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

**MEMORANDUM**

**DATE:** June 2, 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

| COMMENT | DATE | SIGNED BY | AFFILIATION |
|---|---|---|---|
| **CP98-3-1** | 3/6/98 | Emil Berro<br>Associate Director | Pharmacia & Upjohn Company<br>7000 Portage Road<br>Kalamazoo, MI 49001 |
| **CP98-3-1a** | 5/20/98 | 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 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 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 |
| **CP98-3-5** | 5/29/98 | Joseph Zanga<br>MD, FAAP<br>President | American Academy of Pediatrics<br>The Homer Building<br>601 Thirteenth St, NW<br>Suite 400 North<br>Washington, DC 20005 |

cc: OGC

# 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

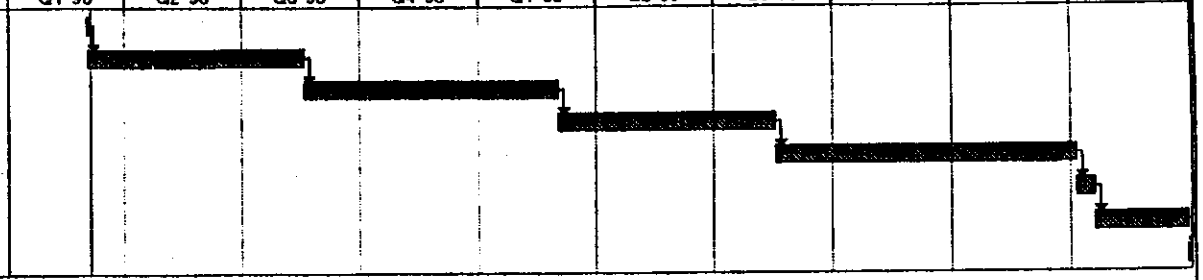
Emil C. Berro
Associate Director
OTC Regulatory Affairs

cc: Suzanne Barone

ECB:cek

ROGAINE CR&F APPLICATOR

| ID | Task Name | 1st Quarter Q1 '98 | 2nd Quarter Q2 '98 | 3rd Quarter Q3 '98 | 4th Quarter Q4 '98 | 1st Quarter Q1 '99 | 2nd Quarter Q2 '99 | 3rd Quarter Q3 '99 | 4th Quarter Q4 '99 | 1st Quarter Q1 '00 | 2nd Quarter Q2 '00 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | ROGAINE 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&F Sprayer
Date: 3/6/98

Task | Milestone | Rolled Up Task | Rolled Up Progress
Progress | Summary | Rolled Up Milestone

CP98-2-10 bag 5/20/98

# 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

May 20, 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 Commision for it's deliberations on March 2, 1998.

Based on discussions with a nationally recognized supplier of sprayer devices, Calmar Inc., we have determined a more realistic timetable to develop, test, and implement a CR/SF sprayer system (see attached timeline). We estimate it will take 134 weeks (roughly 34 months) to bring the metered finger sprayer replacement to market at a minimum cost of $1.62 million dollars capital investment and a per unit cost of approximately $ 0.34. We anticipate that this project will commence at the date of the Final Rule. (A table listing development costs is attached. The cost per unit was determined by Calmar Inc. and utilizes our projected sales volume at the time of market introduction. In comparison, the new CR sprayer will cost $0.19 more than the current non CR sprayer. )

