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UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

Memorandum

Date: DEC 21 2004

TO : The Commission
Todd Stevenson, Secretary

THROUGH: John Gibson Mullan, General Counsel JGM
Patricia Semple, Executive Director PS

FROM: Jacqueline Elder, Assistant Executive Director for Hazard Identification and Reduction
Suzanne Barone, Ph.D., Project Manager for Poison Prevention, Directorate for Health Sciences for SB

SUBJECT : Healthcare Compliance Packaging Council (HCPC) Response to CPSC Staff's Recommendation to the Commission Regarding the Petition to Amend Child-Resistance Testing Pass/Fail Criterion for Unit Packaging (PP03-1)

This memorandum addresses the issues outlined by the HCPC in its response to the CPSC staff's briefing package and recommendation to the Commission regarding petition PP03-1 to amend child-resistance testing pass/fail criterion for unit packaging.

BACKGROUND

The CPSC staff forwarded a briefing package dated November 19, 2004, to the Commission with the recommendation to deny Petition PP03-1 to amend the child-resistance testing pass/fail criterion for unit packaging submitted by the HCPC. On December 13, 2004, the HCPC submitted a response to the staff's recommendation. A copy is at Tab A. The correspondence outlines three areas where the HCPC "commends CPSC staff for its determinations." The HCPC also expresses disagreement with the following three staff conclusions:

A. Granting the HCPC's petition would somehow lower the threshold of safety that currently exists.

B. Available data fail to show that unit dose packaging is safer than cap-and-vial closures.

C. That the only two options for the Commissioners to consider are: 1) accept the petition with a numerical pass/fail criterion of access to more than 8 dosage units; or 2) reject the petition.

NOTE: This document has not been reviewed or accepted by the Commission
Initial DL Date 12/21/04

STAFF'S RESPONSE

The HCPC did not provide any additional information that was not previously included in its petition or other prior submissions. In the current comments, the HCPC highlights two main areas, the safety of unit packaging and the limited number of options outlined by the staff in the briefing package.

Safety of Unit Packaging

The HCPC notes that the staff's analysis did not generate the same conclusions about the relative safety of unit packaging over reclosable packaging as the HCPC's analysis. As stated by staff in its briefing packaging, the data from the CPSC databases do not establish the general safety of unit dose packaging over reclosable packaging for drug products. While the data include fewer ingestion exposures involving unit dose packaging, the analysis by HCPC did not take into account the markets for these two packaging types, the number of units available, or the toxicity of the drug products. The HCPC analysis does not make a distinction between incidents involving child-resistant and conventional (non-child-resistant) packaging either for unit packaging or for reclosable packaging. The number of units available and whether a unit package is child-resistant will greatly influence the number of units accessed by a child. Because the data lack these descriptive details, they cannot be used to make general conclusions about the relative safety of unit packaging. In any event, if the packaging meets the pertinent child-resistance requirements applicable to it, its "safety" relative to other conforming packages is not particularly relevant. Also, the HCPC espouses many "safety" benefits of unit packaging that involve the practice of pharmacy which is not related to the child protection mandate of the PPPA.

The CPSC staff continues to maintain that it is not possible to conclude, based on available data, that unit packaging is safer than reclosable packaging.

Options for the Commission

The HCPC requests that the Commission consider an option of a numerical pass/fail criterion that is greater than one but less than eight. The arguments against a standard that specifies four units or five units as the HCPC suggests are the same as those for eight units. It does not protect children from the most toxic drug or chemical products. In addition, the HCPC petitioned for elimination of the toxicity criterion. They did not petition for a "moving target" change to the other "more than eight" criterion. Thus, elimination of the toxicity criterion is the issue before the Commission under Petition PP03-1.

The briefing package contains a description of tests conducted with conventional and child-resistant unit packaging by the CPSC staff in 1997.[1] The unit package with

[1] C. Wilbur and Barone, S. "Is Unit Dose packaging Inherently Child-Resistant? Presented at the 6th International Conference on Product Safety Research, Amsterdam, The Netherlands, May 15-16, 1998.

