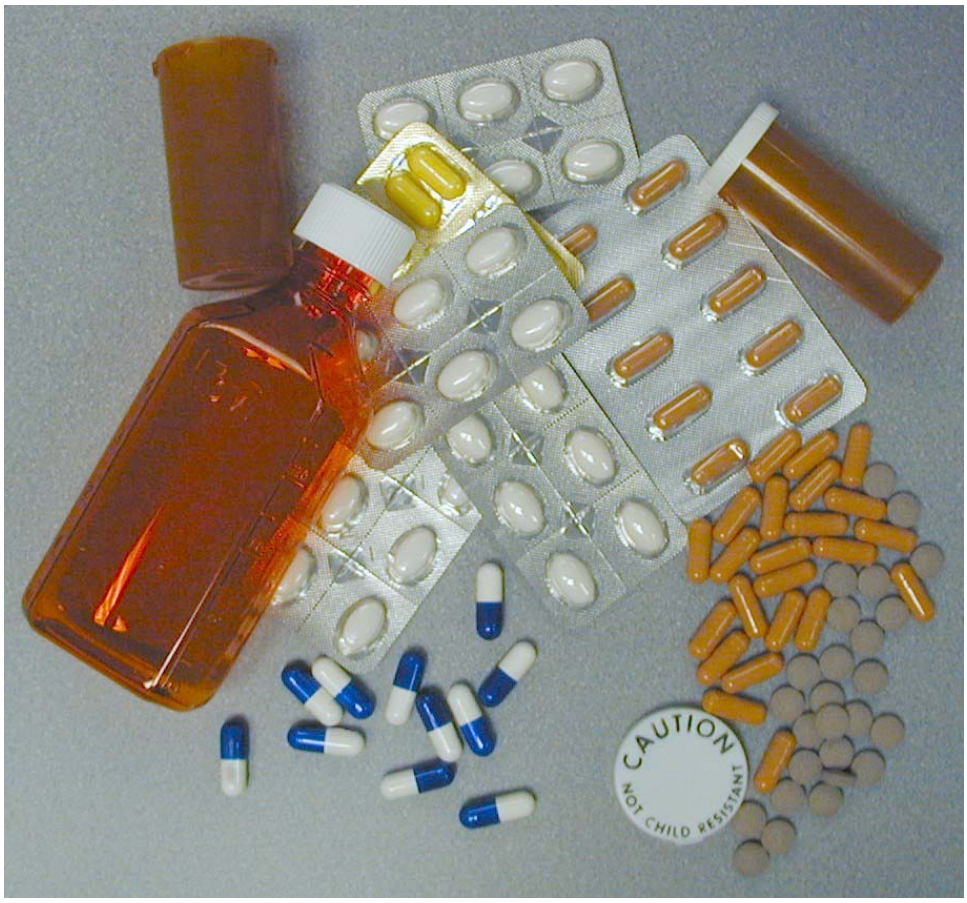
Poison Prevention Packaging:

A Guide For Healthcare Professionals



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Poison Prevention Packaging: A Guide

For Healthcare Professionals

(revised 2005)

Preface

The U.S. Consumer Product Safety Commission (CPSC) administers the Poison Prevention Packaging Act of 1970 (PPPA), 15 U.S.C. §§ 1471-1476. The PPPA requires special (child-resistant and adult-friendly) packaging of a wide range of hazardous household products including most oral prescription drugs. Healthcare professionals are more directly involved with the regulations dealing with drug products than household chemical products.

Over the years that the regulations have been in effect, there have been remarkable declines in reported deaths from ingestions by children of toxic household substances including medications. Despite this reduction in deaths, many children are poisoned or have "near-misses" with medicines and household chemicals each year. Annually, there are about 30 deaths of children under 5 years of age who are unintentionally poisoned. Data from the National Electronic Injury Surveillance System (a CPSC database of emergency room visits) indicate that in 2003, an estimated 78,000 children under 5 years of age were treated for poisonings in hospital emergency rooms in the United States. The American Association of Poison Control Centers reports over a million calls to poison control centers following unintentional exposure to poisons of children under 5 years of age each year.

Some of the reasons for the continuing ingestions are: availability of non-special packaging, on request, for prescription medication; availability of one non-special packaging size of over-the-counter medications; inadequate quality control by manufacturers leading to defective closures; misuse of special packaging in the home (leaving the cap off or unsecured, transferring the contents to a non-special package); and violations of the law by the pharmacist and/or the dispensing physician. Each of these factors has resulted in specific CPSC programs designed to address the issues.

This guidance was designed to educate pharmacists, physicians, and other healthcare professionals about their responsibilities under the PPPA. It is intended to be incorporated into the ongoing curricula of medical, pharmacy, nurse practitioner, and physician assistant programs and schools with the hope that healthcare professionals will become more aware of their responsibilities under the law. By learning the advantages of special packaging and by making a concerted effort to promote its use, healthcare professionals will help to further decrease ingestions by young children.

POISON PREVENTION PACKAGING: A GUIDE FOR HEALTHCARE PROFESSIONALS

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PART I

The History of Poison Prevention

Background

> "A child learns by doing. He gains experience by investigating the world around him. For his experiences to be constructive, they must be conducted in an environment where hazards are kept to a minimum."[1]

Before the Poison Prevention Packaging Act (PPPA) was enacted in 1970, poisonings by common household substances, including medicines, had long been considered by pediatricians to be the leading cause of injuries among children under 5 years of age. At one point, state death certificates reported about 500 fatalities a year in children under 5 due to poisoning caused by unintentional ingestion of drugs and household products.

