Child-Resistant Packaging Statements in Drug Product Labeling

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document contact (CDER) Richard Lostritto 301-796-1697 or (CBER) Office of Communication, Outreach and Development at 1-800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
August 2017
Labeling

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Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
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Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Room 3128
Silver Spring, MD 20993
Phone: 800-835-4709 or 240-402-8010
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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not create any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance is intended to assist applicants, manufacturers, packagers, and distributors (collectively referred to as firms) who choose to include child-resistant packaging (CRP) statements in their drug product[2] labeling. The guidance discusses what information should be included to support CRP statements in labeling for new drug applications (NDAs), abbreviated new drug applications (ANDAs), biologic license applications (BLAs), and supplements to these applications. In addition to recommendations for labeling of prescription drug products, this guidance also includes recommendations for labeling both for nonprescription drug products[3] approved under an NDA or ANDA and those that are marketed under the Over-the-Counter (OTC) Drug Review. This guidance is intended to help ensure that such labeling is clear, useful, informative, and, to the extent possible, consistent in content and format.[4]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research at the Food and Drug Administration.

[2] References to drugs and biological products include drugs approved under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C) and biological products licensed under section 351 of the Public Health Service Act (PHSA) that are drugs. For the purposes of this guidance, *drug product* or *drug* will be used to refer to human prescription drug and biological products that are regulated as drugs.

[3] For the purposes of this guidance, the term nonprescription drug products refers to over-the-counter (OTC) drug products.

[4] This guidance is intended to apply to FDA-regulated drug products that bear CRP statements, regardless of whether CRP is required for such products under 16 CFR 1700. For example, bulk packages of prescription drugs that are shipped to pharmacies for repackaging by a pharmacist are not required to utilize CRP, but a firm may nevertheless choose to use CRP (and a CRP statement) for such drugs. 16 CFR 1701.1.

II. DISCUSSION

In 1970, the Poison Prevention Packaging Act (PPPA) was enacted to protect children (under 5 years of age) from unintentional exposure to household substances including food, drugs, and cosmetics.[5] Under the Federal Food, Drug, and Cosmetic Act (FD&C Act), a drug that has packaging or labeling that is in violation of a regulation issued pursuant to section 3 or 4 of the PPPA is deemed to be misbranded.[6] FDA was responsible for enforcing the PPPA until 1973, when jurisdiction was transferred to the U.S. Consumer Product Safety Commission (CPSC).[7] Because of FDA's authority to regulate labeling for prescription and nonprescription drug products, if firms choose to make statements in their labeling for such products about child-resistant packaging, such statements must comply with FDA's statutory and regulatory requirements.[8]

CPSC's regulations list "special packaging standards"[9,10] (also referred to herein as child-resistant packaging, or CRP) for a wide range of household products, including most oral prescription drugs and many nonprescription drug products.[11] There are different ways to make packaging child-resistant, with the most common forms being a child-resistant closure (e.g., a "safety cap") and certain unit-dose blister packaging (e.g., puncture-resistant and peel-push blisters). However, not all container closures (i.e., packaging components that contain and protect drug products), including unit of use packaging, are child-resistant. Further, "child-resistant" should not be equated with "child-proof," because CRP is not designed to completely eliminate the possibility of an accidental pediatric ingestion. It can only impede access to harmful products.

Child-resistant packaging is regarded as an important public health safety tool for avoiding harmful outcomes related to unsupervised pediatric ingestions.[12] However, the use of the child-resistant packaging is also recognized by public health experts as only one component of preventing these events. Public health campaigns emphasize the need for consumer education on safe storage practices for medications.[13] When medications are stored in reach and sight of children, children are able to gain access to and defeat the child-resistant closure in some instances, thereby reducing the effectiveness of the packaging measure. Therefore, FDA

[5] Poison Prevention Packaging Act of 1970 (PPPA), (Pub. L. 91-601, 84 Stat. 1670-74), enacted December 30, 1970.
[6] See FD&C Act, § 502(p).
[7] Consumer Product Safety Act, Public Law 92-573; 86 Stat. 1207, October 27, 1972, Sec. 30.
[8] See, e.g., FD&C Act § 502(a), (c).
[9] See definitions in section 2 (4) of the PPPA.
[10] *Special packaging* and *child-resistant packaging* (CRP) are used interchangeably in this guidance.
[11] See 16 CFR 1700 for substances requiring special packaging and the relevant packaging standards and testing procedures.
[12] Early studies in the 1960s demonstrated nearly a tenfold reduction in unsupervised pediatric ingestions with medicines with special packaging distributed from the Fort Lewis-McChord Air Force Base in Washington. Subsequent research on effectiveness has been published, and in 2005 CPSC estimated that special packaging has saved the lives of more than a thousand children. See http://www.cpsc.gov/en/Regulations-Laws--Standards/Statutes/Poison-Prevention-Packaging-Act/.
[13] As an example, see the Up and Away Campaign led by the Centers for Disease Control at www.upandaway.org.

advocates that all drugs, irrespective of the type of packaging, be stored safely out of reach and sight of children to further the overall public health efforts to address this safety issue.

FDA regulates certain aspects of drug products' container closure systems related to safety and efficacy as part of the drug application review and approval process.[14,15] During FDA's review of an NDA, ANDA, or BLA (and nonprescription drugs marketed under an application), various data related to container closure systems are evaluated, including, for example, the type of closure employed, the stability of the product in the container closure system, and whether the closure design is suitable for the product. FDA's review does not include evaluation of testing reports to determine whether a product meets the applicable standards for special packaging set forth in the PPPA and its implementing regulations.

With respect to nonprescription drug products marketed under the OTC Drug Review, FDA does not review data related to container closure systems, as applications for individual drug products under the OTC Drug Review are not submitted to FDA for review or approval. In addition, although manufacturers of nonprescription products marketed under the OTC Drug Review must comply with the labeling requirements under 21 CFR 201.66, they are not required to submit labeling to FDA prior to marketing. In this guidance, we recommend text[16] that may be appropriate to consider when including CRP statements on the containers and packaging of products marketed under the OTC Drug Review.

III. LABELING

Because healthcare professionals and consumers may not be able to determine on visual inspection whether packaging is child-resistant, a labeling statement may help to identify this attribute. As a general matter, if a drug product is packaged using CRP and the firm elects to include labeling statements that identify the product as packaged with CRP, the CRP should be described using words and not abbreviations (e.g., "CRP," "CRC," or "CR") or symbols because abbreviations and symbols may not be readily understood. Because it is important to clarify that CRP statements in labeling describe how the product is supplied from the manufacturer, versus how the product is dispensed by a pharmacist, the term "supplied" as opposed to "available" is preferred.

Section 502(a) of the FD&C Act provides that a drug is deemed to be misbranded if its labeling is false or misleading in any particular. In general, to ensure that CRP statements on labeling are not false or misleading, such statements should only be used when the drug product packaging

[14] FDA does not regulate retail pharmacy vials or other containers used by pharmacies to repackage drugs to dispense to patients.

[15] See FDA guidance for industry *Container Closure Systems for Packaging Human Drugs and Biologics*. This guidance is available on the Internet at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm under Guidances (Drugs).

[16] See section III. B.

has been shown to comply with the applicable CPSC regulatory standards and test procedures for CRP.[17,18]

We provide additional recommendations for the labeling of prescription drug products and nonprescription drug products below.

A. Prescription Drug Products

1. Prescribing Information

If a firm chooses to include information about CRP in the prescribing information, such information should appear in the HOW SUPPLIED/STORAGE AND HANDLING section as this is generally where practitioners look to ascertain information about a product's packaging. It is important that the CRP statements be linked clearly to a particular package, especially when multiple packages are supplied and not all have been demonstrated to be child-resistant.

Examples include the following:

HOW SUPPLIED/STORAGE AND HANDLING

- Drug X is supplied in 30 g, 4 oz. tubes with a child-resistant cap.

- Drug X is supplied as child-resistant sachets.

- The 50 mg tablet is film-coated, round, biconvex, pink, scored, and is debossed with XXX on one side and scored on the other side.
  Bottles of 30 with child-resistant closure, NDC xxxx-xxx-xx
  Bottles of 60 with child-resistant closure, NDC xxxx-xxx-xx
  Bottles of 500, NDC xxxx-xxx-xx"

2. Patient Information

If a firm chooses to include information about CRP for a prescription drug product whose commercial container bearing the CRP is designed to be dispensed directly to patients, the CRP information should be included in the patient labeling (e.g., medication guides, patient package

[17] See 16 CFR 1700.15 for poison prevention packaging standards and 16 CFR 1700.20 for special packaging testing procedures. In order to make household substances that are subject to the PPPA's special packaging requirements readily available to elderly or handicapped persons who are unable to use those substances in special packaging, section 4(a) of the PPPA authorizes manufacturers and packers to package such substances in non-complying packaging of a single size provided that: 1) complying packaging is also supplied, and 2) the non-complying packages are conspicuously labeled to indicate that they should not be used in households where young children are present. In order to comply with CPSC regulations, any non-complying packages a firm elects to market pursuant to section 4(a) of the PPPA must bear the labeling described in 16 CFR 1700.5.

[18] We note that if a product is subject to the special packaging requirements of the PPPA, but its packaging or labeling is in violation of applicable regulations issued pursuant to section 3 or 4 of the PPPA, it may also be misbranded under section 502(p) of the FD&C Act.

inserts). Information about the CRP in patient labeling should appear under a heading titled "How should I store Drug X?" The description should be consistent with the CRP statement(s) included in the HOW SUPPLIED/STORAGE AND HANDLING section of the full prescribing information.

Examples of the CRP description on the patient labeling include the following:

How should I store Drug X?

- Drug X comes in a child-resistant package.