"child-resistant" features tested by CPSC staff for this study had a child-resistance of approximately F= 4. In this testing, 53 of the 100 children tested opened at least 1 unit. If the substance contained in this package causes serious injury after access to one unit, more than half of the children tested would have been in danger. If this is the unit package that the HCPC is describing in the scenario on page 7 of its December 13, 2004 letter, then a child-resistant bottle/closure system (where 85% of the children cannot open the package) would permit far fewer children to have access to an amount that would cause serious injury or illness.

In the briefing package, the CPSC staff noted that the only single numerical standard that would provide ample protection from all toxic chemicals and drugs is F=1. The staff does suggest that companies could use this packaging voluntarily if they do not want to assess the toxicity of the products to be packaged. Because this packaging is too restrictive in many instances, the staff did not (and does not) recommend that the Commission consider requiring F=1 packaging as an option at this time.

STAFF RECOMMENDATION

The staff continues to recommend that the Commission deny Petition PP03-1 to amend the child-resistance testing pass/fail criterion to delete the toxicity criterion for unit packaging. The HCPC December 13, 2004 letter provided no additional information or data than that provided in the petition or its prior additional submissions. The CPSC staff believes that eliminating the consideration of toxicity of the packaged product would weaken the existing child-resistance failure criteria for unit packaging and result in little or no protection of children from the most toxic products on the market.

TAB A

December 13, 2004

VIA FACSIMILE: 301/504-0127

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

RE: HCPC RESPONSE TO CPSC STAFF'S RECOMMENDATION TO THE COMMISSIONERS REGARDING PETITION PP 03-1

Dear Mr. Secretary:

I am writing on behalf of the Healthcare Compliance Packaging Council (HCPC) in response to a document entitled *Briefing Package, Petition PP 03-1: Petition to Amend Child-Resistance Testing Pass/Fail Criterion for Unit Dose Packaging* released by the U.S. Consumer Product Safety Commission (CPSC) on November 19, 2004.

After reviewing this document, the HCPC commends CPSC staff for its determinations that:

- "...the amount of a substance that will cause serious injury or illness to a young child can be difficult [to determine] especially when data are limited (e.g., for a new drug)." p. 14

- "The staff analysis produced similar but not identical numbers to those [included in the HCPC petition demonstrating that unit dose formats are safer than cap-and-vial closures]. We believe that the numbers presented in the petition are plausible." Tab B, p. 55.

- "Generally, manufacturers could use any of the available F=1 packaging with product requiring lower levels of child-resistance since it would be child-resistant at all F levels. In addition, those manufacturers that do not know or do not wish to determine the appropriate packaging for toxicity level of their product could use F=1 packaging." Tab D, p. 79

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There are, however, certain findings included in the briefing package with which we most definitely disagree. Specifically, we take issue with staff's conclusions that:

- Granting the HCPC's petition would somehow lower the threshold of safety that currently exists.
- Available data fail to show that unit dose packaging is safer than cap-and-vial closures.
- That the only two options for the Commissioners to consider are: 1) accept the petition with a numerical pass/fail criterion of access to more than 8 dosage units; or 2) reject the petition.

With regard to the first and second points, the HCPC continues to maintain that the establishment of a numerical pass/fail standard for unit dose formats used with pharmaceuticals would *not* lower the threshold of safety that currently exists. We maintain, as we did in the original petition – and subsequent correspondence to the Commission that is included in the briefing package – that a numerical standard would actually increase safety because it would remove a significant obstacle to greater adoption of unit dose formats as manufacturers' original packaging. This, in turn, would:

- Reduce the need to re-package drug products in the pharmacy – a practice that leads to dispensing errors and other negative repercussions to consumers.
- Ensure that the efficacy of drug products is protected from the time the drug has been manufactured until the time the drug is ingested.
- Allow for the use of technologies that ensure drug products have not been adulterated, counterfeited, or produced in a non-FDA-approved facility.
- Provide consumers with tamper-evident packaging for their pharmaceuticals.
- Ensure that a greater percentage of pharmaceuticals are actually dispensed to consumers in a format capable of passing the CPSC protocol. And,
- Provide consumers with pharmaceutical packaging that does not have a CR feature which relies on proper use by adults each time the package is accessed.

