(*AEP Order*),[1] the Commission adopts new interim generation market power screens to identify those applicants for electric market-based rate authority that may possess generation market power. An analysis of whether an applicant possesses generation market power has for many years been one of the four prongs of analysis the Commission has used to assess whether an applicant should be granted market-based rate authority. The other three prongs that the Commission has considered are (1) whether the applicant has transmission market power, (2) whether the applicant can erect barriers to entry, and (3) whether there are concerns involving the applicant that relate to affiliate abuse and/or reciprocal dealing. In today's *AEP Order* and in prior orders in the same dockets, the Commission stated that the generation market power screen it was adopting in that proceeding was only an interim screen, and that the Commission intended to initiate a generic rulemaking proceeding on potential new analytical methods for assessing markets and market power. The Commission has also stated that as part of this process it intended to hold a series of outreach meetings with industry experts on these matters.[2] The purpose of this notice is to initiate a rulemaking proceeding with respect to the adequacy of the current four-prong analysis and whether and how it should be modified to assure that electric market-based rates are just and reasonable under the Federal Power Act.

2. The Commission's four-prong market-based rate test was developed nearly 15 years ago, in the context of specific market-based rate proposals filed with the Commission, and currently there are no comprehensive codified regulations governing what applicants must demonstrate in order to obtain market-based rate authorization from the Commission. Much has changed in the industry since the Commission began using the four-prong test in the 1980s, and we believe it is important not only to ensure that our test is sufficient to support market-based rates in today's energy markets, but also to provide clarity, by way of codified regulations, as to what applicants must demonstrate in order to obtain (and retain) authority to sell at market-based rates.

3. This generic proceeding will address, but not be limited to, whether the Commission should retain or modify its existing four-prong test (*e.g.*, whether the analysis should explicitly address vertical market power issues); whether the factors the Commission considers under the existing prongs should be revised; whether the interim generation market power screens that are adopted today in the *AEP Order* should be retained over the long-term; whether the Commission should adopt different approaches to affiliate transactions than it currently does; and whether there should be new Commission regulations promulgated expressly for electric market-based rate filings. The Commission intends the scope of this rulemaking proceeding to be broad, and to include market-based rate authorizations associated with ancillary services.

4. In order to have a better understanding of the issues that need to be considered, as well as the procedural direction the rulemaking should take, as a first step the Commission intends to convene a series of technical conferences that will be open to the public. The Commission will hold the first such technical conference on June 9, 2004, at the Commission's headquarters. The purpose of this conference will be to frame the issues that will comprise the rulemaking proceeding, including a discussion of how all four parts of the current test interrelate, as well as what other factors the Commission should consider in granting market-based rate authorizations.

5. The conference will be transcribed. Those interested in acquiring the transcript should contact Ace Reporters at 202–347–3700 or 800–336–6646. Transcripts will be placed in the public record 10 days after the Commission receives the transcripts. Additionally, Capitol Connection offers the opportunity for remote listening and viewing of the conference. It is available for a fee, live over the Internet, by phone or via satellite. Persons interested in receiving the broadcast, or who need information on making arrangements, should contact David Reininger or Julia Morelli at Capitol Connection (703–993–3100) as soon as possible or visit the Capitol Connection Web site at *http://www.capitolconnection.org* and click on "FERC.''

6. For more information about the conference, please contact Michelle Barnaby at 202–502–8407 or *Michelle.Barnaby@ferc.gov*.

7. A supplemental notice of this conference will be issued later that will provide details of the conference, including the panelists.

By direction of the Commission.

Magalie R. Salas,

Secretary.

[FR Doc. 04–9099 Filed 4–21–04; 8:45 am]

BILLING CODE 6717–01–P

[1] 107 FERC ¶ 61,018 (2004) (*AEP Order*).

[2] *See, e.g., AEP Order,* 107 FERC ¶ 61,018 at P1–2; AEP Power Marketing, Inc, *et al.*, 97 FERC ¶ 61,219 at 61,967 & n.2 (2001); Notice Delaying Effective Date of Mitigation and Announcing Technical Conference, December 20, 2001 at 1; Notice of Technical Conference on Supply Margin Assessment Screen and Alternatives, December 19, 2003, at 1, 3, and attached Staff Paper at 1.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 201, 208, and 209

[Docket No. 2003N–0324]

RIN 0910–AC35

Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend its regulations governing the format and content of labeling for human drug products for which an application is approved under section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355). The proposed rule would require the addition of a statement that includes a toll-free number and advises that the number is to be used only for reporting side effects and is not intended for medical advice (the side effects statement). When finalized, this rule will bring FDA regulations into compliance with provisions of the Best Pharmaceuticals for Children Act (the BPCA).

DATES: Submit written or electronic comments by July 21, 2004. See section IV of this document for the proposed effective date of any final rule based on this proposal.

ADDRESSES: You may submit comments, identified by Docket No. 2003N–0324 and RIN 0910–AC35, by any of the following methods:

- Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.
- Agency Web site: *http://www.fda.gov/dockets/ecomments*. Follow the instructions for submitting comments on the agency Web site.
- E-mail: *fdadockets@oc.fda.gov*. Include Docket No. 2003N–0324 and RIN 0910–AC35 in the subject line of your e-mail message.

- FAX: 301-827-6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD–ROM submissions]: Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the agency name and Docket No. 2003N–0324 and RIN 0910–AC35 or Regulatory Information Number (RIN) for this rulemaking. All comments received will be posted without change to *http://www.fda.gov/dockets/ecomments*, including any personal information provided. For detailed instructions on submitting comments and additional information on the rulemaking process, see the "Comments'' heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to *http://www.fda.gov/dockets/ecomments* and/or the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Carol Drew, Center for Drug Evaluation and Research (HFD–7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–2041.

SUPPLEMENTARY INFORMATION:

I. Background

A. BPCA Requirements

Section 17 of the BPCA (Public Law 107–109) requires 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 act (21 U.S.C. 355) 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, not to seek or obtain medical advice. The BPCA states that the final rule must implement the labeling requirement so as to reach the broadest consumer audience and minimize the cost to the pharmacy profession.

B. MedWatch

FDA already has an adverse drug events reporting program. FDA's existing MedWatch safety information and adverse event reporting program (MedWatch program) includes a toll-free number to facilitate the reporting of adverse events directly to the agency by both health care practitioners and consumers.

Under the existing MedWatch program, consumers and health care practitioners may report serious adverse events, side effects, or problems they suspect are associated with drug products they use or prescribe. To obtain accurate and complete reports of side effects with a potential association to drug products, FDA generally recommends that consumers advise their health care practitioners to report side effects to the drug manufacturer or MedWatch program. However, consumers may also report side effects to FDA directly. A postage-paid MedWatch 3500 form will be mailed or faxed to a consumer who calls 1–800–FDA–1088 and requests a form. A completed form can be mailed or submitted to MedWatch's fax number, 1–800–FDA–0178. Reporting also may be done online at *http://www.fda.gov/medwatch*. FDA encourages consumers to use the MedWatch Website to report adverse events. Consumers who call the MedWatch phone number are given the MedWatch Website address and the option of completing and submitting the reporting form on the Internet.

Currently consumers receive an acknowledgement from FDA after their report is received. Consumers are personally contacted only if additional critically important information is needed. All reports are entered into a database and are evaluated by a safety evaluator. All information is submitted in confidence and protected to the fullest extent of the law.

C. Existing Labeling Requirements

Section 505 of the act describes requirements for the agency's approval of new drug applications (NDAs) and abbreviated new drug applications (ANDAs). FDA regulates many forms of drug labeling for drug products approved under section 505 of the act. Regulated labeling includes: A prescription drug product's approved labeling directed to health care practitioners (physician labeling), FDA-approved Medication Guides, patient package inserts (PPIs) for certain drug products, and over-the-counter (OTC) drug product labeling.

II. Description of the Proposed Rule

A. FDA's Approach to the BPCA Requirements

FDA is proposing that the MedWatch system should be used to fulfill the requirements of the BPCA for providing a toll-free number for the purpose of receiving adverse event reports regarding drug products.

FDA is proposing that the side effects statement be distributed with each prescription drug product, both new prescriptions and refills, approved under section 505 of the act and dispensed to consumers by pharmacies and authorized dispensers in an outpatient setting. FDA is proposing a number of options/alternatives to meet this proposed requirement. FDA also is proposing to require the side effects statement in two categories of drug product labeling: (1) FDA-approved Medication Guides for drugs approved under section 505 of the act, and (2) the labeling for OTC drug products approved under section 505 of the act. Manufacturers may include the side effects statement in PPIs or Medication Guides on a voluntary basis for products not approved under section 505 of the act. In addition, FDA has proposed adding FDA's toll-free MedWatch telephone number to physician labeling in the proposed rule entitled "Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels'' (65 FR 81082, December 22, 2000). FDA believes that this approach will be most likely to reach the broadest consumer audience and minimize the cost to the pharmacy profession.

B. Labeling Not Covered Under this Proposed Rule

1. Physician Labeling

FDA is not proposing to modify the requirements for physician labeling at this time. Although consumers have access to physician labeling as reprinted in the Physician Desk Reference (PDR), physician labeling is not written for the consumer audience. In the **Federal Register** of December 22, 2000, the agency issued a proposed rule to revise the physician labeling requirements in 21 CFR 201.56 and 201.57 (the physician labeling rule). The proposed changes to the labeling format included the addition of adverse drug reaction reporting contact information for health care practitioners, including FDA's toll-free MedWatch telephone number. Because physician labeling is directed to health care practitioners, and FDA anticipates that this labeling will be updated with the toll-free MedWatch number, the agency is not proposing modifications to physician labeling at this time. However, FDA is soliciting comments on this issue.

2. PPIs

PPIs are required by FDA for certain drug products, including oral contraceptives and estrogen drug products (§§ 310.501 and 310.515 (21 CFR 310.501 and 310.515)). Some manufacturers also voluntarily produce PPIs for drug products. PPIs are an extension of physician labeling and are often distributed to consumers when the

drug product is dispensed. FDA is not proposing to require the side effects statement in PPIs at this time because the proposed requirement in this rule that pharmacies distribute the side effects statement will ensure that a broad consumer audience receives it. FDA believes that requiring changes to PPIs in addition is unnecessary; however, FDA is soliciting comments on this issue. Manufacturers may provide the side effects statement voluntarily in PPIs.

C. Benefits of the Proposed Rule to Public Health

FDA has determined that this proposed rule will promote the agency's mission to protect the public health by informing consumers of FDA's adverse event reporting program under MedWatch. Data reported as a result of this proposed rule will supplement data currently reported and assist the agency in identifying trends in reported adverse events for specific drug products. These data may result in a review of the safety and/or effectiveness of particular drug products on the market. Once an adverse event or product problem is identified, the agency can initiate various actions to address the problem, such as labeling changes (*e.g.,* boxed warnings), medical or safety alerts to health care practitioners, and product withdrawals. For further discussion of the benefits of this proposed rule, see the agency's analysis of economic impacts in section V.C of this document.