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

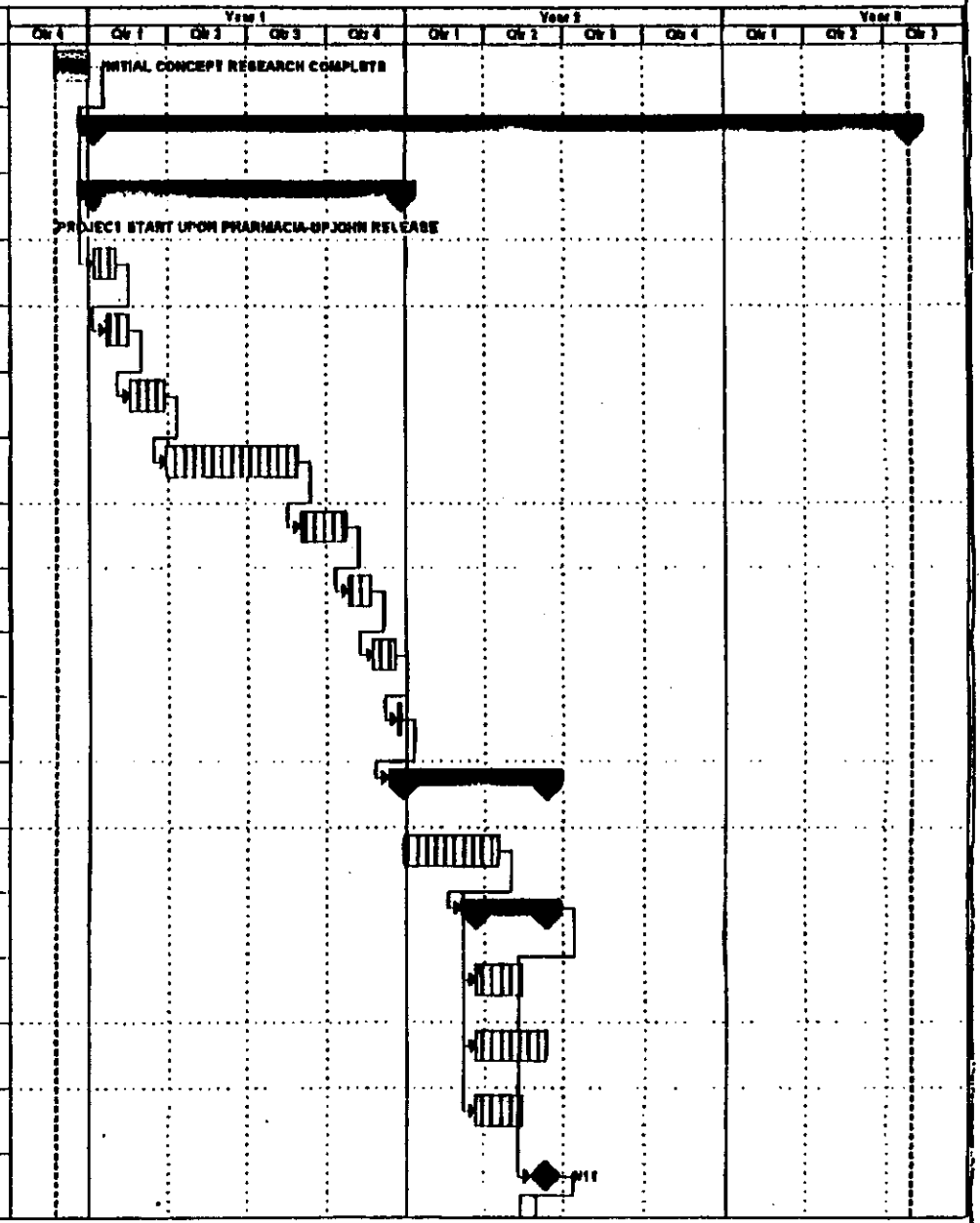
cc: Suzanne Barone
Chuck Wilbur

ECB:cek

# MARK II CHILD RESISTANT SPRAY PUMP DEVELOPMENT AND COMMERCIALIZATION

CONFIDENTIAL

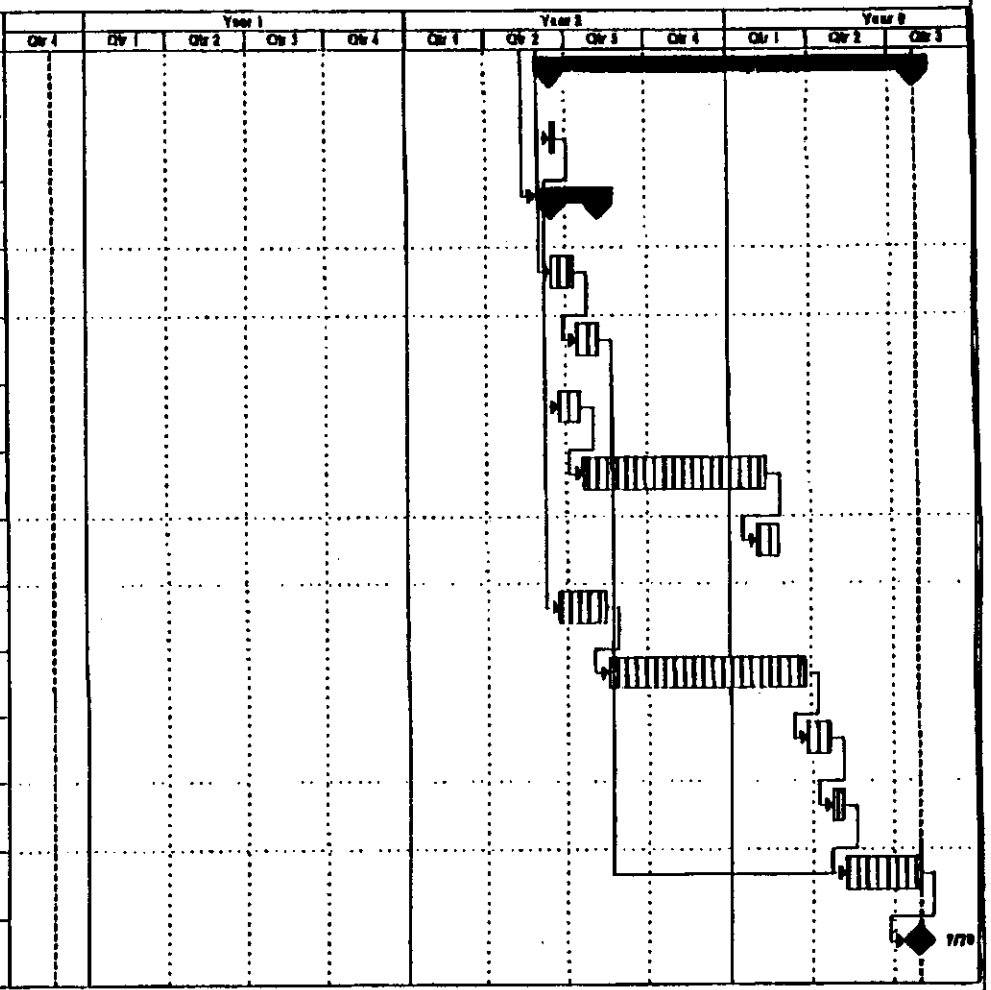
| ID | Task Name | Dur |
|---|---|---|
| 1 | CONCEPT EVALUATION & PROJECT PROPOSAL | 6 w |
| 2 | **PROJECT ROLL UP** | **134 w** |
| 3 | **PRODUCT DEVELOPMENT ROLL UP** | **61 w** |
| 4 | PRODUCT DESIGN | 4 w |
| 5 | COMPUTER ANALYSIS | 4 w |
| 6 | HAND BUILT PROTOTYPE / SOFT TOOLING | 6 w |
| 7 | STEEL UNIT CAVITY DESIGN & BUILD | 22 w |
| 8 | PART DEVELOPMENT | 8 w |
| 9 | PROCESSING DOE | 4 w |
| 10 | PUMP QUALIFICATION TESTING | 4 w |
| 11 | MAKE SAMPLES FOR CUSTOMER QUALIFICATION | 1 w |
| 12 | *PHARMACIA & UPJOHN QUALIFICATION TESTING FOR 2 & 5% MINOXIDIL* | 24 w |
| 13 | *CPSC CHILD & SENIOR FRIENDLY TESTS* | 16 w |
| 14 | *NDA REQUIRED TESTS* | 12 w |
| 15 | *DOSE ACCURACY TESTING* | 8 w |
| 16 | *LONG TERM USE TESTS* | 12 w |
| 17 | *PACKAGE\PRODUCT INTEGRITY TESTS* | 8 w |
| 18 | *DECISION TO COMMERCIALIZE* | 1 d |