The point here is that staff did not even address the primary reason why the HCPC filed the petition in the first place: pharmaceutical manufacturers have repeatedly stated that they do not use unit dose formats as original packaging in the United States due to concerns with PPPA compliance. This is despite the fact that unit dose formats offer tremendous consumer benefits, and pharmaceutical manufacturers routinely use these formats for the exact same products when they are sold in other markets throughout the world.

CPSC staff also failed to note in the briefing package that pharmaceutical manufacturers routinely avoid PPPA compliance by shipping product in bulk containers which are exempted from the Act. This practice results in a paradigm whereby drug products *must* be repackaged in the pharmacy again, to the detriment of U.S. consumers. Moreover, it institutes reliance on cap-and-

vial closures which – unlike unit dose formats – have to be properly resealed *each time the container is accessed* to ensure the CR properties of the container.

Bulk distribution also requires that CPSC enforce PPPA compliance by policing pharmacies (of which there are at least 71,000 chain and independent drug stores in the United States) instead of pharmaceutical manufacturers (of which there are approximately 150 in the United States).

Simply stated, by granting the HCPC's request for a straight numerical standard that can be used to determine whether unit dose containers used for pharmaceuticals can legally be considered "child resistant" in the United States – an ability that Congress placed solely in the hands of the CPSC – the Commission would be opening the door to greater adoption of unit dose formats as manufacturers' original packaging and, in turn, significantly increasing the safety of pharmaceutical distribution. This action would simultaneously reduce CPSC's burden of ensuring PPPA compliance.

We also remind the Commissioners that virtually every comment sent to CPSC in response to the HCPC's petition by toxicologists, pediatricians, poison prevention centers, and other healthcare experts endorsed greater use of unit dose formats as a means of increasing safety. These comments agreed with CPSC staff, however, that a pass/fail standard of access to more than eight units is unacceptably liberal.

Which leads to our third concern with the staff's conclusion: that CPSC staff only identified two options for the Commissioners to consider. We reiterate that our petition called for the creation of a numerical standard for determining whether unit dose formats intended to be used with pharmaceuticals can be considered PPPA-compliant in the United States. While we *suggested* that this standard be set at access to more than eight dosage units during a 10-minute protocol test in the original petition, we quickly recognized that this would not be acceptable. For that reason we included in correspondence to the Commission – which is included in the briefing package – an offer to work with CPSC to create a numerical standard that is more acceptable. We also repeated this offer during numerous conversations with CPSC staff over the past 18 months.

We were surprised, therefore, when staff concluded that only two options were available to the Commissioners: 1) adopt a standard for unit dose formats that is pegged at access to more than eight units during protocol testing; or 2) reject the petition.

We urge the Commissioners, therefore, to consider a third option in evaluating our petition: remove the current pass/fail criterion that applies solely to unit dose formats under the existing protocol and replace it with a numerical standard that is more than one but less than eight.

While we agree with staff's conclusions that F=1 unit dose formats can be used to package pharmaceuticals with no need for determining the amount of product that could cause serious personal injury or serious personal illness to a small child, we also note it is not practical or necessary for all drug products to be dispensed in an F=1 format. There are, in fact, only a very small number of drug products that can cause serious personal injury or illness to small children if only a single dosage unit is ingested. From a safety standpoint and with regard to Congressional intent with the PPPA, therefore, the creation of such a rigid standard would be overly restrictive.

