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Attachment

**BRIEFING PACKAGE**

**FINAL RULE TO REQUIRE SPECIAL PACKAGING FOR MINOXIDIL**



**For Information Contact**  
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NOTE: This document has not been  
reviewed as a final rule. Comments are  
not to be submitted.

*TS* 10/9/98

CPSA 6 (1)(1) Cleared

*10/9/98*  
No Other Products

Products: *Puberty*

Except: *Puberty*

Firm: *Puberty*

Comments: *Puberty*

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## Executive Summary

On March 17, 1998, the Commission proposed child-resistant packaging requirements for preparations containing more than 14 mg of minoxidil in a single package (63 FR 13020). Minoxidil is a potent vasodilator capable of causing serious effects on the heart and blood pressure. Serious injuries from minoxidil ingestions have been documented in the medical literature. Topical minoxidil solutions on the market today contain an amount of minoxidil which exceeds an amount expected to cause serious injury to a young child.

The proposed child-resistant packaging requirement also includes any applicators which it is reasonable to expect may be used to replace the original closure. Of the topical minoxidil packages examined by the staff some droppers and all finger sprayers supplied with the product packages were not child-resistant.

The Commission received five comments in response to the notice of proposed rulemaking. Several commenters provided information and comments on issues including packaging technical feasibility, costs, and effective date. However, no information was received that changes the staff recommendation.

The staff concludes that data support a finding that child-resistant packaging for minoxidil is technically feasible, practicable, and appropriate. Child-resistant primary closures and child-resistant dropper applicators are readily available and in use by many firms. Child-resistant finger sprayers can be commercialized according to a pump manufacturer. The staff believes that the child-resistant finger sprayer can be modified to accept the extended sprayer.

Child-resistant primary packaging and applicators are readily available or can be developed at costs that are not substantial relative to the retail costs of these products. Therefore, the requirements for child-resistant packaging for minoxidil-containing products will not have a significant effect on a substantial number of small businesses.

In order to protect children from serious personal injury following ingestion, the staff recommends that the Commission issue a special packaging standard for preparations containing more than 14 mg of minoxidil in a single package. The standard should include primary closures and applicators packaged with minoxidil products which it is reasonable to expect would replace the primary closure when used and stored in the home. The staff recommends a six month effective date for child-resistant primary and dropper packaging. A one year effective date is recommended for the finger sprayer and extender sprayer. However, because additional time will be necessary to commercialize a child-resistant finger sprayer, the staff recommends that the Commission specifically include a provision so that companies may request additional time in the form of a temporary stay of enforcement immediately after the rule is published.



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

**MEMORANDUM**

**DATE:** OCT 9 1998

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

**Through :** Jeffrey Bromme, General Counsel *JB*  
 Pamela Gilbert, Executive Director *PG*

**From :** Ronald L. Medford, Assistant Executive Director for Hazard *RLM*  
 Identification and Reduction  
 Suzanne Barone, Ph.D., Project Manager for Poison Prevention *SB*  
 Directorate for Epidemiology and Health Sciences

**Subject :** Special Packaging Standard for Minoxidil

The purpose of this memorandum is to address the comments received in response to the proposed rule to require child-resistant (CR) packaging of products containing more than 14 mg of minoxidil in a single package. The staff recommendation that the Commission issue the rule is also presented. A copy of the draft final rule Federal Register notice is at Tab E.

**BACKGROUND**

The Poison Prevention Packaging Act of 1970 (PPPA) authorizes the U.S. Consumer Product Safety Commission (CPSC) to establish special packaging standards for household substances that may cause serious injury or illness to young children. The PPPA currently requires CR packaging of most oral prescription drugs. However, topical drugs and nonprescription or over-the-counter (OTC) drugs are not generally regulated by current PPPA standards, unless the Commission specifically requires it.

One such drug is minoxidil. Minoxidil is available OTC in liquid topical form that can be applied to the scalp to stimulate hair regrowth in men and women with a common form of genetic hair loss. This topical form of minoxidil does not currently require CR packaging. However, minoxidil is also available, by prescription only, in oral tablet form to treat severe high blood pressure. This form of minoxidil currently requires CR packaging. The potential for adverse effects from the topical form is the same as from the oral tablet if topical minoxidil is

NOTE: This document has not been reviewed or accepted by the Commission.  
 Initial *10/9/98*

CPSA 6 (b)(7) Cleared  
 No Mfrs/PrvtLbrs or  
 Products Identified  
 Exempted by *Richardson*

ingested. The staff documented the potential for topical minoxidil to cause serious injury in children in a briefing document to the Commission dated February 10, 1998.

On March 17, 1998, the Commission proposed CR packaging requirements for preparations containing more than 14 mg of minoxidil in a single package (63 FR 13020) (Tab A). This proposed requirement includes any applicator packaged with the minoxidil preparation which it is reasonable to expect may be used to replace the original closure. Packages of topical minoxidil contain droppers and/or finger sprayers that are used to administer the product onto the scalp.

A copy of the Federal Register notice was sent to 23 trade associations, drug manufacturers, and closure manufacturers that are known to be involved with the packaging of minoxidil. The Commission received five comments in response to the notice of proposed rulemaking. The staff responses to these comments are described below.

Before finalizing a CR packaging standard for minoxidil, the Commission must find that minoxidil presents a threat of serious injury or illness to young children when ingested or otherwise handled. The Commission also must find that CR packaging for minoxidil is technically feasible, practicable, and appropriate. In addition to complying with these requirements in the PPPA, the Commission must either assess the impact of a regulation on small businesses, or certify that there will not be a significant economic effect on a substantial number of small entities. The Commission must also examine the potential for adverse effects on the environment.

The information to support these findings is presented in the staff memoranda (Tabs C and D) and discussed below.

## **RESPONSE TO COMMENTS**

Comments were received from five different associations and drug manufacturers. A copy of the comments is at Tab B. The American Academy of Pediatrics (CP98-3-5) supported the rule. Several other commenters provided information and comments on issues including packaging technical feasibility, costs, and effective date. The comments and staff responses follow.

### **Packaging Issues**

Comment: One commenter (CP98-3-2) stated that the Commission had no data to demonstrate that CR extender spray applicators were technically feasible and practicable. The commenter stated that CPSC noted in the Federal Register that, "...the technology does not exist for the development or use of finger sprayers

with extenders that are CR." The commenter went on to state that CPSC could not go further with a minoxidil rule since this was a violation of the statute.

Response: The commenters provided no data to demonstrate that an extender sprayer cannot be made and mass produced. The commenter misinterpreted the Commission statement in the Federal Register notice. The Federal Register notice stated that CR extender sprayers are not currently on the market. This does not imply that current technology cannot be modified to produce a CR finger sprayer with attachment. This is especially true since two other commenters presented information to demonstrate that the CR finger sprayer can be commercialized. The staff believes that the technology for a child-resistant finger sprayer can be adapted for the extender sprayer. However, none of the drug companies that currently use an extender sprayer specifically commented about it. In addition, the PPPA does not mandate that all package designs must be made child-resistant. The extender sprayer attachment is used by several companies on products for women only. Other companies do not use an extender sprayer on their women's product. There are alternative applicators currently used for these products. Child-resistant packaging is technically feasible, practicable, and appropriate for minoxidil. Therefore, to proceed is not a violation of the statute.

Comment: One commenter (CP98-3-4) indicated that CR droppers are not a good barrier because children can chew through the bulb turning it into a nipple thus aiding ingestion.

Response: When testing CR dropper packaging, chewing through or pulling out the dropper bulb counts as a failure since the child gains access to the product. The CPSC has data indicating that dropper assemblies pass the child-resistant packaging test protocol and meet the standards. Therefore, CR dropper assemblies are available that provide protection as mandated by requirements of the PPPA.

Comment: One commenter (CP98-3-4) requested that the Commission prohibit all applicators that could be used as substitutes for the original closure because of the cost, time, and competitive balance.

Response: The Commission proposed that any applicator packaged with the minoxidil preparation which is reasonably expected to replace the original closure shall be child-resistant. It is an acceptable alternative to use applicators that cannot replace the original closure, for example, the use of a dropper without an attached closure assembly. The commenters request that this alternative option be the only option permitted. The PPPA prevents the Commission from prescribing specified packaging designs (15 USC 1472(d)). Any package type which meets the requirements can be used. Any applicator, with the capability to replace the original closure, that prevents child-access to the product as defined by the regulations of the PPPA, is acceptable.

## Effective Date

**Comment:** Three commenters indicated that the effective date of one year for the sprayer was too short (CP98-3-1,3,4). One commenter requested a total of 34 months (22 months in addition to a 1 year effective date). Another commenter indicated that 27-36 months is necessary to incorporate a child-resistant finger sprayer.

**Response:** The staff reviewed the steps and timing involved with the commercialization of a child-resistant finger sprayer and agrees that more than 12 months is necessary. The complex nature of making more than one feature child-resistant adds to the timing. Further discussion is found in the EFFECTIVE DATE section of this memorandum.

## Cost Considerations

**Comment:** One commenter (CP98-3-4) indicated that the additional cost of purchasing child-resistant rather than nonchild-resistant droppers was greater than \$0.05.

**Response:** The CPSC staff obtained this estimated incremental cost of purchasing child-resistant droppers from a dropper manufacturer. The commenter has since indicated to CPSC staff that the cited incremental cost was within the range of the increased cost.

**Comment:** One commenter (CP98-3-4) stated that it would be a competitive disadvantage to generic manufacturers if exclusive agreements for sprayer applicators were made with the manufacturer of the brand product.

**Response:** The commenter supplied no data and the CPSC staff have no data to support this claim. The fact that two different commenters provided information about the timing for the development of a finger sprayer may provide evidence to the contrary. Even if there was an exclusive agreement, it would not prevent other companies, such as the commenter, from developing a child-resistant finger sprayer independently. The estimated incremental cost of the CR sprayer will be a little more than double the 13-15 cents currently paid for the nonCR finger sprayer, according to one commenter. This is not a substantial cost increase relative to the retail prices (\$20-\$30) of preparations known to be supplied with a finger sprayer, even for the less expensive generic minoxidil products. In addition, several of the generic brands do not currently include a finger sprayer with their products. It is also important to note that generic does not necessarily mean small business. The commenter is a large generic pharmaceutical manufacturer.

## **TOXICITY UPDATE**

The February 10, 1998, briefing package to the Commission contained poisoning data that demonstrated access to the products and the potential for serious injury from ingestion of minoxidil. Information on ingestions of minoxidil was obtained from several sources. The staff updated the information on poisonings since the last submission to the Commission. No additional reports of accidental ingestion by children appeared in the medical literature or were reported by the Food and Drug Administration's Spontaneous Reporting System.