As a result of the many injuries, individual poison control centers were established to provide specialized diagnoses and treatment for poisonings within their communities. The first poison control center started in Chicago in 1953. As these centers proliferated, the need for a coordinating body became apparent so that duplicative work could be avoided. In 1957, the National Clearinghouse for Poison Control Centers was established with the mandate to collect data from the centers and provide them with diagnostic and therapeutic information on the myriad of household products involved in childhood poisonings.[2] The Clearinghouse became the largest repository of poisoning case reports in the world. These reports became the primary source of data to evaluate the incidence of childhood poisoning. The Clearinghouse data collection ended in 1984. Poisoning cases reported to poison control centers are currently documented in the Toxic Exposure Surveillance System (TESS) maintained by the American Association of Poison Control Centers. The National Electronic Injury Surveillance System (NEISS) run by the U.S. Consumer Product Safety Commission (CPSC) is a source of national estimates of poisoning cases treated in hospital emergency rooms and it provides a follow-up mechanism when additional details about a particular drug or type of incident are needed.

A review of reports from poison control centers revealed a direct relationship between the stage of a child's development and the type of substance being ingested.[3] For example, youngsters still in the crawling stage were much more apt to get into those products stored on the floor of the bathroom or the cabinet below the kitchen sink (soaps and detergents, drain, and bowl cleaners). Toddlers were able to reach products left on low lying tables (uncapped bottles of furniture polish, for example). By the time youngsters were able to climb, they were reaching into the medicine cabinet.

Early Preventive Programs

The earliest attempts at controlling the problem of poisonings of young children surfaced after World War II, when there was a proliferation of household chemicals. Working with the American Medical Association (AMA) and industry, the Food and Drug Administration (FDA) drafted what in 1960 became the Hazardous Substances Labeling Act. This law stated that certain products, identified as “hazardous substances” within the meaning of the law, had to carry on their labels specific cautionary statements. Later, amendments to the law provided the authority to ban substances found too hazardous to be used safely around the household - notwithstanding cautionary labeling.[4]

Another activity geared to the prevention and control of childhood poisonings was the passage of Public Law 87-319 which requested the President to designate the third week in March each year as National Poison Prevention Week (NPPW), “… to aid in encouraging the American people to learn of the dangers of unintentional poisoning and to take such preventive measures as are warranted by the

seriousness of the danger."[5] It was a pharmacist who was the driving force behind the Resolution. In 1950, Homer George, of Cape Girardeau, Missouri, convinced his mayor to proclaim a Poison Prevention Week in his community. Mr. George then followed this up with the Governor of Missouri and subsequently prevailed on his congressman to introduce national legislation for a nationwide observance of poison prevention week.[6]

The introduction of a poison prevention week on a nationwide scale provided community organizations an opportunity to initiate poison prevention programs or highlight ongoing ones. While NPPW was beneficial in developing and fostering community interest, child poisonings and deaths continued.

In 1966, to address his concern about the number of aspirin ingestions, Dr. James Goddard, Commissioner of the FDA, convened a conference of aspirin producers, representatives of poison control centers, and public health officials.[7] One of the results of the conference was a voluntary agreement on the part of the manufacturers to restrict the number of children's aspirin tablets in a single container to 36, 1¼-grain tablets, generally accepted as a not highly toxic dose. Although this limitation would do little to affect the frequency of ingestions, it was hoped it would have an effect on severity should a child gain access to the aspirin.

Creating A Barrier

Another decision of the conferees laid the groundwork for a far-reaching change in U.S. consumers' experiences with the packaging of household products. The Chairman of the FDA-Industry Committee, Dr. Edward Press, appointed a subcommittee to look into the state of the art with respect to child-resistant packaging in 1966. One major manufacturer of children's aspirin was already using safety packaging for its product on a voluntary basis. The firm offered to make available whatever data it had that might be useful to the Subcommittee.[8] As part of this new approach to the prevention of poisonings, two independent studies were undertaken.

One of these took place in the State of Washington in the Fort Lewis-McChord Air Force Base area.[9,10] Prescription drugs were dispensed to the military population serviced by this area in packaging that utilized two dissimilar motions for opening (pushing and turning). The study included a preliminary test program (May 1967 – December 1970) which demonstrated that the new package design was much more effective in preventing access by young children than the standard screw caps and snap caps that were used on prescription vials. The effectiveness of this approach in controlling unintentional ingestions was shown by a decrease in ingestions. There were 27 incidents reported instead of the 210 ingestions that would have been anticipated during this time period.[11]

The other study took place in Essex County in Ontario, Canada, where there had been a vigorous educational campaign in effect for 10 years trying to reduce childhood unintentional ingestions. The campaign met with little success. A program to use child-resistant packaging for all prescription tablets and capsules was initiated by area pediatricians and pharmacists. The reduction in ingestions was as dramatic as that in the U.S.[12]

Backed by this and related information showing that childhood ingestions could be reduced through the use of child-resistant packaging, Congress enacted legislation. In 1970, the Congress passed, and the President signed, Public Law 91-601, the Poison Prevention Packaging Act (PPPA).[13] The legislation formed the basis for a new attack on the problem of unintentional poisoning among young children. It was now possible to control the agents responsible for these toxic episodes by creating a barrier between the harmful chemical and the child.

The FDA was responsible for enforcing the PPPA until 1973 when jurisdiction was transferred to the newly formed CPSC.[14] The PPPA gives the CPSC the authority to require "special packaging" of household products and drugs to protect children from serious injury or illness.

The PPPA defines special packaging as, "…packaging that is designed or constructed to be significantly difficult for children under 5 years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time and 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."[15]

Human performance tests were developed to measure child-resistance and adult-use-effectiveness. Children aged 42 to 51 months were chosen as the test subjects. The test method was developed to try to mimic the situation found at home. The test involved giving packages to pairs of children. The children were given 5 minutes to try to open the package. If they did not open their package within that time period, the children were given a single visual demonstration and then given another 5 minutes to attempt to open the package. The package was considered to be child-resistant if not more than 20 percent of 200 children tested could open the package.

