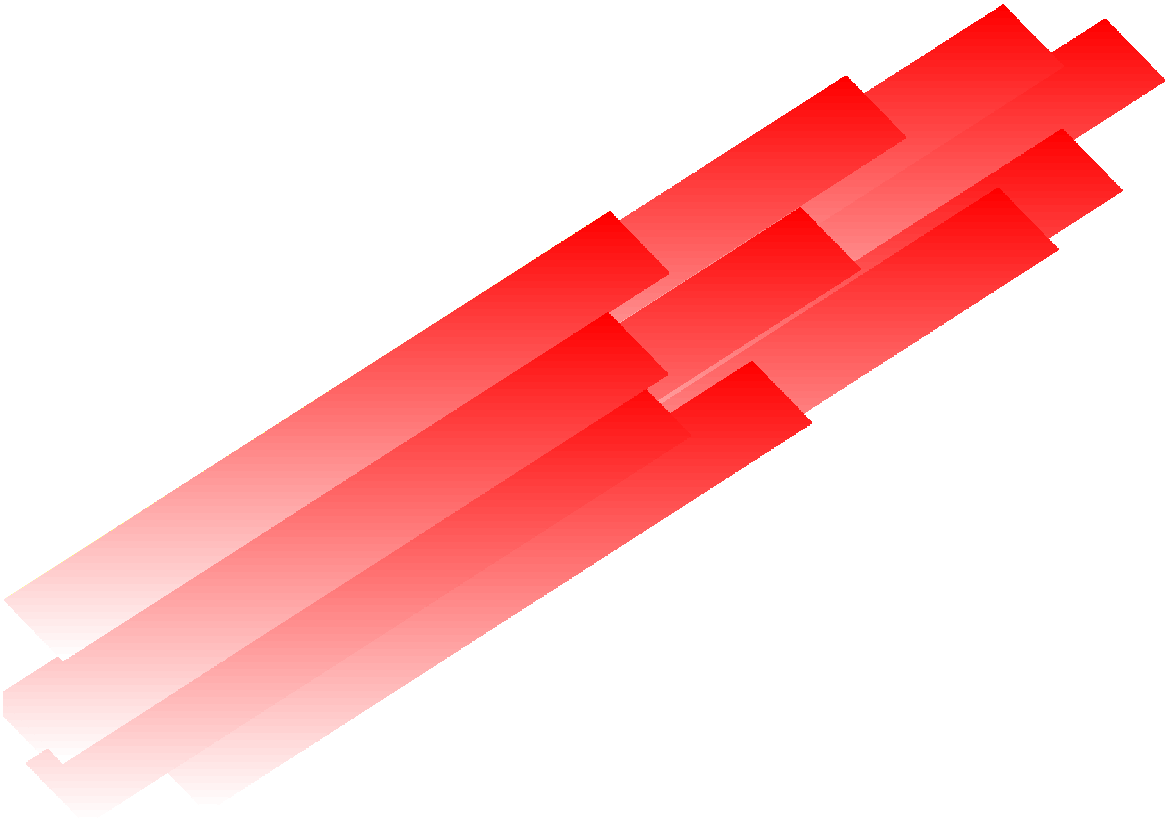
Guidance for Industry

Implementation of Section 126 of the Food and Drug Administration Modernization Act of 1997 — Elimination of Certain Labeling Requirements



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)

Procedural Guidance #3

Revised, July 1998

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(Fax) 888-CBERFAX or 301-827-3844
(Voice Information) 800-835-4709 or 301-827-1800

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GUIDANCE FOR INDUSTRY[1]

Implementation of Section 126 of the Food and Drug Administration Modernization Act of 1997 — Elimination of Certain Labeling Requirements

I. INTRODUCTION

Section 126 of Title I of the Food and Drug Administration Modernization Act of 1997 (Modernization Act), signed into law by President Clinton on November 21, 1997, amends section 503(b)(4) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 353(b)(4)) to require, at a minimum, that prior to dispensing, the label of prescription products contain the symbol "Rx only." In addition, section 502(d) of the Act (21 U.S.C. 352(d)), which required the labels of certain habit-forming drugs to bear the statement "Warning-May be habit forming," is repealed. The amendments to section 503(b)(4) and the repeal of 502(d) of the Act became effective February 19, 1998.

This guidance has been revised to extend the time period during which FDA does not intend to object if a sponsor has not yet implemented the labeling changes required by section 126 of the Modernization Act, and to answer certain frequently asked questions.

II. DISCUSSION

Prior to the enactment of the Modernization Act, section 503(b)(4) of the Act stated that a prescription drug product would be deemed to be misbranded if, at any time prior to dispensing, its label fails to bear the statement "Caution: Federal law prohibits dispensing without prescription." In addition, section 502(d) of the Act required the labels of certain habit-forming drugs to bear the statement "Warning-May be habit forming."

The amendment of section 503(b)(4) and repeal of section 502(d) in section 126 of the Modernization Act affect drug labels and labeling requirements in the following ways:

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[1]This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) in consultation with the Center for Biologics Evaluation and Research at the Food and Drug Administration (FDA). This guidance represents the Agency's current thinking on implementation of elimination of certain labeling requirements. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

1. Prior to dispensing, the label of prescription drugs must bear, at a minimum, the symbol "Rx only" (see, e.g., 21 CFR 201.100(b)(1), 201.120, 201.122, 610.60(a)(6), 610.61(s) and 606.121(c)(8)(i), which the Agency intends to amend). It was the intent of the Agency and Congress to simplify the labeling requirements in that the "Rx only" statement would replace the "Caution: Federal law prohibits...." statement. The new label statement may be printed as "Rx only" or "℞ only."

