Lowest reported dose for moderate and severe poisoning

Medication	No. of dose units
atenolol	<1
nifedipine	<1
propranolol	<1
amoxapine	1
dapsone	1
dothiepin	1
quinine	1
sulphonylureas	1
Lomotil ®	1,3
carbamazepine	1,5
hyoscine	1,5
methadone	2
imipramine	3
temazepam	3

All of the investigated substances can lead to moderate or severe poisonings if less than 8 units are ingested.

There are some other pharmaceuticals which could also lead to serious effects at low doses and should be investigated. These include all tricyclic antidepressants, products containing large doses of opioids, chlormethiazole, chloral hydrate, chlorpromazine, clozapine, dextropropoxyphene, codeine, flecainide and clonidine, verapamil, orphenadrine, risperidone, thioridazine, flecainide, theophylline, and chloroquine. Due to financial and time constraints it was not possible to incorporate them in the study.

Guidelines

The guidelines for determining and predicting toxic doses of pharmaceuticals for children contain a scheme including a flow chart for the determination of a toxic dose (the dose which requires medical intervention. It also discusses the methodology, specificities of the child's body response to ingestion of medications, extrapolation of adult data for paediatric use, strengths and weaknesses of various data sources and other things. Some practical examples for the application of the guide are given.

These guidelines clearly demonstrate that it is feasible to determine a toxic dose for a child which is a prerequisite for the deduction of a maximum number of accessible units in the context of child panel testing of child-resistant packaging.

Conclusions about the study by ANEC

The report provides clear evidence that the ingestion of low numbers of tablets of pharmaceuticals can do serious damage to children. In certain cases less than one pill can kill a child.

Hence, the approach of the draft European standard prEN 14375 to consider packages as child-resistant although the specified percentage of test children can open up to 8 units in a child panel test is questionable and needs to be reconsidered.

At least for certain highly toxic medications a different approach is needed. The maximum number of units for the child panel test must correspond to the toxicity of the pharmaceutical. Therefore the 8 units criterion contained in the draft standard irrespective of the dose is not acceptable. The standard must be revised.

Reaction of the CEN Working Group

The ANEC project advisor presented the study referred to above at the comments resolutions meeting of the responsible CEN Working Group in November 2002. Whilst the scientific validity of the study was fully recognised there was no willingness to make any change regarding the acceptance criterion. A proposal made by the ANEC project advisor just to define a test method in the standard and to let the legislator define the number of units allowed to be opened was rejected.

However, the limitations of the standard were acknowledged by inserting the following note in the normative text:

"NOTE The figure of eight units is based on existing national standards published by certain CEN members and does not address the issue of toxicity. Some pharmaceutical products on the market can cause harm to children by the ingestion of fewer than eight units. However, reliable data on child toxicity exists for few pharmaceutical products. A harmful dose can be established for some existing pharmaceutical products and a maximum safe dose can be established for all pharmaceutical products by one means or another. Such information is not currently available for all products and there is no central register where this information could be held. In the absence of European legislation on this topic the drafters of this European Standard acknowledge these concerns and believe that research and collection of data should continue with a view to considering the substitution of a toxicity based pass/fail criterion for the child panel test in a later revision".

In addition, it was decided to draw the attention of the CEN Management Centre and the responsible department of the Commission to this note and further action to be taken.

The formal vote was launched in May 2003. Presumably the standard will receive a positive vote despite ANEC's lobbying against it.

Future activities – call for legislation

It is evident that the European standard cannot be regarded as a long term solution from a consumer protection perspective. German health authorities have questioned the standard and have suggested an immediate revision.

Irrespective of any future action within the European standardisation institution CEN the implementation of European legislation for child-resistant packaging of pharmaceuticals is necessary. At present only a few countries (UK, Germany, Holland, Italy) have legal requirements in place. However, these requirements differ strongly in terms of comprehensiveness and in terms of requirements. A harmonised European solution may be preferable also from a trade point of view.

The future European legislation should:
- require child-resistant packages for pharmaceuticals which can harm the health of a child
- provide for a procedure and a scientific body to identify and assess the toxicity of these pharmaceuticals for children
- be based on the US philosophy of prescribing packages of different degrees of difficulty in terms of opening depending on the dose and toxicity of the medications
- shall identify the acceptance criteria in terms of dose/units allowed to be opened in child panel tests
- refer to a European standard which should be a test method only
- provide for a register of type approved packages

ANEC has been made aware of the fact that manufacturers in the US try to get rid of the stringent provisions concerning child-resistant packaging for medications. The US Consumer Product Safety Commission has received a petition from the Healthcare Compliance Packaging Council (HCPC) aiming at the removal of the toxicity based criterion following the questionable CEN approach. The US CPSC solicited written comments on the request in June 2003. ANEC will forward the study and additional comments.

Stevenson, Todd A.

From: Tania VANDENBERGHE [tania@anec.org]
Sent: Tuesday, June 24, 2003 5:12 AM
To: Stevenson, Todd A.
Cc: Franz Fiala (E-mail)
Subject: Petition PP 03-1: comments from ANEC

03011tr.pdf | MTU Report final 0205.pdf | MTU Report Guidelines final 02... | ch042-03.pdf

Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

Dear Sir,

Please find enclosed comments from ANEC on the above mentioned petition.

Yours sincerely,
--
Tania Vandenberghe
Programme Manager

ANEC - European Association for the Co-ordination
of Consumer Representation in Standardization
Tervurenlaan 36/4 - B-1040 Brussel/Bruxelles/Brussels

Tel. +32 2 743 2470 - E-mail: anec@anec.org
Fax +32 2 706 5430 - Direct E-mail: tania@anec.org
Internet: http://www.anec.org

CR Testing Comment

Stevenson, Todd A.

From: RBrooke@KVPharmaceutical.com
Sent: Monday, July 28, 2003 11:08 AM
To: Stevenson, Todd A.
Subject: Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

<<...OLE_Obj...>>

July 28, 2003
Office of the Secretary
Consumer Product Safety Commission
Washington, DC 20207

Comments to: "Petition PP 03-1, Petition for Amendment of the Child-resistance Testing Requirements for Unit Dose Packaging"

After reviewing the petition for amending the Child-Resistance Testing Requirements for Unit Dose Packaging KV Pharmaceuticals agrees that the current requirements impose an unnecessarily stricter standard for unit dose packaging then those required for bottle packages. We agree with the Healthcare Compliance Packaging Council's proposal that the child resistance testing requirements should be based on an objective standard regardless of the content of the package, similar in nature to bottled packages.

Sincerely,
Robert R. Brooke, MS JD
Vice President Quality Assurance/Quality Control
KV Pharmaceutical
St. Louis, MO 63043

CRS test post comment

Stevenson, Todd A.

From: Steven Marcus [smarcus@njpies.org]

Sent: Wednesday, July 30, 2003 1:08 PM

To: cpsc-0s@cpsc.gov

Cc: MEDDIRECTORS-L@LISTSERV.AAPCC.ORG; DIRECTORS-L@LISTSERV.AAPCC.ORG

Subject: Petition PP 03-1

I am writing in response to the Proposed Rules changes reported in the Federal Register Vol 68, No 115/Monday, June 16,2003

As a rather senior pediatrician, toxicologist and medical director of a regional poison control center, I am amazed at an apparent reversal in position of the CPSC as far as rules for child resistant containers. I am old enough to remember children getting very sick from ingesting a **single** dose of Lomotil, a rather obsolete drug these days, but a model for the problem of setting an absolute standard to the number of doses to be exceeded after which a packaging is no longer considered child resistant.

There are medications used today which are hazardous to toddlers in even a single dose administration. This is particularly troubling in an era when more pharmaceuticals are being prepared in sustained release forms so that once ingested absorption may continue for many hours. A perfect example exists in the form of sustained release verapamil preparations. These calcium channel blockers are potentially very toxic even in low doses. If such a product is used as a model for this change, than a child could ingest up to 7 sustained release verapamil and the package still considered as child-resistant. Once ingested, we have little in our armamentarium to avoid disaster. Once the drug is absorbed it may create hypotension and bradycardia, which can be life threatening, very resistant to medical therapy. The "sh

There are many other substances in this category ranging from pharmaceuticals which are frequently found in homes, such as oral hypoglycemic agents, to antibiotics, such as isoniazide, all of which are models in which 7 or fewer doses can prove to be life-threatening overdoses.

May I remind the commission of Paracelsus' alleged statement that all things are poisons, it is the dose which makes something not a poison!

There is very little hard evidence to use in debating this issue. I know of no way to prove efficacy without endangering the lives of children-subjects, something no Institutional Review Board I know would ever approve anyway.

I understand the commission's desire to simplify the regulation, but by so doing, it risks the welfare and lives of the very children it is charged with protecting.

Steven M Marcus, MD
Executive Director
New Jersey Poison Information & Education System

<<Steven Marcus (E-mail).vcf>>

CRTSA pet comment

03-1

Stevenson, Todd A.

From: Anthony S. Manoguerra [amanoguerra@ucsd.edu]
Sent: Wednesday, July 30, 2003 1:32 PM
To: Stevenson, Todd A.
Subject: Petition 03-1

Office of the Secretary
Consumer Product Safety Commission
Washington, DC 20207

Re: Petition 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging.

I am writing to express my strong opposition to the petition submitted by the Healthcare Compliance Packaging Council to change the testing requirements for unit dose packaging. Their proposal appears to not consider toxicity as a factor in the assessment. The current language allows for differences in packaging for highly toxic drugs as opposed to those with a lower level of toxicity. I can understand where the industry would like a single standard that could be applied across the board but as proposed, the standard would not provide a safeguard to the health of children. If one uses toxicity of the drugs to be packaged as the most important standard, then the single standard must make the packaging safe and effective for the most highly toxic drugs. There are many drugs where 8 dosage units would be a fatal ingestion in a typical two or three year old child. For example, calcium channel blocking drugs, beta-adrenergic blocking drugs, oral hypoglycemic agents, isoniazid, tricyclic antidepressants, sustained release oxycodone and morphine products, digoxin, etc. The complete list would be very long. For some of these drugs, the only acceptable standard would be no more than one dosage unit in ten minutes, as two dosage units could be a life-threatening ingestion.

I agree that child-resistant unit dose packaging is preferable to child-resistant cap and vial packaging. However, the implementation of a standard must not be a relaxation of protection for children. The Poison Prevention Packaging Act has been the single most effective measure that has reduced deaths in children from drug and other poison ingestions. We cannot accept a standard that relaxes the level of protection and places children at risk.

Thank you for this opportunity to provide input.

Sincerely,

Anthony S. Manoguerra, Pharm.D., DABAT, FAACT
Director, San Diego Division, California Poison Control System
Professor of Clinical Pharmacy, University of California San Francisco School of Pharmacy
Clinical Professor of Pharmacology and Pediatrics, University of California San Diego School of Medicine
Past-President, American Association of Poison Control Centers

Stevenson, Todd A.

CPSC/DX 03-?

From: Suzanne Doyon [sdoyon@rx.umaryland.edu]
Sent: Wednesday, July 30, 2003 2:38 PM
To: Stevenson, Todd A.
Subject: PP 03-1

Petition PP 03-1: Amendment of Child Resistance Testing Requirements for
Unit Dose Packaging.

I strongly oppose the proposed Amendment. There are a large number of substances for which 8 unit doses would pose a risk to a toddler:

Clonidine
Sulfonyureas
Lomotil
Isoniazid
Calcium Channel blockers
Olanzapine other antipsychotics
High concentration iron products (e.g. pre-natal vitamins)
Opioids
Bupropion
etc.

High concentration iron products are now packaged in blister packs thanks to a July 1997 FDA regulation. This novel regulation has resulted
in a dramatic reduction of pediatric Emergency Department visits related to iron ingestions (2190 in 1997, 840 in 1998). More importantly, it has resulted in a reduction in pediatric iron fatalities
in the US (1-2 1997, 0 in 1998). The numbers are even more impressive if
you extend the observation period!(1)

1. Morris CC: Pediatric iron poisonings in the United States. South Med
J 2000;93:353-358.

Need I say more. Blister packaging works!

I would support more widespread use of blister packaging. I advocate to use blister packaging for any pharmaceutical product that can cause serious personal injury or serious illness to a child.

Suzanne Doyon, MD
Medical Director
Maryland Poison Center

Suzanne Doyon, MD
Medical Director
Maryland Poison Center

My new e-mail address is:
sdoyon@rx.umaryland.edu

Suzanne Doyon, MD
Medical Director
Maryland Poison Center

My new e-mail address is:
sdoyon@rx.umaryland.edu

CR Todd

Stevenson, Todd A.

From: Mowry, Jim [JMowry@clarian.org]

Sent: Friday, August 01, 2003 6:15 PM

To: Stevenson, Todd A.

Subject: Petition PP 03-1, Petition for Amendment of the Child-Resistant Testing Requirements for Unit Dose Packaging

I am writing in response to the Proposed Rules changes reported in the Federal Register Vol 68, No 115/Monday, June 16,2003, page 35614.

As a clinical pharmacist and director of a regional poison control center for over 20 years, I am opposed to the proposed change in method of assessing child-resistant failure for "special" packaging by the CPSC.

I am confused as to the products this proposed regulation would cover? Are these prescription drugs which have lower therapeutic indices, or OTC drugs that, by the virtue of their being placed on OTC status, have higher therapeutic indices and therefore lower potential for toxicity?

If the proposed change would include prescription drugs, the petitioner's rationale eludes me. They would like to remove the "subjective" standard of "the amount that may cause serious personal injury or serious illness", but keep the "objective standard of "more than eight individual unit doses" without regard to the inherent toxicity of the product. This "objective" standard does not take into account the inherent toxicity of a drug product which varies considerably. Many prescription drugs are toxic with ingestion of less than 8 dosage units. Typical classes would include oral hypoglycemics (sulfonylureas) and calcium antagonists and some individual drugs such as isoniazid. Taking inherent toxicity into account would actually make the "objective" standard of 8 dosage units just as subjective as "the amount that may cause serious personal injury or serious illness" which at least has a outcome that related to the safety of the patient, as opposed to an arbitrary number.

Their assertion that unit dose packaging is "inherently" safer is also disingenuous and based on very limited data. Again, they base their argument solely on the number of tablets potentially accessed, but do not address the relative toxicity of the drugs involved. While not having the CPSC data to review, based on the usage of unit dose packaging for consumer use, it would be entirely possible that the drugs in CRC cap-vial closure systems causing fatalities were prescription drugs versus OTC drugs packaged in unit-dose packages. They also do not report the complete data on CRC cap-vial closure system amounts reported to CPSC, reporting instead that data (only cases in which > 10 dosage units were ingested) which tends to support their contentions that unit-dose packaging is safer. How many cases reported to CPSC over that two year period, had less than 10 dosage units ingested? That information is not presented.