The Commission obtains annual data from the American Association of Poison Control Centers (AAPCC) on pediatric exposures to drugs and other household substances. For 1997, the AAPCC reported 52 children under 5 years of age who had ingested topical minoxidil. Half of the children were referred to a healthcare facility for observation or treatment. However, no serious outcomes were reported. The AAPCC data base reported 43 ingestion cases of topical minoxidil for 1996 and 4 cases for 1995. Prior to 1995, topical minoxidil was not given a specific code within the database.

Two childhood poisoning cases associated with minoxidil were reported in the National Electronic Injury Surveillance System (NEISS) database since the last update. One case was minoxidil tablets and the other was topical minoxidil in a spray bottle. Neither child was hospitalized. No other details are available. The amount of ingested minoxidil was not determined for the NEISS and AAPCC cases. There were no minoxidil-related deaths found in the CPSC Death Certificate files.

## **LEVEL FOR REGULATION**

The Commission proposed that preparations containing more than 14 mg of minoxidil be packaged in accordance with the special packaging provisions of the PPPA. This level was chosen based on the maximum recommended therapeutic dose of minoxidil which corresponds to 1.4 mg/kg for the average 70 kg adult and is equivalent to a 14 mg dose level for a 10 kg child. No additional information has been obtained to recommend changing this proposed level. The American Academy of Pediatrics (CP98-3-5) supported the Commission's intention to require child-resistant packaging of minoxidil products containing more than 14 mg per package.

## **TECHNICAL FEASIBILITY, PRACTICABILITY, AND APPROPRIATENESS**

The Commission preliminarily determined that the available data on packaging for minoxidil support the findings that child-resistant packaging is technically feasible (producible), practicable (lends itself to mass production), and

appropriate (compatible with the contents of the package) for these products. This information is discussed in more detail at TAB C.

Child-resistant continuous threaded closures are widely available and in use on the primary packaging for topical minoxidil and many other products. Child-resistant dropper applicators of a size that accommodate current topical minoxidil containers are also available and in use.

Unlike child-resistant continuous threaded packaging and dropper applicators, there are no commercially available child-resistant metered finger sprayers or extender attachments for topical minoxidil products. However, in the briefing package of February 10, 1998, the staff described a prototype CR finger sprayer that was developed but not commercially produced or tested with the senior test protocol. In addition, a pump manufacturer has indicated that it is technically feasible to make and produce a child-resistant finger sprayer. The technology for a child-resistant finger sprayer could be adapted for the extender sprayer since they operate by the same mechanism.

These data support a conclusion that child-resistant packaging for minoxidil-containing products is technically feasible, practicable, and appropriate.

#### **EFFECTIVE DATE**

The Commission proposed an effective date of six months for the primary packaging and dropper applicators. The Commission proposed an effective date of one year plus the possibility of a stay of enforcement if necessary for finger sprayer commercialization.

No additional information has been supplied that would change the proposed effective date of six months for manufacturers to provide continuous threaded child-resistant packaging and dropper applicators for topical minoxidil products. The primary product containers identified by the staff are already child-resistant. In addition, child-resistant droppers are commercially available and used with many of the minoxidil products examined by the staff that contained droppers.

More than twelve months will be necessary to convert to a child-resistant metered finger sprayer. Two commenters have indicated that a design could be modified, tested, and in commercial use in approximately 27-36 months. The CPSC staff reviewed the timelines and agrees that the time seems reasonable because of the complex nature of the development of a finger sprayer that has two child-resistant features. In addition, the finger sprayer must be metered to give a correct dose. The staff believes that it is necessary to provide time in addition to the one year effective date for those companies who wish to develop a child-resistant finger sprayer. One company requested an additional 22 months over the

one year effective date in their comment to the Commission (CP98-3-1). Because of the commitment of resources to the development of this type of packaging, the staff recommends that in addition to a one year effective date, companies be given the option of requesting the stay of enforcement immediately after the final rule is published. Companies requesting a temporary stay of enforcement should provide a timeline or schedule for completion, outlining the steps involved in the development, and including an estimated initial production date for the child-resistant version of the product. Companies should also include current and proposed packaging specifications.

## **ECONOMIC AND ENVIRONMENTAL CONSIDERATIONS**

The effect of a child-resistant packaging requirement on small businesses is described in detail at Tab D.

The Commission preliminarily concluded that a special packaging requirement for minoxidil would not be expected to have a significant economic impact on a substantial number of small firms. This was because there are few small businesses (only two known small manufacturers) that would be impacted by the special packaging requirement. These firms can use child-resistant continuous threaded closures at costs competitive with nonchild-resistant closures. Child-resistant droppers are available at an incremental cost of about five cents per unit. At the time of the proposal, the incremental costs of child-resistant finger sprayers was not available, but was not expected to be large relative to the retail price of the topical minoxidil products known to be supplied with a finger sprayer. In addition, firms had the option of supplying only a child-resistant dropper applicator, since many of the generic products are packaged that way.

Further information regarding the potential impact on small businesses was requested in the Notice of Proposed Rulemaking. The notice was specifically sent to known small firms in addition to other companies and trade associations involved in the packaging of minoxidil. No small business commented on the proposed rule. One commenter, representing a large company, supplied cost estimates for the child-resistant finger sprayer. The expected cost is not substantial relative to the retail cost of the product. Moreover, the staff is unaware of any small firms that supply a finger sprayer with their product.

The staff concludes that the final action to require child-resistant packaging for products that contain more than 14 mg of minoxidil will not have a significant economic effect on a substantial number of small entities.

A special packaging requirement will have no significant effects on the environment since the manufacture, use, and disposal of CR/SF closures will present the same environmental effects as non-CR closures.

## **OPTIONS**

1. The Commission may finalize a rule requiring special packaging for products containing more than 14 mg of minoxidil in a single package if the Commission finds that special packaging is required to protect young children from serious personal injury or illness from handling, using or ingesting the product; and that special packaging is technically feasible, practicable, and appropriate.

Or

2. The Commission may decline to finalize a special packaging rule for minoxidil if it is unable to make these findings.

## **RECOMMENDATION and CONCLUSION**

The staff recommends that the Commission issue a child-resistant packaging standard for products that contain more than 14 mg of minoxidil in a single package. Minoxidil is a potent vasodilator capable of causing serious effects on the heart and blood pressure. Serious injuries from minoxidil ingestions have been documented in the medical literature. Topical minoxidil solutions on the market today contain at least 1200 mg of minoxidil which far exceeds an amount expected to cause serious injury to a young child.

Packages of topical minoxidil can be readily purchased by consumers without a prescription. These products do not now require special packaging. It is reasonable to expect an increase in accidental childhood ingestions with the greater consumer access that accompanies OTC status and additional entry into the market of products without child-resistant applicators. The data from the AAPCC seem to demonstrate this trend even though it is not a statistical sample.

The staff recommends that the Commission adopt the long held staff position that the requirement for child-resistance extend to all applicators which are expected to replace the original closure. No commenter challenged this position and the American Academy of Pediatrics supported it. Of the topical minoxidil packages examined by the staff some droppers and all finger sprayers supplied with the product packages were not child-resistant. This requirement will ensure that current and future suppliers will provide adequate child-resistance with their products.

The staff concludes that data support a finding that child-resistant packaging for minoxidil is technically feasible, practicable, and appropriate. Child-resistant primary closures and child-resistant dropper applicators are readily available and in

use by many of the firms. Child-resistant finger sprayers can be commercialized according to a pump manufacturer. The staff believes that the child-resistant finger sprayer can be modified to accept the extender sprayer.

Many different packaging options exist and are currently used for minoxidil-containing products. Child-resistant packaging is readily available or can be developed at costs that are not substantial compared to the retail costs of these products. Therefore, the requirements for child-resistant packaging for minoxidil-containing products will not have a significant effect on a substantial number of small businesses. In addition, child-resistant packaging requirements will have no significant effects on the environment.

The staff recommends that the Commission adopt an effective date of six months for primary and child-resistant dropper packaging since these types of packaging are readily available and are already being used with many topical minoxidil preparations. The staff recommends a one year effective date for the finger sprayer or extender sprayer attachments. However, because additional time is necessary to commercialize a child-resistant finger sprayer, the staff recommends that the Commission specifically include a provision so that companies may request additional time in the form of a temporary stay of enforcement immediately after the rule is published.

**TAB A**

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**CONSUMER PRODUCT SAFETY  
COMMISSION**

**16 CFR Part 1700**

**Requirements for Child-Resistant  
Packaging; Minoxidil Preparations  
With More Than 14 mg of Minoxidil Per  
Package**

**AGENCY:** Consumer Product Safety  
Commission.

**ACTION:** Proposed rule.

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**SUMMARY:** The Commission is proposing a rule to require child-resistant ("CR") packaging for minoxidil preparations containing more than 14 mg of minoxidil in a single package. The Commission has preliminarily determined that child-resistant packaging is necessary to protect children under 5 years of age from serious personal injury and serious illness resulting from handling or

ingesting a toxic amount of minoxidil. The Commission takes this action under the authority of the Poison Prevention Packaging Act of 1970.

**DATES:** Comments on the proposal should be submitted no later than June 1, 1998.

**ADDRESSES:** Comments should be mailed to the Office of the Secretary, Consumer Product Safety Commission, Washington, D.C. 20207, or delivered 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](mailto:cpsc-os@cpsc.gov).

**FOR FURTHER INFORMATION CONTACT:** Suzanne Barone, Ph.D., Division of Health Sciences, Directorate for Epidemiology and Health Sciences, Consumer Product Safety Commission, Washington, D.C. 20207; telephone (301) 504-0477 ext. 1196.

**SUPPLEMENTARY INFORMATION:**

**A. Background**

*1. Relevant Statutory and Regulatory Provisions*

The Poison Prevention Packaging Act of 1970 ("PPPA"), 15 U.S.C. 1471-1476, 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.

Special packaging, also referred to as "child-resistant" ("CR") packaging, is (1) designed or constructed to be 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 performance requirements for special packaging. 16 CFR 1700.15, 1700.20. Under these requirements, most special packaging must be child-resistant (85 percent of a

panel of 200 children cannot open it without a demonstration and 80 percent cannot open it with a demonstration) and senior-friendly ("SF") (90 percent of a panel of 100 adults ages 50 to 70 must be able to open the packaging in a 5 minute test period and open and (if appropriate) properly reseal it in a 1 minute test). 16 CFR 1700.20(a)(2) and (3).