- Drug X comes in a sealed child-resistant foil pouch.

The following statement should also appear at the end of the "How should I store Drug X?' section:

- Keep Drug X and all medicines out of the reach of children.

3. Carton Labeling and Container Labels

If a firm chooses to include information about the CRP on carton labeling and container labels, it may do so as long as there is sufficient space to include such information in addition to information required to be included.[19] If space permits, a firm may also include a storage statement in conjunction with the CRP statement to recommend that the package be kept out of reach of children, particularly for those packages which may be dispensed directly to patients. Statements about CRP are most appropriately displayed on the side panels of the carton labeling and container labels in close proximity to storage information.

Examples include the following:

- This package is child-resistant. Store at 20°C-25°C (68°F-77°F); excursions permitted to 15°C-30°C (59°F-66°F).

- This package is child-resistant. **Keep out of reach of children**. Store at 20°C-25°C (68°F-77°F); excursions permitted to 15°C-30°C (59°F-66°F).

B. Nonprescription Drug Products

1. Drug Facts Labeling

FDA regulations do not specify where to place CRP statements on labeling for nonprescription drug products. If firms choose to include the statement in the drug facts labeling (DFL), it

[19] If the container label is too small, see 21 CFR 201.10(i).

should appear under the subheading "Other information" with the storage statement.[20] Placement of CRP statements on the labeling must not interfere with required information on the labeling.[21]

"Other information" is the subheading used for additional information that is not included under the other DFL subheadings, but which is required or is made optional under an OTC drug monograph(s), other nonprescription drug regulation(s), approved drug application, statute, or guidance. A CRP statement would be considered to be "additional information"[22] and as such would follow any required statements.

The following examples illustrate types of information considered to be "other information," including a CRP statement:

- Read the directions and warnings before use.
- Keep the carton. It contains important information.
- This package is child-resistant.
- Store at 20-25°C (68-77°F) and protect from moisture.

2. Carton Labeling and Container Labels

Even if the CRP statement(s) are included in the DFL, their placement on the carton labeling and/or container labeling outside the DFL is still optional. And, if the CRP statement is not included in the DFL, it is still permissible to include a CRP statement(s) on the carton labeling and/or the container labeling outside the DFL, space permitting.[23] Appropriate text could read "this package is child-resistant." For small containers and/or cartons, appropriate text could read "child-resistant package." Although any available panel or part of a panel, outside the DFL, is appropriate for this use, consumers may find this information to be more useful if displayed on the principal display panel(s).

IV. PROCESS FOR INCLUDING STATEMENTS REGARDING CRP ON THE LABELING

If firms choose to include CRP statements on their product labeling, they should verify in writing for FDA that the CRP meets the standards set forth by the CPSC in 16 CFR 1700, as applicable, as discussed below.[24,25] FDA also recommends that firms retain the data demonstrating that the packaging meets applicable CPSC standards.

[20] See § 201.66(c)(7).
[21] See FD&C Act § 502(c).
[22] See § 201.66(c)(7)(iii).
[23] In such circumstances, we encourage applicants to discuss their plans with FDA.
[24] The written verification discussed in this guidance is intended for FDA only, and is separate from the certification required to be provided to CPSC under 15 USC 2063 and 16 CFR 1110.
[25] Firms should provide such written verification to FDA to support CRP statements even in circumstances where they have elected to use CRP for products that are not subject to the special packaging requirements of 16 CFR 1700.

A. Prescription Drug Products and Nonprescription Drug Products Approved Under an Application

1. Original NDA, BLA, or ANDA submission

In an original NDA, BLA, or ANDA submission, written verification that the CRP meets the CPSC's standards under 16 CFR 1700 should appear in the container closure section of Module 3 of the Electronic Common Technical Document (eCTD). An example of the written verification may be "We verify in this submission that the following package (or packages) meet CPSC's standards under 16 CFR 1700."

2. Postapproval Change

If there is a postapproval change to the package or labeling of a product approved under an NDA, BLA, or ANDA, refer to appropriate regulations and guidances to determine the appropriate pathway to implement these changes.[26] Submissions for changes to add CRP statements on labeling should verify in writing that the CRP meets the CPSC's standards under 16 CFR 1700 and should appear in the detailed container closure description section of Module 3 in the eCTD. An example of the written verification may be "We verify in this submission that the following package (or packages) meet CPSC's standards under 16 CFR 1700."

B. Nonprescription Drug Products Marketed Under the OTC Drug Review

There is no defined process for submission of a written verification to FDA that a nonprescription drug product marketed under an OTC monograph meets CPSC's standards under 16 CFR 1700. However, if you elect to include a CRP statement on the labeling of a nonprescription drug product marketed under an OTC monograph, you should retain the data demonstrating that the packaging meets applicable CPSC standards and follow the labeling recommendations in this guidance.

[26] See 21 CFR 314.70 and 601.12 for reporting requirements for changes to approved applications for drug products and licensed biological products.