

Food and Drug Administration
Docket No. 2003N-0342
RIN 0910-AC35
Division of Dockets Management
5630 Fishers Lane
Room 1061
Rockville, MD 20852

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

To whom it may concern,

First DataBank (FDB) is providing comments on the agency's implementation of Section 17 of the Best Pharmaceuticals for Children Act of 2001 (P.L. 107-109) that requires pharmacies to include as part of the labeling of each consumer prescription package a toll-free number maintained by the Secretary of HHS to report to the FDA adverse reactions from medications. This statement or phrase proposed by the FDA is "Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088." See 69 Fed. Reg. 21 778 (April 22, 2004).

FDB is a leading provider of medical and pharmaceutical databases to the entire spectrum of healthcare, from governmental agencies to third party payers to software vendors and pharmacies/clinics/institutions nationally and internationally.

FDB understands the intent to enhance the reporting of post-marketing adverse drug reactions (ADRs) to the FDA. These reports help practitioners understand the impact of the broader use of medications beyond the limited population of patients included in clinical trials. However, there are problematic issues raised by the proposed FDA plan.

First of all, FDB can incorporate the Medwatch toll-free number statement into the Side Effects Section of all the patient education monographs (aka Consumer Medication Information or CMI) provided to our customers without a great deal of difficulty. We would recommend that CMI not be the only vehicle for communicating the toll-free number, as we are aware that some pharmacies may not dispense CMI for refill prescriptions. **A physical sticker containing the Medwatch toll-free number statement (as opposed to a software-generated statement on the prescription label etc) is suggested as an additional method available to the pharmacist.** The reason a physical sticker is recommended is as follows:

Our auxiliary warning label database is structured on a priority system. The most important labels are rank-ordered. Due to space considerations, some customers may only use the first three to five labels out of the entire set assigned to a certain product. To assure that the toll-free number label was received by all possible consumers, we would be faced with the very problematic decision of which label to bump in order to add the toll-free number label to the highest priority label group. This would result in very important labels covering useful consumer advisories being bumped down the priority list, and possibly not reaching the consumer audience. Hence, the recommendation that the toll-free number advice be available on a physical sticker separate from our auxiliary label warning database.

The agency could also minimize the impact on pharmacy by **requiring manufacturers of unit of use products, and those that have to distribute patient package inserts (PPIs) with their**

prescription packaging, to provide this number on their containers or on the PPI, obviating the need for pharmacies to generate this information. This is especially important when a container such as a bronchodilator device is involved. Frequently, the patient may discard the outer packaging, so printing the toll-free number statement on the device itself is useful. Additionally, we support the idea of a small **magnet with the toll-free number embossed on it** being made available to patients, obviating the need for repeated dispensing of this information each time a patient visits their pharmacy.

In our view, implementation of this program in its proposed form will not only be burdensome to pharmacies, but will be extremely burdensome to FDA. That is because it will result in the reporting of thousands of insignificant, commonly-known adverse events of prescription drugs that have been on the market for decades, to say nothing of the false reports (i.e., events not actually caused by the drug in question). Instead, **this program should be targeted to encourage consumer reporting of adverse reactions from newer drugs**. Certain new adverse effects may be identified once a newer drug is used in the broader population that was not identified in more limited clinical trials or early use experience.

However, by proposing a wide-ranging program in this proposed rule, rather than a more targeted and effective program, FDA runs the risk that the public will dismiss the importance of reporting adverse events for newer drugs. That could happen if the system becomes overwhelmed with reports of commonly-known adverse events (i.e. gastrointestinal distress with antibiotics; somnolence with benzodiazepines). The agency may have no choice but to establish voice recording systems to allow all the patients calling in to the FDA to leave information about their suspected event. Because patients may not be able to easily reach the agency with more important unknown events for newer drugs, the relevance of this system will decline and important adverse events that are occurring from newer drugs could be missed.

Regarding the agency's proposed language for both Rx and OTC products:

FDA's Proposed RX language: Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

FDB's suggested RX language: Call your doctor **or pharmacist** for advice about side effects. **FDA does not give medical advice**, but you may report side effects to FDA at 1-800-FDA-1088.

COMMENT: The first sentence is general in nature, with no specific urgency attached to the process of consulting a healthcare professional re: particular side effects. We believe this is appropriate, as our CMI already provides 3 levels of urgency for various adverse effects, depending on their seriousness. There does not appear to be an ideal way to express this idea, however. Specifically, some consumers may still be confused re: the urgency of reporting specific adverse effects when comparing the first sentence of this Medwatch advisory to the urgency levels in CMI. For example, the highest level of urgency is expressed in our accelerated hypersensitivity statement (paraphrased): "seek immediate medical attention if the following symptoms of a serious allergic reaction occur: rash, itching, swelling, dizziness, trouble breathing." It seems apparent that some consumers may be confused by the disparity between the "seek immediate medical attention" statement in the CMI, and the much less urgent "Call your doctor for advice about side effects" statement. This could lead to patient harm if they focus on the Medwatch statement and not on the CMI advice.

The pharmacist should also be included in the process, as the healthcare professional most accessible to the patient, and as the drug therapy expert, hence the suggested inclusion of the pharmacist in the first sentence language.

The second sentence is not explicit enough re: the fact that FDA is not offering medical consultation. In our experience writing CMI, patients need very explicit, concrete information. Failure to create a more explicit second sentence could lead to patient harm, as some consumers will interpret the existing sentence to mean that they can receive side effect advice from FDA. If the adverse effect is serious and urgent, and medical treatment is delayed while the patient is calling FDA, the resulting patient harm is counterproductive to the overall intent of the rule.

FDA's proposed OTC language: Stop use and ask a doctor if side effects occur. You may report side effects to FDA at 1-800-FDA-1088.

***FDB's suggested OTC language:* Call your doctor or pharmacist for advice about side effects. FDA does not give medical advice**, but you may report side effects to FDA at 1-800-FDA-1088.

COMMENT: Regarding the first sentence, one would assume the logic used was that OTC meds are not critical for the patient, so drug discontinuation before professional consultation is reasonable. However, consider the patient using aspirin OTC for cardiovascular prophylaxis as an example. In these types of situations (effective OTC meds used for diagnosed, significant medical conditions, as opposed to self-diagnosis of minor ailments) it seems more logical and prudent to advise the patient to seek professional advice before drug discontinuation, in case the adverse effect is either minor or risk/benefit considerations would dictate continuing the medication. Hence the suggestion that the first sentence of the Rx and OTC advisories be identical. This approach should be reasonable for all OTC usage situations, since the patient could speak to the more accessible pharmacist about OTC products, perhaps obviating the need to contact their physician. This would be especially true for minor/self-limited conditions, and the pharmacist could suggest alternative products, or refer the patient if necessary -- depending on symptoms. The second sentence is not explicit enough re: the fact that FDA is not offering medical consultation. Hence, we would suggest the same language as the RX statement's second sentence.

We would be willing to explain any of the above comments/suggestions in more detail, or offer additional input should that be deemed useful by the agency.

Sincerely,

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