

TAB D



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

MEMORANDUM

DATE: August 24, 1998

TO : Suzanne Barone, Ph.D., EH
Project Manager, Minoxidil

Through: Warren J. Prunella, AED, EC *GR for WJP*

FROM : Marcia P. Robins, EC ^{*mpr*}
(504-0962)

SUBJECT: Child-Resistant Packaging for Preparations Containing
Minoxidil: Small Business Effects

The Regulatory Flexibility Act (RFA [PL 96-3451]) generally requires agencies to prepare and make available for public comment an initial regulatory flexibility analysis describing the impact of the rule on small businesses and other small entities, when a general notice of proposed rulemaking is published in the *Federal Register* (FR). However, under section 605, no such analysis is required if the Commission certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities.

On March 17, 1998, CPSC published a Notice of Proposed Rulemaking (NPR) to require child-resistant (CR) packaging for preparations containing more than 14 mg minoxidil in a single package. The requirement extends to applicators that are included in the package and may reasonably be expected to replace primary closures when used and stored in the home. In this notice the Commission concluded that the proposal would not have a significant economic effect on a substantial number of small businesses or other small entities.

This conclusion was based primarily on the fact that many firms are voluntarily using CR packaging on the bottle (primary package) and on its dropper applicator. Firms that are not using CR packaging and firms that enter this market in the future will be readily able to find primary packaging at prices competitive with nonCR packaging. Substitution of a CR dropper will result in an estimated 5 cent per package incremental cost to the supplier, a cost increase that is small relative to the average retail price of the product. Information regarding the incremental cost of a CR finger sprayer was not previously available because the finger sprayer was not in commercial production. However, it too, was not expected to be large

relative to the retail prices (\$20-\$30) of the preparations known to be supplied with a finger sprayer.

A copy of the FR notice containing the proposed rule was sent to 16 individual large and small businesses known to manufacture or repackage/relabel minoxidil-containing preparations. A copy of the proposal was also sent to some individual closure manufacturers and additionally to trade associations representing manufacturers of OTC drug products and manufacturers of closures.

Public comments on the proposal were provided only by large pharmaceutical manufacturers. One manufacturer provided confidential information on the projected time and costs to develop, test, and make available commercial quantities of a CR finger sprayer. The expected cost of a CR finger sprayer is not substantial relative to the retail price of the product. Staff is unaware of any small manufacturers that supply a finger sprayer or an extended finger sprayer with their product.

One large generic pharmaceutical manufacturer expressed concern over the possibility that the manufacturer of a CR finger sprayer might enter into an exclusive agreement with a brand name supplier thus creating a competitive disadvantage to generic suppliers. However, no data were provided to support this possibility. Additionally, a finger sprayer is not supplied with many generic minoxidil products currently in the market. No information regarding potential adverse impacts on small businesses or other small entities was received. Based on all of the economic information available on the proposed rule, the Directorate for Economic Analysis concludes that the final action to require CR packaging for OTC drug preparations containing more than 14 mg minoxidil in a single package will not have a significant economic effect on a substantial number of small entities.

T A B E

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CONSUMER PRODUCT SAFETY COMMISSION

16 CFR Part 1700

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

AGENCY: Consumer Product Safety Commission.

ACTION: Final rule.

SUMMARY: The Commission is issuing 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 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 authority of the Poison Prevention Packaging Act of 1970.

DATE: For primary packaging and dropper applicators, the rule will become effective on _____ [insert date that is six months after publication in the **FEDERAL REGISTER**]. For metered finger mechanical sprayer applicators and extender attachments, the rule will become effective on _____ [insert date that is one year after publication in the **FEDERAL REGISTER**]. The effective dates apply to preparations packaged on or after those dates. Companies intending to develop a CR finger sprayer and/or extender may apply to the Commission for a temporary stay of

enforcement.

FOR FURTHER INFORMATION CONTACT: Laura Washburn, Directorate for Compliance, Consumer Product Safety Commission, Washington, D.C. 20207; telephone (301) 504-0400 ext. 1452.

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 the 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.

