bodies; (8) simplify or clarify language in regulations; (9) revise regulations to address changes in technology, economic conditions, or other factors; (10) determine if matters in an existing regulation could be better handled fully by the states without Federal regulations; (11) reduce burdens by incorporating international or industry consensus standards into regulations; (12) reconsider regulations that were based on scientific or other information that has been discredited or superseded; and (13) expand regulations that are insufficient to address their intended objectives or to obtain additional benefits.

Comments should focus on regulations that have demonstrated deficiencies. Comments that rehash debates over recently issued rules will be less useful. Particularly where comments relate to a rule's costs or benefits, comments will be most useful if there are data and experience under the rule available to ascertain the rule's actual impact. For that reason, we encourage the public to emphasize those rules that have been in effect for a sufficient amount of time to warrant a fair evaluation. Furthermore, the public should focus on rule changes that will achieve a broad public impact, rather than an individual personal or corporate benefit. Where feasible, comments should reference a specific regulation, by Code of Federal Regulations (CFR) cite, and provide the Department information on what needs fixing and why. Comments do not necessarily need to address how to fix the perceived problem, though such comments are welcome. Lastly, we also want to stress that this review is for existing rules; the public should not use this process to submit comments on proposed rules.

The public meeting will begin with a discussion of and taking comments on the Department's preliminary plan for regulatory review required by Executive Order 13563. After that, we plan to allow for comments on candidate rules for review. The Department's General Counsel will preside over the meeting. Other senior officials from the Department and its OAs will also attend. It is our intent that the public meeting will provide an opportunity for these officials to interact with individuals or stakeholder representatives. To enable them to effectively participate in the public meeting, they will need some information in advance. As a result, we are establishing the following process.

1. Suggestions for Discussion at Public Meeting:

a. By March 3, 2011, the Department requests that commenters submit their suggestions for discussion at the public meeting and indicate whether they want time allocated to them at the public meeting. Commenters are welcome to indicate how much time they would like to be allocated, but the Department reserves the right to allocate time as necessary to ensure that as many commenters as possible may participate in the public meeting in a meaningful manner.

b. The initial comments from those intending to participate in the public meeting should contain enough details to permit DOT officials to sufficiently prepare and ask questions.

c. The initial comments may be augmented anytime before the end of the full comment period.

d. Anyone who needs auxiliary aids and services, such as sign language interpreters, to effectively participate in the meeting should contact the Department via the "**FOR FURTHER INFORMATION CONTACT**" information provided above.

2. Public Meeting:

a. After receiving this initial round of public comment, the Department will organize those suggestions by topic and OA for discussion during the public meeting.

b. By having the public meeting after receiving initial public comment and by organizing the discussion around topics and OAs, the Department will be better positioned to discuss issues regarding a particular rule, broad category of rules, or affected group or industry, rather than merely recording public comment for later review.

c. The Department will hold its public meeting beginning at 9:30 a.m. ET on March 14, 2011 at the Department of Transportation, West Building, Ground Floor, DOT Conference Center, Oklahoma Room, 1200 New Jersey Avenue, SE., Washington, DC. We will make a meeting outline available on *http://regs.dot.gov* in advance of the meeting. Furthermore, we are exploring the use of technology to enable remote participation in the meeting. We will update *http://regs.dot.gov* with information about opportunities for the public to participate remotely.

3. Other Written Comments:

The Department will continue to accept written comments through April 1, 2011. Those who do not wish to attend the public meeting may, of course, submit comments at any time during the comment period.

4. Follow-up Action by DOT:

a. We will place a transcript or summary of the public meeting in our public docket (*http://www.regulations.gov*) as soon as possible after the end of the meeting. We note that because the docket is Internet accessible, it should allow those with Internet access to review those proceedings as well as other comments. We hope this will further improve the interchange of ideas.

b. This review will provide meaningful and significant input to the Secretary, the General Counsel, OA Administrators, and other DOT senior officials. As soon as possible, depending on the number of comments we receive and the issues raised, the Department will publish a report providing at least a brief response to the comments we have received, including a description of any further action we intend to take.