D. Specific Proposed Changes to the Regulations

1. Side Effects Statement

Section 17 of the BPCA requires that the labeling for each drug approved under section 505 of the act include: (1) A toll-free number maintained by FDA for the purpose of receiving reports of adverse events regarding drug products, and (2) a statement that the number is to be used for reporting purposes only, not to seek medical advice. FDA has considered these requirements and has developed a conforming statement: "Call your doctor for medical advice about side effects. You may report side effects to FDA at 1–800–FDA–1088.'' FDA believes this statement comports with the mandate in the BPCA and is brief enough to convey the appropriate message and fit on the labeling of drug products. However, FDA is soliciting comments on the wording of the proposed statements. As stated previously in this document, FDA is using the established MedWatch toll-free number for consumer reporting. For OTC products, the side effects statement has been modified to correspond to the specific requirements for OTC drug product labeling. FDA consulted with an agency communications specialist in developing the side effects statement.

FDA is proposing that the side effects statement first direct consumers to call their doctor for medical advice. FDA is concerned that consumers may misinterpret a statement to report side effects and call the agency at the time they or members of their family experience a side effect, rather than calling their own doctor for immediate, and possibly critical, medical advice. To make it clear that consumers experiencing side effects and in need of medical advice should call their doctor first, FDA has included the first sentence instructing consumers to call their doctor for medical advice.

FDA is proposing to use the term "side effects'' rather than "adverse events'' because of concern that some consumers may not understand the meaning of the term "adverse event.'' FDA believes the term "side effects'' will be understood by a broader consumer audience than would the term "adverse event.''

The current MedWatch program distinguishes serious adverse events, defined in 21 CFR 314.80, as those where the patient outcome is: death, life threatening (real risk of dying), hospitalization (initial or prolonged), disability (significant, persistent or permanent), congenital anomaly, or required intervention to prevent permanent impairment or damage. The BPCA does not qualify the type of adverse event reported to the toll-free number. Therefore, FDA is not proposing that consumers report only serious adverse events to the MedWatch program. This is likely to result in more reports to FDA than under the existing system. The agency solicits comments on whether the term "side effects'' should be further qualified.

2. Medication Guides

FDA-approved Medication Guides are required for prescription drug products that the agency has determined pose a serious and significant public health concern. Because these products have increased risks, FDA believes that the side effects statement should be included in Medication Guides required for drug products approved under section 505 of the act.

Part 208 (21 CFR part 208) sets forth the requirements for this type of patient labeling. Medication Guides provide information when FDA determines that the information is necessary to patients' safe and effective use of drug products. Medication Guides have been approved for approximately 18 prescription drug products, only some of which are approved under section 505 of the act. Some biological products have Medication Guides, but those products are not approved under section 505 of the act, and therefore are not covered by these BPCA provisions. These provisions would apply, however, to any biological products approved under section 505 that carry Medication Guides.

FDA is proposing that manufacturers be required to include the side effects statement under the heading, "What are the possible or reasonably likely side effects of (name of drug)?''. Manufacturers who ship drug products for which a Medication Guide is required are responsible for ensuring that the Medication Guide is available for distribution to patients by providing sufficient numbers of Medication Guides to authorized dispensers of drug products. Consumers who receive the appropriate Medication Guide with their dispensed prescription drug product will be made aware of FDA's toll-free number to report side effects by reading the appropriate section of the Medication Guide.

Under § 208.20(a)(4), the letter height or type size for Medication Guides must be no smaller than 10 points (1 point = 0.0138 inches). FDA is not proposing to modify this requirement; therefore, the side effects statement in Medication Guides will appear in no smaller than 10-point letter height or type size.

While FDA is not requiring manufacturers to add the side effects statement to Medication Guides for those drug products not approved under section 505 of the act, manufacturers may do so voluntarily.

3. OTC Labeling

Because certain OTC drug products are approved under section 505 of the act, FDA is proposing that the labeling of those products approved under NDAs or ANDAs must also contain the side effects statement as mandated by the BPCA. FDA estimates that there are approximately 350 OTC products approved under an NDA and 172 approved under an ANDA.

In 1999, FDA published a final rule on the labeling of OTC drug products. The final rule was intended to assist consumers in reading and understanding OTC drug product labeling and introduced a new format (drug facts format). In this proposed rule, FDA has modified the side effects statement for OTC products to correspond to the drug facts format. Section 201.66 (21 CFR 201.66) addresses format and content

requirements for OTC drug product labeling. Section 201.66(c) lists the content requirements for OTC drug product labeling, and § 201.66(d) specifies the format requirements for OTC drug product labeling, including the letter height and type size.

The format and content labeling requirements for OTC drug products in § 201.66 include specific subheadings for presenting "warnings'' information. The subheading in § 201.66(c)(5)(vii) is "Stop use and ask a doctor if''. The agency considers this language similar to the language in the first sentence of the side effects statement for prescription drug products that advises patients to "Call your doctor for medical advice about side effects.'' Accordingly, for OTC drug products, the agency is proposing to use the existing subheading in § 201.66(c)(5)(vii) and include after it the bulleted statement "side effects occur.'' The second sentence would remain the same as for prescription products: "You may report side effects to FDA at 1–800–FDA–1088.'' This approach incorporates the side effects statement in OTC product labeling in the appropriate location, using existing consumer-friendly language and a minimal amount of additional labeling space.

The letter height or type size for subheadings and all other information described in §§ 201.66(c)(2) through (c)(9) in OTC labeling is no smaller than 6-point letter height or type size (§ 201.66(d)(2)). Therefore, the OTC side effects statement would appear in a minimum 6-point letter height or type size. Consistent with § 201.66(c)(9), the telephone number would appear in a minimum 6-point bold letter height or type size. This requirement is repeated in the revisions to § 201.66(c)(5)(vii).

4. Pharmacy Provisions

FDA is proposing to add new part 209 (21 CFR part 209) to the regulations to require pharmacies and authorized dispensers to distribute the side effects statement to consumers with each prescription drug product approved under section 505 of the act. Under this part, the term "pharmacies'' includes, but is not limited to, retail, mail-order, hospital, university, or clinic pharmacies, as well as public health agencies that dispense prescription drugs. The term "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. The term includes health care practitioners who dispense prescription drug products from their offices, but does not include the dispensing of drug samples. FDA does not intend that part 209 apply to health care practitioners administering medication 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 believes that patients receiving drugs under these circumstances will rely on their health care practitioners to monitor and report adverse events.

While section 17 of the BPCA requires FDA to reach the broadest consumer audience, it also requires FDA to minimize costs to the pharmacy profession. To minimize the cost of the requirement for pharmacists to distribute the side effects statement, FDA is proposing to provide a range of options from which pharmacists may choose. These options are included in proposed § 209.11(b). FDA invites comments on other options pharmacies might use to distribute the side effects statement.

Proposed § 209.11(b) provides that pharmacies and authorized dispensers may choose one of the following methods, or any combination of the following methods, to distribute the side effects statement to consumers: (1) Attach a standard-size sticker (1 1/2 by 7/16 inches) containing the side effects statement to the vial, package, or container of the prescription drug product; (2) use a pharmacy prescription vial cap preprinted with the side effects statement; (3) distribute a separate sheet of paper containing the side effects statement; (4) distribute consumer medication information such as that provided by pharmacy software and third party data processing vendors that contains the side effects statement; or (5) distribute the appropriate FDA-approved Medication Guide that contains the side effects statement.

a. *Option 1—sticker*. The first option for distribution of the side effects statement by pharmacies and authorized dispensers is to attach a standard-size pharmacy sticker to the unit package, vial, or container of the prescription drug product dispensed to the consumer. FDA is proposing that the letter height or type size of the side effects statement on any sticker attached to the unit package, vial, or container of a prescription drug product be no smaller than 6 points. The side effects statement should be printed in any single, clear, easy-to-read type style. To minimize the cost of this option for pharmacies, FDA has determined that the proposed side effects statement will fit on a standard-size (1 1/2- by 7/16-inch) pharmacy sticker.

FDA recognizes there may be reasons that the sticker option is not practicable for some drug products, e.g., the packaging of the drug product is too small to accommodate a sticker, or there are stickers already necessary that preclude adding another. FDA is not proposing to require this option. Therefore, a pharmacy or authorized dispenser may choose any other option.

b. *Option 2—preprinted vial cap*. The second option for distribution of the side effects statement by pharmacies and authorized dispensers is to use a pharmacy prescription vial cap preprinted with the side effects statement. As with the sticker option, FDA is proposing that the letter height or type size of the side effects statement be no smaller than 6 points. The side effects statement should be printed on the vial cap in any single, clear, easy-to-read type style. Use of a preprinted vial cap should be useful when the necessary number of stickers on a prescription vial precludes the addition of another sticker.

c. *Option 3—separate sheet of paper*. The third possible method of distribution is to provide a separate sheet of paper with the side effects statement to consumers. FDA is proposing that the letter height or type size of the side effects statement be no smaller than 10 points to ensure readability. The side effects statement should be in a single, clear, easy-to-read type style. FDA is not proposing any further requirements on how this information is presented. The agency believes that this flexibility will allow pharmacies and authorized dispensers who choose this option to use existing systems to meet this requirement.

d. *Option 4—consumer medication information*. Some pharmacies voluntarily distribute written information about prescription drug products to consumers as part of patient medication counseling activities (consumer medication information). This information is often attached to or placed in the bag into which the pharmacist puts the prescription drug product prior to providing it to the consumer. Consumer medication information is often produced by third party data processing vendors. Therefore, FDA is providing pharmacies and authorized dispensers with the option of complying with this regulation by providing the consumer with consumer medication information updated to include the side effects statement. FDA is proposing that the letter height or type size of the side effects statement be no smaller than 10 points to ensure readability. Distributing this consumer medication information

with each original and refill prescription dispensed to consumers will satisfy the requirements of this part.

e. *Option 5—FDA-approved medication guides.* FDA is proposing that manufacturers include the side effects statement in FDA-approved Medication Guides for drug products approved under section 505 of the act. Medication Guides are typically produced by the manufacturer of the drug product. By regulation manufacturers are required to provide Medication Guides or the means to produce them to authorized dispensers for distribution to the patient (§ 208.24). Medication Guides are required to be printed in no smaller than 10-point letter height or type size. Pharmacists and other authorized dispensers may comply with this regulation by distributing Medication Guides that include the side effects statement for those drug products approved under section 505. Pharmacists and other authorized dispensers will need to choose a different compliance option if an FDA-approved Medication Guide for a drug product approved under section 505 of the act has not yet been updated with the side effects statement, or if the prescription drug product they are dispensing does not have a Medication Guide.