But a middle ground exists that would be acceptable under the PPPA while simultaneously removing the primary obstacle cited by pharmaceutical manufacturers as the major impediment to greater use of unit dose formats as original packaging. Specifically, we ask that:

CPSC create a standard for PPPA-compliant unit dose formats intended to package pharmaceuticals based on whether children are able to open X number of units during the entire 10-minute protocol test.

What number could be used as "X" under this recommendation? Again, the HCPC is willing to work with the Commission to answer this question. But a good argument can be made that F=4 or F=5 would be reasonable.

We note, for instance, that the objection to CEN standard EN 14375 which was filed by the German government earlier this year, and is referenced on page 11 of the staff briefing package, seeks to replace the EU-adopted CR criterion for non re-closable pharmaceutical packaging that was adopted in September, 2003 – and includes a pass/fail standard of access to more than eight dosage units during protocol testing – with a straight numerical standard of access to more than 4 dosage units constituting failure.

Indeed, officials from the German government who have participated in CEN discussions have categorically rejected the concept of establishing the amount of individual drug products that could injure a small child as is currently required by CPSC *only* when unit dose formats are used. It was also estimated at the most recent CEN meeting (held in England October 21-22, 2004) that the research needed to determine a "tolerable dose" for the most dangerous drugs that are actually being ingested by small children – not all drugs by any stretch of the imagination – would take at least four years to develop and cost, at a minimum, approximately $1 million.

It is for these reasons that officials from the German government who filed the objection realize that a straight numerical pass/fail criterion is far more practical than a vague and undefined standard based on the amount of drug product that could cause serious personal injury or serious illness to a small child.

CEN members also recognize that protocol testing is not reflective of real world scenarios. It is impossible to imagine, for instance, any rational premise other than protocol testing in which an adult would actively encourage small children to open a package intended to contain potentially harmful drug product. Or any other premise in which an adult would demonstrate proper opening technique to children – and tell children they can use their teeth – if the kids cannot open a drug package after five full minutes of trying, then grant five minutes more to get the package open.

Simply stated, it is universally recognized that the existing CPSC protocol is tilted to facilitate a child's ability to open the package. Considering the legislative requirements contained in the PPPA, it is clear that a pharmaceutical package tested under such a scenario could realistically be considered "child resistant" if children were only able to access 3, 4, or 5 dosage units under existing protocol testing conditions.

And for those relatively few drug products that could be considered dangerous if a child ingested one or two dosage units, authorities in Germany and throughout the EU have concluded it would be unlikely for children to remove a harmful amount of product *under real world circumstances*

from a non re-closable pharmaceutical package capable of passing the rigorous CPSC protocol at an F=4 or even an F=5 level.

Moreover, as CPSC staff note in the briefing package "The Pharmaceutical Research and Manufacturers of America, a major pharmaceutical trade association, stated that its member companies would not knowingly use packaging that was insufficiently protective for children." So even if a unit dosage pharmaceutical package capable of passing protocol at, say, F=5 was legally considered to be "child resistant" in the United States it is unlikely, according to CPSC staff, that manufacturers would use such a format for a product which could harm a small child if only a single unit were to be ingested when F=1 packaging is readily available.

A unit dose format capable of passing the CPSC protocol at F=4 or F=5 would, therefore, offer ample protection to meet PPPA requirements established by Congress that a CR package be "designed or constructed to be significantly difficult for children under age 5 to open or obtain a toxic or harmful amount of the substance within a reasonable time...and is not difficult for normal adults to use properly."[1]

We also want the CPSC Commissioners to know of our continued assertion that unit dose packaging is inherently safer than other packaging formats as a poison prevention device, and that this is true for a host of reasons. We maintain this position despite CPSC staffs' conclusion found in Tab B of the briefing package that data does not exist to definitively prove the poison-prevention superiority of unit dose formats.

In the first place, we repeat our point that drug products must be removed one at a time from a unit dose format. This slows children down, allowing more time for them to lose interest and/or for an adult to intervene. We also repeat our assertion that unit dose formats are safer because, by design, they are non re-closable and – unlike other alternatives – the CR features of unit dose formats do not rely on proper use by adults each time the contents are accessed.