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 substance in CR packages of a popular size, and the non-CR packages bear conspicuous labeling stating: "This package for households without young children." 15 U.S.C. 1473(a), 16 CFR 1700.5.

*2. Minoxidil*

Topical minoxidil is a liquid medication that is applied to the scalp to stimulate hair regrowth for individuals with a common form of genetic hair loss (androgenetic alopecia). In February 1996, the Food and Drug Administration ("FDA") approved the sale of topical minoxidil as an over-the-counter ("OTC") drug available without a prescription. There is also a tablet form of minoxidil for treatment of severe hypertension that is available only by prescription. Like most oral prescription drugs, the prescription form of minoxidil must be in special packaging. 16 CFR 1700.14(a)(10). However, special packaging is not required for topical drugs unless the Commission takes specific action to require it.

Topical minoxidil first became available by prescription in 1988. The OTC preparation is currently marketed as a two percent solution in 60 percent alcohol, propylene glycol, and water. The package instructions direct the user to apply one milliliter (20 milligrams of minoxidil) to the scalp twice a day. This application generally must continue for four months for there to be any noticeable hair growth. Continuous application is necessary to maintain the newly grown hair. The most prevalent package size contains 60 milliliters of the preparation (1200 milligrams of minoxidil) which is a 30-day supply if used as directed.<sup>1</sup> On November 14, 1997, the FDA approved for OTC use a 5% minoxidil solution for men. The package size is also 60 milliliters, and the recommended dosage is one milliliter (50 milligrams of minoxidil)

<sup>1</sup> Numbers in parentheses refer to documents listed at the end of this document.

applied twice a day. The total contents of the package is 3000 milligrams.

The Commission is aware of ten manufacturers that have FDA's approval to market the OTC two percent minoxidil solution. In addition, the Commission knows of six other companies—probably repackagers or relabelers—that sell the OTC minoxidil formulation. The year after FDA approved OTC status for topical minoxidil preparations, retail sales of topical minoxidil were about \$200 million (approximately 8 million packages).<sup>(3)</sup>

Topical minoxidil formulations are generally packaged either for men or for women. Although the formulations are the same, the packaging and instructions are different. All the bottles the Commission is aware of are secured with CR/SF continuous threaded closures. In addition to the primary closure, the packages the Commission staff examined contain one or more applicators that are reasonably expected to be used to replace the primary closure once the product has been used for the first time.

The Commission staff examined nine topical minoxidil packages for men. These packages contained dropper applicators. In six of these, the droppers were CR/SF, the other three droppers were non-CR. Four of the packages for men also contained a metered finger mechanical sprayer applicator (hereafter referred to as a "finger sprayer") in addition to the dropper applicator. The finger sprayer releases the solution in a mist which the package insert claims may be more useful than a dropper for broader areas of hair loss. None of the finger sprayers are CR.<sup>(4)</sup>

Hair loss for women occurs as a thinning of the hair over a broad area on the top of the scalp rather than at the vertex. All four of the topical minoxidil packages for women that the staff examined contained the metered finger mechanical sprayer applicator. Two products for women included a CR/SF dropper in addition to the finger sprayer. Three packages for women included an extender attachment to fit onto the finger sprayer applicator allowing the solution to be applied closer to the scalp than the pump spray alone would manage. Neither the finger sprayers nor the extenders in the packages intended for women were CR.<sup>(4)</sup>

*3. CR Packaging for Applicators*

Because the topical minoxidil formulations are packaged with applicators that are reasonably expected to replace the primary closure of the product after its first use, the question

arises whether the applicators themselves must be CR if the Commission requires CR packaging for the product. The Commission has not previously addressed this issue.

Under the PPPA, a "package" is the "immediate container" that holds a substance when it is located in the household. Specifically, the term "package" is defined as:

the immediate container or wrapping in which any household substance is contained for consumption, use, or storage by individuals in or about the household.

15 U.S.C. 1471(3). The focus of this definition is on how the product is packaged in the home where it is "contained for consumption, use or storage" rather than its packaging in the store. This is fully consistent with the purpose of the statute, to reduce child poisonings from available household substances.

The exclusions from the definition of "package" also indicate that Congress was concerned with the package as maintained in the home. Congress excluded containers used only to transport the product. Thus, "package" does not include:

(A) any shipping container or wrapping used solely for the transportation of any household substance in bulk or in quantity to manufacturers, packers, or processors, or to wholesale or retail distributors thereof, or

(B) any shipping container or outer wrapping used by retailers to ship or deliver any household substance to consumers unless it is the only such container or wrapping

*Id.*

The legislative history of the statute also supports the view that the "package" includes applicators that are reasonably expected to be used as closures in the home. The Senate Commerce Committee Report notes: "The term 'package' was defined here to [sic] in order to make explicit that special packaging refers to that package in which the substance is kept in or around the house." S. Rep. 845, 91st Cong., 2d Sess. 9 (1970).

Thus, the Commission believes that when an applicator is packaged with a product that requires CR packaging and the applicator is reasonably expected to replace the original closure of the packaging, that applicator must also be CR. This does not mean that every applicator packaged with a substance requiring CR packaging must itself be CR. It is permissible for an applicator, such as a dropper, to be packaged with a product so long as the applicator cannot be used to replace the original closure.

Early in the Commission's administration of the PPPA, the staff

recognized the potential problem posed by applicators used to replace original closures. Accordingly, the staff advised that dropper bottles are not excepted from the PPPA's requirements. In 1974, the staff advised the Arizona State Board of Pharmacy that if a manufacturer of prescription drugs dispensed with droppers could not provide CR closures incorporating the dropper, the drug could be packaged with a conventional CR closure accompanied by a separate non-closing dropper. (See letter to Alfred J. Duncan, Executive Secretary of the Arizona State Board of Pharmacy from Robert Poth, April 11, 1974.) This position was reiterated in an internal staff memorandum stating "when a prescription drug is packaged in a dropper bottle, it is the dropper bottle that is the 'package' and any packaging exterior to this cannot be considered the 'package.'" The memo continues: "[U]ntil special packaging is available for the dropper unit itself, manufacturers should place the drug in a specially packaged bottle, with a separate dropper provided for proper administration of the drug. However, in our view, the separately provided dropper should not contain a cap, since the consumer would be apt to use the dropper and noncomplying cap permanently, and discard the special cap." (Memo from Poth and Lemberg, June 12, 1974.) The staff discussed this position with staff at the FDA a few months later. The FDA staff agreed with the Commission staff's approach. (Memorandum of meeting between FDA and CPSC representatives, October 15, 1974.)

Because the Commission has not previously addressed this question explicitly in a regulation, the proposed rule that the Commission issues today expressly states that applicators packaged with topical minoxidil that are reasonably expected to replace the original closures would be required to be CR and SF. The Commission recognizes that its other rules, such as the rule covering oral prescription drugs, do not contain such a provision. When previous special packaging rules were issued, few packages contained applicators that could be used as closures. Thus, previous rules did not expressly state that such applicator closures are "packages" under the PPPA. In order to clarify the issue, the Commission proposes to include such a statement in the proposed rule for minoxidil. The lack of such a statement in previous PPPA rules is not to be construed to mean applicator closures are exempt from special packaging

requirements. As stated above, the Commission agrees with the staff's longstanding interpretation that special packaging requirements extend to applicators reasonably expected to replace primary closures when used and stored in the home.

#### B. Toxicity of Minoxidil

The Commission's Directorate for Epidemiology and Health Sciences reviewed the toxicity of minoxidil. This includes both information concerning the therapeutic ingestion of prescription minoxidil tablets to treat hypertension and ingestion of topical minoxidil. In either form, when it is ingested, minoxidil is rapidly and almost completely (over 95 percent) absorbed by the gastrointestinal tract and is distributed systematically throughout the body. In contrast, minoxidil is very poorly absorbed through the skin, and insufficient levels of minoxidil reach the bloodstream to cause effects on vascular and cardiac function. This is why a topical solution of two percent minoxidil is considered safe when used on the skin as directed but can be harmful if ingested.(2)

The tablet form of minoxidil is prescribed for use as an antihypertensive drug. It lowers blood pressure by relaxing the smooth muscle of the arteries. The body's nervous system responds by causing the heart to beat faster (tachycardia) and with more force (increased cardiac output) to compensate for the drop in blood pressure. Minoxidil tablets are typically used in combination with a  $\beta$ -adrenergic blocking agent and a diuretic to maximize its effect on blood pressure while minimizing associated side effects (the cardiac response and retention of fluids).(2)

The most prominent effects from therapeutic ingestion of minoxidil are increased heart rate, increased cardiac output and decreased blood pressure. When blood pressure becomes abnormally low (hypotension), it can lead to lethargy and lightheadedness with the possibility of damage to the heart and other tissues with high oxygen demand, if left untreated. Less frequent effects include salt and fluid retention and edema, aggravation of angina, and pericardial effusion (massive fluid accumulation around the heart) in patients with renal impairment. Repeated ingestion over several months can produce hypertrichosis (overstimulated hair growth) particularly to the face and to a lesser extent to the limbs and scalp. Less severe symptoms of nausea, headache, fatigue, and dermatologic reactions have been occasionally reported.(2)

Prescription minoxidil is available as 2.5 mg, 5 mg, and 10 mg tablets. The effective dosage is usually between 0.2 to 1 mg/kg/day (roughly 5 to 40 mg/day for an adult) depending on the individual and the desired antihypertensive response. Use in children has been limited with a similar effective body weight-normalized dose range as adults (0.2 to 1 mg/kg/day). Because of possible adverse effects, the maximum recommended daily therapeutic dosage is 100 mg in adults and 50 mg for children under the age of 12.(2)

### C. Incident Data

The staff reviewed several sources for information of adverse health effects from ingestions of minoxidil. These sources are the American Association of Poison Control Centers ("AAPCC"), the FDA Spontaneous Reporting System ("SRS"), published reports in the medical literature, and reports from the injury surveillance databases maintained by the Commission. The most commonly cited injuries are prolonged hypotension and tachycardia that require hospitalization. There were reports of two deaths associated with minoxidil overdose.

#### AAPCC Data

The AAPCC collects reports made to participating poison control centers throughout the United States. A retrospective study evaluated AAPCC records of all minoxidil exposures from 1985 through 1991. (The study did not distinguish between ingestions of minoxidil tablets and topical solution.) During this time period, 285 incidents were reported. About half (51 percent) of these occurred in children under six years of age. Most of the 285 incidents were reportedly accidental ingestions (80%) and some involved co-ingestions (21%) of other substances. The most frequently reported adverse effects from 16 incidents involving moderate to severe poisoning were hypotension (69%), tachycardia (38%), and lethargy (31%) with 44% requiring medical treatment. Most of the more serious poisonings were intentional ingestions (69%) and involved co-ingestions (81%). It was not reported how many of these incidents occurred in children. There was one reported death caused by an intentional ingestion of minoxidil with other vasodilators, and acetaminophen.(2)

CPSC obtains annual AAPCC data on pediatric exposures to children under six years of age. Four accidental ingestions of topical minoxidil liquid were reported in 1995. (Prior to 1995, topical minoxidil was not given a

specific code within the AAPCC database.) None of these four incidents led to serious toxicity. In 1996, the number of reported cases increased to 43. One of these exhibited moderate effects.

Because incidents involving minoxidil tablets (rather than topical solutions) are coded in a category that includes "other vasodilators," it is not possible to isolate incidents specific to minoxidil tablets. There were two childhood ingestions of "other vasodilators" reported in 1995 that resulted in a moderate toxicity.(2)

#### FDA/SRS Database

The SRS is a database maintained by the FDA for reports of adverse reactions detected after a drug goes on the market. Drug manufacturers are required to report any known incidents of adverse effects associated with their products. However, the incident reports are not verified by the FDA, and therefore, the adverse effects may reflect underlying diseases or reactions to multiple drugs.

There have been 16,795 SRS reports on topical minoxidil between 1983 and March 1997. Most of the reported adverse effects were dermal reactions to excessive application of topical minoxidil to the scalp. However, FDA specifically cited five overdose ingestion cases involving topical minoxidil. Three of these led to serious outcomes.(2)

One of these cases was a suicide in which an adult male ingested the contents of five bottles (6 grams in 300 ml) of topical minoxidil and died. No other details were provided. A second case was an adult male who mistakenly ingested 15–20 ml (300–400 mg) of topical minoxidil and experienced fainting, severe hypotension, cardiac effects, and acute renal failure. The person was taking anti-hypertensive medication at the time of the poisoning but no other details of his prior medical condition were cited. The third case was an ingestion of topical minoxidil by a two-year-old child. She was found with an empty bottle that had been full earlier. She was admitted to an intensive care unit in a lethargic state with a pulse of 160 (above normal range), blood pressure of 106/60 (within normal limits), but was discharged the same day. The amount of minoxidil actually ingested was never established.(2)

In addition, two possible childhood ingestions of topical minoxidil were reported in SRS to result in hospital visits. In both incidents, no adverse outcomes were recorded but the children were retained at the hospital for observation. While the children

gained access to the medication in these cases, the hospital suspected that no minoxidil was consumed.(2)

#### CPSC Databases

CPSC has several databases for poison incidents. The staff reviewed cases from 1988 to 1997 in the National Electronic Injury Surveillance System ("NEISS"). NEISS monitors emergency room visits to a statistically-based sample of selected hospitals throughout the United States. One childhood poisoning case associated with minoxidil was reported in the NEISS database during that time period. This was an ingestion of an unknown quantity of topical minoxidil by a two-year-old male. The child was seen in an emergency room with normal temperature, pulse, and respiration and was released the same day without treatment. It is not known whether the minoxidil package was secured with a child-resistant closure at the time of the incident.(2)

The staff also reviewed CPSC's Injury and Potential Injury Incident ("IPII") files of consumer product-related incidents reported through letters, telephone calls, media articles and Death Certificate files of consumer product-related deaths. There were no minoxidil-related injuries or deaths found in these databases for the 1988 to 1997 time period.(2)

#### Medical Literature

Five case reports of injuries following minoxidil ingestion were found in the published literature. Two cases involved young children. In one instance, a two-year-old ingested an unconfirmed number of minoxidil tablets. In the second instance, a three-year-old swallowed an estimated 1–2 milliliters of three percent minoxidil solution (30–60 milligrams). Both children were seen at hospitals experiencing moderate tachycardia but no other reported abnormalities. The three other reports were intentional ingestions by adults of minoxidil tablets (one case) or two percent liquid (two cases). The latter two cases involved consumption of several hundred milligrams of minoxidil (10–20 mg/kg) along with alcohol and, in one case, several other substances. The clinical courses were similar. A few hours after ingestion, each individual was admitted to a hospital, usually in a disoriented and unresponsive state. They became moderately to severely hypotensive with tachycardia and elevated cardiac output. Medical treatment was administered and the patient's cardiac and vascular signs eventually normalized over the next 36 to 72 hours. In each instance it was concluded that minoxidil was

primarily responsible for the observed effects, and that co-ingested substances were not consumed in amounts sufficient to cause the reported symptoms. (2)

#### D. Level for Regulation

The Commission is proposing a rule that would require special packaging for minoxidil products containing more than 14 mg of minoxidil in a single package. This is based on the maximum recommended therapeutic dose of minoxidil for an adult. The 14 mg dose level corresponds to 1.4 mg/kg for a 10 kg child. The equivalent minoxidil dose for the average 70 kg adult would be approximately 100 mg. The regulated dose level is expected to reasonably protect children under five years of age from serious personal injury or illness. (2)

#### E. Statutory Considerations

##### 1. Hazard to Children

As noted above, the toxicity data concerning ingestion of minoxidil demonstrate that minoxidil can cause serious illness and injury to children. Moreover, it is available to children in OTC topical minoxidil preparations. Although as far as the Commission is aware, all primary product containers for topical minoxidil products currently use CR packaging, all applicators are not CR. Some packages contain applicators meant to be used as closures after first use which are not CR. The Commission preliminarily concludes that a regulation is needed to ensure that products subject to the regulation, including applicators which it is reasonable to expect may be used to replace the original closures, will be placed in CR packaging by any current as well as new manufacturers.

Pursuant to section 3(a) of the PPPA, 15 U.S.C. 1472(a), the Commission preliminarily finds that the degree and nature of the hazard to children from handling or ingesting minoxidil is such that special packaging is required to protect children from serious illness. The Commission bases this finding on the toxic nature of minoxidil products and their accessibility to children in the home.

##### 2. Technical Feasibility, Practicability, and Appropriateness

In issuing a standard for special packaging under the PPPA, the Commission is required to 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 substance and not interfere with its intended storage or use.

##### a. Primary Product Containers

The primary product containers for all topical minoxidil products that the Commission is aware of have continuous threaded reclosable packaging. All of these closures that the staff examined were CR and SF. Thus, it is clear that CR packaging for primary product containers is technically feasible, practicable and appropriate. (4)

##### b. Applicators

As discussed above, topical minoxidil packages contain applicators—droppers and/or metered finger mechanical sprayers—which it is reasonable to expect may replace the original closures. Eight products have droppers that are CR and SF. This indicates that such droppers are technically feasible, practicable and appropriate. (4)

The Commission knows of eight minoxidil products that include a non-CR finger sprayer. Child-resistance for a finger sprayer means that it must be significantly difficult for children to (1) remove the finger sprayer closure from the container and (2) activate the finger sprayer mechanism to obtain an amount above the regulated level. One packaging manufacturer has developed a prototype CR metered finger sprayer applicator which the manufacturer believes can be modified to pass senior adult effectiveness testing in approximately 12 months. Additional time may be required to provide commercial quantities of this type of packaging. As discussed above, an applicator that cannot be used as a closure does not need to be CR. (4)

Three products for women also contain an extender to be used with the finger sprayer. Under the proposed rule, when the extender is attached to the finger sprayer, this applicator mechanism must be CR. That is, it must be significantly difficult for children to (1) remove the combined finger sprayer and extender from the container and (2) activate the combined finger sprayer and extender to obtain an amount above the regulated level. Currently no finger sprayers with extenders are CR. As noted above, CR/SF finger sprayer could be developed within 12 months. Some modifications to the extender may be

needed so that it would operate with the CR finger sprayer. (4)

#### 3. Other Considerations

In establishing a special packaging standard under the PPPA, the Commission must consider the following:

- The reasonableness of the standard.
- Available scientific, medical, and engineering data concerning special packaging and concerning childhood accidental ingestions, illness, and injury caused by household substances.
- The manufacturing practices of industries affected by the PPPA; and
- 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.

#### F. Effective Date

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

Senior-friendly special packaging is currently commercially available for most types of CR packaging. Primary product containers for topical minoxidil are already CR and SF. Most droppers that can be used to replace the original closures are also CR and SF. One packaging manufacturer has developed a prototype CR finger sprayer that the manufacturer believes can be modified to pass senior adult effectiveness testing in approximately 12 months. Additional time may be required to provide commercial quantities of this type of packaging. Modifications to the extender would likely require a similar amount of time. Thus, the Commission proposes that a final rule would take effect (1) six months after publication of the final rule for primary closures and dropper applicators and (2) 12 months after publication of the final rule for metered finger sprayer applicators and extenders. The Commission also proposes that if additional time is necessary to produce commercial quantities, manufacturers could request a temporary stay of enforcement for the finger sprayer and extender. A final rule would apply to products that are packaged on or after the effective date.

### G. Regulatory Flexibility Act Certification

When an agency undertakes a rulemaking proceeding, the Regulatory Flexibility Act, 5 U.S.C. 601 *et seq.*, generally requires the agency to prepare proposed and final regulatory flexibility analyses describing the impact of the rule on small businesses and other small entities. Section 605 of the Act 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 require special packaging topical minoxidil products containing more than 14 mg of minoxidil in a single package.

This assessment reports that the staff is aware of 16 marketers of minoxidil-containing products. Ten of these are manufacturers, and two of the ten are small companies. (3)

As mentioned above, at the present time, the primary packaging for all topical minoxidil products is CR. Thus, there will be no additional cost to existing firms to use CR primary packaging. Firms entering the market in the future will find readily available CR primary packaging at prices competitive with non-CR packaging. (3)

Similarly, companies now using CR dropper applicators that can be used as closures will not incur any additional cost. For other companies to switch from non-CR droppers, there is an estimated 5 cent incremental cost of a CR dropper compared with a non-CR dropper. This cost is small relative to the retail price of a minoxidil product (\$6-\$30). (3)

Because there are no CR metered finger mechanical sprayer applicators or extenders currently on the market, the staff has no information on the incremental cost of senior friendly CR finger sprayers and extenders. (3) Firms do have the option of supplying only a CR/SF dropper applicator. They also could supply any type of applicator that cannot be used as a closure.

Based on this assessment, the Commission preliminarily concludes that the proposed requirement for minoxidil products would not have a significant impact on a substantial number of small businesses or other small entities. The Commission seeks additional information on the possible impact on small business.