I suspect that the petitioner's real aim is covered in the second item of the petition, e.g., to not have to test each unit-dosing packaging based on the drug it is packaged in, but "type-testing" of unit-dose packaging (like for CRC cap-vial closure systems) which would ultimately reduce their costs of design and production.

Granting this petition would weaken the Poison Prevention Packaging Act, successful and effective legislation.
Sincerely,
<<...OLE_Obj...>>
James B. Mowry, PharmD, DABAT, FAACT
Director, Indiana Poison Center
Indianapolis, Indiana

Pfizer Inc
235 East 42nd Street
New York, NY 10017
Tel 212 733 4210 Fax 212 309 4420
Email marc.b.wilenzcik@pfizer.com

PP03-1
CR Comments

Marc B. Wilenzick
Senior Corporate Counsel

August 1, 2003

VIA HAND DELIVERY

Todd A. Stevenson, Secretary
Office of the Secretary
U.S. Consumer Product Safety Commission
Room 501
4330 East-West Highway
Bethesda, Maryland 20814

Re: Comments of Pfizer Inc. on Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

Dear Mr. Stevenson:

Pfizer Inc., a leading manufacturer of prescription and over-the-counter drugs, submits these comments in response to the request by the U.S. Consumer Product Safety Commission (CPSC) for comments on a petition submitted by the Healthcare Compliance Packaging Council (HCPC) to amend the definition of a unit dose packaging test failure in 16 C.F.R. § 1700.20(a)(2)(ii).

Pfizer agrees that the public health and safety would benefit from an increase in the use of unit dose formats, and that a revision to the definition of unit dose test failure would help accomplish this objective. Specifically, Pfizer proposes that CPSC revise the second sentence of § 1700.20(a)(2)(ii), in relation to child-resistance (CR) testing, to state:

> "In the case of unit packaging, however, a test failure shall be any child who opens or gains access to the number of individual units, during the full 10 minutes of testing, which constitute the amount that may produce serious personal injury or serious illness."

Thus, we do not advocate that the definition of a test failure exclude access to the amount that may produce serious personal injury or serious illness; rather we believe that the phrase "or a child who opens or gains access to more than eight units during the test period" should be eliminated from the definition of a test failure for unit dose packaging.

Pfizer plans to make a separate submission to CPSC regarding the un-docketed portion of HCPC's petition relating to "type testing."[1]

A. Background

The purpose of the PPPA is to reduce the risk of "serious personal injury or serious illness" to young children from the accidental handling or ingestion of hazardous household substances. The PPPA gives the CPSC the authority to require "special packaging" for such substances. The PPPA defines "special packaging" as "packaging that is designed or constructed to be significantly difficult for children under five years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable amount of time and not difficult for normal adults to use properly." 15 U.S.C. § 1471(4). However, "special packaging" does not mean "packaging which all such children cannot open or obtain a toxic or harmful amount within a reasonable time." *Id.*

CPSC regulations require prescription drugs to be distributed in special packaging, absent a specific exemption. The packaging must be both child-resistant (CR) and reasonably easy for adults to open when tested in accordance with CPSC's prescribed testing methodology. Although CPSC does not require that companies test packaging for compliance with the PPPA, the distribution in commerce of products that fail to comply with the CR packaging requirements, when tested in accordance with test methodology prescribed in the regulations, is prohibited under the Federal Hazardous Substances Act.

---

1 As discussed during Pfizer's meeting with CPSC on July 30, 2003, Pfizer believes that the public interest and goals of the PPPA would be furthered if CPSC were to encourage the development of a system for peer-review and publication of CR specifications for particular packaging systems. Under such an initiative, packaging manufacturers could CR test individual packaging configurations, and submit the specifications to an expert panel (such as ASTM) for peer review and publication. Pfizer believes that CPSC's participation in such a process would be critical to its success. And, ultimately, Pfizer believes that CPSC, either as an enforcement guidance or otherwise, should provide a "safe harbor" for manufacturers and distributors that use such package types that have been demonstrated to comply with requirements for "special packaging" under the Poison Prevention Packaging Act (PPPA) and implementing regulations.

CPSC regulations provide that, for unit packaging, a test failure means "any child who opens or gains access to the number of individual units which constitute the amount that may produce serious personal injury or serious illness, or a child who opens or gains access to more than 8 individual units, whichever number is lower, during the full 10 minutes of testing." 16 C.F.R. § 1700.20(a)(2)(ii). Thus, according to this definition, even if a substance packaged for household use is not toxic, access to more than eight units during the test period constitutes a test failure.

The stated rationale for imposing an upper numerical limit – which initially was five units – was to "provide the packaging industry with parameters within which to develop unit packaging. It also involved an evaluation of an estimated attention span of children relative to opening unit dose packaging." 38 Fed. Reg. 1510, 1510 (Jan. 8, 1973). FDA, which at the time was responsible for enforcing the PPPA, subsequently found that the five unit limit was "unnecessarily restrictive and thus tended to stifle industry initiative in this area." 38 Fed. Reg. 12738, 12738 (May 15, 1973). FDA also stated that such restriction was "undesirable since unit packaging has the potential for being an effective form of child protection packaging for many applications, particularly in the drug field." *Id.* Accordingly, FDA increased the upper limit for a test failure from five to eight units.

To our knowledge, there is no scientific rationale for the eight unit ceiling in the definition of a test failure.

B. Benefits of unit dose packaging

The HCPC petition makes well-founded points regarding the safety benefits of unit dose formats over cap-and-vial closure systems in preventing the accidental ingestion of drug products. In particular, HCPC correctly states, among other things, that cap-and-vial closure systems require repeated, proper usage by adult consumers to prevent a child from having instant access to the entire contents of the package. Unit dose systems, on the other hand, need not be re-secured after each use and, therefore, their CR properties are not dependent on proper adult usage. Moreover, products packaged in CR bottles are far more likely to be repackaged into non-CR containers than are CR unit dose systems. Therefore, encouraging the use of CR unit dose systems can further the CPSC's mission of decreasing the risk of accidental ingestion by children of hazardous household substances.

In addition, unit dose formats have the safety advantage of separating each pill or capsule into its own cavity. This requires that each dosage unit be removed one-at-a-time, slowing children down, and allowing more time for adult intervention or for children to lose interest. Again, encouraging the use of unit dose packaging can improve on the successes of the PPPA in protecting against accidental ingestion by young children.

In addition to these observations made in the HCPC petition as to the reasons why unit dose packaging can further the CPSC's mission (of deterring accidental ingestion by children of household substances), there are other health and safety benefits of unit dose packaging which include the following.

- Patient Compliance. Unlike other closure systems, unit dose packaging allows manufacturers to provide easy-to-read directions on the container itself. This is important, particularly for medicines which have more complicated dosing or titration regimens. Manufacturers can design unit dose formats to enhance compliance with such dosing regimens (*e.g.*, mnemonic packaging for oral contraceptives), where the same information cannot be readily conveyed through cap-and-vial packaging. Unit dose packaging therefore can improve patient compliance and proper dosing.

- Medication error and cross-contamination. Unit dose packaging can reduce the likelihood of medication error and cross-contamination. Unit dose packages allow for prominent disclosure of drug name, strength, and are color-coded, thereby making it much more difficult to confuse one medication for another with unit dose packages (as opposed to pharmacy bottles). Further, pharmacists need not repackage substances in unit dose formats to help patients manage their medication regimens. A reduction in the repackaging of such drugs will correspondingly reduce medication errors that result from repackaging. Such a reduction in repackaging will correspondingly reduce the incidence of inadvertent cross-contamination of drugs that can occur when multiple drugs are counted and dispensed in the same area (e.g., by pharmacists or by repackagers).

- Product stability. Unit dose packaging can enhance product stability, by protecting each dosage unit from the time of manufacture until the time of consumption. Manufacturers expend significant resources to ensure that products, particularly those that are moisture sensitive, remain stable in their packaging system. Pharmacy repackaging, which occurs more frequently with products that are not originally contained in unit dose packages, diminishes the product stability associated with original packaging.

- Deterring Counterfeits. Unit dose packaging is a deterrent to the introduction of counterfeit drugs into commerce, since such packages are dispensed in their original packaging. In contrast, most medicines that are dispensed in cap-and-vial containers have been repackaged, by dedicated repackagers and/or individual pharmacists, before distribution to consumers. Unit dose packages are expensive to de-blister/repackage and

> there is no need to hand count the pills (into small bottles). Thus, increased simplicity in qualifying CR packages would help deter the introduction of counterfeits, at both the pharmacy level and the repackager level.[2]

C. <u>The eight unit threshold in CPSC's definition of a test failure is not required to prevent harm to children, discourages the use of unit dose packaging, and can ultimately harm consumers.</u>

The eight unit numerical standard imposes an arbitrary requirement that is unrelated to child safety and does not further the purposes of the PPPA. As above noted, the purpose of the PPPA is to reduce the risk of harm to children from accidentally ingesting or otherwise gaining access to hazardous substances. However, the arbitrary ceiling of eight units is not based on the toxicity of particular substances, nor does it help to protect children from the risk of harm.

The PPPA itself contemplates that packaging requirements shall be linked directly to safety concerns. The statute defines "special packaging" to be packaging that is "designed or constructed to be significantly difficult for children under five years of age to open or <u>obtain a toxic or harmful amount of the substance contained therein</u> within a reasonable amount of time. . . ." 15 U.S.C. § 1471(4) (emphasis added). Pfizer's proposal – to define a test failure solely based upon the number of units that may cause serious injury or illness – is fully consistent with that legislative intent. Further, this proposal is consistent with a risk-based regulatory approach. By contrast, the eight unit ceiling unnecessarily limits the use of unit dose packaging without benefiting child safety.

Typically, manufacturers, including Pfizer, convene child test panels whenever a unit dose package will contain either (a) a toxic dose of eight units or fewer, or (b) more than eight units, regardless of toxicity.[3] However, such testing should not be necessary if a unit package contains a non-toxic amount of a substance, regardless of the number of units in the package. The time and cost considerations associated with convening child test panels deter manufacturers from making greater use of such formats. Specifically, the testing, re-working of tooling and re-testing to ensure compliance with CPSC's

---

2 Although these additional health and safety benefits are outside the scope of the PPPA, they help further demonstrate the importance of Pfizer's requested regulatory change.

3 Under the current rule, medicines may be packaged in quantities of eight units or less without passing tests involving panels of children, when the package contains a non-toxic amount of the medicine.

standards for unit dose packaging can take nine months or more to complete, once the final dose is established and a package design finalized, at a cost of approaching $100,000 per package (multiplied by the number of strengths for the product). Such burdens and barriers to the use of unit dose packaging cannot be justified on safety grounds if the package in question contains a non-toxic dose of the substance in question.[4]

Thank you in advance for considering these comments. If you have any questions, please feel free to contact my colleague, Rich Hollander of Pfizer Global Manufacturing, me, or our outside counsel, Eric Rubel of Arnold & Porter (202/942-5729).

Sincerely,

Marc B Wilenzick

Marc Wilenzick
Senior Corporate Counsel
Pfizer, Inc.

cc: Suzanne Barone, Ph.D. (CPSC)
Eric Rubel, Esq.
Matthew Eisenstein, Esq.

---

4 Given timing constraints in qualifying new packaging for the launch of new products (typically not initiated until the final dosing is established), the existing exemption process under 16 C.F.R. § 1702.7 is of limited use for obtaining relief from the eight unit ceiling for substances with favorable (low) toxicity profiles. For example, it took over two years for a final rule to be issued regarding the exemption of certain conjugated estrogens tablets. *See* 53 Fed. Reg. 41159 (Oct. 20, 1988). More recently, it took nearly a year and a half for a decision to be issued regarding the oral prescription drug Sucraid. *See* 63 Fed. Reg. 66001 (Dec. 1, 1998). Further, once a product has been launched, there are commercial and manufacturing barriers to switching existing production lines over (rendering the existing exemption process of limited use).

EMORY UNIVERSITY SCHOOL OF MEDICINE
DEPARTMENT OF PEDIATRICS
69 Butler Street, S.E. Atlanta, Georgia 30303

Division of General Pediatrics
and
Adolescent Medicine

(404) 616-3544

CP Test comment
03-1-8

2003 ... A 11:01
OFFICE OF THE SECRETARY
CPSC

August 4, 2003

Office of the Secretary
US Consumer Product Safety Commission
Washington, DC 20207

Dear Sir:

I am writing in reference to the petition labeled PP03-1 requesting a redefinition of the child resistant closure rule for unit dose packaging.

The efficacy of child resistant closures is excellent. A review of the incidence of poisoning of product classes during the period when the Poison Prevention Packaging Act was being implemented shows that, as preventive packaging was implemented for each class, poisonings involving that class declined over several years. Classes of products not regulated showed no changes. Ultimately, each regulated class showed a decline of about 66% in poisoning events in children.

I believe that an objective standard for testing unit dose packaging is appropriate. However, I do not agree with the petitioner's suggestion of more than 8 individual units during the full 10 minutes of testing.

I believe that a more appropriate rule would be:

> no more than 1 individual unit ("accessible dose") can be accessed by 90% of children during the 10 minutes of testing, *unless* the product manufacturer or their representative can demonstrate that their proposed "accessible dose" has not been shown to be toxic to a child of 10 kg under any circumstances.

Thank you for the opportunity to comment on this matter.

Sincerely yours,

Robert J. Geller, MD, FAAP, ACMT
Medical Director, Georgia Poison Center, and
Associate Professor of Pediatrics, Emory University School of Medicine

References:

Lembersky RB et al. Vet Hum Toxicol 1996; 38:380-383
Keram S. Williams ME. J Am Geriatrics Soc 1988;36:198-201
Walton WW. Pediatr 1982; 69:363-370.

[illegible] comment

August 4, 2003

Office of the Secretary
US Consumer Product Safety Commission
Washington, DC 20207

Dear Sir:

I am writing in reference to the petition labeled PP03-1 requesting a redefinition of the child resistant closure rule for unit dose packaging.

The efficacy of child resistant closures is excellent. A review of the incidence of poisoning of product classes during the period when the Poison Prevention Packaging Act was being implemented shows that, as preventive packaging was implemented for each class, poisonings involving that class declined over several years. Classes of products not regulated showed no changes. Ultimately, each regulated class showed a decline of about 66% in poisoning events in children.

I believe that an objective standard for testing unit dose packaging is appropriate. However, I do not agree with the petitioner's suggestion of more than 8 individual units during the full 10 minutes of testing.

I believe that a more appropriate rule would be:

> no more than 1 individual unit ("accessible dose") can be accessed by 90% of children during the 10 minutes of testing, *unless* the product manufacturer or their representative can demonstrate that their proposed "accessible dose" has not been shown to be toxic to a child of 10 kg under any circumstances.

Thank you for the opportunity to comment on this matter.

Sincerely yours,

Robert J. Geller, MD, FAAP, ACMT
Medical Director, Georgia Poison Center, and
Associate Professor of Pediatrics, Emory University School of Medicine

References:
Lembersky RB et al. Vet Hum Toxicol 1996; 38:380-383
Keram S. Williams ME. J Am Geriatrics Soc 1988;36:198-201
Walton WW. Pediatr 1982; 69:363-370.