The packages also had to be opened and properly closed by adults. Adults aged 18 to 45 years were chosen as the test subjects. The adults had a 5-minute time period to open and properly close the package. If 90 percent of 100 adults tested could open and close the child-resistant package, it passed.

Improving the Packaging

The test methods and standards described above were adopted in the early 1970s. The CPSC enforced these standards to make sure that special packaging on the market complied. Packaged products that did not meet the standards were recalled.

The CPSC staff continued to monitor ingestions. In 1986, the CPSC conducted an ingestion study with the AAPCC.[16] The results indicated that children were being poisoned by drugs that belonged to their grandparents. Many of these incidents occurred because special packaging was not being used properly; the closures were loose or left off. In other cases, the drugs were not in special packaging at all.

The CPSC tested the packaging with adults over a wide range of ages up to 75 years. Many adults, especially seniors, could not open special packaging. Children were being poisoned because adults could not use the packaging properly. The CPSC worked with the industry to revise the adult test methods to increase the age of adults tested. In 1995, the CPSC issued new requirements that amended the test procedures.[17] Adults aged 50 to 70 years old are now tested to measure adult-use effectiveness for most packages. These changes became effective in January 1998. Special packaging is improving. Packages are easier for adults to use properly while still maintaining child-resistance.

Success

Special packaging saves lives. CPSC analyzed child fatality data for unintentional ingestions of oral prescription medicines during the 1964 through 1992 timeframe. The results of the analysis showed that the death rates for oral prescription medicines declined even after taking into account the changes in the consumption of the medications over time and the long-term decline in the overall unintentional death rate of children from all causes.[18]

The CPSC study showed that special packaging reduced the oral prescription medicine-related death rate by up to 1.4 deaths per million children under age 5. This represents a reduction in the rate of fatalities of up to 45 percent from levels that would have been projected in the absence of special packaging requirements, and equates to about 24 fewer child deaths annually.[19]

A similar study of the effectiveness of special packaging of aspirin estimated that special packaging reduced the aspirin-related mortality rate by 34 percent. This equates to about 90 fewer child deaths from aspirin during the 1973-1990 study period.[20]

When combining the statistics for aspirin with those for prescription drugs, the staff of the CPSC estimates that special packaging saved the lives of more than 900 children since the requirements went into effect in the early 1970's. This estimate relates to aspirin and oral

prescription medicines only and does not include additional lives that may have been saved by special packaging on other products.

PART II

Substances Covered by Regulation

Background

The PPPA gives the Commission the authority to require special packaging of hazardous household substances to protect children. Section 3 of the PPPA details the findings that the Commission must make prior to promulgating a special packaging standard. The Commission may require special packaging of a household substance if it finds that:

> 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
>
> The special packaging to be required by such standard is technically feasible, practicable, and appropriate for such substance.

In establishing a standard the Commission also considers:

1. the reasonableness of such standard;
2. available scientific, medical, and engineering data concerning special packaging and concerning childhood unintentional ingestions, illness, and injury caused by household substances;
3. the manufacturing practices of industries affected by the PPPA; and
4. the nature and use of the household substance.

The scope of products, which may potentially be subject to special packaging standards is quite broad and includes products customarily produced for use in or around the household. Foods, drugs, cosmetics, as defined by the Federal Food, Drug and Cosmetic Act, hazardous substances as defined by the Federal Hazardous Substances Act (FHSA), and pre-packaged fuels are all within the jurisdiction of the legislation.

The responsibility for administration and enforcement of child-resistant packaging for pesticides (including cleaning products that make antimicrobial claims) lies entirely with the Environmental Protection Agency (EPA) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). It should be noted that the same test methods for determining whether a package is child-resistant and senior friendly apply to pesticides because the FIFRA was amended to recognize packaging and labeling violations under the PPPA.

In the years since enactment of the PPPA, many household chemicals or categories of household substances have been added to the list of regulated substances[21]. Those standards dealing with drug products, particularly prescription drug products, will be discussed in somewhat greater detail. A list of substances that require special packaging as of 2005, is presented below. Please refer to the PPPA regulations at 16 CFR § 1700.14 for the most current list of regulated substances and for the specific details of each regulation.

Substances Regulated At 16 CFR § 1700.14

- Aspirin: Any aspirin-containing preparation for human use in oral dosage form.
- Furniture Polish: Low-viscosity, non-emulsion type liquid furniture polish containing 10 percent or more petroleum distillates, unless packaged in pressurized spray containers. (These products also require restricted flow so that not more than

2 milliliters is obtained when the package is inverted, squeezed or otherwise activated once.)

- Methyl Salicylate (oil of wintergreen): Liquid preparations containing more than 5 percent by weight, unless packaged in pressurized spray containers.

- Controlled Drugs: Preparations intended for oral human use, which are subject to the Comprehensive Drug Abuse Prevention and Control Act of 1970.

- Sodium and/or Potassium Hydroxide: Household substances in dry form (granules, powders, flakes, etc.) containing 10 percent or more by weight and all other household substances (aerosols, liquids, pastes) containing 2 percent or more by weight, of chemically unneutralized sodium and/or potassium hydroxide.

- Turpentine: Household substances in liquid form containing 10 percent or more by weight of turpentine.

- Kindling and/or Illuminating Preparations: Prepackaged low viscosity substances (i.e., cigarette lighter fluids, charcoal lighter fluids, camping equipment fuel, torch fuel, and fuel for decorative or functional lanterns) which contain 10 percent or more by weight of petroleum distillates.

- Methyl Alcohol (Methanol): Household substances in liquid form containing 4 percent or more by weight of methyl alcohol, unless packaged in a pressurized container.

- Sulfuric Acid: Household substances containing 10 percent or more by weight of sulfuric acid, except in wet cell storage batteries.

- Prescription Drugs: Any drug for human use in oral dosage form and which is required by federal law to be dispensed only by or upon an oral or written prescription of a practitioner licensed to administer such drug.

- Ethylene Glycol: Household substances in liquid form containing 10 percent or more by weight of ethylene glycol.

- Iron-Containing Drugs: Non-injectable animal and human drugs providing iron for therapeutic or prophylactic purposes which contain a total amount of elemental iron equivalent to 250 milligrams or more per package.

- Iron-Containing Dietary Supplements: Most dietary supplements that contain an equivalent of 250 milligrams or more of elemental iron per package.

- Solvents for Paint or Similar Surface Coatings: Prepackaged low-viscosity liquid solvents for paints or other surface-coating material that contain 10 percent or more by weight of benzene, toluene, xylene, petroleum distillates, or any combination thereof.

- Acetaminophen: Preparations for human use in oral dosage forms containing more than 1 gram of acetaminophen in a single package.

- Diphenhydramine: Preparations for human use in oral dosage forms containing more than the equivalent of 66 milligrams of diphenhydramine base in a single package.

- Glue removers containing acetonitrile: Household glue removers in a liquid form containing more than 500 milligrams of acetonitrile in a single container.

- Permanent wave neutralizers: Liquid home permanent wave neutralizers, containing more than 600 milligrams of sodium bromate or more than 50 milligrams of potassium bromate in a single container.

- Ibuprofen: Preparations for human use in oral dosage forms containing 1 gram or more of ibuprofen in a single package.

- Loperamide: Preparations for human use in oral dosage forms containing more than

0.045 milligrams of loperamide in a single package.

- Mouthwash: Most mouthwash containing 3 grams or more of ethanol in a single package.

- Lidocaine: Products containing more than 5 milligrams of lidocaine in a single package.

- Dibucaine: Products containing more than 0.5 milligrams of dibucaine in a single package.

- Naproxen: Preparations for human use in oral dosage forms containing 250 milligrams or more of naproxen in a single package.

- Ketoprofen: Preparations for human use in oral dosage forms containing more than 50 milligrams of ketoprofen in a single package.

- Fluoride: Products containing more than 50 milligrams of elemental fluoride and more than 0.5 percent fluoride in a single package.

- Minoxidil: Preparations for human use containing more than 14 milligrams of minoxidil in a single package.

- Methacrylic Acid: Liquid products containing more than 5 percent (weight to volume) methacrylic acid in a single package.

- Over-the-Counter Drug Products: Preparations in oral dosage forms that contain any active ingredient that was previously available for oral administration only by prescription.

- Hazardous substances containing low-viscosity hydrocarbons: Products containing 10 percent or more hydrocarbon by weight with a viscosity of less than 100 SUS at 100ºF.

- Drugs and cosmetics containing low viscosity hydrocarbons: Products containing 10 percent or more hydrocarbon by weight with a viscosity of less than 100 SUS at 100ºF.

Review of the list of categories reveals a wide range of household products and chemicals. Healthcare professionals are more directly involved with those regulations dealing with drug products than household chemical products.

Aspirin and Acetaminophen

Aspirin was the first substance to be regulated under the PPPA. Note that while acetaminophen is regulated at a level of more than 1 gram per package, no level has been established for aspirin and aspirin-containing products. Thus a substance containing any amount of aspirin is required to be in special packaging. There are two exemptions to each of these regulations; each based primarily upon physical characteristics of the dosage forms, which have been found to inhibit or limit unintentional ingestion of these products by children. These exemptions are:

1. Effervescent tablets or granules containing not more than 15 percent acetaminophen or aspirin, provided the dry tablet or granules have an oral LD_{50} of 5 grams or more per kilogram of body weight.

2. Unflavored acetaminophen or aspirin-containing preparations in powder form (other than those intended for pediatric use) that are packaged in unit doses providing not more than 13 grains of acetaminophen or 15.4 grains of aspirin per unit dose.

Methyl Salicylate

This regulation covers liquid preparations containing more than 5 percent by weight of the substance and specifically exempts pressurized spray containers. The cream and ointment preparations are not included.

Controlled Drugs

All controlled drugs intended for oral administration to humans are covered without exception, including over-the-counter preparations.

Iron-Containing Drugs and Dietary Supplements

Iron-containing drugs and dietary supplements that contain 250 mg or more elemental iron have required special packaging since 1978. Iron was responsible for many poisoning deaths. Consumers may be unaware of the toxicity of iron. It is important for Healthcare Professionals to educate their patients about the toxicity of iron.

Lidocaine, Dibucaine, and Minoxidil

All three of these drugs are available in topical formulations. The regulations for lidocaine and dibucaine, two topical local anesthetic drugs, are noteworthy because they extend to all dosage forms including creams, sprays, and transdermal patches. Minoxidil is available as an oral prescription drug used for hypertension; this formulation requires special packaging under the prescription drug rule. Minoxidil is also available in topical form for hair regrowth. The CPSC regulated minoxidil to require the topical forms to be sold in special packaging. Many minoxidil preparations are sold with applicators (i.e., droppers or spray pumps) that are intended to replace the original closure on the package of minoxidil. The package is required to comply with the special packaging requirements of the PPPA for the life of the product. Thus the package must continue to meet the special packaging requirements when the provided applicators are affixed to the package.[22]

Human Oral Prescription Drugs

The special packaging requirement for oral prescription drugs, which became effective on April 16, 1974, has had great impact on both pharmacists and drug manufacturers. As described previously, the PPPA requires that a number of findings be made before a special packaging standard can be promulgated. The key finding is the establishment that the substance, because of the way it is packaged, has a significant potential for causing serious personal injury or illness in children. However, some human oral prescription drugs may not have the potential to cause serious injury or illness to children. Why then did the Federal government choose to require all human oral prescription drugs to be dispensed in special packaging?