2. The Agency intends to revoke 21 CFR 329.10 labeling requirements for habit-forming drugs.

III. FDA POLICY

To minimize the burden faced by sponsors dealing with a variety of labeling changes, FDA advises that for the time periods stated below, in the exercise of its enforcement discretion, the agency does not intend to object if a sponsor does not comply with the new labeling requirements of section 503(b)(4) and 502(d) of the Act, as amended by the Modernization Act, under the following circumstances:

1. For currently approved products, the sponsor implements the new requirements of section 126 of the Modernization Act at the time of next revision of its labels, or by February 19, 2003 (5 years from the effective date of the Modernization Act), whichever comes first, and reports these minor changes in the next annual report in accordance with 21 CFR 314.70(d)(3) or 601.12(f)(3).

2. For pending (unapproved) full or abbreviated applications received by the Agency prior to February 19, 1998, the sponsor implements the new requirements of section 126 of the Modernization Act at the time of next revision of its labels or by February 19, 2003, whichever comes first, and reports these minor changes in the next annual report in accordance with 21 CFR 314.70(d)(3) or 601.12(f)(3).

Full or abbreviated applications, including unapproved original and supplemental applications, received by the Agency after February 19, 1998, should provide labels and labeling in compliance with the amendments.

IV. FREQUENTLY ASKED QUESTIONS

Since the passage of the Modernization Act, the Agency has received numerous calls raising questions about certain aspects of implementation. The following represents some of the questions received and advice provided:

1. What was the genesis of these two changes to the Federal Food, Drug, and Cosmetic Act?

In November of 1991, a joint USP/FDA Advisory Panel on Simplification and Improvement of Injection Labeling made several recommendations to simplify the labeling requirements for parenteral drug products. This was in response to concerns about deaths and injuries from accidental misuse of injectable products because of overcrowded labels. These recommendations may be found in the *Pharmacopeial Forum,* Volume 20, Number 4, pages 7885-7888. In addition, the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) identified a series of recommendations that, when implemented, could help to reduce the incidence of medication errors in which product labeling and package design had been identified as a contributing factor. The recommendations of NCC MERP included the changes in section 126 of the Modernization Act and broadened the recommendations to all dosage forms. These recommendations were supported by the sixteen NCC MERP member organizations comprising medicine, pharmacy, nursing, industry, government, health care facilities, and standard-setters.

2. Does the original "Caution: Federal law...." statement satisfy the new statutory requirement?

The previous requirement that the "Caution: Federal law...." statement appear on the label is no longer in the Federal Food, Drug, and Cosmetic Act. The new requirement under section 126 of the Modernization Act provides that the label shall bear "at a minimum, the symbol 'Rx only.'" Since the "Caution: Federal law...." statement does not include the symbol "Rx only," it would not satisfy the new statutory requirement. Although it would be legally permissible to include BOTH statements on the label, the Agency believes that in the interests of simplification, it would be preferable to have only the "Rx only" statement.

3. What prominence (e.g., font size, capital letters, bold print) does the Agency want the "Rx only" statement to have? Where should it appear?

The statement should be prominent and conspicuous, as is required by section 502(c) of the Act and 21 CFR 201.15. If space permits, the Agency prefers that the statement appear on the main panel of container labels and carton labeling. The "Rx only" statement is not required for package insert labeling. However, if a manufacturer chooses to include

the statement, the Agency prefers that it be placed in the TITLE section of the package insert.

4. Do we have to include the quotation marks that surround the "Rx only" statement? In addition, does the word "only" have to be in lower case letters?

Manufacturers may exercise discretion as to whether to include the quotation marks and whether the word "only" appears in upper or lower case letters.

5. How does section 126 of the Modernization Act affect the labels of veterinary products, medical devices, bulk drugs, and drugs used for compounding?

Section 126 does not affect the labels of veterinary products or medical devices. For bulk drugs and drugs used for compounding, FDA does not intend to object if a sponsor implements the new requirements of section 126 of the Modernization Act at the time of next revision of its labels, or by February 19, 2003, whichever comes first.

6. Does the implementation date, cited above, mean that products remaining in the marketplace after February 19, 2003, must be in compliance and labeled accordingly?

It is not the intent of the Agency that products already labeled with the "Caution: Federal law...." statement be destroyed or relabeled to meet the new requirements. Changes to comply with section 126 should be implemented when labeling is revised for the products. The date of February 19, 2003, should allow a reasonable time frame to accomplish this goal. After February 19, 2003, all products shipped from the manufacturer, distributor, or repacker should be labeled according to section 126 of the Modernization Act.

7. During this implementation period, is it acceptable to have a product's immediate container labels state "Rx only" while other parts of the labeling (carton and/or package insert) state "Caution: Federal law...."?

FDA does not intend to object to inconsistencies between different pieces of labeling regarding the prescription legend statement while firms implement the new requirements.

8. Is the Agency publishing a proposed rule for implementing these changes?

The Agency intends to initiate rulemaking to incorporate the changes made by section 126 into FDA's regulations.

9. Can the "WARNING - MAY BE HABIT FORMING" statement be maintained on the immediate container labels?

The language repealing section 502(d) does not prohibit labeling a product with the "WARNING - May be habit forming" statement and it could, therefore, be maintained. However, the Agency believes that the habit forming characteristics of a drug product should be adequately described in the Drug Abuse and Dependence section of the package insert and that further labeled warnings are not necessary for the safe use of the product. Such warnings should be provided to the patient by health care providers. In most cases, with the exception of unit-of-use containers, the statement provided on the immediate container only provided the warning to the dispensing pharmacist and not to the patient. As such, the responsibility to warn the patient rested with the prescribing and dispensing health care team. In addition, the symbol used for designating the schedule of a controlled substance conveys the meaning that the drug is potentially habit forming.