Regulatory Notices

Privacy Act: Anyone may search the electronic form of comments received into any of our dockets by the name of the individual submitting the comment (or signing the comment, if submitted on behalf of an association, business, labor union, etc.) You may review DOT's complete Privacy Act Statement in the **Federal Register** published on April 11, 2000 (65 FR 19477–78) or you may visit *http://www.gpoaccess.gov/fr/browse.html* and browse under 2000 for April 11, looking under Department of Transportation.

Authority: 5 U.S.C. 610; E.O. 13563, 76 FR 3821, Jan. 21 2011; E.O. 12866, 58 FR 51735, Oct. 4, 1993.

Issued on February 10, 2011, in Washington, DC.

Robert S. Rivkin,

General Counsel.

[FR Doc. 2011–3492 Filed 2–11–11; 8:45 am]

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CONSUMER PRODUCT SAFETY COMMISSION

16 CFR Part 1700

[CPSC Docket No. CPSC–2011–0007]

Poison Prevention Packaging Requirements; Proposed Exemption of Powder Formulations of Colesevelam Hydrochloride and Sevelamer Carbonate

AGENCY: Consumer Product Safety Commission.

ACTION: Proposed rule.

SUMMARY: The Consumer Product Safety Commission ("CPSC," "Commission," or "we") is proposing to amend its child-resistant packaging requirements to exempt powder formulations of two oral prescription drugs, colesevelam hydrochloride and sevelamer carbonate. Colesevelam hydrochloride, currently

marketed as Welchol®, is available in a new powder formulation and is indicated to reduce elevated LDL cholesterol levels and improve glycemic control in adults with type 2 diabetes mellitus. Sevelamer carbonate, currently marketed as Renvela®, is available as a new powder formulation and is indicated for the control of elevated serum phosphorus in chronic kidney disease patients on dialysis. The proposed rule would exempt these prescription drug products on the basis that child-resistant packaging is not needed to protect young children from serious injury or illness from powder formulations of colesevelam hydrochloride and sevelamer carbonate because the products are not acutely toxic, lack adverse human experience associated with acute ingestion, and in powder form, are not likely to be ingested in large quantities by children under 5 years of age.

DATES: Comments on the proposal should be submitted no later than May 2, 2011.

ADDRESSES: You may submit comments, identified by Docket No. CPSC–2011–0007, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following way:

Federal eRulemaking Portal: http://www.regulations.gov. Follow the instructions for submitting comments.

To ensure timely processing of comments, the Commission is no longer accepting comments submitted by electronic mail (e-mail) except through *http://www.regulations.gov.*

Written Submissions

Submit written submissions in the following way:

Mail/Hand delivery/Courier (for paper, disk, or CD–ROM submissions), preferably in five copies, to: Office of the Secretary, U.S. Consumer Product Safety Commission, Room 820, 4330 East West Highway, Bethesda, MD 20814; telephone (301) 504–7923.

Instructions: All submissions received must include the agency name and docket number for this rulemaking. All comments received may be posted without change, including any personal identifiers, contact information, or other personal information provided, to *http://www.regulations.gov.* Do not submit confidential business information, trade secret information, or other sensitive or protected information electronically. Such information should be submitted in writing.

Docket: For access to the docket to read background documents or comments received, go to *http://www.regulations.gov.*

FOR FURTHER INFORMATION CONTACT: Adrienne Layton, PhD, Division of Health Sciences, Directorate for Health Sciences, Consumer Product Safety Commission, Bethesda, MD 20814–4408; telephone (301) 504–7576; *alayton@cpsc.gov.*

SUPPLEMENTARY INFORMATION:

A. Background

1. The Poison Prevention Packaging Act of 1970 and Implementing Regulations

The Poison Prevention Packaging Act of 1970 ("PPPA"), 15 U.S.C. 1471–1476, gives the Commission authority to establish standards for the "special packaging" of household substances, such as drugs, when child-resistant ("CR") packaging is necessary to protect children from serious personal injury or illness due to the substance and the special packaging is technically feasible, practicable, and appropriate for such substance. Accordingly, CPSC regulations require that oral prescription drugs be in CR packaging. 16 CFR 1700.14(a)(10). The powder forms of cholestyramine and colestipol, two drugs that are chemically similar to colesevelam hydrochloride and sevelamer carbonate, currently are exempt from CR packaging. *Id.* 1700.14(a)(10)(v) and (xv).

CPSC regulations allow companies to petition the Commission for exemption from CR requirements. 16 CFR part 1702. Among the possible grounds for granting an exemption are that the degree or nature of the hazard that the substance poses to children is such that special packaging is not required to protect children against serious personal injury or serious illness (16 CFR 1702.17).

2. The Products for Which Exemptions Are Sought

a. Welchol® (Colesevelam Hydrochloride)

On February 24, 2009, Daiichi Sankyo, Inc. ("Daiichi") petitioned the Commission to exempt the powdered form of colesevelam hydrochloride, which it markets as Welchol®, from the special packaging requirements for oral prescription drugs. The petitioner stated that the exemption is justified because of lack of toxicity and lack of adverse human experience with the drug. Welchol® has been marketed in tablet form and dispensed in CR packaging. On October 2, 2009, the U.S. Food and Drug Administration ("FDA") approved a new powder formulation of the drug. The petition requested an exemption only for the powder dosage form of Welchol®. Tablets would continue to be in CR packaging.

Welchol® (colesevelam hydrochloride) is a bile acid sequestrant indicated as an adjunct to: (1) Reduce elevated low-density lipoprotein cholesterol (LDL–C) levels; and (2) improve glycemic control in adults with type 2 diabetes mellitus. The new dosage form of Welchol® provides 1.875 g or 3.75 g of the powdered drug in unit dose packages to be mixed with water and taken orally as a suspension. (A unit dose package of Welchol® or Renvela® is a pouch that contains an individual dose.)

b. Renvela® (Sevelamer Carbonate)

On March 6, 2009, Genzyme Corporation ("Genzyme") petitioned the Commission to exempt the powdered form of sevelamer carbonate, which it markets as Renvela®, from the special packaging requirements for oral prescription drugs. The petitioner stated that the exemption is justified because of lack of toxicity and lack of adverse human experience with the drug.

Renvela,® sevelamer carbonate, is a phosphate binder indicated for the control of serum phosphorus in patients with chronic kidney disease on dialysis. The tablets are marketed with a pill crusher for patients who have trouble swallowing the tablets. The company reformulated Renvela® as a powder to be taken as an oral suspension and received approval from FDA for this powder formulation on August 12, 2009. The new dosage form of Renvela® provides either 0.8 g or 2.4 g of Renvela® powder in unit dose packages to be mixed with 2 ounces of water.

B. Toxicity and Human Experience Data

Welchol® and Renvela® have similar chemical structures, biological properties, and powder formulations. Therefore, we are considering the two petitions together, and staff reviewed related toxicity data together. CPSC staff found that colesevelam hydrochloride and sevelamer carbonate are not absorbed from the gastrointestinal tract. This limits the systemic toxicity of the drugs.

No data indicate that either drug is acutely toxic, which is the type of toxicity of concern when considering whether CR packaging is appropriate. Even in patients taking these drugs chronically, the adverse effects are mostly minor, such as diarrhea, nausea, constipation, flatulence, and dyspepsia.

