



Expanding the Use of Child-Resistant Packaging

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With more countries evaluating child-resistant (CR) packaging standards and related testing protocols, harmonization may be at hand.

With several national and international groups working on standards and regulations for child-resistant (CR) packaging, its use for drug products is broadening and is hoped to become more harmonized worldwide. By expanding the use of this final barrier to potentially toxic products, more children can be saved from traumatic experiences, injury, and death.

However, less-positive effects of increased use may include challenges for sight- and dexterity-impaired adults who reportedly have difficulty opening CR packaging. Furthermore, changes in CR packaging requirements can mean more compliance issues for drug companies and, in some cases, may necessitate the time-consuming and costly process of package redesign and retesting.

During the past 12 months, considerable activity has occurred both in the United States and abroad that is related to using CR packaging for certain pharmaceutical products. In

December 2001, the British Standards Institute published *BS 8404:2001, Packaging — Child-Resistant Packaging — Requirements and Testing Procedures for Nonreclosable Packages for Pharmaceutical Products*. The standard specifies a testing protocol, using child and adult test groups, for non-reclosable drug packages such as blister cards or strip packs. The protocol is based on a draft European Standard being prepared by a technical committee of the European Committee for Standardization (CEN), which works to promote volunteer harmonization in Europe. If passed, the draft standard, CEN/TC 261, Packaging, may supercede BS 8404:2001.

Noting that “child-resistant packaging cannot be a substitute for other safety measures,” *BS 8404:2001* warns that “CR packaging is only the last in a series of protective measures and does not release parents or guardians from their duty to keep medicinal products out of the reach of

children.” Like its US and German counterparts, *BS 8404:2001* does require that a CR package be “capable of providing a satisfactory degree of resistance to opening by children and a satisfactory level of accessibility to its contents by adults.” Thus, both child and adult test panels are specified.

Each child panel must consist of as many as 200 children between 42 and 51 months of age and be divided equally between boys and girls. Each adult group must contain 100 individuals between 50 and 70 years of age who are capable of reading and have no disabilities that might affect dexterity. Of the participants, 25 each are drawn from the 50–54 and 55–59 age groups; the remaining 50 are drawn from the 60–70 age group. The male–female ratio of each group is 30:70.

Various tests have been designed for the test panels. The children’s test consists of dividing the group into pairs and giving each pair an unprinted primary package to open. If the package has not been breached within 5 minutes, a supervisor silently demonstrates how to open the package, and the children are given another 5 minutes to gain access. Results are charted sequentially and could be completed with as few as 27 subjects if no child gains access within 10 minutes.

The adult test consists of each subject receiving a package, any associated opening tools that would be supplied with the product, written instructions if applicable, and 5 minutes to study and open the package. If the subject successfully opens the package, a second package is provided with instructions to open it as quickly as possible (within 1 minute).

If in the course of the children’s test all 200 participants are tested, the package is considered to pass if at least 85% of the children are unable to access more than a total of eight units in the first 5 minutes, and at least 80% are unable to access more than eight units in 10 minutes. For the package to pass the adult-panel test, at least 90% of the subjects must be able to access at least one unit within 1 minute. Such accessibility standards for both child and adult panels must be met for the package to be considered an acceptable CR design.

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An effective date for the *BS 8404:2001* testing protocol is at least two years away. The United Kingdom's Medicines Control Agency first must prepare draft legislation for presentation to Parliament, and Parliament then must vote in favor of it. Details that must be determined include what products would be obligated to meet the CR protection standard as well as an effective date that would give the industry sufficient time to test CR packaging alternatives for affected products. This likely would be accomplished in a period of 12–24 months. Once Parliament passes the legislation, it would be submitted to the European Union in Brussels for approval, a process that can take as long as six months.

A range of products would fall under *BS 8404:2001*. For example, because reclosable CR packaging regulations in the United Kingdom apply to aspirin and paracetamol (acetaminophen) products, these two drug families may be included in nonreclosable CR packaging requirements. Iron-containing products also may be scrutinized because ingestion of iron-sulfate tablets that were in non-CR blister packaging resulted in the well-publicized death of a toddler about two years ago. The incident provided the impetus for the development of the *BS 8404:2001* standard.