PP03 CR

Comments- Petition PP03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

We support the idea that well-designed compliance packages increase patient compliance. We agree that unit dose packages can be more child resistant than cap and vial closure systems because children may access fewer units of medication per "breach." We agree that there is no need for the medication user to properly re- secure a closure after each use. This is a basic distinction between unit dose and multiple unit packages in the ASTM classification (ASTM D3475, Standard Classification of Child Resistant Packages). However, lowering the acceptance criteria for unit dose packaging, as HCPC has argued, is not the proper way to encourage manufacturers to use it. Promotion of the aforementioned features is a better approach to increasing the use of unit dose packaging by manufacturers.

On changing failure level

Several of the arguments presented by HCPC are biased. The HCPC review of CPSC data indicates that unit dose packages are rarely involved in poisonings, and that from 1983-2002 84.6% of poisonings were attributed to cap and vial systems while 6.8% were attributed to unit dose packaging. However, in HCPC's own words, "unit dose formats are not widely used in the United States." As a result, the percentages should be normalized to reflect the prevalence of cap and vial systems in order to compare performance fairly. The difference in percentage of incidents is probably due in part to the smaller number of unit dose packages in the market.

Another issue raised by the HCPC is that the current protocol puts them at a disadvantage by "requiring" toxicity data, which is subjective, and not "required" for cap and vial systems. There are problems with this argument.

1. CPSC does not "require" testing or submission of data. The language that the CPSC uses is "request."
2. The current test protocol recognizes the inherent child resistance of unit dose packaging by allowing a unit dose package to pass even if it has been breached (provided that a toxic quantity or 8 blisters has not been accessed). When a cap closure system is breached, it is considered an automatic failure under the current test protocol. CPSC has actually given the manufacturers of unit dose a second chance at passing once a breach has occurred by allowing for the fact that a toxic dose has not been accessed.
3. If the subjectivity of toxicity levels is truly the driving force behind this petition, the HCPC should err on the side of safety and make the failure level 1, not 8. This will take the subjectivity that is uncomfortable for the manufacturers away and not allow a potentially toxic dose to be considered acceptable under the test protocol, and this would be parity with cap and vial; a single opening is a failure.

An additional argument made by HCPC is that the Poison Prevention Packaging Act (PPPA) of 1970 indicates that a standard should be set that makes packaging

> "significantly difficult for children under five years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time and not difficult for normal adults to use properly, *but does not mean packaging which all such children cannot open or obtain a toxic or harmful amount within a reasonable time.*"

HCPC emphasizes the last line of the quotation to make the point that a potentially toxic dose should be allowed to pass the test protocol. CPSC has addressed the spirit of this quotation through the use of their sequential test table, which allows a package design to pass, despite the fact that packages within the test have failed.

Another factor that CPSC should consider prior to implementing HCPC recommendations is the potential ramifications presented below.

Under the proposed protocol a package would pass if:

Package	Outcome	Outcome Under Proposed Protocol
Bottle	80% (or less) of children get none	Pass
Unit dose	80% (or less) of children access less than 8 blisters	Pass
	100% of children get into between 1-7 blisters (despite the level of toxicity)	Pass

Theoretically, 100% of the children tested could access a toxic dose, but the package passes the protocol. Is this congruent with CPSC's mission to "protect the public against unreasonable risks of injuries and deaths associated with consumer products"? Under this scenario the proposed blister end point is more risky by the assurance that 1-7 openings are accepted but the toxicity level may be between 1 and 7.

Laura Bix
Assistant Professor
Michigan State University
153 Packaging
East Lansing, MI 48824
517-355-4556

Hugh Lockhart
Professor
Michigan State University
155 Packaging Building
East Lansing, MI 48824
517-355-3604

Stevenson, Todd A.

From: Laura Bix [Bixlaura@msu.edu]

Sent: Thursday, August 07, 2003 10:15 AM

To: Stevenson, Todd A.

Cc: lckhrt@msu.edu; bixlaura@pilot.msu.edu

Subject: Petition PP03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

Hello... Please accept our comments on Petition PP-03-1 Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging. Please feel free to contact myself (information below) or Hugh Lockhart (517-355-3604) regarding any difficulties with the file. Thank you
Laura

Laura Bix, PhD
Assistant Professor
153 Packaging
East Lansing, MI 48824
517-355-4556

CMM Comment 03-1

Bristol-Myers Squibb
Pharmaceutical Research Institute

P.O. Box 4000 Princeton, NJ 08543-4000
Tel: 609 252-5992 Fax: 609 252-3619
laurie.smaldone@bms.com

Laurie Smaldone, M.D.
Senior Vice President
Global Regulatory Sciences

July 23, 2003

Office of the Secretary
Consumer Product Safety Commission
4330 East-West Highway
Bethesda, MD 20814

Re: Petition PP 03-1; Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose: 68 Federal Register 35614 (June 16,2003)

Dear Sir or Madame:

Bristol-Myers Squibb is a diversified worldwide health and personal care company with principal businesses in pharmaceuticals, consumer medicines, nutritionals and medical devices. We are a leader in the research and development of innovative therapies for cardiovascular, metabolic and infectious diseases, neurological disorders, and oncology. In 2002 alone, Bristol-Myers Squibb dedicated $2.2 billion for pharmaceuitcal research and development activities. The company has more than 5,000 scientists and doctors committed to discover and develop best in class therapeutic and preventive agents that extend and enhance human life.

For these reasons, we are very interested in and well qualified to comment on this Petition to CPSC requesting Amendment to Child-resistance Testing Pass/Fail Criterion for Unit Dose Packaging (Petition No. PP 03-1).

Summary of BMS Comments on Proposal

We commend the CPSC for their continued pursuit of child resistant packaging. However, BMS does not agree with the HCPC petition as it may affect the safety of children for whom this regulation was originally intended to protect. The following are points in the proposed petition that we at Bristol-Myers Squibb respectfully request be given additional consideration.

Specific comments (Items that Need Clarification and Recommended Action).

1) **The petition is requesting that the CPSC modify the current definition of a child resistant test failure for unit dose packaging under the Poison Prevention Packaging Act (PPPA). This modification would eliminate reference to substance toxicity as part of the pass/fail criteria for unit dose packaging.**

BMS does not agree that the criteria related to the "toxicity of the substance to be packaged" should be eliminated as part of the pass/fail determination. BMS believes the "toxicity of the substance to be packaged" to be a critical part of determining the pass/fail criteria for any child resistant package regardless of whether it is unit dose or other.

Recommendation: BMS recommends that toxicity data continue to remain as part of the design criteria for a Child-Resistant package.

2) **The petition also recommends the pass/fail definition of test failure for unit dose packaging be "any child who opens or gains access to more than 8 individual units during the full 10 minutes of testing."**

Recommendation: BMS believes protecting children from serious personal injury or serious illness should be the basis of determining how protective the package should be and that in the absence of toxicity data, a test failure should be "any child who opens or gains access to 1 individual unit during the full 10 minutes of testing."

Bristol-Myers Squibb appreciates the opportunity to provide comment and respectfully requests that CPSC give consideration to our recommendation.

Sincerely,

L Sma

Laurie F. Smaldone, M.D
Senior Vice President
Global Regulatory Sciences

CHPA®
FOUNDED 1881

Advancing Quality Healthcare
Through Over-the-Counter Medicines
and Nutritional Supplements

CP 03-11

CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

August 7, 2003

Office of the Secretary
Consumer Products Safety Commission
Washington, DC 20207

Re: Petition No. PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

Dear Sir or Madam:

On behalf of member companies who manufacture and distribute over-the-counter drug products and dietary supplements, the Consumer Healthcare Products Association provides the following comments on the petition for amendment of the child-resistance testing requirements for unit dose packaging.

The petition by the Healthcare Compliance Packaging Council (HCPC) requests that the definition of test failure for unit dose packaging only be an "objective standard," defined as any child who opens or gains access to more than eight individual units during the full 10 minutes of testing. HCPC further requests that the criterion of a child gaining access to the number of individual unit doses that constitute the amount that "may cause serious personal injury or serious illness" be omitted from the definition of a child-resistance test failure.

CHPA disagrees that this second criterion should be eliminated and that the pass-failure of unit dose packaging rest solely on the child's ability to open eight individual units. This objective parameter alone does not consider the potential toxicity of the drug and the fact that, if a child were to gain access to even less than eight individual units of certain drugs, serious illness or harm could develop. We believe that the assessment of the toxicity of the drug being packaged in individual unit doses is a necessary component to ensure the safety of products using this packaging and that this provision for evaluation of "serious personal injury or serious illness" in the testing requirements should be retained. The deletion of this provision could have a negative impact on the safety of products in the marketplace.

1150 Connecticut Avenue, N.W., Washington, D.C. 20036-4193 • Tel: 202-429-9260 • Fax: 202-223-6835 • www.chpa-info.org

CHPA agrees, however, with the concerns expressed by HCPC about the guidance provided by CPSC for "serious personal injury or serious illness" being subjective. The guidance provided by CPSC in 16 CFR 1700.20 states:

> "The determination of the amount of a substance that may produce serious personal injury or serious illness shall be based on a 25-pound (11.4 kg) child. Manufacturers or packagers intending to use unit packaging for a substance requiring special packaging are requested to submit such toxicological data to the Commission's Office of Compliance."

We support CPSC providing clearer guidance on what constitutes "serious personal injury or serious illness" and that this guidance be developed based on scientific and toxicological principles. We recommend CPSC work with industry and other stakeholders to develop guidelines that define best approaches for the types of data to be considered in making an assessment of toxicological information.

Further, we support placing no additional burden on manufacturers or packagers to require CPSC approval before marketing in unit packaging products for which a toxicological assessment has been made. We believe it the responsibility and the obligation of the manufacturer or packager to determine whether the unit packaging meets all of the criteria for child-resistance testing. This allows the manufacturers and packagers using unit packaging to meet the testing requirements without an undue time restriction.

Finally, we agree with the HCPC petition to allow type testing of unit dose packaging. We advocate that once a packaging has successfully passed protocol testing it be allowed for use for other products so long as the safety profile of the drug products being packaged is not dissimilar. Additional testing would not be necessary, because the integrity of the unit packaging does not change even if the product in the unit packaging changes.

We appreciate the opportunity to comment on the proposed HPCP petition. We support child-resistance testing of unit dose packaging. While we do not support deletion of the "serious personal illness or serious injury" provision in the testing requirements, we are supportive of CPSC developing clearer guidance of what constitutes "serious personal injury or serious illness" and adopting the provision that toxicology/risk assessment does not need prior approval from CPSC before the unit packaging may be marketed.

Sincerely,

Douglas Ws. Bierer, Ph.D.
Vice President of Regulatory and Scientific Affairs

CPSC letter/DB/LT

CRTest Comm

03-2

Stevenson, Todd A.

From: Pakmax@aol.com

Sent: Monday, August 11, 2003 6:12 PM

To: Stevenson, Todd A.

Subject: Petition PP 03-1

I am writing regarding the Petition for Amendment of the Child Resistance Testing Requirements for Unit Dose Packaging.

This petition if allowed would give the Child access to drugs that could severely injury them and still pass the protocol requirements and be considered safe. Does this make any sense or am I missing something? How can you justify this change? The law was written to protect children and now the Healthcare Compliance Packaging Council Lobby wants to change it so their sponsors can sell more blisters.

I just can't believe that the CPSC would give this serious consideration.

Regards, Stu DeJonge

Sharp

c R Pal comm

August 11, 2003

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

Re: Petition PP 03-01

Dear Mr. Secretary,

Sharp is a pharmaceutical contract packaging company that has been involved with the design, development and manufacturing of child resistant unit dose packaging for over 30 years. As one of the founding members of the HCPC, we want to express our full support of the petition to amend the 16 CFR 1700.20 (a) (2) (ii) of the CR/SF protocol.

The petition lists all the quantitative statistics that support our point of view, which would change the existing pass/fail criteria to a standard numerical value of 8 dose units that a child can remove during the course of the ten-minute test. The subjectivity and variability of the current protocol creates an environment, which discourages the use of unit dose packaging. We doubt that this was the original intent of this regulation.

The proposed changes will even out the playing field and might in fact create more standardization of designs for unit dose child resistant packaging. Unit dose packaging allows the dispensing of pharmaceutical products from the pharmacy into the home in the manufacturer's original package. This ensures the stability of the product/package system as well as providing the consumer with information, which identifies the name, strength, lot number and expiration date of each individual unit of use. This information can only enhance pharmacy and consumer compliance with regard to proper dispensing and use of pharmaceutical products. As you are aware, compliance is a major issue affecting the health and welfare of the public.

The growth of safer unit dose packaging in this country has also been restricted by the variability of pharmaceutical company's interpretations of toxicity levels for new drug entities which is currently used to determine the protocol pass/fail criteria for a new product. This imposes a degree of severity on the design, success and expense of creating new compliant, adult friendly, child resistant unit dose packages.

The many current and yet to be developed pharmaceutical products will support the healthy aging of our population. We need to encourage the design and use of packaging that will maintain the best product integrity, offer the consumer the most information about the drug, limit access to young children, as well as provide senior citizens opening features that are understandable and easy for them to use. Unit dose packaging has the flexibility to encompass all of these important features.

Thank you for your consideration. We hope that your agency will give its full support to implementation of this change.

Sincerely,

Kathleen Baszczewski

Kathleen Baszczewski
Director of Compliance
Sharp Corporation

03-1/14

PERRITT
LABORATORIES

145 South Main Street
Post Office Box 147
Hightstown, NJ 08520 USA
Tel. (609) 443-4848
Fax (609) 443-5293

August 12, 2003

Office of the Secretary
Consumer Product Safety Commission
4330 East West Highway, Room 600
Bethesda, MD 20814-4408

SUBJECT: Opposed to Petition No. PP 03-1

Dear Commissioners:

We disagree with Petition No. PP 03-1.

It is not sensible to lessen child-resistant safety standards for unit packaging, potentially exposing more children to toxic/harmful products, especially since the technology already exists to produce child-resistant unit packaging with access to as little as one unit being a failure. The CPSC would be lowering the bar of public safety.

If the petition were to pass, highly toxic products, where a lethal dose could be a single tablet/pill, could be placed in "protocol passing" packaging where children were able to access up to eight tablets/pills during protocol testing and still be deemed as "passing." This is absurd.

Perritt Laboratories has conducted thousands of studies on child-resistant packaging, which have demonstrated that it is indeed possible to meet the child-resistant requirements of products, with a range of toxicity levels, placed in unit packages. Many unit packaging studies intended for highly toxic drugs, have passed with access to just one tablet being a failure. Unit packaging has been regulated by way of product toxicity since 1973. This regulation has proven to be successful. These proposed changes seem to be aimed more for a specific industry group to sell more of their packages rather than the safety of our children.

Perritt Laboratories is an independent testing laboratory specializing in child-resistant package testing. We have been testing packaging since 1973 when the protocol was first enacted. Our clients range from major pharmaceutical companies, packaging manufacturers, household products manufacturers, pesticide producers, to small contract packagers and inventors. Every day we are working with child-resistant packaging of various designs and concepts. Our founder and CEO, Dr. Alexander M. Perritt, has been involved with child-resistant packaging since 1968 when the FDA was developing the original child-resistant packaging protocol. Perritt Laboratories holds accreditations for testing CR packaging from the United Kingdom Accreditation Service (UKAS) for United States standards and well as Canadian (CSA), European (CEN), British (BSI), and International (ISO) standards. We have worked on every protocol development contract from the CPSC over the past 25+ years. We conduct annual seminars on child-resistant packaging and are considered to be the leaders in our field. It is with this background of experience and expertise that we offer our insights and knowledge throughout this response.

There are numerous discrepancies throughout the petition that are misleading to the reader. Some of the notable ones are:

- The petitioner tries to show support for the petition by citing international standards, but fails to mention the fact that these same standards acknowledge the benefits of toxicity based pass/fail criteria.
  - It is stated in the petition (March 17, 2003, page 8, last paragraph) that, *"We also note that CR standards for non-reclosable packaging that have been adopted in Great Britain, and are currently under consideration throughout the entire European Union, set a failure criteria at more than eight units. These decisions were not made arbitrarily, nor were then made in a vacuum. Rather, these standards are based on nearly three decades of data and experience with the U.S. protocol, and in consultation with ASTM and other bodies in the United States..."*
  - The petitioner fails to mention statements in the proposed CEN (European) standard which states, [1]*"NOTE: The figure of eight units is based on existing national standards published by certain CEN members and does not address the issue of toxicity. Some pharmaceutical products on the market can cause harm to children by the ingestion of fewer than eight units. However, reliable data on child toxicity exists for few pharmaceutical products. A harmful dose can be established for some existing pharmaceutical products and a maximum safe dose can be established for all pharmaceutical products by one means or another. Such information is not currently available for all products and there is no central register where this information could be held. In the absence of European legislation on this topic the drafters of this European Standard acknowledge these concerns and believe that research and collection of data should continue with a view to considering the substitution of a toxicity based pass/fail criteria for the child panel test in a later version."*
    - The FDA did not arbitrarily select access to greater than eight units as a failure when they initially regulated child-resistant unit packaging. The greater than eight number was based on the toxicity of the first product regulated, aspirin. Aspirin tablets were dispensed in tablets of 5 grains each and 45 grains was deemed to be the toxic dose for a 25 pound child. Thus, access to nine tablets was considered to be a failure for aspirin. With the toxicity feature in mind, it was indicated that future products packaged in unit packaging would have their own access level failure based on the toxicity of the product. Examples of toxicity thresholds requiring child-resistant packaging include:

Acetaminophen	1000mg	two adult tablets
Diphenhydramine	66mg	one tablet
Loperimide	0.045mg	one tablet
Ibuprofen	1000mg	two adult tablets

The greater than 8 access level was logically chosen by the FDA based upon the toxicity of aspirin.

[1] CEN TC 261, December 2002, Child-resistant non-reclosable packaging for pharmaceutical products – Requirements and testing, 4.2.1, page 7.

- The Poison Prevention Packaging Act is not only aimed at pharmaceuticals. Household products are also included. Changes to the regulation could potentially sway manufacturers to package extremely toxic substances (such as lye) in unit packaging. These packages would only have to pass protocol testing with eight or less units being opened, even though one unit would be lethal to a child. EPA regulated products can also fall into this unit packaging category.
- France had a problem with an oven cleaning product placed in unit packaging (pouch). A number of children accessed a toxic dose and as a result, they forced CEN to fast-track a regulation on this type of packaging.
- Canadian Standards Association (CSA) standards nearly mirror United States standards, and include the toxicity feature.

❖ The petitioner repeatedly makes the statement (or closely similar), "unit dose packaging is inherently safer than cap-and-vial closures." For years, this position has been held in the United Kingdom and across Europe, until February of 2000 when an English child was tragically poisoned by access to many (40+) iron tablets packaged in unit packaging. This tragedy created a public outcry in the UK to fast track a standard for unit packaging.

❖ The petitioner cites the statement in the current US protocol, "…significantly difficult for children under five years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time and not difficult for normal adults to use properly." The petitioner then makes the argument, "…but does not mean packaging which all such children cannot open or obtain a toxic or harmful amount within a reasonable time."

➢ If a child is able to access as many as eight units during a protocol test (still indicating a passing result), how can the petitioner justify a situation where a child accesses just a single unit of the "easier to pass protocol test package" and is tragically poisoned. It is unreasonable.

❖ The petitioner infers that children loose interest in opening packaging when dealing with unit packaging. This is not the case as indicated by the poisoning in the UK and in studies we have conducted. Once the children find they can open packaging they often don't stop.

In summary, the FDA based its original failure pattern, of greater than eight units, on the toxicity of adult aspirin, and indicated other products should have their failure patter based on product toxicity. The technology exists to make unit packaging safe for children. Why revert to packaging that would result in more child poisonings. It makes no sense.

As for us, the father of four children and grandfather of 12; father of three; and father of three, we feel the CPSC would be acting counter to its responsibility to the safety of the U.S. public in approving this petition.

Sincerely,
PERRITT LABORATORIES, INC.

Alexander M. Perritt
Alexander M. Perritt, Ph.D.
CEO

Scott J. Perritt
President

Richard A. Ward /SMK.
Richard A. Ward
VP, Consumer
Product Testing

Child Res. Test comm
CP03-1-1

C E PACKAGING PARTNERSHIP

C. Scaife Managing Partner.
Independent Consultant to the Pharmaceutical Industry.

29, DENE ROAD
COTTINGHAM,
East Yorkshire.
HU16-5PD

BusinessTelephone: 01482 846416
Business Fax: 01482 844955
Home telephone: 01482 840336

Date: 11th August 2003

Mr. Todd A. Stevenson,
Office of the Secretary, Room 501
Consumer Product Safety Commission,
4330 East West Highway,
BETHESDA.
Maryland, 20814.
USA.

Dear Mr. Stevenson,

Comments on the HCPC Petition.
"Petition PP 03-1 Petition for Amendment of the Child-Resistance Testing Requirement for Unit Dose Packaging.

I have read with interest the petition submitted to you by the Healthcare Compliance Packaging Council for a change to your 16 CFR Part 1700.

Whilst my comments are based on my personal view point, as Convenor of the CEN/TC 261/ SC 5/ Working Group 27 drafting European Standards for Child Resistant Packaging; I am interested in the outcome of this petition as for the last few years WG 27 has been considering the issue of product toxicity as a basis for the Child Panel Test Fail Criteria.

You may therefore be interested in the background to the current draft Standard prEN 14375 " Child Resistant non-reclosable packaging for medicinal products – Requirements and testing." which is currently out for "Formal Vote" for acceptance.
This Standard has "Access to 8 or more unit doses" as the fail criteria for the child panel test; the adult test follows your protocol.

It has taken several years to reach this stage; the initial draft based on a "Product Toxicity Fail Criteria" being defeated at the "Internal Enquiry" voting stage.

This was because it was felt that insufficient product toxicity data existed on a European basis. This issued is now addressed in a non mandatory "note" in the prEN 14375 Standard drawing attention to the topic and requesting the compilation of a European Toxicity Database.

The European Consumer Safety Committee (ANEC) commissioned the UK National Poisons Unit to conduct research into the determination of product toxicity dosage levels relative to accidental ingestion by young children. Their published report was inconclusive and did not convince the UK BSI Child Resistance Standards Committee that a "Toxicity" based fail criteria could be promoted at this stage and that further research needed to be carried out.
The CEN WG 27 was of a similar opinion.

CEN WG 27 comprises representatives from the various EU States Standards Bodies nominated for their expertise. Hence Industry, Consumer Safety, Government departments and accredited CR Testing establishments are present on the Working Group and we invite representation from the USA (Dr. A. Perritt) as observers and to provide advice on the USA viewpoint.
The WG has was formed in about 1991 in response to a mandate from the EU Commission to develop Standards in support of their Directive requiring CR Packaging for potentially harmful household products.

The EU Directive for regulated household products for retail sale specified the use of reclosable child resistant packages complying with the ISO Standard which was adopted as an EU Standard EN 28317 but no Standard existed for non-reclosable packages for such products hence the formation of the Working Group (WG 27).

It was recognized by the WG that there is a significant difference between non-reclosable packages for household products and pharmaceutical products hence a need for two Standards.
EN 862 was developed for Non-reclosable CR Household Product Packages based on a single entry as the "fail criteria" because the packs contained a quantity of product for a single application. These packages tended to be either sachets or specific application style packs (i.e Oven cleaner).
The adult test is optional because customer selection would determine whether the packaging is appropriate to themselves.
PrEN 14375 has been developed specifically for Pharmaceutical product CR packaging and after several attempts, what is thought to be its final form, has a Child Panel Test "Fail criteria" of access to 8 or more units. The Standard includes a note bringing the attention of the user to the issue of product toxicity but is for guidance and is not mandatory. The Adult test criteria are the same as that in your 16 CRF Part 1700
This Standard is now similar to the German DIN 55.559 and United Kingdom BS 8404 the only two European States with Child Resistant Packaging Standards for Pharmaceutical products.

The European Pharmaceutical market is heavily dependant on the use of unit dose packaging for the distribution and dispensing of its pharmaceutical products in meeting its obligations for patient pack dispensing, providing patient information, as an aid to patient compliance as well as the benefits of hygiene and shelf life guarantees.

Adult access to their medication can sometimes be critical in the treatment of a life threatening ailment and the patient has no choice in the medication prescribed and its packaging, hence the adoption of your adult test protocol as the screening test embodied in it recognizes the inabilities of the old and infirm.

However the use of "Product Toxicity" as the "Fail Criteria" in the child panel test of non-reclosable pharmaceutical CR packaging seems to result in compliant packaging which is senior unfriendly and puts an obligation on such packaging which is not recognized in the testing of reclosable packaging.
Reclosable CR packaging can contain more than a "toxic" quantity of product and there does not seem to be a limit in the USA on pack contents as there is in Europe in meeting Patient Pack Dispensing Regulations.

The introduction of Child Resistant Packaging Regulations in the UK in 1975 had the effect of reducing accidental ingestion by children under 5 years old of regulated products and the data collected by the Home Accident Surveillance System operated by the Department of Trade and Industry has supported the styles of packaging adopted and shown that the decrease has been maintained.

Given the UK experience I personally would advocate that there has to be differentiation between CR reclosable and non-reclosable packaging and that this is best done by having a specified number of entries into non-reclosable packaging as the "Fail Criteria" as adopted by the United Kingdom, Germany and proposed in prEN 14375.

You may be interested to learn of an EU Funded Research Project into the development of a Mechanical Testing machine for assessing the child resistance of non-reclosable packages. The objective being to reduce the reliance on child panel testing and support the principle of "Type Testing" for such packaging. This is a two year project and at the end of the first year significant progress has been made. The next phase is to validate the test methods possible on the machine – twisting, bending, puncturing and piercing of unit dose packages which are compliant with prEN 14375.

Given that only a few countries worldwide have regulations for Child Resistant Packaging; I believe we should try to standardize methods of testing.
This is especially true for pharmaceutical products which are sold on a worldwide basis. Whilst appreciating the views expressed by Consumer Safety Groups on the issue of "Toxicity", I also believe that such Groups have an increasing obligation in the protection of the increasing numbers of elderly and possibly infirm in being able to comply with their medicine's dosage regimes. Such people often live alone and have no one to help them with their medication whilst children have parents.

These parents have to face their obligations, a fact identified in all CR Standards.

I would therefore ask you to give serious consideration to the adoption of the HCPC's petition.

The opinions expressed in these comments are my personal viewpoint based on 28 years experience in Child Resistant packaging and are not meant to represent the opinions of all the members of WG 27.

Finally if you have data on pharmaceutical product toxicity, its determination and how you enforce your protocol's "toxic level criteria" I would be grateful if you would send it to me as this issue will be again debated at the next CEN WG 27 meeting on the 11th & 12th September.

Yours sincerely,

Colin Scaife.
Convenor of both the CEN & ISO Child Resistant Packaging Working Groups.
Member of UK BSI Committee for Child Resistance Standards.
Member of ASTM D10-31 Committee.

AMERICAN ACADEMY OF
CLINICAL TOXICOLOGY, INC.
777 EAST PARK DRIVE, P.O. BOX 8820, HARRISBURG, PA 17105-8820, 717-558-7847 • FAX 717-558-7841
WEBSITE: WWW.CLINTOX.ORG

August 1, 2003

Office of the Secretary
Consumer Products Safety Commission
Room 501, 4330 East-West Highway
Bethesda, Maryland 20814-4408

Dear CPSC:

RE: Petition PP03-1
Petition for Amendment of the Child-Resistance
Testing Requirements for Unit Dose Packaging

The American Academy of Clinical Toxicology is the largest organization concerned with the prevention and treatment of poisoning. Its membership consists of physicians, pharmacists and nurses. Many of these members are directors, managers and rank and file poison control center staff. The Academy notes with concern this petition of the Healthcare Compliance Packaging Council (HCPC), who represent the manufacturers of unit dose blister and strip packaging of pharmaceuticals. By this letter, the Academy opposes their petition.

The Academy notes that this petition does not question the efficacy of blister and strip packaging in the prevention of the unintentional poisoning of young children. A prime example is iron poisoning. In the middle of the past decade, the high incidence of iron poisoning deaths of young children resulted in the regulatory change to the requirement for blister packaging of this medication. Academy members were active in effecting this change. The resultant dramatic decrease of mortality due to iron poisoning bears witness to the power of this preventive intervention.

Rather, the intent of this petition is to modify the requirements for this type of packaging. The current criteria specify that a child gain access to the number of individual unit doses that constitute the amount that "may cause serious personal injury or serious illness" or more than eight individual unit doses, whichever is less. The HCPC's petition requests that the Commission amend that requirement to eliminate the first criterion related to the toxicity of the drug and define a unit dose packaging failure as a child gaining access to more than eight individual unit doses.

This flies in the face of the fundamental pillar of clinical toxicology - "the dose makes the poison." Drugs have differing potencies and hence differing hazards. Some examples of drugs that pose a serious threat to young children when fewer than eight unit doses are consumed are clonidine, morphine and the sulfonylurea family of drugs. The latter group is used to treat diabetes and is very commonly prescribed. Therefore, relying upon more than eight individual unit doses as the sole criterion is arbitrary, non-evidence based and frankly dangerous. Granting this petition would weaken the Poison Prevention Packaging Act, universally acknowledged as successful and effective legislation.