Generally, chronic studies are not useful in determining whether a drug should be in CR packaging (because CR

packaging is intended to protect against the child's access and likely one-time use of the drug). Nevertheless, staff reviewed such data. Animal studies involving 3 to 6 month administration of Welchol® and Renvela,® respectively, resulted in hemorrhage. However, this result was not related directly to the mechanism of action of the drugs, but rather to a side effect involving the inhibition of vitamin K absorption. Chronic administration of Welchol® and Renvela® can cause an alteration in the absorption of vitamins A, D, E, and K. Vitamin K is required by the liver to produce functional blood clotting factors. When vitamin K levels are low, nonfunctional blood clotting factors are produced, which can lead to hemorrhage. This can occur following the chronic administration of a drug that inhibits vitamin K, but not after the acute administration of such a drug. Daiichi Sankyo's submission mentions one 4-year-old girl who was prescribed Welchol® off-label to treat a skin irritation secondary to liver disease. She died from an intracranial hemorrhage. There are confounding factors in this case, and the death occurred after chronic, not acute, exposure. Because of the confounding factors, the death cannot be attributed solely to Welchol®. A trial of Renvela® in a limited number of pediatric patients (18) for eight weeks resulted in primarily minor GI effects. (Pieper A.K., Haffner D., Hoppe B., Dittrich K., Offner G., Bonzel K.E., John U., Frund S., Klaus G., Stubinger A., Duker G. and Querfeld U. (2006).) Other effects, such as metabolic acidosis, can be attributed to the underlying chronic kidney disease in these children. These effects would occur after chronic, but not acute, exposure.

If a child were to ingest accidentally colesevelam hydrochloride (Welchol®) or sevelamer carbonate (Renvela®), the potential for the occurrence of mild to moderate GI discomfort, such as indigestion, constipation, nausea, and vomiting does exist. However, a review of relevant data indicates that an acute ingestion of these drugs would not result in serious toxicity. Any serious toxicity would result only after chronic administration.

As noted, the CPSC's CR packaging regulations exempt cholestyramine and colestipol in powder form, two bile acid sequestrants that are similar chemically to Welchol® and Renvela®. CPSC staff has not found any articles in the medical literature describing toxic effects following the acute ingestion of either cholestyramine or colestipol from 1975 through 2010.

CPSC staff searched the following databases for incidents related to Welchol® and Renvela® occurring between 2000 and 2009: the Injury and Potential Injury Incident database ("IPII"), the National Electronic Injury Surveillance System database ("NEISS"), and the Death Certificates database ("DTHS"). Staff found one incident involving Welchol® in the NEISS database. In that incident, 11-month-old twin boys were taken to the emergency room after they had been playing with their grandmother's prescription medications. It is not clear how many, if any, pills the boys ingested, but the children were treated and released from the hospital. CPSC staff also searched Poisindex®, Pub Med, and Google for Welchol®, Renvela®, Colestipol, and Cholestyramine, and found no incidents of acute poisoning in humans.

CPSC staff also analyzed Medwatch reports obtained from the FDA. Medwatch is the FDA's program for reporting a serious adverse event, product quality problem, product use error, or therapeutic inequivalence/failure that may be associated with the use of an FDA-regulated drug, biologic, medical device, dietary supplement, or cosmetic. (*See http://www.fda.gov/Safety/MedWatch/HowToReport/default.htm*.) There may be adverse events that have occurred and are not reported in the Medwatch database. Also, the existence of a report in the database does not mean necessarily that the product actually caused the adverse event.

The FDA provided CPSC staff with 151 distinct incidents of adverse events associated with colesevelam hydrochloride (Welchol®) reported through the Medwatch system. CPSC staff excluded incidents where other medications may have caused the adverse event reported, resulting in 22 adverse events. Most adverse events reported to Medwatch were gastrointestinal or involved muscle pain, which is to be expected considering the adverse effects reported from clinical trials of Welchol®.