The answer is twofold. First, it provides the best protection of children. Second, it eliminates the formidable task for dispensing pharmacists of having to maintain complete and accurate listings of regulated and non-regulated drugs. Since new drugs and drug classes are being approved by the FDA at an increased rate, promulgation of separate regulations for drugs or classes of drugs known to be a potential hazard to young children upon unintentional ingestion would have been an extremely onerous task. In addition, the burden upon individual pharmacists would have been great since they would have to check each drug, dosage strength, and amount before dispensing. These problems were resolved by regulating all human oral prescription drugs and then establishing a procedure for exempting products that do not pose a hazard to children (described below). This approach was possible with the support and cooperation of the various pharmaceutical, trade, and professional associations.

Oral investigational drugs for outpatient clinical trials require special packaging under the Human Oral Prescription Drug Rule. Because of the special circumstances surrounding the use of investigational drugs, the CPSC staff has issued guidance on the packaging of these products.[23]

Oral prescription drug samples and “starter kits” dispensed by the prescribing practitioners require special packaging. However, the current CPSC position is that manufacturers are not responsible for the special packaging of these products since they are distributed by a licensed medical practitioner who has the authority to specify non-complying packaging for his/her patients. This is not the case for oral prescription drugs, including samples, that are dispensed by pharmacists, since pharmacists do not have the authority to specify that prescriptions be dispensed in non-complying packaging.[24]

Drugs Switched from Rx to OTC Status

Diphenhydramine, ibuprofen, loperamide, naproxen, and ketoprofen are drugs that were originally available by prescription. The FDA allowed the over-the-counter (OTC) sale of certain formulations of these drugs. When these drugs were granted OTC status, they were no longer required to be packaged in special packaging under the oral prescription drug rule. The CPSC had to initiate separate rulemaking activity in order to require special packaging of each drug. In 2001, the CPSC issued a rule to require special packaging of oral prescription drugs that are granted over-the-counter (OTC) status by the FDA. This will ensure that special packaging will continue to be required for these products when they are more readily available to the public. Separate rulemakings such as those for diphenhydramine, ibuprofen, loperamide, naproxen, and ketoprofen will be unnecessary in the future for these types of drugs.

Exceptions and Exemptions

The section above describes the substances that must be in special packaging. However, there are several situations when special packaging is not required. Since the PPPA applies only to substances used in or around the household, the special packaging requirements do not extend to products used in institutional settings such as hospitals and traditional nursing homes. However, if the patients are taking the drugs home, including assisted-living types of homes where patients are responsible for taking their medication, the substances need to be in special packaging.

Congress had concerns about the ability of elderly or handicapped individuals to access products in special packaging. Therefore, the PPPA contains provisions to facilitate access of products by these special populations. Section 4(a) of the PPPA provides for the marketing of "non-complying" or non-special packages of regulated substances other than prescription drugs in order to facilitate access to regulated products by the elderly and handicapped.[25]

A manufacturer or packager may package any over-the-counter household substance (subject to a PPPA standard) in packaging of a single size that does not comply with such standard if:

1. The manufacturer (or packager) also supplies such substance in packages that comply with such standard; and

2. The packages of such substance that do not meet such standard bear conspicuous labeling stating: "This package for households without young children"; (or “Package Not Child-Resistant” for small packages).

As a result, manufacturers of over-the-counter household products regulated under the PPPA, have the option of marketing one size in a conventional package as long as that same product is supplied in popular-sized complying packages. There is one exception. Under the Federal Hazardous Substances Act, household products containing more than 10 percent sodium/potassium hydroxide are banned unless marketed in special packaging.[26] The effect of this is to essentially remove the option of producing a single non-complying package of the substance.

Section 4(b) of the PPPA addresses the need for facilitating access to prescription drugs by elderly and handicapped individuals who have difficulty using special packaging.[27]

> "In the case of a household substance which is subject to such a [PPPA] standard and which is dispensed pursuant to an order of a physician, dentist, or other licensed medical practitioner authorized to prescribe, such substance may be dispensed in noncomplying packages only when directed in such order or when requested by the purchaser.”

The pharmacist's role in implementing this section is further discussed in Chapter III.

In addition to the scenarios described above, the regulations of the PPPA contain a procedure whereby exemptions from special packaging requirements may be granted by the Commission. An exemption request, in the form of a formal petition, is generally initiated by the

manufacturer of a product. The majority of such requests are from manufacturers of human oral prescription drugs. Generally such requests seek exemption for a specific package size of a drug, normally a package designed for direct dispensing to the consumer after appropriate labeling by the pharmacist.

The petitioner must submit various data relating to the toxicity of the product, and, generally must establish that the amount of product contained within the requested exemption would not be harmful to a child under 5 years of age. Formal exemption criteria exist to guide manufacturers in submitting petitions.[28] The exemption procedure involves rulemaking by the Commission.

As of 2005, the following prescription drugs are exempt from the PPPA standards and may be dispensed in conventional packaging, as long as they contain no other substance subject to 16 CFR § 1700.14(a).[29] The specific exemptions are in the PPPA regulations at 16 CFR § 1700 (a)(10).

1. Sublingual dosage forms of nitroglycerin,

2. Sublingual and chewable forms of isosorbide dinitrate in dosage strengths of 10 milligrams or less.

3. Erythromycin ethylsuccinate granules for oral suspension and oral suspensions in packages containing not more than 8 grams or the equivalent of erythromycin.

