Guidance for Industry

Toll-Free Number Labeling and Related Requirements for Over-the-Counter and Prescription Drugs Marketed With Approved Applications

Small Entity Compliance Guide

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

June 2012
Procedural

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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance is intended to help small businesses better understand and comply with FDA's final rule regarding labeling of drugs with a toll-free number for adverse event reporting, which was published in the *Federal Register* on October 28, 2008 (73 FR 63886). The Food and Drug Administration (FDA) has prepared this guidance in accordance with section 212 of the Small Business Regulatory Enforcement Fairness Act (Public Law 104-121).

FDA's guidance documents, including this guidance, 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.

II. BACKGROUND

FDA issued the toll-free number final rule (Final Rule) to comply with certain requirements of section 17 of the Best Pharmaceuticals for Children Act (BPCA), as amended by section 502(f) of the Food and Drug Administration Amendments Act of 2007 (FDAAA). The BPCA (Public Law 107-109) directed FDA to issue a final rule requiring the labeling of each human drug product for which an application is approved under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) to include (1) a toll-free number maintained by FDA for the purpose of receiving reports of adverse events regarding drugs and (2) a statement that the number is to be used for reporting purposes only, and not to receive medical advice.

The Final Rule became effective November 28, 2008, and requires that toll-free number labeling be:

(1) included in all FDA-approved Medication Guides for products approved under a New Drug Application (NDA) or an Abbreviated New Drug Application (ANDA) (i.e., approved under section 505),
(2) provided to patients by authorized dispensers or pharmacies with each prescription drug product approved under an NDA or ANDA (i.e., approved under section 505), and
(3) included in the labeling of certain over-the-counter (OTC) drugs approved under an NDA or ANDA (i.e., approved under section 505) (discussed in detail below).

FDA has previously issued a guidance for industry entitled *Medication Guides—Adding a Toll-Free Number for Reporting Adverse Events* (June 2009)[1] to assist new drug application holders with revising FDA-approved Medication Guides to comply with the first of these requirements. Persons interested in the Medication Guide requirements should refer to that guidance document; it will not be further discussed here.

This guidance is intended to assist small businesses and others with implementing the two other requirements in the Final Rule — distribution of toll-free number information to patients with each prescription (or refill), and adding toll-free number information to the labeling of certain OTC drugs.

III. DISTRIBUTION OF SIDE EFFECTS STATEMENT BY AUTHORIZED DISPENSERS AND PHARMACISTS

Under the toll-free number Final Rule, each authorized dispenser or pharmacy must distribute a "side effects statement" with each prescription drug product approved under section 505 of the FD&C Act that they dispense, including both new and refill prescriptions. "Side effects statement" is defined as the following verbatim statement: "Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088" (21 CFR 209.2).

A. Authorized Dispenser or Pharmacy

Under FDA regulations at 21 CFR 209.2, as amended by the Final Rule, an "authorized dispenser" means an individual licensed, registered, or otherwise permitted by the jurisdiction in which the individual practices to provide drug products on prescription in the course of professional practice, including licensed physicians and pharmacists. The Final Rule defines "pharmacy" as including, but not limited to, a retail, mail order, Internet, hospital, university, or clinic pharmacy, or a public health agency, that is regularly and lawfully engaged in dispensing prescription drugs. FDA regulations, as

[1] Available on the Internet at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances.

amended by the Final Rule, require any authorized dispenser providing a prescription drug that is approved under section 505 to a patient to provide the side effects statement with each new and refill prescription (21 CFR 209.11(a)).

B. Distribution of Side Effects Statement

The regulations require the dispenser to choose one or more of the following options to distribute the side effects statement (21 CFR 209.11(b)):

(1) Distribute the side effects statement on a sticker attached to the unit package, vial, or container of the drug product;
(2) Distribute the side effects statement on a preprinted pharmacy prescription vial cap;
(3) Distribute the side effects statement on a separate sheet of paper;
(4) Distribute the side effects statement as part of other consumer medication information (written information voluntarily provided to consumers by dispensing pharmacists as part of patient medication counseling activities); or
(5) Distribute an appropriate FDA-approved Medication Guide that contains the side effects statement.

FDA has received a number of questions about whether the regulations require the side effects statement to be provided to patients in situations where the authorized dispenser or pharmacy is located in a hospital, nursing home, or similar health care facility. As adopted by the Final Rule, 21 CFR 209.1 excludes from the requirements "authorized dispensers dispensing or administering prescription drug products to inpatients in a hospital or health care facility under an order of a licensed practitioner, or as part of supervised home health care." FDA's position is that when the drug is being administered in the presence of a trained health care provider, usually a single dose at a time, the requirement to provide the side effects statement does not apply. Generally, in such circumstances the patient is relying on the health care provider to monitor and report any adverse events. Such patients would also not ordinarily receive printed patient counseling information provided by most commercial pharmacies. For example, a nurse administering a single dose of medication at bedside to a patient in a nursing home wing of an independent living/nursing home facility would not be required to provide the side effects statement. Similarly, the regulations do not require providing a side effects statement each time a medication is administered to a patient by a home health care provider.