CPSC staff also received reports from the FDA of 40 distinct incidents of adverse events associated with sevelamer carbonate (Renvela®). CPSC staff excluded incidents where other medications may have caused the adverse event reported, resulting in five in-scope incidents. Two of the five incidents were deaths, which most likely were related to the underlying disease and not sevelamer carbonate (Renvela®) treatment. One of the five incidents involved intestinal obstruction and perforation, which the patient's physician thought were related to the patient's treatment with sevelamer carbonate (Renvela®). In the two remaining incidents, one patient experienced gastroenteritis, and the other (who had asthma and chronic obstructive pulmonary disease) suffered severe breathing problems while on Renvela®. Neither of these two results likely was related to sevelamer carbonate (Renvela®).

CPSC staff also evaluated the likelihood of children younger than 5 years old ingesting powdered substances. The powdered form of these substances makes them more difficult to ingest than medicines in other forms and therefore, likely will keep children from ingesting significant quantities. CPSC staff believes that it would be difficult for children under 5 years old to eat large amounts of powder quickly without aspirating or coughing. It would also be difficult for children to mix powder thoroughly in a liquid, and the resulting lumpy quality may be unappealing to children who try to drink it. Although children are likely to be able to tear open the non-child-resistant packets used for Welchol® and Renvela,® they are likely to spill much of the contents; therefore, they would have to open a number of packages to access a significant quantity of the drug. Most unintentional poisonings among children occur during short lapses in direct visual supervision. The difficulty posed by ingestion of powder introduces a delay in the poisoning scenario, and supervision is likely to resume before a child can take in a significant quantity.

The packages used with the powder formulations of Welchol® and Renvela® also reduce the likelihood of child poisoning. Both drugs are provided in small foil-lined packages containing individual doses. The Renvela® package is easy to tear only at the notch. Because the package must be opened at a precise location, it is less accessible, especially to young children. The Welchol® package does not have a notch and has uniform resistance to tearing, which makes it more difficult to open than Renvela®. Although both packages tear easily enough to be opened by children under 5 years of age, the fine motor skills of this age group of children are still developing, and children age 2 and younger are likely to spill most of the powder.

C. Action on the Petition

After considering the information provided by the petitioner and other available toxicity and human experience data, the Commission concluded preliminarily that the degree and nature of the hazard to children presented by the availability of powder formulations of colesevelam hydrochloride (currently

marketed as Welchol®) and sevelamer carbonate (currently marketed as Renvela®) do not require special packaging to protect children from serious personal injury or serious illness resulting from handling, using, or ingesting the substance. Therefore, the Commission voted to grant the petition and begin a rulemaking proceeding to exempt powder formulations of colesevelam hydrochloride containing not more than 3.75 grams per package and sevelamer carbonate containing not more than 2.4 grams per package from the special packaging requirements for oral prescription drugs.

D. Regulatory Flexibility Act Certification

Under the Regulatory Flexibility Act, 5 U.S.C. 601 et seq., an agency that engages in rulemaking generally must prepare initial and final regulatory flexibility analyses describing the impact of the rule on small businesses and other small entities. Section 605 of the Act provides that an agency is not required to prepare a regulatory flexibility analysis if the head of an agency certifies that the rule will not have a significant economic impact on a substantial number of small entities.

The Commission's Directorate for Economic Analysis prepared a preliminary assessment of the impact of a rule to exempt powder formulations of colesevelam hydrochloride (currently marketed as Welchol®) and sevelamer carbonate (currently marketed as Renvela®) from special packaging requirements.

Daiichi Sankyo, Inc., a subsidiary of the Japanese firm Daiichi Sankyo Co, Ltd, the company that markets colesevelam hydrochloride under the trade name of Welchol®, employs approximately 1,500 people in the United States. Net sales of Welchol® were approximately $243.1 million in 2008. Genzyme Corporation, the company that markets sevelamer carbonate under the trade name of Renvela®, is a U.S. firm headquartered in Cambridge, Mass., with more than 12,000 employees worldwide. Annual revenue for 2008 was $4.6 billion. Given that both firms that would be affected by a CR packaging exemption for these drugs are large, the exemption would not have a significant economic effect on a substantial number of small entities. Moreover, because the action at issue is an exemption from special packaging requirements, it would allow companies to avoid the costs associated with CR packaging.