## MARK II CHILD RESISTANT SPRAY PUMP DEVELOPMENT AND COMMERCIALIZATION

CONFIDENTIAL

| ID | Task Name | Dur |
|---|---|---|
| 19 | **PRODUCTION UNIT COMMERCIALIZATION ROLL UP** | 59 w |
| 20 | COMMERCIALIZATION PLANNING | 1 w |
| 21 | *PHARMACIA & UPJOHN REGULATORY TASKS* | 8 w |
| 22 | *PREPARE & SUBMIT SNDA FOR SPRAYER* | 4 w |
| 23 | *SNDA APPROVED BY FDA* | 4 w |
| 24 | PRODUCTION MOLD DESIGN | 4 w |
| 25 | PRODUCTION MOLD BUILD | 30 w |
| 26 | PRODUCTION MOLD QUALIFICATION | 4 w |
| 27 | ASSEMBLY MACHINE DESIGN | 8 w |
| 28 | ASSEMBLY MACHINE BUILD | 32 w |
| 29 | ASSEMBLY MACHINE QUALIFICATION | 4 w |
| 30 | PRODUCTION FINAL QUALIFICATION | 2 w |
| 31 | *PHARMACIA & UPJOHN PRODUCTION PART ORDER & PACKAGING RELEASE* | 12 w |
| 32 | *USE IN NEW MINOXIDIL PACKAGES* | 1 d |



Calmar inc.
Personal Care Products Div.

May 11, 1998

Wayne Leblong
Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
616 833 5151

Dear Wayne,

Per our phone conference, the following is a cost break out for the Mark II Child Resistant Spray Pump development , commercialization and qualification along with the revised project schedule.

| ITEM | COST |
|---|---|
| | |
| **CALMAR DEVELOPMENT** | |
| Prototype Molds and Tooling | $92,500 |
| Engineering & Technical Services | $25,000 |
| **SUBTOTAL** | **$117,500** |
| | |
| **CALMAR COMMERCIALIZATION** | |
| Production Molds | $569,000 |
| Production Assembly Machines | $713,500 |
| Installation & Qualification | $20,000 |
| **SUBTOTAL** | **$1,292,500** |
| | |
| **TOTAL** | **$1,420,000** |
| | |
| **PHARMACIA-UPJOHN TESTING & QUALIFICATION** | **$200,000** |
| | |
| **COMPLETE PROJECT COST** | **$1,620,000** |

CPSC-D-01 61-01C 5/26/98 FR2

CLOSURE
MANUFACTURERS
ASSOCIATION

CMA



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).

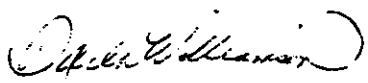
The proposed rule seeks to require special child-resistant packaging for minoxidil preparations that contain over 14 milligrams of the substance and which are packaged with applicators, including droppers, metered-finger mechanical sprayers, and finger sprayers with extenders. Pursuant to the Poison 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)

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

Pharmaceutical Division | 8500 Hidden River Parkway Tampa FL 33637 | 813 975 7700 Fax 813 975 7770

65 01C 5/29/98 a

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

Donald H. Chmielewski
Director, Regulatory Affairs

CP98-5-4

TEVA

Deborah A. Jaskot
Sr. Director, Regulatory Affairs

**Corporate Headquarters:**
TEVA PHARMACEUTICALS USA
650 Cathill Road, Sellersville, PA 18960

Toll Free: (888) TEVA USA
Phone: (215) 256 8400
FAX: (215) 721 9669

**Corresponding Address:**
TEVA PHARMACEUTICALS USA
1510 Delp Drive, Kulpsville, PA 19443

Toll Free: (888) TEVA USA
Phone: (215) 256 8400
FAX: (215) 256 7855

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,

Deborah Jasmot

DAJ

6017 5/29/98
CP98-5-5

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: iuds1st@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 orignal 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