



**American Pharmacists Association**  
Improving medication use. Advancing patient care.

July 21, 2004

Division of Dockets Management  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

Re: Docket No. 2003N-0342 / RIN 0910-AC35

Dear Sir/Madam:

Thank you for the opportunity to comment on the Food and Drug Administration's (FDA) proposal to require drug product labeling to include a toll-free number for the reporting of adverse events. The American Pharmacists Association (APhA), founded in 1852 as the American Pharmaceutical Association, represents more than 50,000 practicing pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in advancing the profession. APhA, dedicated to helping all pharmacists improve medication use and advance patient care, is the first-established and largest association of pharmacists in the United States.

Adverse event reports are a crucial component of post-marketing surveillance for both prescription and over-the-counter drug products. Post-marketing surveillance allows the Agency, in conjunction with product manufacturers, to monitor patterns of use and the harmful or beneficial effects of drug products as they are used in the general population. Although drug products are carefully evaluated as part of the drug approval process, a drug product's effects may not be apparent until after the product is widely used in the general population. Adverse event reports are a primary mechanism of obtaining information about a product's effects in the post-marketing environment.

To date, the majority of adverse events reports are submitted by pharmacists, prescribers, and other health care professionals. To increase the number of adverse events reported by consumers, Section 17 "Adverse Event Reporting" of the Best Pharmaceuticals for Children Act (BPCA) [Public Law 107-109] requires medication labeling to include a toll-free number maintained by the Department of Health and Human Services (HHS) for the purpose of receiving reports of drug-related adverse events. The number must be included on the labeling of human drug products approved through a new drug application (NDA) or abbreviated new drug application (ANDA), including over-the-counter products originally approved as a NDA or ANDA. The proposed rule, as published in the April 22, 2004 *Federal Register*, implements Section 17 of the BPCA.

APhA strongly supports efforts to increase active reporting of adverse events. The APhA House of Delegates, the policy-making body for the Association, has adopted several policies in support of post-marketing surveillance efforts. The following policy adopted in 1982 and reaffirmed in 1986 illustrates pharmacy's and the Association's support of adverse event reporting:

APhA recognizes the spontaneous adverse drug reaction reporting system as the basic foundation of post-marketing drug surveillance; as such, APhA believes that this spontaneous reporting system should be maintained and strengthened.<sup>1</sup> [Emphasis added]

APhA welcomes the Agency's efforts to increase adverse event reporting and appreciates the opportunity to comment on the proposed rule. APhA will provide comments and recommendations on two areas of the rule: 1) the proposed language for the side effects labeling statement and 2) the delivery of the labeling statement.

### **Side Effects Statement**

Section 17 of the BPCA directs the Secretary of HHS to develop a labeling statement that contains a toll-free number for reporting adverse events. Although the law does not provide specific language for the labeling statement, it does require that the labeling be accompanied by a statement that the "number is to be used for reporting purposes only, not to receive medical advice." The FDA has proposed that the labeling statement read: "Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088."

In general, the labeling statement offered by the Agency appears to meet the law's two requirements: it includes the toll-free number of the MedWatch Program, the FDA's established system for receiving adverse event reports; and it includes a statement directing consumers to a health care professional for medical advice. However, APhA shares the concern acknowledged by the Agency in the proposed rule that the side effects statement may generate confusion for some consumers. While the statement directs consumers to a health care professional for medical advice about side effects, it may not be clear that medical advice is not available from the Agency. We are concerned that consumers experiencing a serious reaction or problem related to a drug product will call the toll-free number in search of medical advice rather than contact their health care provider. The delay in obtaining medical advice could have deadly consequences. APhA urges the Agency to conduct consumer testing of the proposed statement to evaluate consumer comprehension.

APhA also recommends that the Agency modify the statement to read: "Call your doctor or pharmacist for advice about side effects." While we understand the need for brevity in the labeling statement, pharmacists are the medication experts of the health care team. With an average of six years professional education in pharmacology and therapeutics, pharmacists are the most knowledgeable health care professional with respect to prescription and OTC medications. Pharmacists understand how drugs work, how drugs interact, and how drug side effects should be addressed. Pharmacists are also the most accessible health care professional. With a pharmacy located within five miles of virtually every household in the United States,<sup>2</sup> many of which are open in the evenings and on

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<sup>1</sup> Am Pharm. NS26(6):420. June, 1986); (Am Pharm. NS22(7): 32. July, 1982.

<sup>2</sup> Alliance for Pharmaceutical Care: Pharmacists for Qualify Patient Care. "Your Pharmacist". 2003; pg. 3.

weekends outside of hours physicians are readily available, consumers frequently have more immediate access to a pharmacist than a physician.

APhA strongly encourages the FDA to add “or pharmacist” to the labeling statement. By directing consumers to their physician or pharmacist, the Agency will help ensure that consumers experiencing an adverse event obtain access to a trained health care professional who can provide immediate advice. Patients calling about serious side effects requiring immediate medical attention would be referred by the pharmacist to a physician or hospital.