The adjoining issue of harmonization is significant for global pharmaceutical companies. National CR packaging requirements differ among countries with such rules, including the United States, the United Kingdom, Italy, Germany, Holland, Canada, and the Republic of Ireland. One of the major differences is whether the testing takes product toxicity into account. Germany's *DIN 55 559*, a CR standard for nonreusable drug packaging, and US rules do; however, *BS 8404:2001* does not.

Efforts toward harmonization are moving forward slowly. Colin Scaife, convener of the European Standards Working Group and managing partner of a packaging consultancy, CE Packaging Partnership (Cottingham, England), predicted that a European (CEN) standard likely will be published in 2003. Once the standard is published, Member States will comment, and the draft may be amended. Upon approval, the directive and an implementation date will be issued.

An International Standards Working Group also is busy drafting an ISO stan-

dard, which is expected to resemble the CEN standard (the two committees share many members). Even after European and international standards are in place, specification of which products require CR packaging likely will remain a national decision.

In the United States, the Consumer Product Safety Commission (CPSC, Washington, DC) issues and enforces regulations regarding CR packaging. Recent rulemaking has focused on CR packaging for products switching from prescription to over-the-counter (OTC) status and products containing low-viscosity hydrocarbons.

For OTC-switch products, CR packaging requirements apply to any product for which the application for OTC status was made to FDA after 29 January 2002. Exempt are products for which the sole prescription-only active ingredient is part of an OTC-switch application made before 29 January 2002, according to a 21 December 2001 *Federal Register* clarification to the final rule published on 2 August 2001.

Products such as certain topical lotions that contain low-viscosity hydrocarbons must be in CR packaging by 25 October 2002. This CPSC rule applies to products that contain 10% or more hydrocarbons by weight and have a viscosity of <100 Saybolt University Seconds at 100 °F. Excluded are products that are packaged in aerosol containers and those with mechanical pumps and trigger sprayers, as long as the spray mechanism either is permanently attached to the container or has a CR attachment. Products that do not contain free-flowing contents (fluid-soaked pads) also are exempt.

For clinical trials packaging, CPSC Compliance Officer Geri Niebauer (now Smith) clarified in a 22 June 2000 letter that clinical-trial products dispensed on an outpatient basis "must comply with CR packaging requirements if they are subject to one or more of the other regulations issued under the Poison Prevention Packaging Act." According to 16 *CFR* 1700.14(a), clinical-trials packaging would have to be CR if the products were classified as oral prescription drugs and/or contain ingredients such as aspirin, methyl salicylate, controlled drugs, iron, acetaminophen, diphenhydramine, ibuprofen, loperamide, lidocaine, dibucaine, naproxen, ketoprofen, fluoride, and minoxidil. CPSC

allows a 24-month phase-in compliance period, which will expire on 23 May 2002. Immediately thereafter, packages of all toxic oral drugs intended for human use and dispensed for household use in Phase II, III, or IV clinical trials must be CR. It should be noted, however, that clinical-trial packaging requirements are based on drug toxicity. "Non-CR packaging may be used if the amount of drug that is dispensed into the household will not cause serious injury or illness to a young child," according to the Niebauer (Smith) letter.

Physician-dispensed samples present a different story. If the sample contains a substance regulated under 16 *CFR* 1700.14(a), then it must be in CR packaging. However, the Poison Prevention Packaging Act includes a provision that permits patients to request non-CR packaging or doctors to specify non-CR packaging when writing a prescription. With that in mind, the CPSC currently takes the position that because the doctor is dispensing the sample, it is "up to the physician to determine whether the sample should be in CR packaging," says Compliance Officer Smith.

However, Smith also added that the CPSC's position is subject to change. If poisoning incidents related to physician samples rose to a level that caused concern, the agency undoubtedly would revisit the subject. In fact, the CPSC currently is collecting data related to physician-dispensed samples, but interpreting the data is complicated. Although statistics generally identify the drug involved in poisoning incidents, the data frequently don't specify whether a product was accessed from a sample or a prescription.

Alternatively, many pharmaceutical companies opt to package their physician-dispensed samples in CR packaging as a matter of course. This practice provides a safety measure when doctors are not aware of their responsibility in determining the appropriateness of non-CR packaging for a particular patient.

With international CR packaging standards on the horizon, children worldwide will be better protected from accidental ingestion of toxic drugs, and global pharmaceutical companies will benefit from more-harmonized requirements. **PT**