Based on this assessment, we preliminarily conclude that the proposed amendment exempting powder formulations of colesevelam hydrochloride (currently marketed as Welchol®) and sevelamer carbonate (currently marketed as Renvela®) from special packaging requirements would not have a significant impact on a substantial number of small businesses or other small entities.

E. Environmental Considerations

Pursuant to the National Environmental Policy Act, and in accordance with the Council on Environmental Quality regulations and CPSC procedures for environmental review, we have assessed the possible environmental effects associated with the proposed PPPA amendment.

CPSC regulations state that rules requiring special packaging for consumer products normally have little or no potential for affecting the human environment. 16 CFR 1021.5(c)(3). Nothing in this proposed rule alters that expectation. Therefore, because the rule would have no adverse effect on the environment, neither an environmental assessment nor an environmental impact statement is required.

F. Executive Orders

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

The PPPA provides that, generally, when a special packaging standard issued under the PPPA is in effect, "no State or political subdivision thereof shall have any authority either to establish or continue in effect, with respect to such household substance, any standard for special packaging (and any exemption therefrom and requirement related thereto) which is not identical to the [PPPA] standard." 15 U.S.C. 1476(a). A state or local standard may be excepted from this preemptive effect if: (1) the state or local standard provides a higher degree of protection from the risk of injury or illness than the PPPA standard; and (2) the state or political subdivision applies to the Commission for an exemption from the PPPA's preemption clause and the Commission grants the exemption through a process specified at 16 CFR Part 1061. 15 U.S.C. 1476(c)(1). In addition, the federal government, or a state or local government, may establish and continue in effect a nonidentical special packaging requirement that provides a higher degree of protection than the PPPA requirement for a household substance for the federal, state or local government's own use. 15 U.S.C. 1476(b).

Thus, with the exceptions noted above, the proposed rule exempting powder formulations of colesevelam hydrochloride (currently marketed as Welchol®) and sevelamer carbonate (currently marketed as Renvela®) from special packaging requirements, if finalized, would preempt nonidentical state or local special packaging standards for the substance.

List of Subjects in 16 CFR Part 1700

Consumer protection, Drugs, Infants and children, Packaging and containers, Poison prevention, Toxic substances.

For the reasons given above, the Commission proposes to amend 16 CFR part 1700 as follows:

PART 1700—[AMENDED]

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

Authority: 15 U.S.C. 1471–76. Secs. 1700.1 and 1700.14 also issued under 15 U.S.C. 2079(a).

2. Section 1700.14 is amended by adding new paragraphs (a)(10)(xxii) and (xxiii) to read as follows:

§ 1700.14 Substances requiring special packaging.

(a) *Substances.* The Commission has determined that the degree or nature of the hazard to children in the availability of the following substances, by reason of their packaging, is such that special packaging meeting the requirements of § 1700.20(a) is required to protect children from serious personal injury or serious illness resulting from handling, using, or ingesting such substances, and the special packaging herein required is technically feasible, practicable, and appropriate for these substances:

* * * * *

(10) *Prescription Drugs.* Any drug for human use that is in a dosage form intended for oral administration and that is required by Federal law to be dispensed only by or upon an oral or written prescription of a practitioner licensed by law to administer such drug shall be packaged in accordance with the provisions of § 1700.15 (a), (b), and (c), except for the following:

* * * * *

(xxii) Colesevelam hydrochloride in powder form in packages containing not more than 3.75 grams of the drug.

(xxiii) Sevelamer carbonate in powder form in packages containing not more than 2.4 grams of the drug.

Dated: February 10, 2011.

Todd A. Stevenson,

Secretary, Consumer Product Safety Commission.

[FR Doc. 2011–3437 Filed 2–15–11; 8:45 am]

BILLING CODE 6355–01–P