If further information or clarification is required please contact our spokesperson, Milton Tenenbein, M.D., Immediate Past President, American Academy of Clinical Toxicology, (mtenenbein@hsc.mb.ca; 204-787-2445).

Sincerely,

Donna Seger, M.D.

Donna Seger, M.D.
President, American Academy of Clinical Toxicology

CRTom Comments

ALCOA

Packaging Technology Center
Environmental, Health, Safety & Regulatory Affairs
2101 Reymet Road ● Richmond, Virginia 23237-3768 ● Phone (804) 743-6194
Fax (214) 442-5247 ● Kenneth.C.Stewart@Alcoa.com

August 8, 2003

Office of the Secretary
U.S. Consumer Product Safety Commission
Room 501
4330 East-West Highway
Bethesda, Maryland 20814

RE: Alcoa Flexible Packaging Comments on Petition for Rulemaking Number PP 03-1: "The Definition of Test Failure for Unit Dose Packaging [at 16 CFR 1700.20(a)(2)(ii)] Should be an Objective Standard"

Dear Sir or Madam:

Alcoa Flexible Packaging appreciates the opportunity to provide comments regarding the petition for rulemaking number PP 03-1 under the Poison Prevention Packaging Act (PPPA) the definition of a test failure for unit dose packaging [at 16 CFR 1700.20(a)(2)(ii)] should be an objective standard, ie., "any child who opens or gains access to more than 8 individual units during the full 10 minutes of testing.

Alcoa Inc. has received national and international recognition for sustained excellence in employee safety and health management. We at Alcoa apply these safety principles to our work environment and the products that we produce. Alcoa's safety principles compel us to support this petition and promote the use of unit dose packaging.

Approval of this petition will result in significant improvements in safety for children. The ability of child resistant unit dose packaging to protect small children from accidental poisonings is obvious from statistical analysis of the history of poisoning by ingested drug products.

CPSC Incident Report data records 47 fatalities from 1983 through 2003 in which children aged six years or younger ingested lethal amounts of drug product that had been removed from a closure system. In 22 of these incidents it is specifically noted that the packaging was a "child resistant" cap-and-vial closure system. There are no reported incidents; however, of a child fatality in the United States after he/she removed drug product from a unit dose package.

The existing test protocol - which has been in place since the early 1970's - applies an objective pass/fail standard to most types of drug packaging, but uniquely applies a subjective standard to unit dose formats. While some unit dose formats are capable of passing the current standard, the PP 03-1 petition notes that the existing dichotomy creates a disincentive for pharmaceutical manufactures to adopt unit dose formats for their products. To ensure that similar standards apply to all types of child-resistant packaging, this petition requests that CPSC maintain the "eight pill" criterion as the sole means of determining whether unit dose formats are legally considered child resistant under U.S. law. We also note that granting this request will not require pharmaceutical manufactures to use unit dose packaging.

By approving this petition, CPSC will be increasing safety for children by removing the obstacles that have stood in the way of greater adoption of unit dose formats in the United States for more than 30 years.

Sincerely,

Tom Loredo for Kenneth Stewart

Kenneth C. Stewart
Regulatory Affairs Manager

Michelle B. West

Michelle B. West
Marketing Director

CPSC Comment
CP03-1-19

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Reply To:
Department of Federal Affairs
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
http://www.aap.org

VIA FACSIMILE

August 14, 2003

Office of the Secretary
Consumer Product Safety Commission
Washington, DC 20207

RE: Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

To Whom It May Concern:

I write today on behalf of the American Academy of Pediatrics to express serious concerns about Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging, which was published in the *Federal Register* on June 16, 2003 (68 FR 35614).

The American Academy of Pediatrics (Academy) is an organization of 57,000 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. Throughout is history, the Academy has made poison prevention an integral part of its injury prevention initiatives. Over the years, we have seen many successes. However, data remind us that we must remain vigilant if we are to continue making progress in this area.

One significant success we have seen is the significant reduction in the child death rate from unintentional poisoning. Although the ingestion of potentially poisonous substances by young children remains a common event – the American Association of Poison Control Centers reported approximately 1.2 million such events in the United States in 2001 – the child death rate from unintentional poisoning has decreased dramatically over the past 50 years, falling from 500 per year in the 1940s to just 25 in 1997. The advent of child-resistant closures for hazardous pharmaceuticals is one of the primary reasons this rate has fallen. And, the Poison Prevention Packaging Act (PPPA) is a key tool in requiring child-resistant packaging for pharmaceuticals that pose a risk of serious illness or injury.

As you state in your Notice of Petition, "[t]he current regulatory definition of a child-resistance test failure for unit dose, i.e., non-reclosable packaging under the Poison Prevention Packaging Act (PPPA), is a child gaining access to the number of individual unit doses that constitute the amount that "may cause serious personal injury or serious illness" or more than eight individual unit doses, whichever is less." This two-pronged standard protects children from both high-toxicity (any amount of individual unit doses that may cause serious personal injury or serious illness) and high-volume (more than eight individual unit doses) exposures. It also establishes an objective measurement for test failure ("may cause serious personal injury or serious illness") that can be equally applied to all products.

Filed by Healthcare Compliance Packaging Council, Petition PP 03-1 seeks to weaken current PPPA safety requirements. Specifically, the petition requests that the first protective component of the PPPA standard, which requires that child-resistant packaging prevent access to an amount fewer than 8 individual unit doses if such amount may cause serious personal injury or serious illness, be eliminated. Instead, the petition argues that the definition of test failure should be limited to "any child who opens or gains access to more than 8 individual units during the full 10 minutes of testing."

As pediatricians, we know there are medications that pose serious poisoning risks for children at levels far fewer than 8 individual unit doses. Examples of these medications include morphine, clonidine and the sulfonylurea group of drugs, which are commonly prescribed in the treatment of diabetes. In fact, data establish that only a few doses of sulfonylurea could cause a catastrophic outcome in an infant or young child. Eliminating the first criterion of the current PPPA standard would allow medications such as the sulfonylureas that are known to pose significant risk of serious illness or injury in amounts fewer than 8 individual doses to reach the market in packaging that is accessible to children. This development would, in turn, increase the likelihood that children will gain access to pharmaceuticals at levels that jeopardize their health and safety.

Simply put, reducing the current test failure criteria to one that is based solely on a uniform number of individual unit doses, as requested by Petition PP 03-1, is not consistent with good pharmacologic practice because all medications do not pose a uniform hazard to children. We therefore urge you to reject Petition PP 03-1 and retain the current, two-pronged child-resistance testing standards established by the PPPA.

Sincerely,

E. Stephen Edwards

E. Stephen Edwards, MD
President

ESE/mh

CR Test comment CP03-1-20

Stevenson, Todd A.

From: Ken Kulig [kkmedtox@msn.com]
Sent: Thursday, August 14, 2003 5:22 PM
To: Stevenson, Todd A.
Cc: bobhoff@pol.net
Subject: Petition PP 03-1, Petition for the Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

Office of the Secretary
Consumer Product Safety Commission
Washington DC

Dear Secretary,

I am the chairperson of the Patient Safety Subcommittee of the American College of Medical Toxicology,
a group of physicians specializing in the treatment of human poisoning. Many of the members work full time
in, or are otherwise affiliated with, Poison Centers. I have circulated information about the petition to the
membership of ACMT, and am hereby summarizing the comments received.

First of all, our members are extremely aware of the importance of poison prevention, particularly in children,
and are in favor of measures that will reduce the incidence of pediatric poisoning by pharmaceuticals.

Secondly, we are aware that there are numerous compounds where less than 8 unit doses can cause life-threatening toxicity in toddlers. These include, but are certainly not limited to, opiates, clonidine, sulfonyureas,
Beta blockers, colchicine, lomotil, etc. To eliminate the first criteria for failure of the child resistance test for
blister packs, would leave only the second criteria i.e. more than eight individual doses. One of our members
writes "Using the criterion of a uniform number of dosage forms makes no pharmacologic sense because there
is no uniform hazard for all medications."

In some cases, even one or two tablets of a medication may cause serious toxicity, and for those drugs a test that implies that less than eight is somehow safe is erroneous thinking. The initial criteria, "a number of individual doses that may cause serious personal injury or serious illness" is clearly more rational and takes

into account the varying hazards between various pharmaceutical preparations.

The comments received were favorable to the use of this type of packaging in general, because they do seem to be effective at preventing serious pediatric poisonings. One member from France commented that only blister packs are used in his country for this reason. It was the unanimous opinion of the members who responded that the effectiveness of this type of packaging would be lessened if Petition PP 03-01 were granted.
For this reason we oppose it and request that the CPSC deny it.

Sincerely,

Ken Kulig MD
Chair, Patient Safety Subcommittee
American College of Medical Toxicology

8/15/03

CLOSURE
MANUFACTURERS
ASSOCIATION

CRTest comment
CMA
CP03-1-21

August 15, 2003

VIA FACSIMILE

Office of the Secretary
U.S. Consumer Product Safety Commission
4330 East West Highway
Suite 501
Bethesda, Maryland 20814

Re: Petition PP03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

Dear Sir or Madam:

The Closure Manufacturers Association ("CMA") submits these comments in response to the Consumer Product Safety Commission's ("CPSC's" or "the Commission's") notice of petition filed by the Healthcare Compliance Packaging Council ("HCPC") to amend the CPSC's test failure protocol for child-resistant ("CR") packaging in 16 C.F.R. § 1700.20(a)(2)(ii), as it relates to unit dose packaging.[1/]

Founded in 1984, the CMA is a national non-profit organization dedicated to improving and promoting the manufacture and use of closures. In that capacity, the CMA has developed a strong expertise in and promoted the development of closures that effectively prevent child mortality and injuries that result from the accidental ingestion of harmful or hazardous substances. CMA has actively participated with CPSC in the development of voluntary industry standards for CR closures.

1/ 68 Fed. Reg. 35614 (June 16, 2003).

1-WA/2029385.1

Based on a statutory mandate, the current CR packaging test protocol in CPSC's regulations specifies that a test failure for unit dose packaging is the lesser of either: (1) any child who opens or accesses the number of individual units which constitute the amount that may produce serious personal injury or illness; or (2) a child who opens or gains access to more than 8 individual units in 10 minutes.[2] The HCPC petition, if granted, proposes to eliminate the first prong of the test failure criteria above, such that a test failure for unit dose packaging would be defined only as a child who opens or gains access to more than 8 individual units in 10 minutes.

The CMA opposes the HCPC petition for four reasons and urges the Commission to maintain the CR test failure protocol as it currently appears in the CPSC's regulations. First, under the Poison Prevention Packaging Act ("PPPA" or "the Act"), the Commission does not have the authority to disregard product toxicity to amend the test failure criteria as HCPC has requested. Second, amending the CR test protocol to an objective test criteria of a child who opens or gains access to 8 unit dose packages will not eliminate the need for toxicological analysis because many products are toxic to children at fewer than 8 units. Third, unit dose packaging is not, as HCPC contends, inherently safer than CR closures. Lastly, the PPPA does not authorize consideration of economic or competitive factors in determining toxicity or CR standards. For all of these reasons, the HCPC's petition to CPSC should be denied. Each of these topics will be discussed in detail below.

I. The Commission Does Not Have the Statutory Authority to Disregard Product Toxicity in Establishing Standards for CR Packaging

The PPPA requires special packaging for any particular 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 to be required by such standard is technologically feasible, practicable, and appropriate for such substance.[3]

"Special packaging" is defined as:

> [P]ackaging that is designed or constructed to be significantly difficult for children under five years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time and not difficult for normal adults to use properly, but

---

2/ 16 C.F.R. § 1700.20(a)(2)(ii).

3/ PPPA, §§ 3(a)(1-2); 15 U.S.C. §§ 1472(a)(1-2) (emphasis added).

> does not mean packaging which all such children cannot open or obtain a toxic or harmful amount within a reasonable time.[4/]

As the statute clearly mandates, CPSC first must identify poisonous or toxic substances which require special packaging and then evaluate special packaging by whether it is able to keep children from accessing a toxic or harmful amount of the particular substance contained inside the special packaging. Therefore, under the PPPA, a substance's toxicity is paramount to the analysis of the need for and acceptability of special packaging.

The legislative history supports this interpretation. For example, the report of the House of Representatives' Interstate and Foreign Commerce Committee states that:

> [M]ere reference to the hazards of a particular product will not necessarily mean that its packaging will be regulated under this legislation. Regulation under this legislation must be preceded by a finding that as a result of the degree or nature of the hazard to children in the availability of the product, by reason of its packaging, special packaging is required to prevent serious injury or illness. . . .[5/]

Further, as the CPSC has already pointed out to HCPC, the Senate Commerce Committee Report stated:

> In order to establish standards for the special packaging of a substance, the [CPSC] must find that the substance is responsible for serious personal injury to, or illness of, children and that such illness or injury arises because children are enabled by its packaging to obtain access to the substance. . . . Having found that a substance should be maintained in special packaging, the [CPSC] is authorized to establish standards for special packaging of that substance.[6/]

Moreover, in comments to the legislation submitted by the Department of Health, Education and Welfare ("HEW"), which originally had authority over the administration and implementation of the PPPA through the Food and Drug Administration ("FDA"), HEW stated:

> [w]e feel that the degree or nature of the hazard *presented by a substance* should be stated as the controlling factor in making findings of the need for special packaging. The degree or nature of the hazard of a substance is evidenced in statistics and data on involvement of products in child ingestions, morbidity, and mortality. Certainly 'the

---

4/ PPPA, § 2(4); 15 U.S.C. § 1471(4).

5/ H.R. Rep. No. 91-1642, reprinted in 1970 U.S.C.C.A.N. 5326, 5327.

6/ S. Rep. No. 91-845, at 10.

> availability of a substance, by reason of its packaging' is a factor in the hazards presented by a substance implicated in poisoning episodes.[7]

These references from the legislative history clearly illustrate that it is the hazard presented by a particular substance that drives the determination regarding the need for special packaging. Therefore, the issue of a substance's toxicity or hazardous properties cannot be eliminated from consideration in determining the need for special packaging.

The regulatory history implementing the PPPA's provisions confirms this conclusion, stating that the purpose of the test protocol is "to determine the ability of the special packaging to thwart the efforts of children under 5 years of age to open and obtain a toxic or harmful amount of the contents."[8] As the FDA, which originally maintained jurisdiction over CR packaging, acknowledged in the preamble to a 1973 final rule amending the test protocol, "[t]he ultimate controlling factor in determining the test failure level in the case of unit packaging remains the number of individual units which constitute the amount that may produce serious personal injury or serious illness."[9] Therefore, the relevant regulatory history confirms that product toxicity, including the amount of toxic substance accessible, is the key factor to be considered in evaluating the need for special packaging and, thus, the Commission does not have the authority under the PPPA to eliminate product toxicity from the test failure criteria for unit-dose packaging in 16 C.F.R. § 1700.20(a)(2)(ii).