4. Erythromycin ethylsuccinate tablets in packages containing no more than the equivalent of 16 grams erythromycin.

5. Anhydrous cholestyramine in powder form.

6. Potassium supplements in unit dose forms, including individually wrapped effervescent tablets, unit dose vials of liquid potassium, and powdered potassium in unit dose packets, containing not more than 50 milliequivalents per unit dose.

7. Sodium fluoride drug preparations, including liquid and tablet forms, containing no more than 264 milligrams of sodium fluoride per package.

8. Betamethasone tablets packaged in manufacturers' dispenser packages containing no more than 12.6 milligrams betamethasone.

9. Mebendazole in tablet form in packages containing not more than 600 milligrams of the drug.

10. Methylprednisolone in tablet form in packages containing not more than 84 milligrams of the drug.

11. Colestipol in powder form in packages containing not more than 5 grams of the drug.

12. Pancrelipase preparations in tablet, capsule, or powder form.

13. Cyclically administered oral contraceptives in mnemonic (memory-aid) dispenser packages which rely solely upon the activity of one or more progestogen or estrogen substances.

14. Prednisone in tablet form when dispensed in packages containing no more than 105 milligrams of the drug.

15. Conjugated estrogen tablets when dispensed in mnemonic dispenser packages containing not more than 32.0 milligrams of the drug.

16. Norethindrone acetate tablets in mnemonic dispenser packages containing not more than 50 milligrams of the drug.

17. Medroxyprogesterone acetate tablets.

18. Sacrosidase (sucrase) preparations in a solution of glycerol and water.

19. Hormone Replacement Therapy products that rely solely upon the activity of one or more progestogen or estrogen substances.

CHAPTER III

Responsibilities Under the Act – Frequently Asked Questions

Prescribers/Dispensers of Medications

Q. What is the responsibility of the pharmacist under the PPPA?

A. The pharmacist **must** dispense oral prescription drugs in special packaging unless the drug is exempted or the patient or prescribing practitioner requests non-special packaging.

Q. May an individual request that all of his/her prescriptions be filled in conventional (non-special) packaging?

A. Yes, the law does not preclude a pharmacist from relying upon a specific request from a patient to have all of his/her medications placed in non-special packaging. Many pharmacies choose to have this request in writing, i.e., a blanket waiver. However, a single request from a patient to dispense a specific prescription in non-special packaging is not a basis for the pharmacist to infer the patient wants all subsequent prescriptions to be dispensed in non-special packaging. Such a request is not a blanket waiver.

A patient who previously requested blanket non-special packaging may later change his/her mind about the use of such packaging because of changing personal circumstances, but may not remember to inform the pharmacist of the change in packaging preference. It is a prudent practice for the dispensing pharmacist to periodically check with all patients who have blanket waiver requests on file to ensure that noncomplying packaging continues to be the preferred packaging choice for the patients' prescription drugs.

Q. If the pharmacist is aware that one of his/her customers prefers conventional packaging for his/her prescriptions, can the pharmacist make this decision without the customer's specific request?

A. No. The pharmacist may advise the customer that he/she has the option of having the prescription dispensed in noncomplying packaging, but the choice must be that of the customer.

Q. Must the customer make the choice for conventional packaging in writing?

A. Although many pharmacists do require a written waiver, the law and regulations do not require a written request. The CPSC staff recommends, however, that the pharmacist get a request in writing particularly when a blanket waiver is being requested. This will assist the pharmacist during inspections of the pharmacy by regulatory agencies.

Q. May a pharmacist dispense a prescription drug in a noncomplying package in response to a standing order from a physician that it be so dispensed?

A. This can be done only when it applies to refills of a prescription where the physician has prescribed noncomplying packaging for that prescription. However, a drug dispensed to the same person on a different prescription of the same or another prescriber must be dispensed in special packaging, unless the prescription directs the use of noncomplying packaging or the purchaser requests it.

Q. Can a physician simply check a box on a prescription blank to indicate to the pharmacist that a drug be dispensed in noncomplying packaging?

A. Yes. However, the CPSC staff discourages the use by physicians of prescription blanks having a box to check for noncomplying

packaging, on the basis that the practice would tend to encourage excessive use of noncomplying packaging.

Q. Who is responsible for determining at the retail level whether a prescription drug must be packaged in accordance with PPPA standards?

A. It is the responsibility of the dispensing pharmacist. Unless a prescription drug is expressly exempted from the regulations, or the customer or prescribing physician request noncomplying packaging, the drug must be dispensed in a special package.

Q. How does a pharmacist or physician become aware of which drugs are exempted from PPPA standards?

A. This information listed in the PPPA regulations at 16 CFR § 1700.14 and is available on the CPSC website, http://www.cpsc.gov/businfo/notices.html Announcements are published in the Federal Register, and in news releases issued by CPSC (which may be published in the local press). In addition, the journals and newsletters of pharmaceutical and medical groups, as well as the trade press, publicize these exemptions.

Q. In the case of an antibiotic drug provided by the manufacturer in a granular form to be reconstituted by the pharmacist, who is responsible for providing the special package the pharmacist or the manufacturer?

A. If the product is in the same container intended to be given to the purchaser, the manufacturer and the pharmacist are both responsible.

Q. Does the same rule apply to drugs dispensed in dropper bottles?

A. Yes.

Q. In the case of refills, can prescription bottles and vials be reused?

A. As a general rule, no. This prohibition is based on the wear associated with a plastic vial, which could compromise the package's effectiveness. Since such wear or undetected damage with a glass container is negligible, the CPSC staff has indicated that it would have no objection to the reuse of a glass container, provided a new closure is used. This same consideration would be given to any other package type that is not prone to wear.

Q. Does the regulatory reference to "dosage forms intended for oral administration" include drugs intended for topical application to the teeth or mouth, or in a dosage form intended for inhalation?

A. No. The regulations intend "oral administration" to pertain to drugs that are taken by mouth for a systemic and not local effect. Sublingual preparations are considered "orally administered" even though they are not swallowed. Their effect is systemic and not local to the mouth. Because of the need for quick access to the drug, sublingual nitroglycerin was excluded from the oral prescription drug regulation when it was adopted in 1973.[30]

Q. When a prescription drug is dispensed in a special package, would the pharmacist be in violation of the regulations if he or she included a separate non-complying closure with the package?

A. Although this practice is not prohibited, the CPSC staff discourages the practice in that it is likely to result in the use of noncomplying packaging by those who are able to use special packaging without difficulty.

Q. Are Investigational New Drugs (INDs) subject to the PPPA standards?

A. Yes. Oral INDs are subject to the oral prescription drug regulation, if the IND is a drug that is for oral administration to humans, can be dispensed only on or by an order of a licensed medical practitioner, and is to be dispensed directly to the

patient. Such drugs must be packaged in a special package except as described at http://www.cpsc.gov/BUSINFO/trials.pdf. In addition, if INDs contain any substances regulated under any of the other PPPA regulations, they would be required to be packaged in special packaging if they are dispensed for household use.

Q. May a pharmacist legally use reversible or other types of dual-purpose packaging for dispensing prescription drugs?

A. Although this type of packaging is not prohibited, the CPSC staff discourages its use because it is likely to result in the use of non-special packaging. The potential for children being poisoned thus increases.

Q. What should I advise a consumer who calls for information when there is a suspected poisoning or childhood ingestion emergency?

A. If you are unable to provide the necessary emergency information for the caller or advise him or her as to the proper course of action, refer the caller to the Poison Control Center or nearest hospital emergency room. The national Poison Control Center phone number is 1-800-222-1222. This number should be on or near your telephone, along with those of the fire and police departments. It also would be prudent to suggest that the caller follow up with his/her physician.

Q. May I, as a hospital pharmacist, dispense a regulated drug in a conventional package for use by a patient in the hospital?

A. Yes, provided that the patient is confined in the hospital. Drugs dispensed for outpatient use must be packaged in accordance with the applicable regulations for special packaging.

Q. Our local hospital sometimes calls upon my pharmacy to provide drugs for patient use within the hospital. Must these drugs be dispensed in special packaging?

A. No, provided they are to be used for institutionalized patients. The test is whether the package is likely to enter a home.

Q. My pharmacy provides drugs to a nursing home. Must these drugs be dispensed in special packaging?

A. No, traditional nursing homes where the nursing home staff administers doses to residents are considered to be institutions. This would not be true of senior citizen apartment complexes or assisted living facilities where residents store their drugs in their households. The test is whether the package is likely to enter a home.

Q. I know of several physicians who dispense prescription drugs for a fee. Are they subject to the provisions of the PPPA?

A. Yes. Physicians who dispense drugs (including drug samples), are, and always have been, subject to the regulations under the PPPA. It is important to note, however, that for the purpose of accommodating elderly and disabled consumers who have difficulty using special packaging, Section 4(b) of the PPPA gives medical practitioners the authority to specify conventional packaging for drugs they prescribe.

Q. How can a pharmacist or pharmacy determine if the prescription packages they use meet the special packaging standards?

A. The pharmacy should request special packaging test data from the manufacturer or supplier of the prescription packages. When ordering packaging, pharmacists should be aware that vials and closures from different manufacturers may not function properly when used together. Pharmacists are responsible for ensuring that the packages they use comply with the PPPA.

Manufacturers and Packagers

Q. What is the responsibility of manufacturers of prescription drugs subject to the PPPA?

A. If the manufacturer intends that the package of a particular oral prescription drug is to be dispensed directly to the patient by the pharmacist, the CPSC interprets the PPPA to require the manufacturer to market that drug in special packaging.[31] Such packages are readily recognizable for the most part and often only require relabeling by the pharmacists prior to dispensing. The pharmacist, however, bears the ultimate responsibility for repackaging the drug into special packaging if a manufacturer has failed to comply.[32]

Q. May the manufacturer supply to the pharmacist one size of a regulated prescription drug in a conventional package under Section 4 of the PPPA in the same manner as supplying a non-complying size for over-the-counter drugs?

A. There is no provision for a manufacturer or packager to market a single size of a prescription drug in noncomplying packaging as is the case for over-the-counter medications. Every unit of a prescription drug subject to the PPPA which is packaged by the manufacturer in a package intended to be dispensed to a consumer must be in special packaging. Regulated prescription drugs may be dispensed in non-special packaging only when the prescribing physician directs its use, or the purchaser requests noncomplying packaging. In those cases, the pharmacist would have to repackage the drug with a conventional, non-special package.

Q. Can a supplier of special packaging include an equal number of noncomplying closures with each carton of complying packaging shipped to pharmacies?

A. Yes.

Q. Does the drug manufacturer or packager have to test the packaging to determine if it complies with the PPPA standards?

A. The packages must meet the standards. Failure to meet the standards is a violation of federal law. Most packaging manufacturers will test their packaging to determine if it is complies.

Q. Is unit dose packaging considered to be child-resistant?

A. Any package that contains a substance regulated under the PPPA must meet the special packaging standards regardless of the package type. This includes unit dose packaging such as blisters or pouches. Unit dose packaging is popular for many drugs, especially OTC drugs. The package is evaluated using the same test methods; however, the definition of a package failure is different than that of a bottle/closure package. If a child opens or gains access to a bottle/closure package, it is counted as a failure for that package. However, a failure for unit dose packaging is defined as occurring when a child opens or gains access to more than eight individual units or the number of units representing a toxic amount, whichever is less. The level of child-resistance required of the unit packaging depends on the toxicity of the product in it. A unit package that is compliant for one drug may not be able to be used to package another more toxic drug.