III. Legal Authority

Section 17 of the BPCA requires the agency to issue a final rule mandating that the labeling of each drug approved under section 505 of the act include the toll-free number for reporting adverse events regarding drugs and a statement that the number is for reporting purposes only, not to seek medical advice. The legislation gives FDA broad discretion in designing the rule, requiring only that the labeling requirement be implemented so as to reach the broadest consumer audience and minimize the cost of the rule on the pharmacy profession.

The proposed rule satisfies these two statutory requirements. The proposed rule covers prescription and OTC drugs approved under section 505 of the act, and would require manufacturers, authorized dispensers, and pharmacies to include the side effects statement on certain drug product labeling. The scope of the proposed rule includes these individuals and entities because they all participate in labeling drug products approved under section 505 of the act. Drug manufacturers are subject to comprehensive regulation of drug product labeling under the act and its implementing regulations (e.g., 21 U.S.C. 352, 21 CFR part 201), and section 17 of the BPCA explicitly extends FDA's authority to the side effects statement. Likewise, authorized dispensers (including pharmacists) and pharmacies are subject to statutory labeling requirements under section 503(b)(2) of the act, and the BPCA contemplates that pharmacies and authorized dispensers will distribute the side effects statement with prescription drug products approved under section 505. Including manufacturers, authorized dispensers, and pharmacies within the scope of the proposed rule will ensure that the side effects statement reaches the broadest consumer audience.

FDA is proposing several compliance options for authorized dispensers and pharmacies in order to minimize the cost of the rule on the pharmacy profession. Of these options, authorized dispensers and pharmacies may choose the least costly means to distribute the side effects statement with prescription drug products. FDA recognizes that some pharmacists voluntarily provide consumer medication information to patients. Those who do so may put the side effects statement in that voluntarily provided information, or they may choose to comply using one or more of the other options the agency has proposed. The other options include distributing the side effects statement on: (1) A sticker attached to the unit package, vial, or container of the drug product; (2) a preprinted pharmacy prescription vial cap; (3) a separate sheet of paper; or (4) an FDA-approved Medication Guide, if appropriate.

IV. Proposed Effective Date

FDA considered issuing this rule as an interim final rule to be effective 30 days after the date of its publication in the **Federal Register**. The BPCA directs FDA to issue a final rule within 1 year of the date of the BPCA's enactment on January 4, 2002. FDA is issuing this rule as a proposal, however, to allow the affected entities, including manufacturers and pharmacies, to comment on the proposed changes to the regulations.

FDA is proposing that the final rule be effective 30 days after it is published in the **Federal Register**. FDA is proposing that all manufacturers of drug products, authorized dispensers, and pharmacies be in compliance not more than 1 year after the effective date of any final rule published in the **Federal Register**. FDA anticipates that manufacturers of drug products, authorized dispensers, and pharmacies will require time to update labeling and systems to comply with the new requirements.

Manufacturers of drug products that require FDA-approved Medication Guides will need time to update these Medication Guides with the side effects statement and to distribute them to distributors, packers, and authorized dispensers. Manufacturers who make changes to FDA-approved Medication Guides can submit labeling changes in annual reports as described in § 314.70(d) (21 CFR 314.70(d)) as a minor change in labeling and need not submit a supplemental application to the agency for preapproval.

Manufacturers of OTC drug products will require time to update OTC labeling to make it available to consumers. Manufacturers of OTC drug products approved under an NDA can submit their labeling changes in their annual reports according to § 314.70(d)(3) and need not submit a supplemental application to the agency for preapproval. Manufacturers of OTC drug products approved under an ANDA may also submit these changes in their annual reports according to § 314.70(d)(3) and § 314.97 (21 CFR 314.97) and need not submit a supplemental application to the agency for preapproval.

Pharmacies will require adequate time to make decisions about their least-cost option to comply with the rule and either implement new systems or update established systems. To decrease the burden of this rule on pharmacies and authorized dispensers, as required by the BPCA, FDA is proposing that 1 year should provide adequate time to comply with this rule. However, FDA is soliciting comments on this proposed compliance date.

Manufacturers of products with Medication Guides not approved under section 505 of the act who voluntarily make changes to Medication Guides to include the side effects statement can submit labeling changes in annual reports as described in § 601.12(f)(3)(i)(A) as a minor change in labeling and need not submit a supplemental application to the agency for preapproval. Manufacturers who voluntarily make changes to PPIs required under §§ 310.501 and 310.515 can submit labeling changes in annual reports as described in § 314.70(d) as a minor change in labeling and need not submit a supplemental application to the agency for preapproval.

V. Analysis of Economic Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory

alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule has a significant economic impact on a substantial number of small entities, an agency must consider alternatives that would minimize the economic impact of the rule on small entities. Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million in any one year (adjusted annually for inflation).

The agency believes that this rule is consistent with the regulatory philosophy and principles identified in Executive Order 12866 and in these two statutes. The proposed rule would require pharmacies and authorized dispensers to provide patients with the side effects statement and require drug manufacturers to include the statement on labeling of certain drug products. Potential one-time costs of the proposed rule are projected to range from $1.3 million to $3.7 million with annual compliance costs from $9.2 million to $22.1 million. Annualized for 10 years, total compliance costs would be approximately $9.3 million to $22.6 million at 3 percent discount rate, and $9.4 million to $22.6 million at 7 percent discount rate. Although the agency is unable to quantify the potential benefits of the proposed rule at this time, improved awareness of drug safety reporting may increase the number of serious adverse drug reactions reported by consumers and health care practitioners to the MedWatch program. Potential benefits of the proposed rule are discussed in section V.B of this document. Furthermore, the agency has determined that the proposed rule is not an economically significant rule as described in the Executive order, because annual impacts on the economy are substantially below $100 million. Because the rule does not impose any mandates on State, local or tribal governments, or the private sector that will result in an expenditure in any one year of $100 million or more, FDA is not required to perform a cost-benefit analysis according to the Unfunded Mandates Reform Act. The current inflation-adjusted statutory threshold is about $110 million. With respect to the Regulatory Flexibility Act, the agency believes it is unlikely that this proposed rule will result in a significant economic impact on a substantial number of small entities.

The proposed rule would fulfill the BPCA's statutory requirement to provide consumers with a toll-free telephone number that can be used to report adverse drug events to FDA. The agency believes it receives reports for only a portion of the adverse drug events that occur. Providing consumers with this telephone number is expected to increase public awareness of, and participation in, the agency's voluntary adverse drug events reporting program. To ensure that the side effects statement would cover all drug products approved under section 505 of the act and reach a wide consumer audience as specified in the statute, FDA proposes that labeling of OTC drug products and any required Medication Guide for a drug product approved under section 505 must include the side effects statement, and the side effects statement must accompany each prescription dispensed for outpatient use. The agency also proposes to exercise its discretion to give affected pharmacies flexibility to select a method of compliance from among five options that would minimize the impact of the proposed rule. For a discussion of the alternatives FDA considered in drafting this proposed rule, see section V.C of this document. The rule FDA proposes is the least-expensive alternative that meets the requirements set forth in section 17 of the BPCA.

A. Costs of Regulation

1. Pharmacy Industry

Both retail and nonretail pharmacies may dispense prescription drugs to patients. Retail channels include independent drug stores, chain drug stores, mass merchants, grocery stores with pharmacies, and mail/Internet services. Nonretail channels include health maintenance organizations (HMOs), hospital outpatient pharmacies, offices of health care practitioners, and ambulatory care clinics. Although several sources of information about the retail pharmacy sector exist, data on the number of ambulatory care centers or hospital outpatient departments dispensing prescription drugs are limited.

a. *Number of affected pharmacies.* The proposed rule may affect all locations where an authorized dispenser distributes prescription drug products for outpatient use. According to the NACDS, in 2001 there were 55,581 retail pharmacies, excluding mail order businesses (Ref. 1). Census data from 1997 show there were 314 mail order or electronic shopping establishments with merchandise sales from prescriptions (Ref. 2). In addition, the agency tallied the number of establishments with receipts or revenue from drug products in Health Care and Social Assistance sectors using 1997 Economic Census data (Ref. 3). The Health Care sector data use a single revenue code for nonprescription and prescription drugs. Businesses with receipts or revenues from drug products that would not be licensed to dispense prescriptions (*e.g.,* chiropractors) or would be administering drugs directly to patients (*e.g.,* supervised home health care) were excluded from the analysis.

A study conducted for FDA found that, on average, 89 percent of retail pharmacies currently give patients some type of written consumer medication information (Ref. 4). It is uncertain whether this percentage also represents nonretail pharmacies. Nevertheless, for this analysis we assume that clinics and HMOs are similar to retail pharmacies, distributing consumer medication information with 89 percent of the dispensed prescriptions. In addition, hospital outpatient services and health care practitioners' offices are assumed currently to provide no written drug information. The agency solicits comment on these assumptions.

Whether provided by a third party vendor or prepared in-house, it is anticipated that the side effects statement can be added to existing databases at a negligible one-time cost. Since the statement is not expected to increase the length of existing documents, the agency has assumed that only pharmacies and authorized dispensers not currently providing written consumer medication information will incur compliance costs and be affected by the rule. FDA requests comment on this assumption. Table 1 of this document shows the total number of establishments dispensing prescriptions and the number anticipated to be affected by the proposed rule.

TABLE 1.—ESTIMATED NUMBER OF AFFECTED RETAIL AND NONRETAIL PHARMACIES

Type of Pharmacy	Total No. of Pharmacies	Percentage Not Providing Written Drug Information	No. of Affected Pharmacies
Retail Outlets			
Grocery Store[1]	8,531	11%	938
Independent Pharmacy[1]	20,647	21%	4,336
Mail Order/Electronic Shopping[2]	314	11%	35
Mass Merchant[1]	5,910	2%	118
Traditional Chain Store[1]	20,493	2%	410
Nonretail Outlets:			
HMO Medical Center[3,4]	209	11%	23
Hospital Outpatient Service[3,5]	5,878	100%	5,878
Office of Health Care Practitioner[3,6]	7,867	100%	7,867
Outpatient Care Center, except HMO[3,7]	1,881	11%	207
Total of all Affected Outlets	71,730		19,812

[1] Source: Ref. 1.
[2] Source: Ref. 2, Table 2. Includes number of establishments in North American Industry Classification System (NAICS) code 454110 with merchandise sales for code 0161.
[3] Source: Ref. 3, Tables 1a and 1b.
[4] Includes number of establishments in NAICS 621491 with receipts or revenue from code 8619. Excludes nonemployer statistics.
[5] Includes number of establishments in NAICS 622 with receipts or revenue from outpatient services (code 5250). Excludes nonemployer statistics.
[6] Includes number of establishments in NAICS 62111, 62121, 62132, 62139, with receipts or revenue from code 8619. Excludes nonemployer statistics.
[7] Includes number of establishments in NAICS 62141, 62142, 621492, 621493, 621498, with receipts or revenue from code 8619. Excludes nonemployer statistics.

b. *Prescriptions dispensed*. For those pharmacies not providing written consumer medication information, the compliance costs of the proposed rule would be proportional to the number of outpatient prescriptions that affected pharmacies dispense annually. Consequently, smaller pharmacies dispensing fewer prescriptions than larger pharmacies would incur lower costs. Moreover, the proposed rule requires distributing the side effects statement with both new and refill prescriptions. Since individuals with multiple chronic conditions could potentially receive the side effects statement many times each year, the agency solicits comment on whether the statement could be distributed less frequently to this subset of individuals without increasing the burden on pharmacies.

IMS Health collects data on the number of prescriptions dispensed as well as the number of pharmaceutical products purchased by the retail channels. In contrast, only data on the number of products purchased by nonretail channels are available. Because the types of drugs and dosage forms dispensed to outpatients are expected to be similar for retail and nonretail channels, the agency uses IMS data from both channels to derive estimates of the number of prescriptions dispensed annually by nonretail pharmacies (IMS Health, National Prescription Audit *Plus*, Provider Perspective, Retail Perspective, see appendix for details). Based on volume from 2001, pharmacies are estimated to dispense between 3.28 billion and 3.64 billion prescriptions to outpatients each year (table 2 of this document). However, this number is expected to increase over time. Estimates from NACDS predict that future drug use will increase approximately 26 percent by the year 2005 (Ref. 1). The agency requests comment on these estimates.

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Table 2.--Estimated Number of Outpatient Prescriptions by Type of Pharmacy

Retail Outlets:	Prescriptions Dispensed (million)	
Grocery Store[1]	426.5	
Independent Pharmacy[1]	778.7	
Mail Order or Electronic Shopping[1]	163.5	
Mass Merchant[2]	311.0	
Traditional Chain Store [2]	1,418.0	
	Range of Prescriptions Dispensed(million) [3]	
Nonretail Outlets:	From:	To:
HMO Medical Center	16.6	25.4
Hospital Outpatient Service	98.2	317.1
Office of Health Care Practitioner	8.2	9.2
Outpatient Care Center, except HMO	62.6	194.0
Total Outpatient Prescriptions	3,283.2	3,643.4

[1] Source: IMS Health, National Prescription Audit Plus™, Year 2001, data extracted June 2002.
[2] Source: Ref. 1.
[3] See appendix for methodology used to estimate the number of nonretail prescriptions. Sources: IMS Health, National Prescription Audit Plus™, Year 2001, Data Extracted June 2002; IMS Health, Provider Perspective™, Year 2001, Data Extracted June 2002; IMS Health, Retail Perspective™, Year 2001, data extracted June 2002.

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c. *Compliance costs for pharmacies.* The proposed rule provides several compliance options, allowing pharmacies and authorized dispensers flexibility to select the least costly compliance method. The proposed rule describes five ways pharmacies and authorized dispensers can distribute the side effects statement to patients. These methods may be used individually or together in any combination, and include: (1) Attaching a standard-size sticker to the prescription container, (2) distributing a separate sheet of paper, (3) distributing consumer medication information containing the side effects statement, (4) using an imprinted vial cap, or (5) distributing the appropriate FDA-approved Medication Guide. Moreover, the widespread and growing use of electronic communication presents the opportunity to innovatively inform consumers about public health. FDA solicits suggestions on possible electronic methods to distribute the side effects statement that would comply with the BPCA's statutory mandate, and comment on what burden such solutions might impose on pharmacies and drug manufacturers. FDA also requests comment on whether electronic means of distributing the side effects statement would be consistent with the statutory definition of "labeling.''

The magnitude of the compliance costs will depend on whether a pharmacy is currently using one or more of these methods. For example, although third party vendors of consumer medication information software would incur negligible one-time costs modifying their databases to include the side effects statement, FDA believes that pharmacies using this type of software will incur no additional costs. Similarly, if a drug information database is managed in-house and the pharmacy is already handing out consumer medication information to patients, only a negligible one-time cost to add the statement may be incurred. For prescription drug products with Medication Guides, pharmacies and authorized dispensers will incur no additional costs since they are already required to distribute Medication Guides with those products. Outlets already using imprinted vial caps that elect to add the statement to the cap may incur negligible one-time costs to prepare a new stamping template. In contrast, switching from a non-imprinted vial cap to one imprinted with the side effects statement might increase the cost of each vial cap by an estimated 15 percent.

Some pharmacies, however, might incur new costs for each prescription they dispense. To illustrate the potential impact, the agency calculates the associated costs to affix a sticker, preprinted with the statement, on the prescription container. The agency believes that this option reflects the highest potential cost of the proposed rule to pharmacies and authorized dispensers. A box of series 1 preprinted stickers contains 1,000 stickers at a cost of $2.90, or $0.003 per sticker. In addition to the cost of the sticker, pharmacy personnel may spend about 5 minutes per 1,000 stickers for ordering and inventory control and 5 seconds to affix each sticker to the container. Although in some small establishments a pharmacist may perform these tasks, a pharmacy technician or pharmacy school intern would probably perform these actions. Therefore, a range of labor costs are calculated with a pharmacy technician's mean and 90 percentile loaded hourly wage rates of $14.53 and $20.38, respectively, including 40 percent for benefits (Ref. 5). The annual costs of the proposed rule for affected retail pharmacies may range from $6.4 million to $8.7 million, and from $2.8 million to $11.5 million for nonretail pharmacies. If the entire affected pharmacy industry complied using this option, the proposed rule may cost from $9.2 to $20.2 million annually (table 3 of this document).

Pharmacies could also elect to hand out a piece of paper printed with the side effects statement. Costs for this option depend on the size and quality of the paper. However, based on retail prices, a single sheet of paper and the ink to print the side effects statement cost approximately $0.013. A sheet of paper can comfortably accommodate from 8 to 20 statements in 10-point font, depending on the spacing between statements. Thus, the per statement cost of materials for this option ranges from about $0.001 to $0.002, substantially less than the sticker option. However, because the time required to cut up a piece of paper and distribute it with the prescription may exceed the time needed to affix a sticker, the average total cost to distribute a piece of paper is anticipated to be similar to the average total cost of the sticker option.

TABLE 3.—POTENTIAL COMPLIANCE COSTS FOR PHARMACIES[1]

Type of Pharmacy	No. of Affected Outlets	Average No. of Dispensed R_x[2]	Cost of Stickers ($ mil)	Labor Costs ($ mil)	Total Cost ($ mil)
Retail Outlets:					
Grocery Store	938	49,997	$0.14	$1.00 to $1.41	$1.14 to $1.54
Independent Pharmacy	4,336	37,714	$0.47	$3.50 to $4.91	$3.97 to $5.38
Mail Order or Electronic Shopping	35	520,732	$0.05	$0.38 to $0.54	$0.44 to $0.59
Mass Merchant	118	52,623	$0.02	$0.13 to $0.19	$0.15 to $0.20
Traditional Chain Store	410	69,194	$0.08	$0.61 to $0.85	$0.69 to $0.93
Retail Subtotal	5,837		$0.76	$5.63 to $7.89	$6.39 to $8.66
Nonretail Outlets:					
HMO Medical Center	23	79,244 to 121,688	$0.01 to $0.01	$0.04 to $0.08	$0.04 to $0.09
Hospital Outpatient Service	5,878	16,704 to 53,947	$0.28 to $0.92	$2.10 to $9.52	$2.39 to $10.44
Offices of Health Care Practitioner	7,867	1,042 to 1,171	$0.02 to $0.03	$0.18 to $0.28	$0.20 to $0.30
Outpatient Care Center, except HMO	207	33,262 to 103,126	$0.02 to $0.06	$0.15 to $0.64	$0.17 to $0.70
Nonretail Subtotal	13,975		$0.33 to $1.02	$2.46 to $10.52	$2.80 to $11.53

TABLE 3.—POTENTIAL COMPLIANCE COSTS FOR PHARMACIES[1]—Continued

Type of Pharmacy	No. of Affected Outlets	Average No. of Dispensed R_x[2]	Cost of Stickers ($ mil)	Labor Costs ($ mil)	Total Cost ($ mil)
Industry Total	19,812		$1.10 to $1.78	$8.09 to $18.41	$9.19 to $20.19

[1] Totals may not sum due to rounding.
[2] Average number of dispensed Rx calculated by dividing the number of prescriptions dispensed in Table 2 of this document by the total number of pharmacies in Table 1 of this document.

2. Drug Manufacturers

a. *Number of affected products*. The proposed rule requires that, within 1 year of the effective date of the final rule, manufacturers of OTC drugs approved under section 505 of the act add the side effects statement to drug product labeling, and manufacturers of any prescription drug product with an FDA-approved Medication Guide add the side effects statement to that Medication Guide. The agency estimates that the rule may affect approximately 522 OTC products, including 350 branded and 172 private label products, and up to 18 prescription drug products with Medication Guides.

b. *Cost to modify product labeling*. The proposed rule requires that the side effects statement be included in the "Warning(s)'' section of the "Drug Facts'' box, adding 101 characters to drug product labeling. Because of the brevity of the statement, the agency anticipates that manufacturers of the affected products may incur a one-time cost to modify labeling, but no additional incremental printing or packaging modification costs. The agency solicits comment on this assumption. OTC products marketed under NDAs or ANDAs usually have 2 to 3 stockkeeping units (SKUs), suggesting that up to 1,050 branded packages and 520 private label packages might be affected by the final rule. Revising labeling of branded OTC products may cost about $3,000 for each branded SKU and $1,000 for each private label SKU. Because nonprescription drug manufacturers often use the packaging of OTC products to market their products and change labeling frequently, some labeling costs of the proposed rule would be incurred in the normal course of business. Thus, the per SKU cost estimates are an upper bound. New compliance costs for nonprescription drug manufacturers may range from $1.2 million with one SKU per affected product to $3.7 million with three SKUs per affected product. The agency solicits comment on the number of SKUs affected by the proposed rule and the potential new compliance costs to revise the product labeling of these SKUs.

Manufacturers of prescription drug products change labeling less frequently than OTC manufacturers and therefore may also incur some excess inventory loss because of the 12-month implementation period. Including excess inventory loss and scrap of $1,463, adding the statement to Medication Guides may cost manufacturers an average of $4,177 per product. Within the first year, OTC and prescription drug manufacturers together might incur one-time costs from $1.3 million to $3.7 million to comply with the proposed rule. Annualized for 10 years, compliance costs would range from $0.2 million to $0.4 million at 3 percent discount rate, and from $0.2 million to $0.5 million at 7 percent discount rate.

3. Burden on FDA

Approximately 100 calls are received each week by the MedWatch program. When a consumer contacts the agency directly by telephone, a MedWatch 3500 form and instructions are mailed. Because some questions on the MedWatch 3500 form request clinical information, the instructions recommend that patients work with their health care practitioner to complete the form. However, the confidential nature of the reporting program makes it difficult to track the number of forms consumers return to the agency. In 2001, consumers submitted 1,788 direct reports. This suggests that roughly one-third of the mailed forms are returned.

It is uncertain if receiving the side effects statement with dispensed prescriptions will cause more consumers to call the MedWatch program and report their drug side effects. According to an agency communications specialist, it is likely that some consumers may call the toll-free number with questions or comments unrelated to the intended purpose of safety reporting. Moreover, health care practitioners can report serious adverse drug events to the agency by telephone. From 1998 to 2001, an average of 718 such telephone reports were submitted annually. Even though health care practitioners are not the direct focus of the proposed rule, it is possible that the rule may cause an increase in direct reporting from health care practitioners. Although the agency cannot predict the additional number of calls and reports that might result from the proposed rule, the impact on the agency could be substantial.

It costs the agency an average of $5.60 for each consumer call to the MedWatch program to answer the telephone, process the call, and mail the MedWatch form. Once the MedWatch form is returned, the agency may spend up to $25.00 processing the form and entering the data in the Adverse Events Reporting System (AERS). If only one-third of the calls to MedWatch produce an adverse drug event report, each consumer report would cost the agency about $41.80. However, if every telephone call produces a consumer report, the per report cost decreases to $30.60. Furthermore, reports submitted directly to the MedWatch Website would only cost $25 since there are not additional costs to answer and process the telephone call. Moreover, if there is a substantial increase in the number of telephone calls, the agency might also incur fixed costs for additional telephone and computer equipment.

MedWatch data suggest that telephone reports from practitioners account for approximately 5 percent of the direct reports submitted by mail, facsimile, or telephone. In contrast to consumer reports, telephone reports from health care practitioners may take up to 1.25 hours to process, costing the agency an estimated $67.31 ($53.85 per hour x 1.25 hours). However, the agency does not know the number and source of new direct calls and reports it might receive in response to this rule. Therefore, table 4 presents five scenarios to illustrate the possible impact of the proposed rule on the agency if the volume of consumer calls increased by approximately 0.05 percent, 1 percent, 50 percent, 500 percent, or 1,000 percent over current levels. Because the 3-to-1 relationship of calls to reports could vary, each

scenario shows the impacts on the agency with a range of 1 to 3 calls for each direct report submitted to MedWatch by consumers. Variable costs for FDA could range from $42 to $1,923,308 annually. The agency solicits comments from industry on their experience with consumer telephone calls to toll-free numbers and the proportion of the calls related to safety issues.

TABLE 4.—POTENTIAL ANNUAL COST OF INCREASED DIRECT CALLS AND REPORTS TO FDA'S MEDWATCH PROGRAM[1]

	Potential Scenarios[2]				
	1	2	3	4	5
No. of Additional Calls Received	3	60	3,000	30,000	60,000
No. of Additional Reports Returned by Mail or Fax	1 to 3	20 to 60	1,000 to 3,000	10,000 to 30,000	20,000 to 60,000
Potential Cost for Additional Calls and Direct Reports[3]	$42 to $92	$836 to $1,836	$41,800 to $91,800	$418,000 to $918,000	$836,000 to $1,836,000
No. of Telephone Reports from Health Care Practitioners[4]	0	1	50	500	1,000
Potential Cost for Telephone Reports from Practitioners	$0	$87	$4,365	$43,654	$87,308
Total Potential Annual Cost	$42 to $92	$923 to $1,923	$46,165 to $96,165	$461,654 to $961,654	$923,308 to $1,923,308

[1] Roughly one-third of the MedWatch calls from consumers result in a completed report being returned to FDA. However, calls from other sources may have better yields than calls from consumers. A new telephone call might yield between one and three new reports. Because of this uncertainty, each scenario presents a range of potential costs that could be associated with an increase in the number of telephone calls to MedWatch.

[2] Totals may not sum or multiply due to rounding.

[3] This estimate assumes that all direct consumer reports would be initiated by telephone calls to the MedWatch program and may overstate the potential costs if a substantial number of reports are submitted via the Internet.

[4] Based on FDA data, approximately 5 percent of direct reports received from sources other than the Internet are telephone reports from health care providers. Estimate corresponds to 5 percent of the lower limit of the potential number of new reports.

4. Total Potential Costs of Proposed Rule

As illustrated previously, affected pharmacies and authorized dispensers may incur negligible one-time costs or increased annual costs, FDA may incur increased annual costs, and affected drug manufacturers and third party vendors of consumer medication information may incur one-time costs in the 12 months following the effective date. Table 5 summarizes the range of potential costs of the rule. The agency requests comment on these estimates.

TABLE 5.—SUMMARY OF COMPLIANCE COSTS OF PROPOSED RULE[1]

Affected Sector	One-Time Costs ($ mil)	Annual Costs ($ mil)	Annualized Costs ($mil)	
			3 percent	7 percent
Retail Pharmacies		$6.4–$8.7	$6.4–$8.7	$6.4–$8.7
Nonretail Pharmacies		$2.8–$11.5	$2.8–$11.5	$2.8–$11.5
Drug Manufacturers	$1.3–$3.7		$0.2–$0.4	$0.2–$0.5
PPI Vendors	$0.0		$0.0	$0.0
FDA		$0.0–$1.9	$0.0–$1.9	$0.0–$1.9
Total	$1.3–$3.7	$9.2–$22.1	$9.3–$22.6	$9.4–$22.6

[1] Totals may not sum due to rounding.

B. Benefits of Regulation

The proposed rule would alert patients receiving prescription products to contact their doctor for medical advice about drug side effects and would provide a toll-free telephone number to report side effects to FDA.

All drug products have risks as well as benefits. Every year over 100 NDAs, including about 30 for new molecular entities, are approved in the United States (Ref. 6). Initial approval is based on the risks and benefits identified during the clinical trial phase of drug development. Although designed to detect common serious adverse drug reactions, premarketing clinical trials are not sufficiently large to detect very rare adverse events. Some uncertainty about the risks of approved drugs will always exist, requiring a system of postmarketing surveillance. In the United States, the agency's MedWatch program provides the mechanism for health care professionals and patients to voluntarily report serious adverse events and product problems.

Many adverse drug events in the outpatient setting are not systematically tracked and recorded. The agency

estimates it receives reports of between 1 and 10 percent of the actual adverse drug events that occur (Ref. 7). While drug manufacturers are required to notify FDA of certain adverse drug events, reports from individuals and health care professionals are voluntary. Consumers submitted only 8 percent of the 22,645 voluntary (i.e., direct) reports received by the agency in 2001. Increasing patient awareness of the MedWatch program may enhance patient participation. Moreover, since the agency encourages patients to report serious side effects through their provider, the proposed rule may also increase reporting from health care practitioners.

Drug-related illness costs society billions of dollars in direct medical care and lost productivity every year. Results of a large study of hospital discharge records conducted in Utah and Colorado suggest that adverse drug events cost society at least $42.5 billion each year of which only $18.5 billion would be considered preventable medication errors (Ref. 8). A recent revision of the 1995 Johnson and Bootman cost-of-illness model predicts that drug-related morbidity and mortality occurring in ambulatory care settings cost about $177.4 billion each year (Ref. 9).

The agency has no quantitative information about the value of additional drug safety reports that it might receive once the toll-free number is widely distributed to the public. Reports of adverse drug events provide the agency with "signals'' that a drug product might have previously unidentified risks. Once a signal is detected, the agency can decide whether further action is necessary to protect public health. The proposed rule has the potential to increase the number of direct reports being submitted, thereby providing the agency with more data about potential serious adverse drug events. Having more data may make it easier for the agency to detect signals about previously unknown risks of drugs. However, it is also possible that the toll-free number will encourage calls unrelated to drug product safety. Because the number and nature of calls that will be generated by the toll-free number are unknown, the agency cannot quantify the potential benefits of this rule. Moreover, findings of studies on the effectiveness of warning labels suggest that adding an additional sticker to an overcrowded prescription vial could dilute the impact of existing warnings (Ref. 10). Therefore, the agency solicits comment on the potential effects that could be anticipated from this rule.

C. Impact on Small Entities

1. The Need for the Proposed Rule

The Regulatory Flexibility Act requires the agency justify the need for the proposed rule. As described previously, the proposed rule fulfills the statutory requirement of the BPCA to provide consumers with a toll-free telephone number to report adverse drug events to FDA, along with a statement that the number is not to seek or obtain medical advice.

2. Description of the Affected Small Entities

a. *The pharmacy industry*. The proposed rule will affect pharmacies and authorized dispensers in both the Retail Trade sector and the Health Care and Social Assistance sector that dispense prescriptions to outpatients. For the purposes of this initial regulatory flexibility analysis, affected firms are considered small if they are: (1) A for-profit firm that meets the definition of small according to the current Small Business Administration (SBA) industry size standards; (2) an independently owned and operated, not-for-profit enterprise that is not dominant in its field; or (3) operated by a small governmental jurisdiction with a population of less than 50,000 individuals. Since SBA size standards differ from Census size categories, in the retail sector, all for-profit firms with receipts less than the Census size shown in table 6 of this document are considered small. Using Census data will slightly overestimate the number of small entities.

Although the agency knows of no data on the number of small retail entities dispensing pharmaceutical drugs, the Census Bureau reports the number of establishments with prescription drugs as a merchandise line, and the number of firms by annual sales categories. If the proportion of establishments with merchandise sales from prescription drugs is uniform across all size firms, approximately 26,621 small entities may dispense prescriptions. Furthermore, if the proportions in Table 1 of this document also apply equally to small entities (i.e., the proportion not currently distributing written drug information), approximately 4,879 small retail firms would be affected by the proposed rule (table 6 of this document). FDA solicits comment on these assumptions.

TABLE 6.—ESTIMATED NUMBER OF AFFECTED SMALL RETAIL FOR-PROFIT ENTITIES

Description of Business and NAICS Code	Census Size ($ mil)	SBA Size Standard ($ mil)	No. of Small Entities[1]	Share With Sales From R_x[2]	No. of Small Entities With Sales From R_x	Estimated No. of Affected Small Entities
Supermarkets and other grocery stores, except convenience (445110)	$25.0	$23.0	36,728	17.8%	6,543	720
Convenience stores (445120)	$25.0	$23.0	17,159	1.9%	320	35
Pharmacies and drug stores (4461101)	$10.0	$6.0	19,516	100.0%	19,516	4,098
Discount or mass merchandising department stores, excluding leased (4521102)	$25.0	$23.0	28	47.6%	13	0
Electronic shopping and mail-order houses (454110)	$25.0	$21.0	7,314	3.1%	229	25
Total			80,745		26,621	4,879

[1] Source: Table 4 in Ref. 11. May include small entities that do not dispense pharmaceutical drugs.

[2] Equals the percent of all establishments in the NAICS with sales from merchandise line code 0161 (*i.e.,* prescriptions). Source: Table 2 in Ref. 2.

In the Health Care and Social Assistance sector, both for-profit and not-for-profit entities may dispense prescriptions for outpatient use and would therefore be affected by the proposed rule. Census data exist on the number of establishments with receipts and revenues from prescription or nonprescription drugs as well as on firm size data. Table 7 of this document summarizes the estimated number of small for-profit firms with receipts from prescription or nonprescription drugs, and firms anticipated to be affected by the rule. Based on the Census receipt size most closely matching the SBA size standard and the share of for-profit establishments with receipts from prescription or nonprescription drugs (i.e., Receipt Line (RL) code 8619), there are approximately 6,855 small for-profit entities in this sector. (Again, using Census data slightly overestimates the number of small entities.) Applying the proportion of affected firms from table 1 of this document, an estimated 6,577 small for-profit firms may be affected by the rule.

TABLE 7.—THE NUMBER OF AFFECTED SMALL FOR-PROFIT NONRETAIL ENTITIES

Description of Business and NAICS Code	Census Size ($ mil)	SBA Size Standard ($ mil)	No. of Small Entities[1]	Share of All Non-retail Outlets With Receipts From R_x[2]	No. of Small Entities With Receipts From R_x	Estimated No. of Affected Small Entities
Offices of physicians (62111)	$10.0	$8.50	151,479	2.8%	4,177	4,177
Offices of dentists (62121)	$10.0	$6.00	101,932	1.3%	1,280	1,280
Offices of optometrists (62132)	$10.0	$6.00	14,570	3.0%	441	441
Offices of other health care practitioners (62139)	$10.0	$6.00	11,678	3.5%	404	404
Family planning centers (62141)	$10.0	$8.50	273	9.0%	25	3
Outpatient mental health & substance abuse centers (62142)	$10.0	$8.50	1,507	2.3%	35	4
HMO medical centers (621491)	$10.0	$8.50	14	19.8%	3	0
Kidney dialysis centers (621492)	$50.0	$29.00	355	25.9%	92	10
Free-standing ambulatory surgical & emergency centers (621493)	$10.0	$8.50	1,235	9.5%	117	13
Other outpatient care centers (621498)	$10.0	$8.50	1,891	2.2%	42	5
Hospital outpatient services (622)	$50.0	$29.00	282	85.0%	240	240
Total			285,216		6,855	6,577

[1] Source: Table 4a in Ref. 12. May include small entities that do not dispense prescription drugs.
[2] Equals the percent of all establishments in the NAICS with receipts from code 8619 (i.e., prescription and nonprescription drugs). Source: Table 1a in Ref. 3.

Similar to the table on the number of for-profit small entities in the Health Care sector, table 8 of this document summarizes the estimated number of small not-for-profit firms. For this analysis, single-unit firms exempt from Federal income tax are treated as small. This definition of a small entity may overstate the number of small, government, hospital-based outpatient clinics since some single-unit hospitals are located in jurisdictions with populations larger than 50,000. Similar to other outlets in the Health Care sector, not-for-profit firms dispensing drugs are assumed to be equally distributed across all firm sizes. Therefore, based on the 1997 Economic Census data, about 2,085 small not-for-profit entities may dispense drugs (i.e., have revenues from RL code 8619). Applying the Table 1 proportions, the proposed rule is estimated to affect 1,834 of these small entities.

TABLE 8.—THE NUMBER OF AFFECTED SMALL NOT-FOR-PROFIT NONRETAIL ENTITIES

Description of Business and NAICS Code	No. of Small Entities[1]	Share of All Not-for-Profit Outlets With Revenues From R_x[2]	No. of Small Not-for-Profit Entities With Revenues From R_x	Estimated No. of Affected Small Not-for-Profit Entities
Family planning centers (62141)	454	39%	176	19
Outpatient mental health & substance abuse centers (62142)	698	1%	5	1
HMO medical center (621491)	2	31%	1	0
Kidney dialysis centers (621492)	9	8%	1	0
Freestanding ambulatory surgical & emergency centers (621493)	55	6%	3	0

TABLE 8.—THE NUMBER OF AFFECTED SMALL NOT-FOR-PROFIT NONRETAIL ENTITIES—Continued

Description of Business and NAICS Code	No. of Small Entities[1]	Share of All Not-for-Profit Outlets With Revenues From R_x[2]	No. of Small Not-for-Profit Entities With Revenues From R_x	Estimated No. of Affected Small Not-for-Profit Entities
Other outpatient care centers (621498)	984	10%	96	11
Hospital outpatient services (622)	2,033	89%	1,803	1,803
Total	4,235		2,085	1,834

[1] Source: Table 3b in Ref. 12. May include small single unit firms that do not dispense prescription drugs.
[2] Equals the percent of all establishments in the NAICS with revenues from code 8619 (i.e., prescription and nonprescription drugs). Source: Table 1b in Ref. 3.

Most pharmacies and authorized dispensers currently distribute information to patients using at least one of the five proposed compliance methods. These small entities would incur only negligible one-time costs to add the side effects statement and would not require any additional skills. The agency requests comment on these assumptions. Although pharmacies can choose the least-cost compliance method from among five options, about 11 percent of pharmacies that currently do not distribute consumer medication information to patients could incur new annual costs to comply with the proposed rule. These costs would be proportional to the number of prescriptions dispensed. Because all options involve tasks normally performed in a pharmacy, no additional skills would be required. FDA believes adding a preprinted sticker with the side effects statement would likely be the most costly means of compliance. The agency estimates that adding a preprinted sticker with the statement to a prescription container would cost up to $0.03 per prescription. NACDS reports that in 2001, retailer pharmacies received approximately $10.57 for the average prescription costing $50.17 (Ref. 1). Adding a sticker might reduce affected retail pharmacy revenues by 0.3 percent. FDA believes this would not result in a significant economic impact on a substantial number of small retail pharmacies.

b. *Drug manufacturers.* The proposed rule will also affect drug manufacturers of products with Medication Guides or OTC products approved under section 505 of the act. According to the SBA size standards, Pharmaceutical Preparation Manufacturing firms (NAICS 325412) with fewer than 750 employees are considered small. Since the Census Bureau uses different employment size categories than the SBA, the number of small entities is based on the percentage of establishments with less than 1,000 employees. According to this definition, 97 percent of all establishments operating in 1997 were small (Ref. 13). If a similar share of firms in this sector are small, 1999 data suggest there could be up to 730 small entities in this sector (Ref. 14).

Small manufacturers of drug products with FDA-approved Medication Guides may incur an average of $3,165 in one-time costs to revise labeling of each affected product. Table 9 of this document illustrates the possible impacts on these manufacturers. Depending on production volume, the annualized costs of the proposed rule will add between $0.005 and $0.45 per unit sold. Moreover, NACDS reports that manufacturers receive $37.93 of the average $50.17 cost of a prescription (Ref. 1). If this figure is representative for the small entities affected by the rule, the additional annualized cost might reduce average receipts by less than 1.25 percent. FDA requests comments on these estimates from affected small entities.

Manufacturers of affected OTC products may spend between $1,000 and $3,000 to change their labeling. The effect on individual firms will vary with the number of products the firm must modify. The agency cannot assess the economic impact of the proposed rule on the small OTC manufacturers because Census does not report sales data for OTC products sold through all markets. However, most small firms manufacture few affected stock keeping units and might not incur significant regulatory costs. The agency requests comment from affected small entities.

TABLE 9.—ESTIMATED COST FOR SMALL ENTITIES WITH THREE ALTERNATIVE LEVELS OF PRODUCTION

	No. of Units, With Medication Guides, Sold Annually		
	1,000	10,000	100,000
Annualized cost to revise labeling[1]	$450.58	$450.58	$450.58
Additional cost per unit sold	$0.45	$0.05	$0.005
Additional cost per unit sold as a percentage of average manufacturer's share of retail prescription cost[2]	1.19%	0.12%	0.01%

[1] $450.58 equals the $3,164.71 one-time cost, annualized at 7% for 10 years.
[2] Based on an average share of $37.93 (Ref. 1).

As a result of this analysis, FDA believes that this proposed rule would not have a significant economic impact on a substantial number of small entities.

c. *Alternatives considered.*

Alternative implementation schedule

Because of the requirements of the BPCA, FDA considered a shorter implementation schedule, requiring compliance within 6 months of the effective date of the rule. However, the BPCA also mandates action that minimizes the cost on pharmacies and reaches the broadest consumer

audience. To address all of these requirements, the agency selected a 1-year implementation plan. This longer period will provide adequate time for all affected establishments to comply with the rule and specifically reduce the cost burden on small entities.

Require side effects statement for all drug labeling

The agency considered, but rejected, requiring that the side effects statement be added to the "physician labeling'' of all prescription drug products. The BPCA requires that the statement reach the broadest consumer audience possible. Physician labeling is targeted to health care practitioners and pharmacists. Although consumers may have access to this labeling, it is not intended for the consumer audience. Thus, adding the statement to physician labeling would cause firms of all sizes to incur costs that would not be necessary to achieve the goal of reaching a broad consumer audience.

Furthermore, the agency has proposed changes to physician labeling that will require drug manufacturers to include contact information, including the MedWatch telephone number, so that health care practitioners may report serious adverse drug reactions. These proposed changes will inform consumers who do access physician labeling how to report adverse events to FDA. If the proposed rule also required that firms add the side effects statement to physician labeling, many firms might be required to change labeling twice in a short period of time. This could be especially burdensome on small entities.

The one-time cost of this alternative would be approximately $15.6 million, including any excess inventory losses with a 1-year implementation schedule. However, allowing firms additional time to change labeling would reduce the costs of this alternative. For example, following a schedule staggered over 7 years after the effective date, similar to that proposed for the physician labeling rule, reduces the one-time cost of this alternative to $12.7 million with a present value of $8.0 million. Moreover, with a longer implementation schedule, some firms could avoid these compliance costs by adding the side effects statement when they revise drug product labeling for other reasons.

The agency also considered, but rejected, requiring the side effects statement to be included in PPIs. However, because not all prescription drug products carry PPIs, FDA determined that it was not the most effective way to reach a broad consumer audience, and would be duplicative of other methods the agency is proposing to distribute the side effects statement.

Alternative statement

FDA considered but rejected several alternatives for the proposed side effects statement. The agency considered a more comprehensive side effects statement to clarify when consumers should call FDA. The agency also considered requiring that the side effects statement be formatted in a larger type size than currently proposed for the sticker and vial cap options. The agency determined that these alternatives would require pharmacies to use larger, nonstandard stickers, thereby increasing compliance costs. The agency is proposing a more succinct side effects statement and smaller type size for the sticker and vial cap options in order to reduce the burden on small entities.

Options for pharmacies and authorized dispensers

FDA considered several options pharmacies and authorized dispensers could use to satisfy the requirements of the proposed rule. FDA has included all of these options in its proposal in order to minimize the effects of the rule on the pharmacy profession.

VI. Paperwork Reduction Act

FDA tentatively concludes that this proposed rule contains no collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (Public Law 104–13) is not required. FDA is proposing to amend its regulations to require a labeling statement be added to certain categories of drug product labeling. The proposed labeling statement for prescription drugs products is, "Call your doctor for medical advice about side effects. You may report side effects to FDA at 1–800–FDA–1088.'' For OTC drug products approved under section 505 of the act, the agency is proposing to use the existing subheading in § 201.66(c)(5)(vii) that states, "Stop use and ask a doctor if,'' followed by the bulleted statement "side effects occur.'' The second sentence would remain the same as for prescription products: "You may report side effects to FDA at 1–800–FDA–1088.'' These labeling statements are not subject to review by OMB because they are "originally supplied by the Federal Government to the recipient for the purpose of disclosure to the public'' (5 CFR 1320.3(c)(2)) and are not considered a collection of information under the PRA.

VII. Environmental Impact

The agency has considered the environmental effects of this proposed rule and has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the proposed rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

IX. Request for Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**). Two paper copies of any written comments are to be submitted, except that individuals submitting written comments or anyone submitting electronic copies may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

X. References

The following references have been placed on display in the Division of Dockets Management and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified the Web site address, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.)

1. "2001 Industry Facts-at-a-Glance,'' National Association of Chain Drug Stores, *http://www.nacds.org* (last viewed October 24, 2002).

2. "Summary 1997 Economic Census, Retail Trade,'' U.S. Department of Commerce, U.S. Census Bureau, Publication No. EC97R44S–SM, January 2001, pp. 55, 57, 69, 122, 151.

3. "Sources of Receipts or Revenue, 1997 Economic Census, Health Care and Social Assistance, Subject Series,'' U.S. Department of Commerce, U.S. Census Bureau, Publication No. EC97S62S–LS, August 2000, pp. 7–9, 11–13, 16, 24–27, 29.

4. Svarstad, B. et al., ''Evaluation of Written Prescription Information Provided in Community Pharmacies, 2001,'' Final report to FDA, December 21, 2001, presented at the FDA Drug Safety and Risk Management Advisory Committee Meeting, July 17, 2002, *http://www.fda.gov/cder/reports/prescriptionInfo/default.htm* (last viewed October 21, 2002).

5. 2000 National Occupational Employment and Wage Estimates,'' U.S. Department of Labor, Bureau of Labor Statistics, *http://www.bls.gov.oes/2000/oes292052.htm* (last viewed April 28, 2003).

6. Friedman, M. A. et al., ''The Safety of Newly Approved Medicines: Do Recent Market Removals Mean There Is a Problem?'' *Journal of American Medical Association*, 281(18):1728–34, 1999.

7. ''Adverse Drug Events: The Magnitude of Health Risks Is Uncertain Because of Limited Incidence Data,'' U.S. General Accounting Office, Report No. GAO/HEHS–0021, January 2000, p. 10.

8. Thomas, E. J. et al., ''Costs of Medical Injuries in Utah and Colorado,'' *Inquiry*, 36:255–64, 1999.

9. Ernst, F. R., and A. J. Grizzle, ''Drug-Related Morbidity and Mortality: Updating the Cost-of-Illness Model,'' *Journal of the American Pharmaceutical Association*, 41(2):192–199, 2001.

10. Viscusi, W. K., ''Individual Rationality, Hazard Warnings, and the Foundations of Tort Law,'' *Rutgers Law Review*, 48:625–671, 1996.

11. ''Establishment and Firm Size, 1997 Economic Census, Retail Trade,'' U.S. Department of Commerce, U.S. Census Bureau, Publication No. EC97R44S–SZ, October 2000, pp. 135, 139, 152, 160.

12. ''Establishment and Firm Size, 1997 Economic Census, Health Care and Social Assistance, Subject Series,'' U.S. Department of Commerce, U.S. Census Bureau, publication EC97S62S–SZ, October 2000, pp. 88–90, 97–103, and 106.

13. ''Pharmaceutical Preparation Manufacturing, 1997 Economic Census, Manufacturing, Industry Series,'' U.S. Department of Commerce, U.S. Census Bureau, Publication No. EC97M–3254B, November 1999, p. 9.

14. ''Statistics of U.S. Businesses: 1999, Pharmaceutical Preparation Manufacturing, United States,'' U.S. Department of Commerce, U.S. Census Bureau, *http://www.census.gov/epcd/susb/1999/us/US325412.htm* (last viewed September 12, 2002).

List of Subjects

21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 208

Labeling, Prescription drugs, Reporting and recordkeeping requirements.

21 CFR Part 209

Authorized dispensers, Drugs, Pharmacies, Prescription drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 201 and 208 be amended and part 209 be added as follows:

PART 201—LABELING

1. The authority citation for 21 CFR part 201 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 358, 360, 360b, 360gg–360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 264.

2. Amend § 201.66 by adding two sentences at the end of paragraph (c)(5)(vii) to read as follows:

§ 201.66 Format and content requirements for over-the-counter (OTC) drug product labeling.

* * * * *

(c) * * *

(5) * * *

(vii) * * * For all OTC drug products under an approved drug application, the following text shall immediately follow the subheading: ''[Bullet] side effects occur. You may report side effects to FDA at 1–800–FDA–1088.'' The telephone number must appear in a minimum 6-point bold letter height or type size.

* * * * *

PART 208—MEDICATION GUIDES FOR PRESCRIPTION DRUG PRODUCTS

3. The authority citation for 21 CFR part 208 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 360, 371, 374; 42 U.S.C. 262.

4. Amend § 208.20 by adding paragraph (b)(7)(iii) to read as follows:

§ 208.20 Content and format of a Medication Guide.

* * * * *

(b) * * *

(7) * * *

(iii) For drug products approved under section 505 of the act, 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.''

* * * * *

5. Add part 209 to read as follows:

PART 209—REQUIREMENT FOR AUTHORIZED DISPENSERS AND PHARMACIES TO DISTRIBUTE A SIDE EFFECTS STATEMENT

Subpart A—General Provisions

Sec.

Subpart B—Requirements

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 371; 42 U.S.C. 241.

Subpart A—General Provisions

§ 209.1 Scope and purpose.

(a) This part sets forth requirements for human prescription drug products approved under section 505 of the Federal Food, Drug, and Cosmetic Act and dispensed by authorized dispensers and pharmacies to consumers. This part requires distribution of a side effects statement and applies to new and refill prescriptions. This part is not intended to apply to 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.

(b) The purpose of providing the side effects statement is to enable consumers to report side effects of prescription drug products to FDA.

§ 209.2 Definitions.

For the purposes of this part, the following definitions apply:

Act means the Federal Food, Drug, and Cosmetic Act (sections 201–907 (21 U.S.C. 301–397)).

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.

Consumer medication information means written information voluntarily provided to consumers by dispensing pharmacists as part of patient medication counseling activities.

Medication Guide means FDA-approved patient labeling conforming to the specifications set forth in part 208 of this chapter and other applicable regulations.

Pharmacy includes, but is not limited to, a retail, mail order, Internet, hospital, university, or clinic pharmacy, or a public health agency, regularly and lawfully engaged in dispensing prescription drugs.

Side effects statement means 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.''

Subpart B—Requirements

§ 209.10 Content and format of the side effects statement.

(a) *Content.* The side effects statement provided with each prescription drug product approved under section 505 of the act must read: ''Call your doctor for medical advice about side effects. You may report side effects to FDA at 1–800–FDA–1088.''

(b) *Format.* The side effects statement must be in a single, clear, easy-to-read type style. The letter height or type size used for the side effects statement in accordance with paragraphs (b)(1) and (b)(2) of § 209.11 must be no smaller than 6 points (1 point = 0.0138 inches). The letter height or type size for the side effects statement under paragraphs (b)(3), (b)(4), and (b)(5) of § 209.11 must be no smaller than 10 points.

§ 209.11 Dispensing and distributing the side effects statement.

(a) Each authorized dispenser or pharmacy must distribute the side effects statement with each prescription drug product approved under section 505 of the act and dispensed. The side effects statement must be distributed with new and refill prescriptions.

(b) An authorized dispenser or pharmacy must choose one or more of the following options to distribute the side effects statement:

(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 in consumer medication information; or

(5) Distribute the appropriate FDA-approved Medication Guide that contains the side effects statement.

Dated: December 30, 2004.

Mark B. McClellan,

Commissioner of Food and Drugs.

Dated: December 30, 2004.

Tommy G. Thompson,

Secretary of Health and Human Services.

Note: The following appendix will not appear in the Code of Federal Regulations.

Appendix

IMS Health collects data on the quantity of products purchased by retail and nonretail pharmacies. Data may be reported three ways, by ''extended units'' (EUs), ''eaches'' (EAs), and ''units'' (UNs). IMS defines ''extended units'' as the individual tablet or capsule for solid dosage forms and the weight or volume (i.e., grams or milliliters) for other dosage forms, ''eaches'' as individual product packages (e.g., a vial, bottle or packet of pills), and ''units'' as individual shipping packages. None of these definitions correlates directly to the number of prescriptions dispensed. However, comparing retail prescription volume to the number of products purchased by the sector provides a rough estimate of the average number of EUs, EAs or UNs per prescription. Applying these three averages to the number of drug products purchased by the nonretail pharmacy sector yields rough estimates of the number of prescriptions dispensed by these outlets. Although uncertain, the range of prescriptions derived by this method is used to estimate the impact of the proposed rule on the nonretail pharmacy sector. These estimates were derived by FDA using IMS data. Although they were reviewed by IMS, they do not necessarily represent IMS views. The agency requests comments from nonretail outlets on its derivation of prescription volume.

The number of prescriptions dispensed, and the number of UNs, EAs and EUs purchased for different types of retail pharmacies are shown in Table A–1 of this appendix. In addition, the average number of products purchased per prescription dispensed is calculated for each of the three definitions of purchased products.

TABLE A–1.—NUMBER OF PRESCRIPTION DRUGS DISPENSED, NUMBER OF PHARMACEUTICAL PRODUCTS PURCHASED, AND AVERAGE NUMBER OF PHARMACEUTICAL PRODUCTS PER PRESCRIPTION IN 2001 BY RETAIL CHANNEL

Retail Channel	No. of Prescriptions Dispensed (million)	No. of Products Purchased (million)			Average No. of Products Purchased per Prescription Dispensed[1]		
		UNs	EAs	EUs	UNs	EAs	EUs
Mail Order	163.51	275.47	459.75	24,451.36	1.68	2.81	149.54
Independents	778.68	519.59	860.84	67,534.84	0.67	1.11	86.73
Food Stores	426.52	755.80	1,031.86	156,898.89	1.77	2.42	367.86
Chain Stores[2]	1,715.60	2,159.40	3,089.18	265,991.78	1.26	1.80	155.04

Sources: IMS Health, National Prescription Audit *Plus*, Year 2001, data extracted June 2002; IMS Health, Retail Perspective, Year 2001, data extracted June 2002.