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 applied to the scalp to stimulate hair regrowth for individuals with androgenetic alopecia, a common form of genetic hair loss. 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. A tablet form of minoxidil is also available by prescription for treatment of severe hypertension. 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, and further 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.(2)¹ 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) applied twice a day. The total contents of this 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).(3)

Topical minoxidil formulations are generally packaged either for men or for women. The formulations are the same, but the packaging and instructions are different. All the bottles the Commission is aware of are secured with CR senior friendly ("SF") continuous threaded closures. In addition to the primary

¹ Numbers in parentheses refer to documents listed at the end of this notice.

closure, the packages the Commission staff examined contain one or more applicators that are reasonably expected to be used to replace the primary closure.

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. None of the finger sprayers are CR. (4 and 8)

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 finger sprayer. 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 finger sprayer alone would manage. Neither the finger sprayers nor the extenders in the packages intended for women were CR. (4 and 8)

3. CR Packaging for Applicators

As explained in the notice of proposed rulemaking ("NPR") (63 FR 13019), because the topical minoxidil formulations are packaged with applicators that are reasonably expected to replace the primary closure of the product, the Commission has determined

that the applicators themselves must be CR if the Commission requires CR packaging for the product.

Under the PPPA, a "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). This definition focuses 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. 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 concludes that when an applicator is packaged with a product that requires CR packaging and the applicator is reasonably expected by the Commission 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. As discussed in the NPR, this view reflects the long held interpretation of the Commission staff. 63 FR 13021.

Because the Commission has not previously addressed this question explicitly in a regulation, the minoxidil rule 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 or acetaminophen, 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 is including such a statement in the minoxidil rule. 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.

The Commission did not receive any comments questioning its interpretation of the PPPA as covering applicators that are reasonably expected to be used to replace the primary closure.

4. The Proposed Rule

On March 17, 1998, the Commission issued an NPR that proposed requiring CR packaging for minoxidil preparations containing more than 14 mg of minoxidil in a single package 63 FF 13019.

The Commission received five comments in response to the proposed rule. The American Academy of Pediatrics commented in support of the rule and expressed agreement with the Commission's position that the CR packaging requirement should include applicators expected to replace original closures on minoxidil products. Other comments and the Commission's responses are discussed below. (7)

Packaging Issues

Comment: One comment from the Closure Manufacturers Association ("CMA") stated that the Commission had no data to demonstrate that CR extender finger sprayers are technically feasible and practicable. The commenter stated that the preamble in the NPR had stated that technology does not exist for the development or use of CR finger sprayers with extenders. The commenter concluded that therefore continuing with the proposed rule "would be a violation of the [PPPA] statute and the Administrative Procedures [sic] Act."

Response: CMA apparently misunderstood the statement in the NPR which noted that CR extender sprayers are not currently on the market. The fact that a particular CR closure is not currently being marketed does not mean it is not technically

feasible and practicable. As explained in section E.2. of the preamble, technical feasibility refers to the capability of producing a CR closure, not whether one is actually on the market. Similarly, practicability means that mass production methods can be used to produce CR packaging for the substance, not that it is currently being done. Neither CMA nor any other commenters have presented any information indicating that a CR extender sprayer could not be developed or could not be mass produced. In fact, as discussed below, some companies said they would need more time to produce CR applicators for minoxidil products, but they did not question their ability to make any of the available applicators CR.

CMA's comments refer only to the extended sprayer. It is important to note that the PPPA does not require that every package design must be made CR. The Commission has no information indicating that a CR extended sprayer could not be made. However, even if it could not, other CR packaging applicators exist that are technically feasible, practicable and appropriate exist. Thus, this rulemaking does not violate the PFPA or any other statute.

Comment: One commenter indicated that CR droppers are not a good barrier because children can chew through the bulb.

Response: When testing CR dropper packaging, if a child chews through or pulls out the dropper bulb this would count as a failure since the child gains access to the product. The Commission's data indicate that dropper assemblies currently on

the market pass the CR packaging test protocol and meet the requirements of the PPPA.

Comment: The same commenter requested that the Commission prohibit applicators that could be used as substitutes for original closures because of cost, time, and potential competitive imbalance.

Response: Under the PPPA, the Commission cannot prescribe specific packaging designs. 15 U.S.C. 1472(d). Thus, companies may use any packaging that meets the requirements of the special packaging protocol. Similarly, any applicator (if it is reasonably expected to replace the original closure) that meets these requirements could be used. Moreover, as pointed out in the proposed rule, an applicator that would not be used to replace the original closure, such as a dropper without a reclosable feature, would also be acceptable.

Effective Date for Finger Sprayers

Comment: Three commenters indicated that the proposed effective date of one year was too short. One commenter requested a total of 34 months (22 months in addition to a one year effective date). Another commenter stated that 27-36 months would be necessary to incorporate a CR finger sprayer.

Response: After reviewing the process for commercialization of a CR finger sprayer, the Commission agrees that more than one year may well be necessary. Thus, the Commission will allow companies to request a stay of enforcement to provide additional time to produce CR finger sprayers and extender sprayers, and it

would anticipate granting such requests until such time as it determined that an enforcement stay was no longer appropriate. This issue is discussed further in section F of the preamble.

Cost Considerations

Comment: One commenter indicated that the additional cost of CR droppers instead of non-CR droppers was greater than \$0.05 as suggested in the NPR.

Response: The commenter has since indicated to CPSC staff that the \$0.05 estimate is in fact within the range of increased cost for a CR dropper.

Comment: One commenter stated that there would be a competitive disadvantage to generics if exclusive agreements for spray packaging were made with a brand product.

Response: The commenter supplied no data and the Commission has no data to support this claim. In fact, two different companies commenting on the NPR provided information about the timing for developing a finger sprayer. Even if there were an exclusive agreement, it would not prevent other companies, such as the commenter from developing a CR 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 non-CR finger sprayer, according to one commenter. This is not a substantial cost increase relative to the product cost, even for less expensive generic minoxidil products. Moreover, several of the generic brands do not currently include a finger sprayer with their products. Also, a generic company is not

necessarily a small company. The commenter, for example, is a large generic pharmaceutical manufacturer.

B. Toxicity of Minoxidil

The Commission's Directorate for Epidemiology and Health Sciences reviewed the toxicity of minoxidil. Either as prescription tablets or a topical liquid, 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. Because minoxidil is very poorly absorbed through the skin, 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.(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

As discussed more extensively in the NPR, 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 by AAPCC 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. (2)

Annual AAPCC data on pediatric exposures to children under five years of age reported four accidental ingestions of topical minoxidil liquid in 1995, none of which led to serious toxicity. (Prior to 1995, topical minoxidil was not given a specific code within the AAPCC database.) In 1996, the number of reported cases increased to 43, one of these exhibited moderate effects. For 1997, the AAPCC had 52 reports of children under age five ingesting topical minoxidil. Half of these were referred to a health care facility for observation or treatment. However no serious outcomes were reported. (2 and 6)

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. As discussed in more detail in the NPR, three of these led to serious outcomes. (2)

CPSC Databases

CPSC has several databases for poison incidents. The staff reviewed cases from 1988 to June 1998 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. Three childhood poisoning cases associated with minoxidil were reported in the NEISS database during that time period. One 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)

There is less information concerning the two more recent incidents that were reported since the NPR. One case involved minoxidil tablets and the other resulted from topical minoxidil in a spray bottle. Neither child was hospitalized. No other details are available at this time. (6)

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 June 1998 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) and were discussed in the NPR. (2)

D. Level for Regulation

The Commission is issuing a rule requiring 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) The Commission proposed this level and received no comments on it.

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 that are reasonably expected to be used as closures after first use which are not CR. The Commission 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 future manufacturers.

Pursuant to section 3(a) of the PPPA, 15 U.S.C. 1472(a), the Commission 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, 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 and 8)

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 and 8)

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 obtain an amount above the regulated level by, for example, 1) removing the finger sprayer closure from the container or 2) activating the finger sprayer mechanism. One packaging manufacturer has developed a prototype CR finger sprayer applicator which the manufacturer believes can be modified to pass senior adult effectiveness testing. In addition, two product manufacturers commenting on the NPR indicated that they could develop a finger sprayer that would meet special packaging requirements. As discussed above, an applicator that cannot be used as a closure does not need to be CR. (4 and 8)

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, 2) activate the combined finger sprayer and extender to obtain an amount above the regulated level, and 3) remove the extender. Currently no finger sprayers with extenders are CR. As noted above, CR/SF finger sprayer could be developed. Some modifications to the extender may be needed so that it would operate with the CR finger sprayer. (4 and 8)

As discussed above, the Commission received one comment from CMA questioning whether an extender sprayer was feasible and practicable. However, since the finger sprayer and the extender use essentially the same mechanism, the Commission believes that the extender sprayer could be made CR/SF. The Commission is not aware of any data indicating otherwise.

3. Other Considerations

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

- a. The reasonableness of the standard;
- b. Available scientific, medical, and engineering data concerning special packaging and concerning childhood accidental ingestions, illness, and injury caused by household substances;
- c. The manufacturing practices of industries affected by the PPPA; and
- d. The nature and use of the household substance. 15 U.S.C. 1472(b).

The Commission has considered these factors with respect to the various determinations made in this notice, and 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.

Primary closures and droppers. Primary product containers for topical minoxidil are already CR and SF. Droppers are available CR and SF that can be used to replace the original closures. Thus, the Commission proposed that a final rule with respect to child-resistance of primary closures and dropper applicators would take effect six months after publication of the final rule. The Commission has no additional information that would change this aspect of the proposed effective date.

Finger sprayer and extender. The Commission stated in the NPR that it was aware of one packaging manufacturer that had developed a prototype CR finger sprayer that the manufacturer believed could be modified to pass senior adult effectiveness testing in approximately 12 months. The Commission also recognized that additional time might be needed to provide commercial quantities of this type of packaging. Thus, the Commission proposed an effective date with respect to metered finger sprayer applicators and extenders that would be 12 months

after publication of the final rule. The Commission also proposed that if additional time appeared necessary to produce commercial quantities of these applicators, manufacturers could request a temporary stay of enforcement for the finger sprayer and extender.

As discussed above, the Commission received comments indicating that more than 12 months would be necessary to convert to a CR metered finger sprayer. Two commenters indicated that a design could be modified, tested, and in commercial use in approximately 27 to 36 months. The Commission agrees that this time seems reasonable due to the complexity of developing a finger sprayer that is metered and has two CR features. Because companies will need to commit resources to develop this type of packaging, companies may request a stay of enforcement immediately after this final rule is published, and the Commission would anticipate granting such requests until such time as it determined that an enforcement stay were no longer appropriate. Companies requesting a stay of enforcement should provide the Commission with a timeline or schedule that will outline the steps they will take to bring this type of CR packaging to commercial use. They should include an estimated initial production date and current and proposed packaging specifications.

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.

As noted in the NPR, the Commission's Directorate for Economic Analysis prepared a preliminary assessment of the impact of a rule to require special packaging for topical minoxidil products containing more than 14 mg of minoxidil in a single package. Based on this assessment, the Commission concluded 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 requested additional information on the possible impact on small business, but received no such comments. One commenter (not a small business) supplied cost estimates for the CR finger sprayer. The expected cost is not substantial relative to the retail cost of the product. Moreover, the Commission is unaware of any small firms that supply a finger sprayer with their product. Thus, the Commission continues to conclude that the rule would not have a significant effect on a substantial number of small entities.

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.

In the NPR, the Commission concluded that the rule would have no adverse effect on the environment and that neither an environmental assessment nor an environmental impact statement is required. The Commission has no information that would alter this conclusion.

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). Upon application to the Commission, a State or local standard may be excepted from this preemptive effect if the State or local standard (1) provides a higher degree of protection from the risk of injury or illness than the PPPA standard and (2) does not unduly burden interstate commerce. 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 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 rule does not have sufficient implications for federalism to warrant a Federalism Assessment.

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 amends 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 below 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: _____

Sadye E. Dunn,
Secretary, Consumer Product Safety Commission

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.
6. Briefing memorandum from Suzanne Barone, Ph.D., EH, to the Commission, "Final Rule to Require Child-Resistant Packaging for Topical Minoxidil," October 9, 1998.
7. Memorandum from Martha A. Kosh, OS, Comments on the Proposed Rule for Requirements for Child-resistant Packaging; Minoxidil Preparation with More than 14 mg of Minoxidil per Package (CP98-3), June 2, 1998.
8. Memorandum from Charles Wilbur, EH, to Suzanne Barone, Ph.D., EH, "Technical Feasibility, Practicability, and Appropriateness Determination for the Final Rule to Require

Special Packaging for Products Containing Minoxidil," August 21, 1998.

9. Memorandum from Marcia P. Robins, EC, to Suzanne Barone, Ph.D., EH, "Child-Resistant Packaging for Preparations Containing Minoxidil: Small Business Effects," August 24, 1998.