The Regulatory Agency

Q. What role does the U.S. Consumer Product Safety Commission play in informing and educating the public in the use of, and need for, special packaging?

A. The Commission has issued news releases and other audio-visual material encouraging the use of special packaging. In addition, the CPSC is the Secretary of the Poison Prevention Week Council and plays an important role in Poison Prevention Week each year.

Q. What role does the Commission play in the professional education of health care personnel with respect to the special packaging program?

A. The CPSC staff interacts with the State Boards of Pharmacy. CPSC personnel participate in meetings with pharmaceutical, medical, and packaging groups and prepare articles for publication in their journals. One of the areas where the CPSC staff has been particularly active has been in encouraging pharmacists to demonstrate special package usage to their customers who need help with the proper method of opening and closing a special package.

Q. Precisely what does the term "special packaging" mean?

A. Congress defined the term special packaging in the PPPA. The term "special packaging" means packaging that is designed or constructed to be significantly difficult for children under 5 years of age to open or obtain a toxic or harmful amount of the substance within a reasonable time and not difficult for normal adults to use properly. However, "special packaging" does not mean packaging which all such children cannot open or obtain a toxic or harmful amount within a reasonable time. Normal adults are regarded as those with no overt physical handicaps, which would preclude their manipulating the package. To meet PPPA standards, all children need not be prevented from gaining access to the regulated product. This is why the packaging is called child-resistant and not childproof. Further, all adults need not be able to gain entry into the package. The PPPA does not allow the CPSC to mandate package designs. These stipulations were included in the legislation so that industrial ingenuity would not be stifled.

Q. What is the basis for determining which products will be covered by the PPPA?

A. The Commission must establish a relationship between a particular household substance (because of the way it is packaged) and the potential for serious injury or illness to young children as a result of ingesting, handling, or using that substance. Some substances do not lend themselves to this requirement. Ingestion of a product by children does not automatically result in the need for special packaging. For example, many soaps and detergents are frequently ingested but do not cause serious injury or illness to children. Alternatively, it is not necessary to document serious injury to children for the Commission to require special packaging of a toxic product.

Q. Suppose a pharmacist dispenses a prescription drug in a conventional package. What is the CPSC's position?

A. The law requires that the pharmacist dispense regulated drugs in special packaging. The only exceptions are those instances when the consumer or prescribing physician stipulates that a noncomplying package be used. Pharmacists who violate the regulations may be criminally prosecuted. Individuals may be sentenced to 1 year imprisonment and fined up to $250,000. Organizations may be fined up to $500,000. The Commission could also seek court orders enjoining violators or authorizing seizure of noncomplying products supplied by manufacturers in consumer packages.

Q. What is the basis for selecting the noncomplying package, which the law

permits for over-the-counter drugs, regulated under the PPPA?

A. The manufacturer may select one of its package sizes as its noncomplying package so long as it also supplies the product in popular size packages, which comply with the PPPA standards.

The Commission may require a manufacturer to use only special packaging if the manufacturer has not supplied the product in popular size packages which comply with the standards and the Commission finds, after the opportunity for a hearing, that the exclusive use of special packaging is necessary to accomplish the child protection intended by the PPPA.

Q. The FDA requires tamper-evident packaging for over-the-counter drugs. Does this replace the requirement for special packaging?

A. No, the two systems are independent of one another. Although there are some special packages which are also tamper-evident (blisters, unit-of-use), a tamper-evident package is not necessarily child-resistant. The FDA requires that evidence of tampering be visually determined on initial contact.[33] Special packages must meet specific performance standards. These include maintaining their child-resistance for the number of openings and closings customary for the life of the product.

Q. What types of special packaging have been approved by the Commission for use with prescription drugs and other regulated household substances?

A. The Commission does not approve or certify special packaging. In fact, the PPPA itself specifically prohibits the Commission from prescribing specific package designs, product content, package quantity, and, with the exception of appropriate labeling for allowable single, noncomplying package sizes, labeling. The ultimate determination of whether a particular package complies with the standards is the responsibility of the manufacturer. The Commission assesses compliance on the basis of human performance tests.

Q. What should a pharmacist or physician do if they know or suspect that PPPA regulations are being violated?

A. Contact CPSC Headquarters either by phone, letter, or e-mail. The CPSC operates a toll-free hotline at (800) 638-2772. However, we recommend that you contact the Office of Compliance directly by phone at 301-504-7913, via fax at 301-504-0359, or via e-mail at sect15@cpsc.gov. CPSC staff will review the complaint and take appropriate action as warranted.

Q. Can a State or other political subdivision establish packaging regulations that are more stringent than those promulgated by the CPSC?

A. No. With certain narrow exceptions, they must be identical. However, a State may require child-resistant packaging of a substance not regulated by CPSC.

Q. Can a State or other political subdivision establish packaging regulations that are less stringent than those promulgated by the CPSC?

A. No.

Endnotes

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[25]PPPA, op. cit., Sec. 4; 15 U.S.C. 1473.

[26]Code of Federal Regulations, 16 CFR § 1500.17 (a)(4).

[27]PPPA, op. cit., Sec. 4; 15 U.S.C. 1473

[28]16 CFR § 1702.

[29]16 CFR § 1700.14(a)(10)(i)-(xx)

[30]38 FR 9431, April 16, 1973.

[31]16 CFR § 1701.1(b)

[32]16 CFR § 1701.1(d)

[33]21 CFR § 211.132