### **Delivery of the Side Effects Statement**

The adverse events provision of the BPCA does not specify how the side effect labeling statement should be delivered to the consumer. However, the law directs the Secretary of HHS to implement the labeling statement in a manner “most likely to reach the broadest consumer audience” and to minimize the cost to the pharmacy profession. Under the proposed rule, pharmacists and other authorized dispensers would be required to distribute the side effect statement to consumers with new and refill prescriptions. Pharmacists would be allowed to select from five 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.

APhA applauds the Agency for providing pharmacists and other dispensers with some flexibility to meet the rule’s requirements. While it is most likely that pharmacists will select the fourth option and distribute the side effects statement in consumer medication information (CMI) – a 2001 FDA study found that 89% of pharmacies already distribute CMI to patients with their prescriptions;<sup>3</sup> by providing five options, pharmacists can select the distribution method most appropriate for their pharmacy practice.

We are disappointed, however, that the proposed rule does not require prescription drug manufacturers to include the side effects statement on products manufactured in unit-of-use packages. The rule should require manufacturers to include the side effects statement on products that are not repackaged as part of the dispensing process such as oral contraceptives, insulin, topical ointments, etc. Requiring manufacturers to include the side effects statement on the product packaging will ensure that the statement is provided to the consumer and reduce the administrative burden to the pharmacist. APhA requests that the Agency modify the rule to require manufacturers of unit-of-use products to print the labeling statement directly on the product package. This would mirror the requirement that OTC manufacturers print a similar side effects labeling statement directly on the product package.

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<sup>3</sup> Food and Drug Administration Talk Paper. “Success of Private Sector Patient Information with Prescription Medicines Assessed.” June 18, 2002.

The FDA should also revise the rule to require manufacturers to include the side effects statement in the patient package insert (PPI). While we understand the Agency's rationale that inclusion in the PPI is not necessary because pharmacists will already be required to distribute the statement to patients through other means, we urge the Agency to reconsider its decision. PPIs are designed to be distributed to patients when a medication is dispensed. Developed by the manufacturer, PPIs contain important information about the drug product in lay language geared for a consumer audience. Consumers may turn to the PPI to learn more about their medication – including potential risks associated with its use – or when a medication-related problem occurs. Because the PPI is a source of importation information for consumers that may be referenced when an adverse event occurs, the side effects statement should be included. Although including the statement in the PPI may result in consumers receiving the side effects statement twice (once in the PPI and through one of the five options selected by the pharmacist), this should not be a deterrent for the Agency. Placing important information before consumers multiple times may help ensure that consumers actually observe it.

APhA also recommends that the Agency revise the rule to require distribution of the side effects statement with drug samples. Health care practitioners often provide drug samples to consumers in conjunction with a new prescription for that product. Consumers utilize the drug samples – essentially “trying” the medication – before having the prescription dispensed. In this situation, consumers use the product prior to any interaction with a pharmacist. Not only does this result in the consumer using the medication without the benefit of a pharmacist checking the individual's medication profile for potential drug interactions and contraindications – a service that can reduce the likelihood of adverse events; the pharmacist does not have the opportunity to provide the side effects statement prior to the consumer beginning medication use. It is critical that consumers receive necessary information about their medication – including the side effects statement – when they begin a new medication. Because drug samples often provide a consumer's first exposure to a new medication – when side effects may be most likely to occur – providing side effects information with drug samples appears prudent. APhA implores the Agency to revise the rule to require the distribution of the side effects statement with drug samples.

In conclusion, APhA fully supports the intent of the proposed regulation. Measures to improve patient safety through effective post-marketing surveillance activities are a priority for our Association and our members – and increasing adverse event reporting is an important component of this work. APhA appreciates the efforts of Congress and the FDA to increase adverse event reporting by consumers by promoting the toll-free FDA MedWatch number on prescription and certain OTC medications.

As the Agency continues to work toward implementation of Section 17 of the BPCA, APhA recommends that the Agency:

1. Conduct consumer comprehension testing of the proposed labeling statement;
2. Modify the first portion of the proposed labeling statement to read: “Call your doctor or pharmacist for advice about side effects”;
3. Require prescription drug manufacturers to include the side effects labeling statement on unit-of-use prescription drug product packages;
4. Require prescription drug manufacturers to include the side effects statement in patient package inserts; and
5. Require distribution of the side effects statement with drug samples.

Thank you for your consideration of the views of the nation's pharmacists. Please contact Susan C. Winckler, Vice President, Policy & Communications and Staff Counsel, at 202-429-7533 or [SWinckler@APhAnet.org](mailto:SWinckler@APhAnet.org), or Susan K. Bishop, Senior Manager, Regulatory Affairs & Political Action, at 202-429-7538 or [SBishop@APhAnet.org](mailto:SBishop@APhAnet.org) with any questions.

Sincerely,

A handwritten signature in black ink, appearing to read "John A. Gans". The signature is fluid and cursive, with the first name "John" being the most prominent.

John A. Gans, PharmD  
Executive Vice President

cc: Susan C. Winckler, RPh, Esq, Vice President, Policy & Communications and Staff Counsel  
Susan K. Bishop, MA, Senior Manager, Regulatory Affairs & Political Action