### H. Environmental Considerations

Pursuant to the National Environmental Policy Act, and in accordance with the Council on Environmental Quality regulations and CPSC procedures for environmental review, the Commission has assessed the possible environmental effects associated with the proposed PPPA requirements for minoxidil-containing 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. (3) 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

According to Executive Order 12988 (February 5, 1996), agencies must state in clear language the preemptive effect, if any, of new regulations.

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 exempted 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 a process 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 products containing more than 14 mg minoxidil would preempt non-identical state or local special packaging standards for such minoxidil containing products.

In accordance with Executive Order 12612 (October 26, 1987), the Commission certifies that the proposed rule does not have sufficient implications for federalism to warrant a Federalism Assessment.

### List of Relevant Documents

1. Briefing memorandum from Val Schaeffer, Ph.D., EH, to the Commission, "Proposed Rule to Require Child-Resistant Packaging for Topical Minoxidil," February 10, 1998.

2. Memorandum from Val Schaeffer, Ph.D., EH, to Marilyn Wind, Ph.D., Director, Health Sciences Division, "Toxicity Assessment of Topical Minoxidil," November 14, 1997.

3. Memorandum from Marcia P. Robins, EC, to Val Schaeffer, Ph.D., EH, "Economic Considerations of a Proposal to Require Child-Resistant Packaging for Drug Preparations Containing Minoxidil," January 5, 1998.

4. Memorandum from Charles Wilbur, EH, to Val Schaeffer, Ph.D., EH, "Technical Feasibility, Practicability, and Appropriateness Determination for the Proposed Rule to Require Special Packaging for Products Containing Minoxidil," December 16, 1997.

5. Memorandum from Michael T. Bogumill, CRM, to Val Schaeffer, Ph.D., EH, "Special Packaging of Oral Prescription Drugs in Dropper Bottles," December 17, 1997.

### List of Subjects in 16 CFR Part 1700

Consumer protection, Drugs, Infants and children, Packaging and containers, Poison prevention, Toxic substances  
For the reasons given above, the Commission proposes to amend 16 CFR part 1700 as follows:

#### PART 1700—[AMENDED]

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

Authority: Pub. L. 91-601, secs. 1-9, 84 Stat. 1670-74, 15 U.S.C. 1471-76. Secs. 1700.1 and 1700.14 also issued under Pub. L. 92-573, sec. 30(a), 88 Stat. 1231, 15 U.S.C. 2079(a).

2. Section 1700.14 is amended by adding new paragraph (a)(28) to read as follows (although unchanged, the introductory text of paragraph (a) is included for context):

#### § 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:

(28) *Minoxidil*. Minoxidil preparations for human use and containing more than 14 mg of minoxidil in a single retail package shall be packaged in accordance with the provisions of § 1700.15 (a), (b) and (c). Any applicator packaged with the minoxidil preparation and which it is reasonable to expect may be used to replace the original closure shall also comply with the provisions of § 1700.15 (a), (b) and (c).

Dated: March 11, 1998.

Sadye E. Dunn,

Secretary, Consumer Product Safety Commission.

[FR Doc. 98-6773 Filed 3-16-98; 8:45 am]

BILLING CODE 6355-01-P

## COMMODITY FUTURES TRADING COMMISSION

### 17 CFR Part 1

#### Proposed Rulemaking Concerning Account Identification for Eligible Bunched Orders

**AGENCY:** Commodity Futures Trading Commission.

**ACTION:** Extension of comment period on proposed rulemaking.

**SUMMARY:** The Commodity Futures Trading Commission has repropoed to amend Commission Regulation 1.35(a-1) to permit eligible customer orders to be placed on a contract market without individual customer account identifiers either at the time of order placement or the time of report of execution. Specifically, the proposal would exempt from the customer account identification requirements of Regulation 1.35(a-1)(1), (2)(i), and (4) bunched futures and/or option orders placed by an eligible account manager on behalf of consenting eligible customer accounts as part of its management of a portfolio also containing instruments which are either exempt from regulation pursuant to the Commission's regulations or excluded from regulation under the Commodity Exchange Act. The proposed rule would permit orders entered on behalf of these accounts to be allocated no later than the end of the day on which the order is executed. The proposed rulemaking was in initially published for comment

on January 7, 1998 (63 FR 695) with comments on the proposal due by March 9, 1998. In response to requests from the Futures Industry Association, the Managed Funds Association, the Investment Company Institute, and the New York Mercantile Exchange, the Commission has determined to extend the comment period on this proposal for an additional seven days. The extended deadline for comments on this proposed rulemaking is March 16, 1998. In response to requests from the Futures Industry Association, the Managed Funds Association, the Investment Company Institute, and the New York Mercantile Exchange, the Commission has determined to extend the comment period on this proposal for an additional seven days. The extended deadline for comments on this proposed rulemaking is March 16, 1998.

Any person interested in submitting written data, views, or arguments on the proposals should submit such views and comments by the specified date to Jean A. Webb, Secretary, Commodity Futures Trading Commission, Three Lafayette Centre, 1155 21st Street, N.W., Washington, DC 20581. In addition, comments may be sent by facsimile transmission to facsimile number (202) 418-5521, or by electronic mail to secretary@cftc.gov.

**DATES:** Comments must be received on or before March 16, 1998.

**FOR FURTHER INFORMATION CONTACT:** Duane C. Andresen, Special Counsel, Division of Trading and Markets, Commodity Futures Trading Commission, Three Lafayette Centre, 1155 21st Street, NW, Washington, DC 20581. Telephone: (202) 418-5490.

Issued in Washington, D.C., on this 11th day of March, 1998, by the Commodity Futures Trading Commission.

Jean A. Webb,

Secretary on the Commission.

[FR Doc. 98-6769 Filed 3-16-98; 8:45 am]

BILLING CODE 6361-01-M

## DEPARTMENT OF THE TREASURY

### Customs Service

#### 19 CFR Parts 101 and 122

#### Customs Service Field Organization: Establishment of Port of Entry in Fort Myers, FL

**AGENCY:** U.S. Customs Service, Department of the Treasury.

**ACTION:** Notice of proposed rulemaking.

**SUMMARY:** This document proposes to amend the Customs Regulations pertaining to the field organization of

the Customs Service by designating Fort Myers, Florida, as a port of entry. The new port of entry would include Southwest Florida International Airport, which is currently a user fee airport. The geographical boundaries of the new port will be the same as those of Lee County, Florida. The change is being proposed as part of Customs continuing program to obtain more efficient use of its personnel, facilities, and resources, and to provide better service to carriers importers and the general public.

**DATES:** Comments must be received on or before May 18, 1998.

**ADDRESSES:** Written comments (preferably in triplicate) may be submitted to the Regulations Branch, Office of Regulations and Rulings, U.S. Customs Service, Third Floor, 1300 Pennsylvania Avenue N.W., Washington, D.C. 20229.

**FOR FURTHER INFORMATION CONTACT:** Harry Denning, Office of Field Operations, 202-927-0196.

#### SUPPLEMENTARY INFORMATION:

##### Background

As part of a continuing program to obtain more efficient use of its personnel, facilities, and resources, and to provide better service to carriers, importers, and the general public, Customs is proposing to amend §§ 101.3(b)(1) and 122.15(b). Customs Regulations (19 CFR 101.3(b)(1) and 122.15(b)), by designating Fort Myers, Florida, as a port of entry. The Lee County Port Authority of Florida requested this designation. The geographical boundaries of the new port will be the same as those of Lee County, Florida, and will include the Southwest Florida International Airport (hereafter known as SFIA). SFIA is currently a user fee airport.

The criteria used by Customs in determining whether to establish a port of entry are found in T.D. 82-37 (47 FR 10137), as revised by T.D. 86-14 (51 FR 4559) and T.D. 87-65 (52 FR 16328). Under these criteria, which are not absolute, a community requesting a port of entry designation must: (1) Demonstrate that the benefits to be derived justify the Federal Government expense involved; (2) be serviced by at least two major modes of transportation (rail, air, water or highway); (3) have a minimum population of 300,000 within the immediate service area (approximately a 70 mile radius); and (4) make a commitment to make optimal use of electronic data transfer capabilities to permit integration with Customs Automated Commercial System (ACS), which provides a means for the electronic processing of entries

**TAB B**



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

MEMORANDUM

DATE: June 16, 1998

TO : EHHS

Through: Sadye E. Dunn, Secretary, OS

FROM : Martha A. Kosh, OS

SUBJECT: Requirements for Child-Resistant Packaging; Minoxidil Preparations with More Than 14 mg of Minoxidil Per Package; 63 FR 13019, March 17, 1998

ATTACHED ARE COMMENTS ON THE CP98-3

| <u>COMMENT</u>                        | <u>DATE</u> | <u>SIGNED BY</u>   | <u>AFFILIATION</u>   |
|---------------------------------------|-------------|--|--|
| CP98-3-1                              | 3/6/98      | Emil Berro<br>Associate Director                         | Pharmacia & Upjohn<br>Company<br>7000 Portage Road<br>Kalamazoo, MI 49001  |
| CP98-3-1a                             | 6/15/98     | Emil Berro<br>Associate Director                         | Address same as above  |
| CP98-3-1b<br>(portions<br>restricted) | 8/4/98      | Emil Berro<br>Associate Director                         | Address same as above  |
| CP98-3-2                              | 5/26/98     | Darla Williamson<br>Vice President<br>Closure Activities | Closure Manufacturers<br>Association<br>1627 K Street, NW<br>Suite 800<br>Washington, DC 20006                               |
| CP98-3-3                              | 5/27/98     | Donald Chmielewski<br>Director<br>Regulatory Affairs     | Bausch & Lomb<br>Healthcare and Optics<br>Worldwide<br>Pharmaceutical Division<br>8500 Hidden River Pkwy.<br>Tampa, FL 33637 |
| CP98-3-4                              | 5/28/98     | Deborah Jaskot<br>Sr. Director<br>Regulatory Affairs     | TEVA Pharmaceuticals<br>1510 Delp Drive<br>Kulpsville, PA 19443  |

Preparations with More Than 14 mg of Minoxidil Per Package; 63 FR  
13019, March 17, 1998

CP98-3-5 5/29/98 Joseph Zanga  
MD, FAAP  
President

American Academy of  
Pediatrics  
The Homer Building  
601 Thirteenth St, NW  
Suite 400 North  
Washington, DC 20005

CP98-5-1

KPSA 6 (b)(1) Cleared  
No Min/Priv. Ltr's c  
Products In-  
excepted  
Firm Noted.  
Comments Processed.

# PHARMACIA & UPJOHN COMPANY

7000 Portage Road  
Kalamazoo, MI 49001-0199

Pharmacia & Upjohn Consumer Healthcare  
Office of:  
Emil C. Berro, Associate Director  
OTC Regulatory Affairs

Telephone No. (616) 833-0438  
Telefax No. (616) 833-5612

March 6, 1998

U.S. Consumer Product Safety Commission  
4330 East-West Highway  
Bethesda, MD 20814-4408

Attn: Sadye E. Dunn, Secretary

Dear Ms. Dunn:

After reviewing the briefing package on the "Proposed PPPA Rule Requiring Child-Resistant packing for Topical Minoxidil" dated 2/10/98 and from our understanding of the proceedings on March 2, we have the following comments:

While we agree that it is probably technically feasible to develop a child resistant/senior friendly (CR/SF) sprayer system, we consider the parameters of time and cost to be overly optimistic.

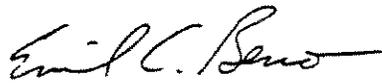
Based on discussions with a nationally recognized supplier of sprayer devices, Calmar, Inc., we have determined a more reasonable time to develop, test, and implement a CR/SF system would be 24-36 months (see attached preliminary timeline).

The development cost to bring such a system to market including our costs for internal compatibility and use testing could be close to \$2-4 million.

We ask that you consider these comments in your deliberations on the "Proposed PPPA Rule Requiring Child-Resistant packing for Topical Minoxidil".

Sincerely,

Pharmacia & Upjohn Consumer Healthcare



Emil C. Berro  
Associate Director  
OTC Regulatory Affairs

cc: Suzanne Barone

ECB:cek

RECEIVED  
MARCH 12 11 11 AM '98  
U.S. CONSUMER PRODUCT SAFETY COMMISSION

ROGAIN CR/SF APPLICATION

| ID | Task Name                                       | 1st Quarter<br>Q1 '98 | 2nd Quarter<br>Q2 '98 | 3rd Quarter<br>Q3 '98 | 4th Quarter<br>Q4 '98 | 1st Quarter<br>Q1 '99 | 2nd Quarter<br>Q2 '99 | 3rd Quarter<br>Q3 '99 | 4th Quarter<br>Q4 '99 | 1st Quarter<br>Q1 '00 | 2nd Quarter<br>Q2 '00 |
|----|---|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| 1  | ROGAIN CR/SF SPRAYER PROJECT-MEDIAN TIMETABLE   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |
| 2  | DEVELOPE ACCEPTABLE DESIGN & PROCUREMENT PLAN   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |
| 3  | DEVELOPE UNIT PARTS & ASSEMBLY SYSTEM           |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |
| 4  | TEST AND QUALIFY NEW SPRAYER FOR 2&5% MINOXIDIL |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |
| 5  | DEVELOPE PRODUCTION PARTS & ASSEMBLY SYSTEM     |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |
| 6  | PRODUCTION PART APPROVAL TESTING                |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |
| 7  | PRODUCTION PART MANUFACTURE & PROCUREMENT       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |
| 8  | USE IN NEW MINOXIDIL PACKAGES                   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |

PROJECT: Rogaine CR/SF Spray  
Date: 3/98

Task:  Milestone:  Summary:

Roll Up: Task  Roll Up: Progress

Roll Up: Milestone

# PHARMACIA & UPJOHN COMPANY

7000 Portage Road  
Kalamazoo, MI 49001-0199

Pharmacia & Upjohn Consumer Healthcare  
Office of:  
Emil C. Berro, Associate Director  
OTC Regulatory Affairs

Telephone No. (616) 833-0438  
Telefax No. (616) 833-5612

August 4, 1998

U.S. Consumer Product Safety Commission  
4330 East-West Highway  
Bethesda, MD 20814-4408

Attn: Todd Stevenson, Freedom of Information Officer

Dear Mr. Stevenson,

In follow up to my telephone conversation with Suzanne Barone on August 4, concerning public disclosure of documents and the confidential nature of portions of our submission dated, May 20, 1998, I would like to offer an amendment to my letter of June 15, 1998. The following attachments are enclosed:

- Attachment I: The letter dated June 15, 1998, which is suitable for public disclosure .
- Attachment II: CR Sprayer Timetable (confidential document, not for public disclosure).
- Attachment III: CR Sprayer Project Costs (confidential document, not for public disclosure).

We feel that the attached letter (alone) adequately conveys our relevant summary comments to the Proposed Rule, 16 CFR 1700, "Requirements for Child-Resistant Package: Minoxidil Preparations With More Than 14 mg of Minoxidil Per Package", which appeared in the March 17, 1998 Federal Register/Vol. 63, No. 51.

Please treat the enclosed timetable and project costs as confidential documents. I apologize for any confusion this may have caused you.

August 4, 1998  
Page 2

If you have questions, please call me at 616-833-0438 or if you can't reach me, contact Ray Dann, at 616-833-0671.

Sincerely,

Pharmacia & Upjohn Consumer Healthcare



Emil C. Berro  
Associate Director  
OTC Regulatory Affairs

ECB:cek

cc: Suzanne Barone  
Chuck Wilbur

# PHARMACIA & UPJOHN COMPANY

7000 Portage Road  
Kalamazoo, MI 49001-0199

Pharmacia & Upjohn Consumer Healthcare  
Office of:  
Emil C. Berro, Associate Director  
OTC Regulatory Affairs

Telephone No. (616) 833-0438  
Telefax No. (616) 833-5612

June 15, 1998

U.S. Consumer Product Safety Commission  
4330 East-West Highway  
Bethesda, MD 20814-4408

Attn: Sadye E. Dunn, Secretary

Dear Ms. Dunn:

After reviewing the Proposed Rule, 16 CFR 1700, "Requirements for Child-Resistant Package: Minoxidil Preparations With More Than 14 mg of Minoxidil Per Package", which appeared in the March 17, 1998 Federal Register/Vol. 63, No. 51, we have the following comments and a request for stay of enforcement:

Pharmacia & Upjohn is the leader in hair regrowth therapy and it is the only non-prescription drug business to market two strengths of topical minoxidil, 2% and 5%, respectively (e.g. ROGAINE® Regular Strength for Men, ROGAINE® For Women, and ROGAINE® Extra Strength for Men). For the period of 1988 through 1997, we estimate that ROGAINE has been used by more than 6 million men and women worldwide.

While we agree that it seems technically feasible to develop a child resistant/senior friendly (CR/SF) metered finger sprayer system, we consider the parameters of time and cost to be overly optimistic, as presented in the CPSC briefing package that was presented to the Consumer Product Safety Commission for its deliberations on March 2, 1998.

Based on discussions with a nationally recognized supplier of sprayer devices, we have determined a more realistic timetable to develop, test, and implement a CR/SF sprayer. We estimate it will take 134 weeks (roughly 34 months) to bring the metered finger sprayer replacement to market at a very substantial capital cost. We anticipate that this project will commence at the date of the Final Rule. We estimate the new CR sprayer will cost more than twice that of the current non CR sprayer per unit.

The development activities and costs for the CR metered finger sprayer have been discussed with Chuck Wilbur, CPSC packaging engineer. We believe these estimates represent realistic projections and we ask that you consider them in your deliberations on the "Final PPPA Rule Requiring Child-Resistant packing for Topical Minoxidil".

Furthermore, we request a stay of enforcement for 34 months, effective the date of issuance of the Final Rule. This time is necessary to permit us to develop a suitable metered finger sprayer

replacement which will have two CR features (i.e. screw closure and actuator), allow for SF utility, verify consumer acceptance in a user study, convert sprayer assembly and packaging to an acceptable production scale and check the sprayer according to the requirements of the existing New Drug Applications for chemical compatibility, in-use stability, establish minimal limits of leakage and verify delivery of an accurate 1 mL dose.

As the leader and pioneer of this product category, we would be pleased to discuss these matters further and answer any of your questions related to the new sprayer design and minoxidil topical solution safety experience.

Sincerely,

Pharmacia & Upjohn Consumer Healthcare



Emil C. Berro  
Associate Director  
OTC Regulatory Affairs

cc: Suzanne Barone  
Chuck Wilbur

ECB:cek

CP98-5-2 66012 5/26/98

**CMA**

CLOSURE  
MANUFACTURERS  
ASSOCIATION  
OFFICE OF THE SECRETARY  
CONSUMER PRODUCT SAFETY COMMISSION

RECEIVED A 10:11

May 26, 1998

Office of the Secretary  
Consumer Product Safety Commission  
4330 East-West Highway  
Room 502  
Bethesda, Maryland 20814  
Washington, DC 20207-0001

Re: Requirements for Child-Resistant Packaging; Minoxidil Preparations with More Than 14 mg of Minoxidil Per Package

Dear Sir or Madam:

The Closure Manufacturers Association ("CMA") is pleased to submit these comments in response to the proposed rulemaking for child-resistant ("CR") packaging for minoxidil preparations containing more than 14 milligrams of minoxidil in a single package. 63 Fed. Reg. 13019 (March 17, 1998).

The proposed rule seeks to require special child-resistant packaging for minoxidil preparations that contain over 14 milligrams of the substance and which are packaged with applicators, including droppers, metered-finger mechanical sprayers, and finger sprayers with extenders. Pursuant to the Poison Prevention Act ("PPPA"), however, the Commission must consider several criteria prior to the establishment of special packaging standards for household products. These include: (1) the degree and nature of the hazard to children caused by the availability of the substance in non-CR packaging; and (2) a finding that the proposed standard is technically feasible, practical, and appropriate. 15 U.S.C. §1472. Under section 1472(a)(2), a finding of technical feasibility requires that the technology exist to produce packaging which meets the standards for child-resistance. See, Senate Report 91-845, 91st Cong., 2d Sess. (1970). Second, the standard of practicality requires that industry have the capability to mass produce and assemble CR packaging. Id. Finally, the standard for appropriateness requires that CR packaging not disturb the integrity, or interfere with the storage or use, of the product. Id.

1627 K Street, NW  
Suite 800  
Washington, DC 20006  
202.223.9050  
202.785.5377 (Fax)

Consumer Product Safety Commission

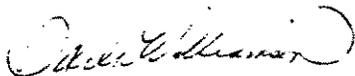
May 26, 1998

Page 2

The current proposed rule would require minoxidil manufacturers to market products that contain a finger sprayer and attachable extender in CR packaging. As CPSC correctly noted in the preamble to the proposed rule, however, the technology does not exist for the development or use of finger sprayers with extenders that are CR. 63 Fed. Reg. at 13023. (There is only a prototype of one kind of package and no evidence of ability to mass produce the packaging.) The statute does not provide for the establishment of a rule based on a presumption, without more, of technology or manufacturing capacity. Moreover, there is no evidence or data that industry has, or will in the near-future possess, the capability to develop CR extenders or have the capability to mass produce and assemble such proposed packaging for these kinds of applicators. Consequently, until such data is available, CPSC is prevented by the statute from imposing these requirements. Accordingly, it would be a violation of the statute and the Administrative Procedures Act to proceed with this proposed rule.

Thank you for the opportunity to comment on the proposed rule. Should you have any questions regarding these comments, please do not hesitate to contact me.

Sincerely,



Darla J. Williamson  
Vice President, Closure Activities

65016  
5/29/98  
e

CP98-3-3

**BAUSCH  
& LOMB**Healthcare and Optics  
Worldwide

May 27, 1998

Office of the Secretary  
Consumer Product Safety Commission  
Room 502  
4330 East-West Highway  
Bethesda MD 20814-4408**Re: Federal Register Proposed Rule Notice of March 17, 1998  
Requirements for Child-Resistant Packaging; Minoxidil  
Preparations With More Than 14 mg of Minoxidil Per  
Package**

We wish to take this opportunity to comment on the above referenced proposed rule regarding the requirement for child-resistant (CR) packaging.

Our concern is about the implementation date of requirement for CR packaging for the finger sprayer. Our current topical 2% products already have CR packaging for the bottle and dropper.

The supplier of our current finger sprayer has stated to us that the timeframe for the availability of commercial supplies of the CR finger sprayer is 18 months. We would then need time after that 18 months to allow for stability testing, the filing of a supplemental application, and FDA-approval. This would be approximately 27-36 months from now. In addition, it must be taken into consideration that there might be an influx of application holders to a sole supplier of a new CR finger sprayer, creating a distribution/supply problem.

Yet the proposed rule states that the requirement for a CR finger sprayer would be effective 12 months after the publication of the final rule. We trust that the above mentioned time periods will be taken into account in the final rule for the establishment of an effective date for the CR finger sprayer.

We request the Commission to be reasonable in the implementation of the proposed rule.

If you have any questions or comments concerning this correspondence, please contact me at the above address or at (813) 975-7786.

Sincerely,



Donald H. Chmielewski  
Director, Regulatory Affairs



CPA-3-4

Deborah A. Jaskot  
Sr. Director, Regulatory Affairs

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May 28, 1998

Office of the Secretary  
Consumer Product Safety Commission  
Washington, D. C. 20207

RE: Proposed Rule of March 17, 1998  
REQUIREMENTS FOR CHILD-RESISTANT PACKAGING; MINOXIDIL PREPARATIONS  
WITH MORE THAN 14 mg OF MINOXIDIL PER PACKAGE

Dear Sir/Madam.

As provided in the above-referenced proposed rule, Teva Pharmaceuticals USA, as a manufacturer of Minoxidil Topical Solution, 2%, herein provides comments.

First we note that four (4) databases have been reviewed in order to assess the historical safety of the current product packaging configuration. These were FDA/SRS, AAPCC, NEISS/IPII and medical literature. Of the cases cited from these databases, those involving children which can reasonably be linked to a topical minoxidil product did not result in death or serious injury. Nonetheless, the issue of child safety should not be easily dismissed. Therefore, while we agree that the intent should be to prevent serious injury to children, we do not agree in the means and time frame proposed toward this end.

A CR dropper assembly, in our estimation, would provide no greater barrier to accidental ingestion by a child than a non-CR dropper. Even with a CR dropper, a young child's first impulse if gaining access to the package will be to bite the rubber bulb. If the rubber bulb were to be punctured, the dropper assembly then very closely resembles a baby bottle in that the child's natural sucking urge would cause the solution to exit through the bulb, thus **aiding** ingestion. Therefore we propose that the proposed rule be revised to require a non-closure dropper assembly. This modification can be easily implemented with dropper assemblies currently commercially available to all manufacturers of minoxidil topical solution.

We also oppose the use of a CR sprayer but for different reasons. Teva has several concerns which are listed below:

1)The proposed rule states that the CR/SF sprayer requirement will be implemented 12 months

after the effective date of the final rule. The single CR sprayer manufacturer discussed in this rule will not have completed senior friendly studies on this sprayer until March 1999 and it will not be commercially available until some unspecified time after that. Given this, a 12 month implementation deadline appears far too short.

2) Additionally, it would not be beyond the realm of possibility or historical precedent that the limited manufacturers of this CR/SF sprayer will be enticed into exclusive agreements with the manufacturer of the brand product, Upjohn in this case. This would leave the generic manufacturers at a competitive disadvantage in that the only option then available to them to comply with the rule would be non-closure applicators for the sprayer and the sprayer extender.

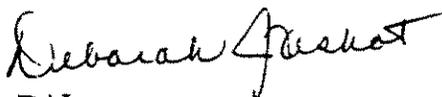
3) If the CR/SF sprayer and sprayer extender were available to all manufacturers of topical minoxidil, the increased cost may render the product of sufficiently decreased profitability that some generic companies may deem it necessary to discontinue manufacture. This again serves the agenda of the brand firm.

4) Teva's materials management function has ascertained that even the incremental cost of a CR/SF dropper assembly will be significantly greater than the \$0.05 estimated in the proposed rule.

Given the concerns of cost and equitable burden/benefit for all manufacturers of minoxidil topical solution, Teva USA proposes that the issue of children's safety can be best addressed by requiring all manufacturers to provide applicators that cannot be substituted for the original CR closure. This solution can be implemented in a shorter time frame and at less cost while more thoroughly safeguarding the small children in the household. It also maintains the competitive balance of the manufacturers currently in the market place.

Thank you for the opportunity to provide these comments and for your consideration of them. If you have any questions on the comments made, please do not hesitate to call me at (215) 256-8400 extension 5249.

Sincerely,



DAJ

*6/01/98*  
*CP98-3-5*

# American Academy of Pediatrics



Department of Government  
Liaison  
American Academy of Pediatrics  
The Homer Building  
601 Thirteenth Street, NW  
Suite 400 North  
Washington, DC 20005  
202/347-8600  
800/336-5475  
FAX: 202/393-6137  
E-mail: kids1st@aap.org  
Web Site: <http://www.aap.org>

May 29, 1998

Office of the Secretary  
Consumer Product Safety Commission  
Room 502  
4330 East-West Highway  
Bethesda, MD 20814  
FAX: 301/504-0127

Re: Proposed rule regarding child-resistant packaging for minoxidil  
(63 Federal Register 13019)

To Whom It May Concern:

The American Academy of Pediatrics (AAP) is an organization of 53,000 primary care pediatricians, pediatric medical subspecialists and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents and young adults.

Given the toxicity data provided in the Notice of Proposed Rulemaking, the Academy supports the Commission's intention to issue a rule to require child-resistant (CR) packaging for minoxidil preparations containing more than 14 mg of minoxidil in a single package. Further, we agree that the CR packaging requirement should include the applicators that are expected to be substituted for the original cap on a number of minoxidil products.

As the Commission has noted, minoxidil is a product that is likely to be readily available to children in the home, since it is available over-the-counter (OTC) and is used by consumers on a daily basis. Moreover, the OTC product is in a liquid form, which can be easily ingested by children.

Please feel free to contact the Academy if we can provide you with additional information or assistance.

Sincerely,

*Joseph R. Zanga, MD*  
Joseph R. Zanga, MD, FAAP  
President

JEG/jeg

#### Executive Committee

##### President

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Lucy S. Crain, MD

San Francisco, California

**T A B C**

UNITED STATES GOVERNMENT

MEMORANDUM

U.S. CONSUMER PRODUCT  
SAFETY COMMISSION  
WASHINGTON, D.C. 20207

8/21/1998

**TO:** Suzanne Barone, Ph.D., Project Manager, Minoxidil,  
Division of Health Sciences

**THROUGH:** Mary Ann Danello, Ph.D., Associate Executive Director  
for Epidemiology and Health Sciences *mad*

Marilyn L. Wind, Ph.D., Director, Division of Health *mlw*  
Sciences, Directorate for Epidemiology and Health  
Sciences

**FROM:** Charles Wilbur, Consumer Safety Officer, Division of *yu*  
Health Sciences, (301-504-0477 ex 1204)

**SUBJECT:** Technical Feasibility, Practicability, and  
Appropriateness Determination for the Final Rule to  
Require Special Packaging for Products Containing  
Minoxidil.

The attached evaluation summarizes the Health Sciences determinations of technical feasibility, practicability, and appropriateness for the final rule for minoxidil-containing products.

PPPA  
FINAL RULE  
MINOXIDIL  
TECHNICAL FEASIBILITY,  
PRACTICABILITY,  
AND  
APPROPRIATENESS  
Charles J. Wilbur

AUGUST 1998



DIRECTORATE FOR EPIDEMIOLOGY & HEALTH SCIENCES  
DIVISION OF HEALTH SCIENCES

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## SUMMARY

Epidemiology and Health Sciences staff concludes that the data support a finding that special packaging requirements for products containing minoxidil are technically feasible (can be produced), practicable (lends itself to techniques of mass production), and appropriate (compatible with the substances contained within the package), for the following:

1) Products requiring continuous threaded and dropper dispensing child-resistant packaging (CRP) with an effective date of six-months. Adequate supplies of senior friendly (SF) continuous threaded and dropper dispenser CRP are available.

2) Products using a metered finger mechanical sprayer (one with an optional extender sprayer) require more than one year to produce commercial quantities. Therefore, an effective date of one year along with a product manufacturer request for a temporary stay of enforcement would be needed. One major child-resistant (CR) metered finger mechanical sprayer manufacturer and a product manufacturer have indicated that with additional time they can develop a new SF CRP. An estimated 34 months will be needed to design CRP, conduct necessary tests, obtain FDA approval, build/modify tools and equipment, etc. for commercialization. Some of the unforeseen additional time is reflected in the need to develop and build equipment to assemble the mechanical pump and with the challenges associated with implementing multiple CR features.

## INTRODUCTION

To require that all minoxidil-containing products be packaged in CRP the Commission must find that CRP is:

- o Technically Feasible - Technology exists to produce packaging conforming to the standards.
- o Practicable - Special packaging complying with the standards, can be produced using modern mass production and assembly line techniques.
- o Appropriate - Packaging complying with the standards, adequately protects the integrity of the substance and does not interfere with its intended storage or use.

The Poison Prevention Packaging Act (PPPA) stipulates that the effective date shall be no sooner than 180 days and no more than one year from the date the final standard was promulgated.