[1] Averages equal the number of UNs, EAs or EUs, divided by the number of prescriptions.

[2] Includes traditional chain stores and mass merchants.

Table A–2 of this appendix displays IMS data for the number of UNs, EAs and EUs shipped to each nonretail channel with outpatient services. Data for clinics and HMOs may include drugs administered to inpatients of these facilities. For this analysis, the agency conservatively assumes that clinics and HMOs dispense all their products to outpatients. Similar to clinics and HMOs, hospital data include pharmaceutical products purchased for both outpatient and inpatient use. Unlike the other health care facilities listed, hospitals administer most drugs to inpatients. Thus the data for hospitals are adjusted by the share of revenue from outpatient services reported in the 1997 Economic Census (Ref. 3).

Although most nonretail channels defined by IMS Health agree closely with NAICS codes, according to Census data, 9,720 offices of health care practitioners reported revenue from pharmaceutical products in 1997. Because the number of products purchased by these offices is minor compared to other nonretail channels, they are not reported separately in the IMS data and would be included with data on other miscellaneous outlets. Therefore, for this analysis, other miscellaneous outlets are considered equivalent to offices of health care practitioners.

TABLE A–2.—NUMBER OF PHARMACEUTICAL PRODUCTS PURCHASED BY NONRETAIL CHANNELS IN 2001[1]

Nonretail Channel	No. Purchased by Quantity Measure (million)		
	UNs	EAs	EUs
Miscellaneous other, excluding prisons and universities	9.86	16.26	1,422.93
Clinics, including universities	121.78	342.24	10,444.36
HMOs	26.79	44.87	2,764.78
Federal and non-Federal hospitals	446.09	2,112.93	81,395.52
Hospitals adjusted by share of revenue from outpatient services[2]	118.11	559.46	21,551.76

[1] Source: IMS Health, Provider Perspective, Year 2001, data extracted June 2002.
[2] The weighted average share of revenue from outpatient services for NAICS 622 equals 26.5% (Ref. 3).

Three weighted averages were calculated based on the retail sector data in Table A–1 of this appendix and vary from 1.20 UNs per prescription to 166.93 EU per prescription (see Table A–3 of this appendix). To derive an estimate of the number of prescriptions dispensed by nonretail channels, the weighted average number of products per prescription shown in Table A–3 of this appendix is applied to the nonretail sector purchase data. This yields estimates that range from approximately 217 million to 546 million prescriptions per year (Table A–4 of this appendix).

TABLE A–3.—PER PRESCRIPTION WEIGHTED AVERAGE BY QUANTITY TYPE AND RETAIL CHANNEL[1]

Retail Channel	Share of Dispensed Prescriptions	Weighted Average No. Per Prescription by Quantity Type		
		UNs	EAs	EUs
Mail Order	5%	0.09	0.15	7.93
Independents	25%	0.17	0.28	21.90
Food Stores	14%	0.25	0.33	50.87
Chain Stores[2]	56%	0.70	1.00	86.24
Total Weighted Average	100%	1.20	1.76	166.93

Sources: IMS Health, National Prescription Audit *Plus*, Year 2001, data extracted June 2002, IMS Health, Retail Perspective, Year 2001, data extracted June 2002.
[1] Each channel's weighted average equals the share of retail prescriptions for the channel, multiplied by the corresponding average in Table A–1. The total weighted average for UNs, EAs, or EUs is the sum of the individual channel's weighted average in the column. Totals may not sum or multiply due to rounding.
[2] Includes traditional chain stores and mass merchants.

TABLE A–4.—ESTIMATED NUMBER OF OUTPATIENT PRESCRIPTIONS DISPENSED BY NONRETAIL CHANNELS

Nonretail Channel by NAICS Code	Estimated No. of Outpatient Prescriptions Dispensed (millions)		
	Based on UNs[1]	Based on EAs[1]	Based on EUs[1]
NAICS 6211, 6212 and 6213: Offices of Health Care Practitioners[2]	8.2	9.2	8.5
NAICS 6214, except NAICS 621491: Outpatient Care Centers, except HMOs[3]	101.2	194.0	62.6
NAICS 621491: HMO Medical Centers[4]	22.3	25.4	16.6
NAICS 622: Hospital Outpatient Services[5]	98.2	317.1	129.1
Total	229.9	545.7	216.8

Sources: IMS Health, National Prescription Audit *Plus*, Year 2001, data extracted June 2002; IMS Health, Provider Perspective, Year 2001, data extracted June 2002; IMS Health, Retail Perspective, Year 2001, data extracted June 2002.
[1] Weighted average quantity/script from Table A–3: UNs/Prescription = 1.20, EAs/Prescription = 1.76, EUs/Prescription = 166.93.
[2] Corresponds to IMS data for miscellaneous-other, excluding prisons and universities.
[3] Corresponds to IMS data for clinics including miscellaneous-universities.
[4] Corresponds to IMS data for HMOs.
[5] Corresponds to IMS data for Federal and non-Federal hospitals adjusted for share of revenue from outpatient services.

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DEPARTMENT OF AGRICULTURE

Forest Service

36 CFR Part 292

RIN 0596–AC00

Sawtooth National Recreation Area—Private Lands; Increasing Residential Outbuilding Size

AGENCY: Forest Service, USDA.

ACTION: Proposed rule; request for comment.

SUMMARY: The Forest Service proposes to revise a building standard for residential outbuildings within the Sawtooth National Recreation Area in Idaho. This proposed rule would increase the allowable size for residential outbuildings to 850 square feet from the current 400-square-foot standard and would limit such outbuildings to one story not more than 22 feet in height. This revision would allow residents to construct two-car garages and increase indoor storage areas to protect personal property and equipment, thereby reducing the need for unprotected and unsightly outdoor storage. Public comment is invited and will be considered in the development of the final rule.

DATES: Comments must be received in writing by June 21, 2004.

ADDRESSES: Send written comments by mail to Sawtooth National Forest, Attn: Private Land Regulations, Kimberly Road East, Twin Falls, ID 83301; via e-mail to *mailroom_r4_sawtooth@fs.fed.us* with "Private Land Regulations'' in the subject line of the message; or via facsimile to (208) 737–3236. Comments also may be submitted via the World Wide Web/Internet at *http://www.regulations.gov*. All comments, including names and addresses when provided, are placed in the record and are available for public inspection and copying. The agency cannot confirm receipt of comments. The public may inspect comments received on this proposed rule in the Office of Public Affairs at the Sawtooth National Forest, 2647 Kimberly Road East, Twin Falls, ID 83301. Visitors are encouraged to call ahead to (208) 737–3200 to facilitate entry into the building.

FOR FURTHER INFORMATION CONTACT: Jonathan Stephens, Recreation, Heritage, and Wilderness Resources Staff, Forest Service, USDA, (202) 205–1701; or Ed Waldapfel, Public Affairs Officer, Sawtooth National Forest (208) 737–3219.

SUPPLEMENTARY INFORMATION: The Sawtooth National Recreation Area (SNRA) in Idaho on the Sawtooth National Forest was created when Congress passed Public Law 92–400 in 1972 to assure the preservation and protection of the natural, scenic, historic, pastoral, and fish and wildife values and the enhancement of recreational values. The act directed the Secretary of Agriculture to develop regulations setting standards for the use, subdivision, and development of privately owned property within the boundaries of the recreation area. The current regulations at title 36 of the Code of Federal Regulations, part 292, subpart C (36 CFR part 292, subpart C), were adopted in 1974 (39 FR 11544) and were amended in 1976 and 1989 (41 FR 29379, 54 FR 3368). The act recognizes that the Secretary may from time to time amend these regulations. The SNRA regulations at § 292.14(b) require that any amendment to the regulations shall include publication of a notice of a proposed rulemaking in the **Federal Register** to provide interested persons the opportunity to comment before adoption of a final rule.

The current SNRA regulations at § 292.16(e)(2)(ii) set out a residential building standard providing that each residence on private land within the SNRA may have not more than two outbuildings at an aggregate area not to exceed 400 square feet.

The Forest Service is proposing to increase this standard for the two allowable outbuildings to 850 square feet and to limit such outbuildings to one story not more than 22 feet in height. The agency previously received numerous comments from the public indicating that the current residential outbuilding size standard is inadequate and supporting the need to increase this size standard. These comments were received in response to the environmental assessment prepared in 2000 for proposed revision of the Sawtooth National Forest land and resource management plan.

This proposed increase in the standard for the maximum square footage of the two allowable residential outbuildings would allow the private landowners to construct two-car garages and increase indoor storage areas to protect personal property and equipment, thereby reducing the need for unprotected and unsightly outdoor storage. Public comment is invited and will be considered in the development of the final rule.

Regulatory Certifications

Regulatory Impact

This proposed rule has been reviewed under USDA procedures and Executive Order 12866 on Regulatory Planning and Review. The Office of Management and Budget (OMB) has determined that this is not a significant rule. This proposed rule would not have an annual effect of $100 million or more on the economy, nor adversely affect productivity, competition, jobs, the environment, public health or safety, nor State or local Governments. This proposed rule would not interfere with an action taken or planned by another agency, nor raise new legal or policy issues. Finally, this proposed rule would not alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients of such programs. Accordingly, this proposed rule is not subject to OMB review under Executive Order 12866.

Proper Consideration of Small Entities

This proposed rule has been considered in light of Executive Order 13272 regarding proper consideration of small entities and the Small Business Regulatory Enforcement Fairness Act of 1996 (SBREFA), which amended the Regulatory Flexibility Act (5 U.S.C. 601 *et seq.*). It has been determined that this proposed rule would not have a significant economic impact on a substantial number of small entities as defined by SBREFA. This proposed rule would impose minimal additional requirements on the affected public, which includes the owners of private property and residences within the Sawtooth National Recreational Area. The proposed increase of the allowable outbuilding size to 850 square feet is responsive to comments already received from the affected public stating that the current allowable square footage under the existing rule is inadequate. These comments were received in response to an environmental assessment prepared in 2000 for the proposed amendment of the Sawtooth National Forest land and resource management plan. The changes are necessary to protect the public interest, are not administratively burdensome or costly to meet, and are well within the capability of small entities to perform.

Environmental Impact

Section 31.1b of Forest Service Handbook 1909.15 (57 FR 43180; September 18, 1992) excludes from documentation in an environmental assessment or impact statement "rules, regulations, or policies to establish