The HCPC acknowledges that "the PPPA requires the Commission to consider toxicity in determining whether a particular substance requires special packaging."[10] Nonetheless, the HCPC argues that, "the PPPA does not require the subjective, zero-tolerance standard that 16

7/ H.R. Rep. No. 91-1642, reprinted in 1970 U.S.C.C.A.N. 5326, 5341 (emphasis in original). Another federal agency that evaluated this legislation at the time of its implementation concurred with this analysis. As the Federal Trade Commission ("FTC") noted, the purpose of the Act is to reduce injuries to, and illnesses of, young children arising from ingestion of toxic or harmful substances customarily produced or distributed for sale for consumption, use, or storage by individuals in or about the household. Child-Resistant Packaging of Household Substances: Hearing on H.R. 6179, H.R. 6180, H.R. 16541, H.R. 16884, and S. 2162 Before the Subcomm. on Commerce and Finance of the House Comm. on Interstate and Foreign Commerce, 91st Cong. 38 (1970) (statement of Caspar W. Weinberger, Chairman, FTC). Again, the toxicity of the substance in the amount accessible drives the analysis.

8/ "Part 295 -- Regulations Under the Poison Prevention Packaging Act," 36 Fed. Reg. 22151, 22152 (Nov. 20, 1971).

9/ "Modification of the Testing Procedure for Special Packaging," 38 Fed. Reg. 12738, 12738 – 12739 (May 15, 1973).

10/ Letter to Stephen Lemberg, Assistant General Counsel, CPSC, from Peter G. Mayberry, Executive Director, HCPC, at 2 (May 5, 2003).

C.F.R. § 1700.20 applies solely to unit-dose packaging."[11/] However, the current test protocol in 16 C.F.R. § 1700.20(a)(2)(ii) does not constitute a zero-tolerance standard. Instead, the test protocol permits the lesser of eight individual units or the number of units that constitute the amount that would cause serious personal injury or illness to a child to trigger the need for special packaging. This is not a zero-tolerance standard. By contrast, for traditional cap-and-vial closures, a test failure is any child who opens the special packaging or gains access to the contents of the package. This is a more stringent standard that does not allow for the flexibility afforded unit dose packaging.[12/]

As illustrated above, the Commission must consider the toxicity of a substance in determining the need for special packaging and the evaluation of special packaging. Consequently, the Commission must deny the HCPC's petition.

II. Product Toxicity Must Remain A Factor in the CR Test Failure Criteria Because, For Some Products, Less Than Eight Units Are Toxic to Children Under Age 5

The CMA believes that an objective test criteria for unit dose packages which defines a test failure as opening or gaining access to more than 8 individual units may, in fact, not be sufficiently stringent for some substances. Pursuant to HCPC's petition, any products packaged in unit dose packaging would be considered CR if packaged in less than 8 individual units. This result would be untenable, because many products pose a risk of serious injury or illness to small children at much lower amounts than 8 units. For example, as many commenters have pointed out, calcium channel blockers, tricyclic antidepressants, opioids, isoniazid, digoxin, and

11/ Id.

12/ Comments from Michigan State University support the argument that cap-and-vial closures are actually subject to a stricter standard than that currently imposed on unit dose packaging. "When a cap closure system is breached, it is considered an automatic failure under the current test protocol. CPSC has actually given the manufacturers of unit dose [packaging] a second chance at passing once a breach has occurred by allowing for the fact that a toxic dose has not been accessed. If the subjectivity of toxicity levels is truly the driving force behind this petition, the HCPC should err on the side of safety and make the failure Level 1, not 8. This will take the subjectivity that is uncomfortable for the manufacturers away and not allow a potentially toxic dose to be considered acceptable under the test protocol, and this would be parity with cap and vial; a single opening is failure." Comments of Laura Bix and Hugh Lockhart, Michigan State University, at 1 (Aug. 7, 2003).

clonidine are all potentially toxic to children in dosage amounts of fewer than 8 units.[13] As one pharmaceutical industry official noted, "[t]oday there are more once-a-day products with higher concentrations and higher potencies. So there are a lot of products where accessing just one or two tablets may be a problem."[14] In addition, because there is an increasing trend to make previously prescription drugs available over-the-counter ("OTC"), and such drugs can be toxic in smaller amounts, CPSC must be more vigilant, not less. Therefore, if CPSC decides to grant the HCPC petition to amend the regulation, CPSC should consider either lowering the test failure number to less than 8 units or removing the reference to 8 or less units, since it is an arbitrary number.

Consequently, because some drugs are toxic to children in fewer than 8 dosages or units, toxicological analysis of particular products is necessary unless a 1 unit access failure rule is adopted. For some substances, CPSC regulations at 16 C.F.R. § 1700.14 specifically set forth the amount or volume of a particular substance that is toxic and requires special packaging.[15]

As pharmaceutical industry officials have acknowledged, the current CPSC CR test protocol has worked effectively for 30 years and has achieved its objective of reducing the number of

---

13/ See Comments of ANEC to HCPC Petition (June 24, 2003); Comments of Steven M. Marcus, M.D., Executive Director, New Jersey Poison Information & Education System, to HCPC Petition (July 30, 2003); Comments of Anthony S. Manoguerra, Pharm.D., DABAT, FAACT, Director, San Diego Division, California Poison Control System, to HCPC Petition (July 30, 2003); Comments of Suzanne Doyon, M.D., Medical Director, Maryland Poison Center, to HCPC Petition (July 30, 2003); and Comments of James B. Mowry, Pharm.D., DABAT, FAACT, Director, Indiana Poison Control Center, to HCPC Petition (Aug. 1, 2003).

14/ "Pharmaceutical Packaging Roundtable: Devising Child-Resistant, Senior-Friendly Packaging," Pharmaceutical and Medical Packaging News, at 62 (June 2001) (statement of Arthur Jaeger, Director of Packaging Development, Merck & Co., Inc.).

15/ For example, acetaminophen must be packaged in special packaging only when a single package contains more than one gram of acetaminophen, which would equate to two 500 mg acetaminophen tablets. By contrast, a single tablet of aspirin is hazardous, and thus, requires special packaging. 16 C.F.R. §§ 1700.14(a)(1) & (16). Therefore, the alleged burden on drug manufacturers to calculate hazardous amounts is alleviated for some substances by the CPSC's regulations. The HCPC attempts to point to a recent journal article from a CPSC staff member analyzing the effectiveness of CR packaging for aspirin as one factor supporting the timeliness of its petition, however, the author's conclusions are incorrectly stated by HCPC. See HCPC Petition, at 2 (Mar. 17, 2003). The author concludes that "additional strategies designed to prevent unintentional drug poisonings need to be developed and evaluated," however, the use of unit dose packaging is not suggested as one such strategy. Gregory B. Rodgers, PhD., "The Effectiveness of Child-Resistant Packaging for Aspirin," Arch. Pediatr. Adolesc. Med., 2002; 156: 929, 932. Instead, the CPSC staffer points to CPSC efforts to increase consumer acceptance of CR packaging as one such strategy. Id.

pharmaceutical-related deaths to one or two per year.[16/] Therefore, for public health reasons, the CPSC should not amend the CR test failure protocol for unit dose packaging as requested by HCPC.

III. Unit Dose Packaging is Not Inherently Safer Than Cap-and-Vial Closures

The HCPC petition is replete with unsubstantiated assertions that unit dose packaging is inherently safer than traditional cap-and-vial closures in preventing accidental ingestions to children. HCPC references only unvalidated CPSC incident data, and provides no evidence of the source of any other data, the sample size, statistical significance or other information to allow CPSC to determine if the analysis is reliable or merely junk science. HCPC acknowledged that the CPSC data it relied upon in its petition are not comprehensive.[17/]

Additionally, the data relied upon by HCPC reveals that the number of incidents occurring with unit dose packaging were actually higher in recent years than cap-and-vial closures. For example, the chart on page 4 of HCPC's petition, summarizing data from November 2000 to January 2003, states that with unit dose packaging, no more than five drug units were ingested at one time, compared to a maximum of 33 units ingested at one time from products packaged with cap-and-vial closures.[18/] What the chart also shows, however, is that during that time, there were only 15 incidents involving cap-and-vial closures, compared to 31 incidents involving unit dose packaging. As one commenter also pointed out, this table only analyzes incidents in which more than 10 dosage units were ingested. There is no corresponding reference to or mention of incidents in which less than 10 units were ingested and no indication of the seriousness of these ingestions.[19/] Therefore, the total number of children exposed to toxic pharmaceuticals from

16/ "Pharmaceutical Packaging Roundtable: Devising Child-Resistant, Senior-Friendly Packaging," Pharmaceutical and Medical Packaging News, at 62 (June 2001) (statement of John Bitner, Manager of Package Design and Development, Pharmacia Corp.). The HCPC also argues that because the Second Circuit recently struck down an FDA rule requiring unit dose packaging for all dietary supplements containing 30 milligrams or more of iron per dosage unit, the CPSC must act to amend the test failure criteria for unit dose packaging. See HCPC Petition at 11. However, this argument misses the mark. The Second Circuit struck down the FDA's rulemaking on the basis that the CPSC, not the FDA, has the authority to prescribe poison prevention packaging, concluding that the FDA had exceeded its statutory authority in prescribing packaging type. See Nutritional Health Alliance v. FDA, 318 F.3d 92 (2d Cir. 2003). Thus, the Court did not address the legitimacy of mandating special packaging for iron-containing dietary supplements. As discussed above, under the PPPA, the need for special packaging for such products can and should be addressed by the CPSC.

17/ HCPC Petition to CPSC, at 4 (Mar. 17, 2003).

18/ See Comments of James B. Mowry, Pharm.D., DABAT, FAACT, Director, Indiana Poison Center (Aug. 1, 2003).

19/ Id.

accidental ingestions involving unit dose packaging is actually higher than the number of such incidents with cap-and-vial closures.

Moreover, the actual percentage of incidents involving unit dose packaging is much higher than the number involving cap and vial closures in view of the much larger number of cap-and-vial systems sold in the United States.[20] As other comments submitted to this petition have noted, HCPC's presentation of its analysis of the data should be "normalized to reflect the prevalence of cap-and-vial systems in order to compare performance fairly."[21] Therefore, HCPC's claims that unit dose packaging is inherently safer than cap-and-vial closures is unsupportable by HCPC's and market data. If CPSC were to make the requirements for unit dose packaging less stringent by removing the need for a toxicological analysis, not only would the number of incidents likely increase, but the number of serious injuries or death of children would likely increase as well.

IV. The PPPA Does Not Authorize the Consideration of Competitive Factors

The PPPA does not authorize the consideration of competitive factors associated with its standards. Nonetheless, the HCPC argues that the current CR test protocol sets forth a standard for blister packaging that requires a drug product manufacturer to conduct a toxicological analysis of its product to use unit dose packaging and to submit these data to CPSC.[22] According to HCPC's unsubstantiated assertions, this creates a disincentive for pharmaceutical manufacturers and packagers to use unit dose packaging, and economically disadvantages unit dose packaging manufacturers compared to cap-and-vial manufacturers.[23] HCPC contends that these testing and data submission steps require "considerable investments of time and money [that] cannot be recovered."[24]

20/ Blister packages are estimated to occupy less than 20% market share. "Pill Blisterpacks Face New BSI Test Regime," Packaging Magazine, at 8 (Jan. 24, 2002).

21/ Comments of Laura Bix and Hugh Lockhart, Michigan State University, to HCPC Petition, at 1 (Aug. 7, 2003).

22/ The HCPC also improperly contends that under CPSC's regulations, a manufacturer that uses unit dose packaging must submit to CPSC toxicological data to support its conclusions regarding the number of units that would cause serious injury or illness and must wait for CPSC's confirmation of the manufacturer's conclusions, and following CPSC review and confirmation of a manufacturer's toxicological data, test the package again. Id. at 6.

23/ HCPC Petition to CPSC, at 5 (Mar. 17, 2003).

24/ Id.

However, HCPC misunderstands the CPSC's regulations in this regard. Manufacturers are requested, not required to submit their toxicological data to CPSC.[25/] Manufacturers are permitted to market products without submission of such data, and to CMA's knowledge, there has never been an enforcement or other action based on failure to provide such data. The CPSC recently confirmed that the submission of such toxicological data is not required. "The current CPSC regulation does not require a company to test, or preclude a company from relying on test data generated by the package manufacturer or from testing of similar packaging."[26/] Thus, product manufacturers and marketers are not required to follow the steps outlined by HCPC above with respect to the submission and review of toxicological data.

Notwithstanding the CPSC rules, product manufacturers and marketers may choose to test products anyway, because, as some product manufacturers have noted, the ultimate responsibility for ensuring package performance lies with the drug product manufacturer. Therefore, even if the package manufacturer has conducted testing, many manufacturers will still conduct their own testing. "When a vendor comes to us with a child-resistant package that's passed with a given tablet, test protocol, and regimen, we still have to test it."[27/] Product manufacturers will still likely test product packaging rather than rely on vendor test results, regardless of the type of packaging, unit dose or cap-and-vial closures. Any such testing is voluntary, however, and is certainly not mandated by CPSC regulations as HCPC erroneously claims.

In addition, even if unit dose packaging manufacturers were economically disadvantaged, the PPPA does not require, and the CPSC is not authorized to consider, market competition factors in its rulemaking. Moreover, even if the CPSC were authorized to consider competition factors, it would likely conclude that manufacturers of cap-and-vial closures, which must meet a more stringent pass/fail product standard than unit dose package manufacturers, represent the industry segment that is economically disadvantaged. To be a truly level playing field, the test failure criteria for unit dose packaging would be the same as the criteria for cap-and-vial closures, i.e., one child who opens or gains access to the contents of one package would constitute a test failure. Rather, it is not the pass/fail standard, as HCPC alleges, but other economic aspects of using unit dose packaging that drive up the cost of the product (e.g., cost of materials, application, etc.). Nonetheless, CPSC does not have the statutory authority to sacrifice child

---

25/ "Manufacturers or packagers intending to use unit dose packaging for a substance requiring special packaging are *requested* to submit such toxicological data to the Commission's Office of Compliance." 16 C.F.R. § 1700.20(a)(2)(ii) (emphasis added).

26/ Letter to Peter G. Mayberry, Executive Director, HCPC, from Stephen Lemberg, Assistant General Counsel, CPSC, at 3 (Apr. 25, 2003).

27/ "Pharmaceutical Packaging Roundtable: Devising Child-Resistant, Senior-Friendly Packaging," Pharmaceutical and Medical Packaging News, at 63 (June 2001) (statement of John Bitner, Manager of Package Design and Development, Pharmacia Corp.).

safety by lowering the pass/fail standard to mitigate the additional costs arising from the use of unit dose packaging.

Finally, at the time that the PPPA was passed, some interested parties contemplated that the law would foster competition in the marketplace, and such competition was regarded as a positive effect of the legislation. In fact, in congressional hearings on this issue, the Federal Trade Commission expressed hope that the enactment of the PPPA would "promote competition among manufacturers to develop and promote the safest possible containers for household substances."[28/] As predicted by FTC, there have been considerable advances in both cap-and-vial and unit dose packaging. Rather than focusing on perceived competitive disadvantages, unit dose package manufacturers should be motivated by competitive forces to continue to develop innovative technologies. For the foregoing reasons, the HCPC's claim that unit dose packaging manufacturers are competitively disadvantaged by the CPSC's test failure criteria misses the mark, and cannot be considered by CPSC as a basis to amend the current CR test failure protocol as HCPC has requested.

V. Conclusion

The CPSC does not have the statutory authority under the PPPA to amend the CR test protocol as requested by HCPC because, as discussed above, under the PPPA, the toxicity of a particular substance cannot be disregarded in determining the need for special packaging. Further, the HCPC's other arguments in support of its petition are without merit. Therefore, the petition should be denied.

The CMA appreciates the opportunity to comment on these issues. Please contact me if you have any questions or comments regarding these issues.

Sincerely,

Darla Williamson

Darla J. Williamson

c: Kathleen M. Sanzo, Esq.
Morgan, Lewis & Bockius, LLP

28/ Child-Resistant Packaging of Household Substances: Hearing on H.R. 6179, H.R. 6180, H.R. 16541, H.R. 16884, and S. 2162 Before the Subcomm. on Commerce and Finance of the House Comm. on Interstate and Foreign Commerce, 91st Cong. 38 (1970) (Memorandum to Accompany Report by the Department of HEW on S. 2162).

1-WA/2029385.1

Morgan, Lewis & Bockius LLP
1111 Pennsylvania Avenue NW
Washington, D.C. 20004
Tel. 202.739.3000
Fax: 202.739.3001
eFax: 877.432.9652
www.morganlewis.com

Morgan Lewis
COUNSELORS AT LAW

FAX MESSAGE

Send To:

Name: Office of the Secretary
FAX Number: (301) 504-0127
Firm: U.S. Consumer Product Safety Commission
Telephone Number: (301) 504-0800

From:

Name Kathleen M. Sanzo
Floor: 11th
Operator Sending:
Telephone Number: (202) 739-5209
Time Sent:
Date Sent: 8/15/03
Number of Pages (INCLUDING COVER PAGE): 11

Note:

Comments: Re: Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

CP03-1-22 C Just

AMERICAN HEALTH PACKAGING®

2550 John Glenn Ave.
Suite A
Columbus, Ohio 43217
614-492-8177
fax 614-492-1903

August 15, 2003

Office of the Secretary
Attn: Mr. Todd A. Stevenson
Consumer Product Safety Commission
Washington, DC 20207

Re: Petition PP03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

Dear Mr. Stevenson:

American Health Packaging is a packaging subsidiary of AmerisourceBergen. The organization has been specializing in pharmaceutical packaging for more than 16 years. We support the Petition initiated by the Healthcare Compliance Packaging Council and recommend the proposals incorporated be adopted by the CPSC.

More specifically, the proposed change in the protocol criteria to more objective criteria merely completes the work the protocols were intended to accomplish in the first place. That original purpose was indeed to provide objective criteria to the subjective requirement for "special packaging" that is child resistant. The task was incomplete as it pertains to unit dose packaging since there remained a somewhat subjective aspect for most manufactures to choose the number of doses that would harm the specified infant.

The recommendation of the eight-dose limit is consistent with previous guidelines issued by the Commission and is consistent with criteria recommended by European Union CEN working groups.

We therefore support adoption of the recommendations in the Petition.

Respectfully Submitted,

Ed Hancock

Ed Hancock
President

cpsc comment CP03-1-23

Alan Goldhammer, PhD
Associate Vice President,
US Regulatory Affairs

PhRMA

August 15, 2003

Todd A. Stevenson, Secretary
Office of the Secretary
US Consumer Product Safety Commission
Room 501
4330 East-West Highway
Bethesda, MD 20814

Re: Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging; 68 Federal Register 35614

Dear Mr. Stevenson:

The following comments on the above noted petition before the Consumer Product Safety Commission (CPSC) are submitted on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies. Our member companies are devoted to inventing medicines that allow patients to lead longer, happier, healthier, and more productive lives. In 2002, our members invested over $32 billion in the discovery and development of new medicines.

As the CPSC is aware, the vast majority of solid oral dosage forms of prescription pharmaceuticals are distributed to pharmacies in bulk packaging. Pharmacies then dispense the requisite number of pills to patients in secondary packaging. These ubiquitous amber plastic vials come in a variety of sizes and can be closed with or without a child resistant cap depending on the patient's preference. Even with the move towards more automated dispensing, pharmacists are overworked and often times do not have the opportunity to counsel or provide other important information to patients. The availability of more unit of use packaging would be beneficial to both pharmacists and patients.

PhRMA member companies are constantly exploring new approaches to the packaging of prescription pharmaceuticals as a way of improving product stability, preventing the introduction of counterfeit medicines into the supply chain, prevention of medication errors, and providing another avenue for the delivery of useful information to patients. Such information improves patient compliance, helps to avoid preventable errors, and results in superior health outcomes. Many nasal sprays, inhalers, ophthalmic drops, creams, and ointments are available to patients in unit of use packaging. This allows manufacturers to include patient package inserts (PPIs) with the prescription pharmaceutical. This useful FDA-approved information provides important information about the drug but unfortunately some consumers do not receive PPIs due to flaws in the distribution system. Innovative packaging designs which integrate useful consumer information into the design itself have recently come onto the marketplace. Much more could be accomplished if the regulatory landscape for the development of unit of use packaging for solid oral dosage forms were improved.

Pharmaceutical Research and Manufacturers of America
1100 Fifteenth Street, NW, Washington, DC 20005 • Tel: 202-835-3533• FAX: 202-835-3597 • E-Mail: agoldham@phrma.org

The petition filed by the Health Care Compliance Packaging Council (HCPC) requests that CPSC amend 16 CFR 1700.20(a)(ii) of the testing procedures for special packaging because it does not provide for an objective approach to development of child resistant packaging. While a pure objective standard of an eight pill blister is appealing, it is unclear how this will serve the end goal of creating more user friendly unit of use packaging. PhRMA member companies will continue to evaluate the underlying toxicity of any unit of use packaged pharmaceutical and make decisions based on package accessibility by children and exposure to the active ingredient. Thus, a company is unlikely to take advantage of an objective standard, in this case an eight pill blister, if in the company's estimation there is likely to be potential exposure to a harmful dose.

While CPSC may be on solid procedural ground in rejecting the second portion of the HCPC petition concerning type testing, PhRMA believes that this issue warrants broad based discussion. Correspondence to HCPC from the Commission states that "current CPSC regulations implementing the Poison Prevention Packaging Act (PPPA) do not restrict a company from relying on child resistance test data generated by the package manufacturer or from testing of similar packaging for a different substance." PhRMA believes that there is a great deal of uncertainty about the current status of type testing and how companies approach this issue. Issues such as the child resistant feature being tested, the design and performance compliance, and the role of standards organizations all need to be discussed by stakeholders.

In order for pharmaceutical manufacturers to utilize more unit of use packaging, expeditious decisions are required during the development process. Companies will not expend the resources to qualify new packaging for the launch of new products under the current regulations outlined in the exemption process under 16 CFR 1702.7. Once a new drug is launched, commercial and manufacturing concerns mitigate against a switch in packaging design. Thus, the type testing process needs to be more transparent than at present in terms of both the type of criteria needed to assure that children will not be exposed to harm and the timeliness of decisions to enable companies to pursue this form of packaging.

To achieve the above goal, PhRMA believes that performance and design standards can be established to facilitate type testing. Working through established standards organizations such as the American Society for Testing and Materials (ASTM) is one avenue to accomplish this goal. PhRMA believes that such a standard will have great utility. For example a company could have the flexibility to use existing packaging designs if the new drug has a similar safety profile to a drug already packaged in blisters.

PhRMA plans to communicate in greater depth to CPSC on type testing and possible approaches to improving the current climate for employing unit of use packaging.

Sincerely,

Alan Goldhammer

Stevenson, Todd A.

From: Alan Goldhammer [AGoldhammer@phrma.org]
Sent: Friday, August 15, 2003 12:54 PM
To: Stevenson, Todd A.
Subject: PhRMA Comments on Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging
Importance: High

Please see the attached Adobe PDF file that outlines the comments of PhRMA on the above referenced petition.

Alan Goldhammer, PhD
Associate Vice President, Regulatory Affairs
PhRMA
1100 Fifteenth Street, NW
Washington, DC 20005

Phone: 202-835-3533
FAX: 202-835-3597

e-mail: agoldham@phrma.org

CR Tab comm CP03-1-24

Honeywell

Specialty Films
Healthcare
101 Columbia Road
Morristown, NJ 07962

August 12, 2003

Mr. Todd Stevenson
Secretary
U.S. Consumer Product Safety Commission
Room 501
4330 East West Highway
Bethesda, Maryland 20814-4408

RE: Petition Number: PP-03-1, Petition for Amendment of the Child Resistance Testing Requirements for Unit Dose Packaging

Dear Mr. Secretary,

In regards to the CPSC request for comment on Petition Number PP-03-01, Honeywell supports the opportunity to further evaluate 16 CFR Part 1700 for the purpose of improving safety and compliance relating to "non-reclosable" packaging.

Sincerely,

Honeywell Intl.
Healthcare Business Team

Honeywell

Sandra E. Luciano
210 N. Fieldcrest Drive
North East, MD 21901
Phone: (410) 658-2080
Fax: (410) 658-2064

To:	CPSC	**Fax#:**	301-504-0127
From:	Sandra Luciano	**Date:**	8/15/03
Re:	Petition Comment	**Pages:**	2

☐ **Urgent** ☑ **For Review** ☐ **Please Comment** ☐ **Please Reply**

Petition Number PP-03-1 Comment

NACDS NATIONAL ASSOCIATION OF CHAIN DRUG STORES

01 Tout

CP 03-1-25

August 15, 2003

Office of the Secretary
Consumer Product Safety Commission
4330 East-West Highway
Room 501
Bethesda, MD 20814

Subject: Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

To whom it may concern:

The National Association of Chain Drug Stores (NACDS) is submitting comments on the June 16, 2003 Petition (PP 03-1), requesting an Amendment to the Child-Resistance Testing Requirements for Unit Dose Packaging. The current regulatory definition of a child-resistance test failure for unit dose, i.e., non-reclosable packaging under the Poison Prevention Packaging Act (PPPA), is a child gaining access to the number of individual unit doses that constitute the amount that "may cause serious personal injury or serious illness" ***or*** more than eight individual unit doses, whichever is less. The petition requests that the Commission amend the requirement to eliminate the first criterion related to the toxicity of the substance to be packaged and define a unit dose packaging failure to be a child gaining access to more than eight individual unit doses.

NACDS represents over 200 chain pharmacy companies that operate nearly 35,000 community-based pharmacies. Our membership provides both prescription and over the counter pharmaceutical products to consumers. Our industry is required to package almost all prescription products in child resistant packaging, unless the consumer requests that such packaging not be used. Many OTC products are also sold in child resistant packaging. We believe that this packaging has helped to significantly reduce the incidence of accidental poisonings from prescription and OTC medications.

NACDS supports the goal of the petition because we understand how the current regulation can unfairly discourage the use of unit dose packaging, which studies show as a safer method of packaging in preventing accidental poisonings by children. By requiring similar objective standards to determine whether a particular unit dose packaging is in fact child resistant, it would give manufacturers a level playing field in determining which packaging is best suited for their products. Moreover, unit dose packaging has several advantages over conventional cap and vial closure packaging, including enhancing the stability of the drug product and helping to protect against potential tampering.

Because there is not an objective pass/fail criteria applied for unit dose packaging, it appears that manufacturers would rather utilize cap-and-vial packaging based on the objective manner in which the pass/fail standard is utilized (i.e., if a child opens the vial, the package fails). We believe that the increased usage of unit dose packaging for over the counter products would help reduce potential accidental poisoning from OTC medications as well.

413 North Lee Street
P.O. Box 1417-D49
Alexandria, Virginia
22313-1480

(703) 549-3001
Fax (703) 836-4869
www.nacds.org

We do have some concerns, however, about the use of a specific number of dosage units as a criteria by which a unit dose package would deemed to have failed. That is because ingestion of more than eight dosage units of a particular drug might cause accidental poisoning, while only four tablets of another product might result in a similar outcome in a child. Having said this, we believe that, given the choice of packaging OTC medications in a unit dose package versus a traditional cap and vial closure that the unit dose package would be inherently more child resistant that the other package. Therefore, Federal regulatory policies should not discourage unit dose packaging.

We support the ability of packagers to do "type testing" on the type of unit dose package, so that the costs of testing are minimized, and the exposure of children to these tests is reduced. If a type of packaging is deemed to be child resistant for one particular product, it will likely be child resistant for another product.

We appreciate the opportunity to submit comments on this issue. Thank you.

Sincerely,

John M. Coster

John M. Coster, Ph.D., R.Ph.
Vice President, Policy and Programs

MeadWestvaco Corporation
World Headquarters
One High Ridge Park
Stamford, CT 06905

Law Department
tel 203 461 7400
fax 203 461 7589

CP03-1-26

MeadWestvaco

August 19, 2003

VIA FACSIMILE (301/504-0127) and HAND DELIVERY

Todd Stevenson
Secretary
U.S. Consumer Product Safety Commission
4330 East West Highway Room 501
Bethesda, Maryland 20814-4408

Petition PP 03-1: Petition for Amendment of the Child-Resistance Testing Requirements for Unit-Dose Packaging

Dear Mr. Secretary:

MeadWestvaco Healthcare Packaging specializes in creating innovative packaging for clinical trial, ethical, OTC, and generic pharmaceuticals, nutriceuticals, cosmeceuticals, medical devices, diagnostic and veterinary products. Our focus is designing unique solutions that contribute to drug efficacy, consumer safety, and health literacy. Extending the value of health care through packaging, we enhance the products developed and marketed by making them engaging, memorable, and easier to administer by physicians, pharmacists, care givers and patients—all while protecting children and giving access to seniors.

MeadWestvaco Healthcare Packaging is a leading supplier to the healthcare industry. Operating under cGMP compliance, MeadWestvaco Healthcare Packaging is comprised of quality driven manufacturing operations integrated with MeadWestvaco's product and systems development resources. MeadWestvaco Corporation is a $7.2 billion dollar company with sales offices and manufacturing facilities in over 33 countries and customers in over 100 nations.

MeadWestvaco is devoting extensive resources toward the efficacy of patient compliance, concordance, and adherence—whether in clinical trial, ethical, or OTC environments. Drug therapy is now the cornerstone of modern medicine. Yet, as you are aware, poor compliance is a leading cause of failed medical treatment. Packaging can offer a number of creative and effective solutions to struggling patients—from education about their disease or condition, to informing about potential side effects, to prompting precisely when they should take each dose, to providing a novel opening mechanism that effectively balances child resistance and ease of use.

In response to the Consumer Product Safety Commission's request for comments regarding Petition PP 03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging, MeadWestvaco offers these observations.

I. Amending the pass/fail criteria for unit-dose formats in 16 CFR 1700.20 (a) (2) (ii) of the testing protocol to permit children to access up to eight units of all unit-dose packages without recording a test failure would significantly weaken the protection the Poison Prevention Packaging Act (PPPA) currently provides in preventing young children from accidentally ingesting potentially hazardous amounts of oral drugs.

A. *Oral medications are becoming increasingly toxic.*

Oral pharmaceutical and OTC dosages are becoming increasingly toxic for a number of reasons. With escalating resistance to commonly used drugs, more effective treatment has led to greater dose toxicity. Meanwhile, there is a growing trend toward combining medications either into a single tablet or into a common package to improve outcomes; although compliance enhancing, the resulting regimen also usually results in a higher combined toxicity. Similarly, to aid better patient compliance, many drugs are now formulated to have more simplified regimens, such as once-weekly and once-monthly dosing. These time-release designs usually require highly toxic individual doses. In addition, titrated regimens can have significant toxicity levels among doses in a single dispensed package. Finally, with the dawning of nanotechnology and customized medicines in biotechnology and gene therapy, newer medications are more often highly toxic.

B. *The HCPC proposal does not take into account drugs that are extremely toxic if taken in small amounts.*

The HCPC proposal separates package performance from child safety. The HCPC petition would define a child resistant unit-dose package as one in which not more than 20% of the children tested could open more than eight units. What this means is that, if every child tested opened and gained access to eight unit-dose packaged tablets or caplets of a product regulated under the PPPA, the package would still be defined as children resistant. The problem with this approach is that it overlooks the fact that many drugs in small quantities can be extremely toxic to young children.

For example, almost all of the commission's regulations that address over-the-counter drugs specify a level of active ingredient above which the Commission has concluded that childhood ingestion can cause serious personal injury or illness. Translating this to actual exposure, the regulated amounts of acetaminophen and ibuprofen equal four 250-mg tablets, respectively. The regulated amount of iron is slightly less than four 325 mg ferrous sulfate tablets. Under the HCPC proposal, if any of these products were packaged in unit-dose packaging, every child tested could open enough units to obtain a harmful amount of the substance. The package would still be regarded as being 100% child resistant, as long as 80% of the children did not get into more than eight units.

As the foregoing demonstrates, granting the HCPC proposal would substantially diminish the protection that the existing regulations under the PPPA provide. This is because, in the case of the products described above, manufacturers who wish to use unit-dose packaging under the current testing rules must tie the definition of an individual package test failure to the amount of the product that is subject to each specific regulation. Thus, in the case of acetaminophen, a package failure would occur each time a child being tested opened more than four units. This common sense approach ensures that the great majority of children (more than 80% under the current definition of a total test failure) will not be exposed to a harmful amount or toxic amount of the product, should they encounter in their homes a unit-packaged product containing acetaminophen.

While we have used over-the-counter drugs as examples to show the effect of the HCPC's requested revisions, both controlled drugs and prescription drugs in lower dosages often present a risk of toxicity to children. Granting the HCPC petition would expose children who ingest small amounts of those types of drugs to injury. Moreover, with more oral medications becoming increasingly toxic, it is not in the interests of young children or to the public to relax the safety that the current CPSC testing protocols afford by taking the action that the petition requests.

C. *Establishing more specific toxicological guidelines may assist manufacturers who wish to consider using unit dose packaging for prescription drugs.*

In part, the HCPC petition is based on the premise that the subjectivity involved in determining the toxic or harmful amounts of substances regulated under the PPPA deters manufacturers from using unit-dose packaging. As the previous discussion outlines, there is no such uncertainty with respect to the over-the-counter drugs that the Commission has regulated.[1] The only regulations in which there is any arguable subjectivity for testing purposes are those covering oral prescription drugs and controlled drugs. This is because, unlike the examples of the OTC drug regulations discussed above, neither of these regulations identifies levels of toxicity for specific products to which manufacturers can refer. Instead, manufacturers who wish to use unit-dose packaging must evaluate the toxicity of specific prescription drugs on a case-by-case basis.

Many manufacturers of prescription drugs have successfully navigated these toxicological issues and now use child-resistant and senior-friendly unit-dose packaging. We believe, therefore, that the HCPC's concerns on this subject may be overstated. Even if, however, the Commission agrees with the premise of the HCPC petition that the subjectivity of toxicological determinations for prescription items discourages the use of unit-dose packaging, the appropriate action is not the amendment to the testing regulations that the

[1] The regulation for aspirin does not specify a regulated amount. However, in the context of this testing discussion, the distinction between aspirin and other regulated OTC drugs is academic, since 45 grains of aspirin (nine 325 mg. tablets) has generally been regard as the threshold for toxicity to children.

HCPC requests. Rather, the Commission should simply address the issue by establishing more specific guidelines with which manufactures can evaluate specific products. Should it be inclined to do so, the Commission could consult with the FDA, which already imposes requirements for toxicological evaluation on manufacturers who wish to market drugs.

II. Viable unit-dose packaging options that meet the PPPA requirements for child-resistance and senior acceptance are commercially available and currently in production.

Sources often concur that an ideal medication package should meet four basic principles: (1) a compliance-enhancing design, (2) sufficient protection, tied to the product's toxicity level, to protect against the unintentional ingestion of the contents by children, (3) ease of use in opening, dispensing, and reclosing, and (4) adequate shelf-life stability or protection against light and moisture[2]. In efforts to create an ideal health care package, MeadWestvaco has placed significant product development and packaging engineering resources to develop commercially viable options that meet these criteria.

In 1999 MeadWestvaco introduced its first unit dose child-resistant and senior friendly (CR/SF) package called Dosepak™. In 2000, the package won the Healthcare Compliance Packaging Council's Compliance Package of the Year award. The Dosepak™ has been tested to the most stringent standard (access to one unit constitutes a child test failure) and has passed.[3] Thus, pharmaceutical manufacturers who use it need not worry about the issue of defining the toxicity of their specific products. Dosepak™ is commercially available and currently being used for both clinical trial and consumer pharmaceutical products globally. Today MeadWestvaco supplies the healthcare industry with over 10 million Dosepak™ packages a year, and the number of applications for its use are growing.

In early 2003, MeadWestvaco launched a second unit-dose CR/SF package concept called Surepak™. By the end of the year, MeadWestvaco Healthcare Packaging division will release additional compliance-enhancing CR/SF unit dose packaging options to the industry.

---

[2] References for key medication packaging attributes include: Rudd P. "Medication Packaging: Simple Solutions to Nonadherence Problems?" *Clinical Pharmacology and Therapeutics*. 1979 Mar; 25(3): 257-65. Task Force for Compliance. "Noncompliance with Medications: An Economic Tragedy with Important Implications for Health Care Reform." A Report of the Task Force for Compliance. 1994 Apr; 20-21, Forcinio H. "Creating Packaging Alternatives." *Pharmaceutical Technology*. 2000 Jun; 24-28., and Forcinio H. "The Future of Pharmaceutical Packaging." *Pharmaceutical Technology*. 2001 Jul; 62-66.

[3] There are other configurations of this package that use access to three or four units in defining test failures.

III. If adopted, "Type Testing" provisions for the protocol must be carefully drafted to avoid loopholes for relaxed CR requirements for oral prescription and OTC drug packaging.

On the subject of type testing, MeadWestvaco believes the HCPC request is somewhat ambiguous. The American Society for Testing and Materials (ASTM) Standard D-3475 currently classifies packages with child-resistant features according to the mechanisms of the packages that provide their child-resistance. ASTM D-3475, however, does not take into account a unit-dose package's child resistant features in relation to the toxicity of its contents or in relation to accessibility to a specific unit dosage of medication. If the HCPC request is so broad that a package needs only to have a feature recognized in the ASTM D-3475 to meet the PPPA standards, MeadWestvaco opposes it.

The ASTM classifications were originally designed to assist manufacturers in developing mechanical tests for different types of packages. Each product within a classification, however, still must be tested to determine whether it is child-resistant. Absent such testing, the classification is meaningless in determining whether a package complies and protects children. [4]

If, by type testing, HCPC means that it supports allowing a unit dose package that has already passed the protocol at a specified failure level to be used for different products without further testing, MeadWestvaco supports this with some reservations. First, the toxicity of the individual units of any product used with the design must be no greater than the level at which the package passed testing. That is, if a package passed with access to five units constituting a test failure, it cannot be used, under type testing, to package a drug that presents toxicity to children at four units or less. Second, it is understood that the package materials and specifications, as well as the methods of fabrication and assembly must remain unchanged. In our experience subtle changes in any one of these characteristics can affect package performance.

Somewhat more problematic is the issue of the degree to which the size, shape, and density of the contents may contribute to unit-dose package failures. This is an issue that the Commission staff will have to consider if the Commission is inclined to deal with the HCPC type-testing request. As long as some reasonable parameters are established, MeadWestvaco believes that allowing type testing should have no significant adverse affect on child safety. For clarity, we also suggest that the Commission more clearly define whether a test failure requires access to the entire contents of each of the individual units tested or whether penetration into the cavity in which the drug is housed is sufficient. In our view, the former is a more realistic and objective test.

[4] The HCPC places a great deal of emphasis on the Commission staff's decision to exercise its enforcement discretion to allow drugs used in clinical trials to be packaged in ASTM-classified packages without testing. As MeadWestvaco understands it, this decision was based on the relatively small number of drugs used in clinical trials, the lack of any ingestion data for clinical trial drugs, and the costs associated with testing children in light of the small number of products used in each trial. The decision did not suggest that the Commission staff generally views the ASTM classification as a substitute for testing.

Conclusion

Over two decades of experience has demonstrated that child-resistant packaging reduces child mortality and injury from the unintentional ingestion of oral prescription and OTC drugs. According to the study conducted by the CPSC, the use of child-resistant packaging was associated with an annual reduction in the oral prescription drug related mortality rate of 1.4 deaths per million children younger than five years. From 1974 to 1992, this translated into the prevention of approximately 460 child deaths, or a mortality reduction rate of 45% from levels projected without the child-resistant requirements.[5]

Child-resistant packaging saves lives. MeadWestvaco concurs the definition of a unit-dose package failure in 16 CFR 1700.20 (a) (2) (ii) should not be amended as the HCPC has proposed. MeadWestvaco however, supports permitting the use of type testing, subject to the conditions and limitations described above.

For further discussion on MeadWestvaco's position on these important matters, please contact Lou Cosentino, Vice President of Sales and Marketing, MeadWestvaco Healthcare Packaging, (212) 318-5663 or lfc6@meadwestvaco.com.

Sincerely,

Mark R. McMahon
Chief Operating Officer
MeadWestvaco Healthcare Packaging
MeadWestvaco Corporation

mrm: aos

[5] Rodgers G.B. "The Safety Effects of Child-Resistant Packaging for Oral Prescription Drugs." JAMA. 1996 June 5;275(21):1661-5.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

August 7, 2003

Office of the Secretary
Consumer Product Safety Commission
Washington, DC 20207

Dear Sirs:

Subject: Petition PP03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging

The Environmental Protection Agency (EPA) in the interest of child safety objects to changing the definition of a unit dose packaging failure to a less stringent definition as proposed in Petition PP03-1, Petition for Amendment of the Child-Resistance Testing Requirements for Unit Dose Packaging.

The EPA has child-resistant packaging, (CRP) regulations. The Federal Insecticide, Fungicide, and Rodenticide Act 25(c)(3) requires EPA CRP regulations to be consistent with those under the Poison Prevention Packaging Act, which is under the Consumer Product Safety Commission's (CPSC) jurisdiction. To accomplish this consistency EPA incorporates the CPSC CRP effectiveness and protocol testing regulations 16 CFR 1700.15(b) and 1700.20 in its regulations (40CFR 157.32). This means when CPSC changes their regulations EPA's CRP regulations will automatically change. Furthermore, EPA has focused more attention on protecting certain susceptible populations (infants and children) from pesticide exposure since the 1996 enactment of the Food Quality Protection Act (FQPA).

EPA has a number of unit dose type pesticide products e.g. swimming pool shock treatment pouches, flea and tick products, ant and roach bait stations, termite bait stations, etc. EPA uses the CPSC definition of a failure for unit packaging[1] for these pesticide products. For EPA pesticide products a unit dose packaging failure may be less than 9 units dependent on the chemical, product formulation, and its toxicity. In determining the amount that may produce serious personal injury or illness

[1] "any child who opens or gains access to the number of individual units which constitute the amount that may produce serious personal injury or serious illness, or a child who opens or gains access to more than 8 individual units, whichever number is lower..."

EPA does not rely on acute oral toxicity alone, we also use No Observable Adverse Effect Level (NOAEL) levels from studies dealing with acute neurotoxicity, developmental toxicity studies, etc. Dependent on the pesticide product, the acute oral LD_{50}, NOAEL levels, etc. from animal studies are combined with an 11.4 kg child's weight to define a failure as the number of units opened/accessed equal to or greater than 11.4 times the acute oral LD_{50}, NOAEL, etc or more than 8 individual units (9 units), whichever number is lower.

The amount of an EPA unit dose type pesticide product that may produce serious personal injury or illness may equal 1, 2, 3, 4, or 7 units. If Petition PP03-1 were granted and more than 8 units (9 units) were defined as a failure then, theoretically all 200 children could open anywhere from 1-7 units (which could be toxic to a child), but if less than 80% of the children open/access 9 units the package would still be CRP. To increase the number of units to more than the amount that may produce serious personal injury or illness means children are potentially exposed to toxic or harmful amounts of a product that is in "CRP". The public perception of CRP is that the child should not be able to access the product as packaged in a reasonable time and their guardians/parents are being given a false sense of security if Petition PP03-1 is granted.

In conclusion, the EPA in the interest of child safety objects to changing the definition of a unit dose packaging failure to a less stringent definition as proposed in Petition PP03-1.

Sincerely,

James J. Jones, Director
Office of Pesticide Programs

CR Testing comment

CP03-1-28

Hammond, Rocky

From: Stevenson, Todd A.
Sent: Thursday, August 21, 2003 3:59 PM
To: Hammond, Rocky
Subject: FW: Petition PP 03-1

From: Corbcohpc03@aol.com[SMTP:CORBCOHPC03@AOL.COM]
Sent: Thursday, August 21, 2003 3:58:50 PM
To: Stevenson, Todd A.
Subject: Petition PP 03-1
Auto forwarded by a Rule

I am writing to express my opposition to the Petition for Amendment of the Child Resistance Testing Requirements for Unit Dose Packaging.

If allowed, this petition would give children access to drugs that have the potential to seriously harm them. But the products would have passed protocol requirements and be considered safe.

This type of change would endanger the very children the original law was meant to protect.

Hipolito Paul Corbacho