## TECHNICAL FEASIBILITY

Minoxidil-containing oral prescription drugs are presently regulated under the PPPA. However, topical over-the-counter (OTC) minoxidil is not. All known OTC minoxidil-containing products are currently in SF CR continuous threaded packaging. In addition, packages contain one or more application devices (i. e. dropper, metered mechanical pump spray, and/or metered mechanical pump spray with an extender sprayer). Some, but not all of the applicators are SF CRP. Table I, Minoxidil Packaging, describes thirteen representative marketed products that were purchased at retail or obtained from the product manufacturer. As indicated in the table, there are SF CR droppers available on the market that are currently packaged with some OTC minoxidil preparations. No SF CR metered finger mechanical sprayer is currently being used. There is at least one CR finger mechanical sprayer that can be made SF.

Various types and designs of SF CR packaging can be obtained. See ASTM D3475, Standard Classification of Child-Resistant Packages. Most, but not all comply with the PPPA senior use effectiveness (SAUE) regulations. Each type of packaging is addressed below:

### PRODUCT CONTAINER

**CONTINUOUS THREADED RECLOSABLE CR PACKAGING:** Thirteen representative products are voluntarily using SF ASTM IA (Push Down and Turn Type) packaging<sup>2-14</sup>. In addition various designs of SF continuous threaded (screw) type reclosable CR packaging are readily available. ASTM in its Standard Classification of Child-Resistant Packages lists several designs of type I packages that are SF. Most minoxidil products use this type of CRP.

### PRODUCT APPLICATORS

**CONTINUOUS THREADED RECLOSABLE CR DROPPER PACKAGING:** Eight known products presently are voluntarily using SF ASTM IA design dropper packaging<sup>5-10,13,14</sup> that are reported to be SF<sup>15-17</sup>. The three products that are using non-CR droppers<sup>3,4,12</sup> can convert to SF CR droppers<sup>16-18</sup>. Alternatively, they could package a dropper that cannot be used as a closure. This may encourage people to close the package with the original SF CRP feature.

**METERED FINGER MECHANICAL SPRAYER CR PACKAGING:** We know of eight minoxidil products using a non-CR metered finger mechanical sprayer dispensing mechanism<sup>19</sup>. Some products contain instructions that include the statement, e. g. "The spray (B) applicator is NOT child-resistant." While not currently commercially available, a similar CR metered finger mechanical sprayer attached to a CR cap can be made available.

**TABLE I: Minoxidil Packaging.**

| MINOXIDIL CONTAINING PRODUCTS, 2% |        |                   |             |                |                    |
|-----------------------------------|--------|-------------------|-------------|----------------|--------------------|
| PACKAGE                           |        |                   |             |                |                    |
| Company                           | For    | Product Container | Applicators |                |                    |
|                                   |        |                   | Dropper     | Finger Sprayer | Extender Sprayer * |
| 3                                 | Women  | SF                | -           | NCR            | NCR                |
| 1                                 | Women  | SF                | -           | NCR            | NCR                |
| 1                                 | Women  | SF                | SF          | NCR            | NCR                |
| 2                                 | Women  | SF                | SF          | NCR            | -                  |
| 1                                 | Men ** | SF                | SF          | NCR            | -                  |
| 1                                 | Men    | SF                | SF          | NCR            | -                  |
| 2                                 | Men    | SF                | SF          | NCR            | -                  |
| 4                                 | Men    | SF                | SF          | NCR            | -                  |
| 5                                 | Men    | SF                | SF          | -              | -                  |
| 6                                 | Men    | SF                | SF          | -              | -                  |
| 7                                 | Men    | SF                | NCR         | -              | -                  |
| 8                                 | Men    | SF                | NCR         | -              | -                  |
| 3                                 | Men    | SF                | NCR         | -              | -                  |

SF=Senior Friendly

NCR=Non-Child Resistant

\* Extender Sprayer Uses Metered Finger Mechanical Sprayer Mechanism.

\*\* Minoxidil, 5%.

A metered mechanical finger pump spray manufacturer and a product manufacturer have agreed that a CR SF metered mechanical finger pump spray is technically feasible and have indicated they can make one available in approximately 34 months<sup>20-22</sup>. The time is needed for the CR mechanical pump manufacturer to design, prototype tool, and provide samples for the product manufacturer to use in testing. The product manufacturer would conduct protocol tests, and do required FDA and use testing. The commercialization phase includes obtaining FDA approval, production tooling, building assembly equipment, making modifications to the equipment and conducting trials. The CRP would most likely consist of a locking mechanism that provides the child resistance for the SF metered finger mechanical sprayer which is mounted on a permanently attached or reclosable SF CR closure that can be attached to a plastic bottle. The time schedule is justified because of the complexity of the CRP. The CRP will have two CR features (three if the extended applicator is included).

Three known products for women have a non-CR extender sprayer that must be attached to the mechanical pump dispensing mechanism<sup>2,11,13</sup>. This extender sprayer is used to "...help you spray ... through the hair, directly onto the scalp." This optional extender sprayer can be made SF and CR by using the same mechanism that provides the SF and CR functions for the finger sprayer special packaging. Another possibility is to use another type of CR mechanism to accomplish the same purpose, i.e., a SF CR dropper<sup>23</sup>. One product for women currently on the market uses the SF CR dropper for this purpose.

The staff believes that data support the finding that special packaging of minoxidil-containing products using SF continuous threaded (screw) CRP, SF dropper CRP, and SF metered mechanical finger pump CRP, with extended spray applicator, are technically feasible.

## **PRACTICABILITY**

### **PRODUCT CONTAINER**

**CONTINUOUS THREADED (CT):** These types of SF CRP are presently being used by many companies for regulated products, i.e., thirteen minoxidil products use SF CT special packaging. Companies have implemented assembly line and mass production techniques in their manufacturing process for the CT CRP. This shows that it is practicable to package regulated products in this type of special packaging. No major problems are anticipated from the manufacturing standpoint.

## **PRODUCT APPLICATORS**

**CONTINUOUS THREADED RECLOSABLE CR DROPPER PACKAGING:** Eight minoxidil products are voluntarily supplied with SF dropper applicators. The companies packaging these products have carried out assembly line and mass production techniques in their manufacturing process. This shows that it is practicable to package regulated products in this type of special packaging. No major problems are anticipated in this change from the manufacturing standpoint. Companies not currently using SF CR dropper applicators can incorporate special packaging into their existing packaging lines.

**METERED FINGER MECHANICAL SPRAYER CR PACKAGING:** No known minoxidil product manufacturer is currently using a CF metered finger mechanical sprayer. However, it is anticipated that a SF CR metered finger mechanical sprayer and a SF CR optional extender sprayer would be similar to the one being used. The mechanical pump manufacturer would need to make changes i.e. build a special assembly machine that would be added to the production line. Additionally, some mass production manufacturing techniques and processes may have to be modified. In the case of the product manufacturer, if the extender sprayer were attached, additional changes to the existing packaging line would be necessary. Two commenters said that with adequate time the necessary changes could be accomplished.

Information is available to support the finding that the special packaging of minoxidil-containing products is practicable.

## **APPROPRIATENESS**

**CONTINUOUS THREADED CRP AND DROPPER SPECIAL PACKAGING:** Some companies are presently using these types of SF special packaging for their products, i.e., thirteen minoxidil products use an SF CR CT package and eight use a CT dropper type special package. Most companies can use existing CR packaging designs and materials that have proven not to be detrimental to the integrity of the substance and have not interfered with its storage or use for these types of CRP. Product shelf life, and integrity would not be expected to change, as it is anticipated that the same packaging materials could be used in contact with the product.

**METERED FINGER MECHANICAL SPRAYER CR PACKAGING:** No known minoxidil product manufacturer is presently using a CR metered finger mechanical sprayer. Assuming the non-CR and the SF CR metered finger mechanical sprayers and the optional extender sprayers use similar materials, we would not expect the materials to be detrimental to the integrity of the substance nor would they interfere with its storage or use. Therefore, product shelf life, and integrity would not be expected to change, as it is anticipated that the same packaging materials could be used in contact with the product.

However, it is anticipated with the configuration change, etc. confirming stability testing would be necessary and may be required by the FDA.

Staff, therefore, believe that the data support the finding that special packaging for minoxidil-containing products is appropriate.

#### **EFFECTIVE DATE**

**CONTINUOUS THREADED CRP AND DROPPER CR PACKAGING:** A six-month effective date is reasonable for these types of special packaging. All known manufacturers are voluntarily using CT SF CRP for the primary container<sup>18,24,25</sup>. As for the applicator, most but not all, manufacturers are voluntarily using SF dropper CRP. Two sizes of SF dropper CRP are commercially available. Most product manufacturing companies would not require any changes to their production lines. The CRP suppliers have the requisite molds, assembly equipment, lining material and plastic resins to supply the required CRP quantities for this product. Adequate supplies of SF CRP for this product are available from the packaging manufacturers.

**METERED FINGER MECHANICAL SPRAYER AND EXTENDER SPRAYER CR PACKAGING:** More than one year is needed for products using the metered finger mechanical sprayer type packaging. One product manufacturer has "estimated it will take 134 weeks (approximately 34 months) to bring the metered finger sprayer replacement to the market..."<sup>21</sup>. This same approximate time frame (27-36 months) was given by another product manufacturer<sup>22</sup>. The additional time required for the CR pump manufacturer, the product manufacturer, and the commercialization phase is necessary and can be made available to companies through a request for a stay of enforcement<sup>26</sup>. If the metered SF finger mechanism sprayer special package were used in combination with the extender sprayer, the timing would be approximately the same.

#### **CONCLUSION**

Staff concludes that data support the findings that ASTM types I (CT), I (Dropper), and IX (Pump Dispenser) special packaging for minoxidil products is technically feasible, practicable, and appropriate.

#### **RECLOSABLE CONTINUOUS THREADED CRP AND DROPPER CRP, (ASTM I):**

There are regulated PPPA products on the market with ASTM type I CRP (with and without a dropper) that comply with SAUE requirements. Adequate supplies of SF CRP are available to support a six-month effective date.

**METERED FINGER MECHANICAL SPRAYER CRP, (ASTM IX) AND EXTENDER SPRAYER CRP:**

One CR metered finger mechanical sprayer manufacturer and one product manufacturer said, given 34 months, they could make commercially available SF special packaging. A one-year effective date with provisions for a 22-month temporary stay of enforcement for a total of 34 months is needed for commercialization of the metered CR finger mechanical sprayer. This additional time is necessary because of the requirements for up to three CR features, building of an assembly machine and the metered spray mechanism tolerance requirements. The same approximate time is needed if the metered finger mechanical sprayer is used with the extender sprayer applicator.

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