This is a critical advantage considering, as CPSC staff note under Tab B, page 54, of the briefing package, "...there is evidence that a *substantial proportion of child poisonings* involved packages that had been *left open* at the time of ingestion (emphasis added)."

We also remind the Commissioners that CPSC staff did conclude that "The data show fewer such adverse events in unit dose packaging, but this *could* also have resulted from the smaller number of unit dose drug products on the market (emphasis added)."[2] While the HCPC applauds the staff's conclusion that existing data show fewer adverse events involving unit dose formats than other package types, we disagree that market share offers a relevant explanation for the differential.

The truth is that more than 20 years of data demonstrate that small children remove far smaller amounts of drug product from unit dose formats than they do from bottles, no matter what the difference in market share is between the two formats. As we noted in our petition, there are literally dozens of instances revealed in CPSC data where children defeated cap-and-vial closures capable of passing the CPSC protocol and ingested 30, 40, 50 or more dosage units.

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[1] Staff briefing package, page 5.
[2] Staff briefing package, Tab B, p. 52

Yet in those instances where unit dose formats were identified as being involved in accidental ingestions, the highest number of dosage units consumed was five. This is true even when children gained access to non-CR unit dose formats used to package oral contraceptives (i.e., birth control pills – which are often the *only* prescription drugs found in homes with small children). In the majority of instances where unit dose formats were identified, in fact, children were only able to ingest one dosage unit or a portion of a single dosage unit, even when non CR formats were involved. And most importantly, the HCPC cannot identify a single instance in more than two decades of CPSC data when a small child removed the entire contents of a drug product that was packaged in a unit dose format.

Additionally, in the event of an accidental ingestion, emergency response personnel can typically make a far better determination regarding the number of dosage units that were ingested when the product was removed from a unit dose format than they can when the product was removed from other package options. As CPSC data show, there are a tremendous number of recorded incidents involving cap-and-vial closures, for instance, where the amount of drug product ingested by a small child is listed as "unknown." This is not the case, however, when unit dose formats were specified as being involved in ingestions.

Overall, therefore, unit dose formats offer the following, demonstrated poison-prevention advantages over cap-and-vial closures:

- Unit dose formats are non re-closable meaning that they cannot be "left open" in normal conditions of use.

- Since medications must be removed from unit dose formats one at a time, these unit dose formats minimize the amount of drug product that a small child can ingest.

- In the event that a small child does ingest a drug product, unit dose formats facilitate the ability of emergency responders to determine the exact amount of product that was involved.

Based on all of this, the HCPC has trouble understanding CPSC staff's conclusion that "Even if we could control for the different number of drug products in each format, it would also be necessary to adjust for possible differences in toxicity of the drugs in each format.... As a result of these competing explanations, none of the analyses in the petition can be used to support the proposition that unit dose packaging is inherently safer than cap and vial format."

After carefully considering this portion of the briefing package, we simply have no idea what sort of additional data could be presented to CPSC staff that would allow them to concede the obvious: that unit dose formats are inherently safer than cap-and-vial closures when it comes to protecting small children from accidental ingestion of drug product.

And due to this frustration, we raise the following question for the Commissioners to consider when making their determinations as to whether unit dose formats are inherently safer than cap-and-vial closures:

> Imagine a child who is less than five years old has come into contact with an Rx drug container, and no adult is present. Which type of container – a unit dose format or a cap-and-vial closure – do you think would minimize the risk that the child will be poisoned?

On behalf of the HCPC, I thank you for the opportunity to express these concerns. We urge the Commissioners to accept our recommendation that a third option be adopted so work can begin as quickly as possible to establish an acceptable numerical pass/fail standard that allows unit dose formats to be considered child resistant under the PPPA.

Sincerely,

Peter G. Mayberry
Executive Director