On the other hand, if the dispensary in the same independent living/nursing home facility fills a doctor's prescription for a 30-day supply of a medication for an independent living resident which the patient will self-administer (in her own apartment within or outside the facility), the Final Rule would require that the patient receive, along with the prescription, the side effects statement with instructions for reporting adverse events to FDA (in the same way as would a patient filling the prescription at a local pharmacy for home use).

The materials would need to be provided to these patients in one of the formats described in section III of this guidance.

IV. TOLL-FREE NUMBER LABEL STATEMENT REQUIREMENTS FOR OTC DRUGS

OTC drugs can be marketed under an application approved under section 505 of the FD&C Act, or without an approved application under an OTC monograph. Because the toll-free labeling requirements of the BPCA and the Final Rule apply only to drug products approved under section 505, under the terms of the FD&C Act, OTC drugs marketed under a monograph are subject to different labeling requirements. The differences in the requirements for application versus monograph OTC drugs are explained below.

A. OTC Drugs With Approved Applications Under Section 505

The toll-free number Final Rule requires OTC drugs with approved applications (NDAs or ANDAs) to comply with the toll-free labeling requirement in either of the following two ways: (1) by including on their packaging a toll-free number through which consumers can report complaints directly to the manufacturer or distributor, or (2) by including a specified label statement in the OTC drug facts format containing FDA's toll-free number for reporting adverse events (FDA's MedWatch telephone number). The label statement must be worded exactly as follows: "[Bullet] side effects occur. You may report side effects to FDA at 1-800-FDA-1088." 21 CFR 201.66(c)(5)(vii).[2] In other words, unless the drug's label contains a toll-free number for reporting adverse events directly to the manufacturer or distributor, the label must include the specified label statement including the 1-800-FDA-1088 number. If the label contains a toll-free number for reporting adverse events to the manufacturer or distributor, the specified label statement and FDA MedWatch phone number are not required.

B. OTC Drugs Marketed Under a Monograph

OTC drugs marketed under an OTC monograph and not under an approved application are not subject to the requirements of the toll-free labeling Final Rule. OTC monograph drugs are subject instead to different labeling requirements established under the Dietary Supplement and Nonprescription Drug Consumer Protection Act of 2006 (DSNDCPA) (Public Law 109-462). Section 2(d) of DSNDCPA added section 502(x) to the FD&C Act to require the label of an OTC drug marketed in the United States without an approved application to contain the domestic address or phone number at which the manufacturer or

[2] Under 21 CFR 201.66(c)(5)(vii), the information is placed in the warning section of the drug facts label.

other "responsible person"[3] may receive a report of a serious adverse event associated with the use of a drug product. In September 2009, FDA issued a guidance on these requirements entitled *Labeling of Nonprescription Human Drug Products Marketed Without an Approved Application as Required by the Dietary Supplement and Nonprescription Drug Consumer Protection Act: Questions and Answers*.[4] Persons interested in more information about that requirement should refer to that guidance.

C. Summary Table For OTC Products

The following table clarifies the type of OTC drug products affected by each statutory provision and answers specific questions about each of the requirements applicable to each category of drugs.

	Toll-Free Number Final Rule	**DSNDCPA and September 2009 Labeling Guidance**
To which OTC drug products does this initiative apply?	OTC products marketed under applications approved under section 505 of the FD&C Act (NDAs or ANDAs).	OTC drug products marketed without an approved application.
What must be on the drug product's label?	Unless the packaging includes a toll-free number through which consumers can report complaints to the manufacturer or distributor, the drug facts label must contain a statement in the content and format specified in 21 CFR 201.66(c)(5)(vii) that includes FDA's toll-free MedWatch telephone number.	The domestic address or phone number at which the manufacturer or other "responsible person" may receive a report of a serious adverse event associated with the use of a drug product.
What is the legislative origin of this initiative?	Best Pharmaceuticals for Children Act of 2001 (BPCA) and Food and Drug Administration Amendments Act of 2007 (FDAAA).	Dietary Supplement and Nonprescription Drug Consumer Protection Act of 2006 (DSNDCPA).
What is the effective date?	The toll-free number Final Rule became effective November 28, 2008.	The DSNDCPA requirements became effective December 22, 2007.

[3] "Responsible person" is defined in the DSNDCPA as "The manufacturer, packer, or distributor whose name (pursuant to section 502(b)(1)) appears on the label of a nonprescription drug marketed in the United States" (section 760(b)(1)).

[4] Available on the Internet at Available on the Internet at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances.