

# **Guidance**

## **Drug Safety Information – FDA’s Communication to the Public**

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

**March 2007  
Drug Safety**

# Guidance

## Drug Safety Information – FDA’s Communication to the Public

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# Guidance<sup>1</sup>

## Drug Safety Information – FDA’s Communication to the Public

This guidance represents the Food and Drug Administration’s (FDA’s) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public.

### I. WHAT IS THIS GUIDANCE ABOUT?

This document provides guidance on how FDA is developing and disseminating information to the public regarding important drug safety issues, including emerging drug safety information.<sup>2</sup> As discussed in more detail below, an *important drug safety issue* is one that has the potential to alter the benefit/risk analysis for a drug in such a way as to affect decisions about prescribing or taking the drug. The term *emerging drug safety information* refers to information about an important drug safety issue that has not yet been fully analyzed or confirmed.

For many years, FDA has provided information on drug risks and benefits to healthcare professionals and patients when that information has generated a specific concern or prompted a regulatory action, such as a revision to the drug product’s labeling. More recently, FDA has begun taking a more comprehensive approach to making information on potential drug risks available to the public earlier, in some cases while the Agency still is evaluating whether any regulatory action is warranted. FDA believes that timely communication of important drug safety information will give healthcare professionals, patients, consumers, and other interested persons access to the most current information concerning the potential risks and benefits of a marketed drug, helping them to make more informed individual treatment choices.

This Guidance<sup>3</sup> describes FDA’s current approach to communicating important drug safety information, including emerging drug safety information, to the public and the factors that influence when such information is communicated. FDA may disseminate important drug safety information by other methods and at other times than those described in this guidance.

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<sup>1</sup> This guidance has been prepared by the Office of Regulatory Policy in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA).

<sup>2</sup> The term *drug* as used in this guidance includes all drug and biological products regulated by CDER. Information about marketed drugs available on the Index to Drug-Specific Information Web page may include approved drugs used for labeled or unlabeled indications, or unapproved drugs.

<sup>3</sup> The draft version of this guidance was called *FDA’s ‘Drug Watch’ for Emerging Drug Safety Information*.

## **II. WHY IS FDA ISSUING THIS GUIDANCE?**

FDA has been reexamining its risk communication program, including how and when we communicate emerging drug safety information to the public. We are issuing this guidance to reaffirm our commitment to communicating important information about drug safety in a timely manner, in some cases while the Agency still is evaluating whether any regulatory action is warranted.

FDA's risk communication efforts are part of a larger drug safety initiative that began in November 2004, when FDA announced an initiative to strengthen the safety program for marketed drugs. This initiative included: (1) sponsoring an independent study by the Institute of Medicine of the National Academies of the effectiveness of the drug safety system, with emphasis on postmarketing risk assessment and surveillance; (2) conducting workshops and Advisory Committee meetings regarding complex drug safety and risk management issues, including emerging concerns; and (3) publishing three risk management guidances.<sup>4</sup>

FDA augmented its drug safety initiative in February 2005 by creating an independent Drug Safety Oversight Board to enhance oversight of drug safety decision making within CDER. FDA also announced its commitment to "increase the transparency of the Agency's decision-making process by establishing new and expanding existing communication channels to provide targeted drug safety information to the public. These channels will be used to help ensure that established and emerging drug safety data are quickly available in an easily accessible form. The increased openness will enable patients and their healthcare professionals to make better-informed decisions about individual treatment options."<sup>5</sup>

To fulfill this commitment, FDA issued for comment a draft guidance titled *FDA's 'Drug Watch' for Emerging Drug Safety Information* in May 2005. In December 2005, FDA held a public hearing regarding "FDA's Communication of Drug Safety Information" that examined the various risk communication tools employed by FDA. Comments from participants emphasized that, increasingly, patients are taking a more active role in their healthcare. Patients want information about the drugs they are taking, and actively seek this information from various sources, including the Internet. Patients and their healthcare providers rely on information from these sources to make important prescribing and treatment decisions (including about consumer self-care). Because of its expertise and access to important information concerning the benefits and safety of medications, FDA is an important source of drug information.

FDA has carefully reviewed the comments it received on the draft guidance (30 comments were submitted to the public docket)<sup>6</sup> and during the public hearing. This final version of the guidance reflects our consideration of these comments, as well as our experience with posting emerging drug safety information.

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<sup>4</sup> See the following guidance documents published in March 2005: *Premarketing Risk Assessment; Development and Use of Risk Minimization Action Plans*; and *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment*, available at <http://www.fda.gov/cder/guidance/index.htm>.

<sup>5</sup> FDA Fact Sheet (February 15, 2005).

<sup>6</sup> See Docket No. 2005D-0062 (available at <http://www.fda.gov/ohrms/dockets/dockets/05d0062/05d0062.htm>).

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Due to potential confusion between the proposed *Drug Watch* and FDA's existing *MedWatch* program, FDA no longer plans to use the name *Drug Watch* to describe the Web page that contains drug safety information. As discussed in more detail in section VII of this guidance, we have identified drugs that have been the subject of a Public Health Advisory or an Alert (see section VI.E of this guidance) on a single Web page linked from FDA's Web site. This is part of our ongoing effort to use and enhance existing FDA communications mechanisms to better convey important drug safety information to the public. In addition, we have revised this guidance to describe the various methods FDA currently uses to communicate established and emerging drug safety information to the public. It should be noted that we will continue to evaluate and enhance the effectiveness of the various methods we use to communicate about important drug safety issues, including the mechanisms described in this guidance and the presentation of drug safety information on the Agency's Web sites (<http://www.fda.gov> and <http://www.fda.gov/cder>). We intend to update this guidance, as appropriate, to reflect any substantial modifications to our communication of drug safety information to the public.

### **III. WHAT DRUG SAFETY INFORMATION DOES FDA COMMUNICATE?**

FDA communicates information about *important drug safety issues*, and under the drug safety initiative, FDA has enhanced its efforts to communicate such information earlier in our decision making process (see section V of this guidance). An *important drug safety issue* is one that has the potential to alter the benefit/risk analysis for a drug in such a way as to affect decisions about prescribing or taking the drug. Examples of important drug safety issues include, but are not limited to:

- Serious adverse drug experiences<sup>7</sup> identified after approval or in the setting of a new use
- Additional serious or more frequent adverse drug experiences in a subpopulation of patients
- Medication errors

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<sup>7</sup> A *serious adverse drug experience* is defined as:

Any adverse drug experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse

(21 CFR 314.80(a)).

#### **IV. HOW DOES FDA EVALUATE DRUG SAFETY INFORMATION?**

All drugs have risks, and healthcare professionals and patients must balance the risks and benefits of a drug when making decisions about medical therapy. FDA monitors and reviews available safety information related to marketed drugs throughout each drug product's lifecycle. When a drug is approved, the product labeling includes, among other things, available information about the benefits and risks of the drug. After drug approval, the Agency may learn of new, or more frequent, serious adverse drug experiences from postapproval clinical studies or from clinical use. For example, additional adverse drug experiences, some of them serious, may be identified as a drug is used more widely and under more diverse conditions (e.g., concurrently with other drugs), or as the drug is prescribed for off-label uses.

As new information related to a marketed drug becomes available, the Agency reviews the data and evaluates whether there is a potential drug safety concern. When a potential drug safety concern arises, relevant scientific experts within the Agency engage in a prompt review and analysis of available data. Often, there is a period of uncertainty while FDA evaluates the new safety information to determine whether there is an important drug safety issue related to a specific drug or drug class and whether regulatory action is appropriate. During this period, FDA also is actively engaged in scientific efforts to gather additional safety information. The Drug Safety Oversight Board may be consulted and provide recommendations to the Director of the Center for Drug Evaluation and Research regarding the management and communication of an emerging drug safety issue. FDA also may consult an Advisory Committee regarding an emerging drug safety issue. Sponsors are also evaluating the new safety information and providing the results of their analyses to FDA during this time. As additional data relevant to an emerging drug safety issue become available (e.g., data from an ongoing study or data from available clinical databases), such data are considered in the analysis and decision-making process. Upon evaluation of additional data, further regulatory action, such as a revision to product labeling or a Risk Minimization Action Plan (RiskMAP), may be appropriate.

Interpretation of postmarketing safety data is complex, involving analysis of postapproval clinical data, detailed review of adverse drug experience reports in the context of relevant clinical studies, estimates of drug usage and adverse drug experience reporting rates, estimates of background rates of the adverse event, and other relevant information. Decisions about how to address a safety concern often are a matter of judgment, about which reasonable persons with relevant expertise may disagree. We engage in vigorous and comprehensive discussions within the Agency regarding potential drug safety issues to ensure that all points of view are considered prior to making a decision on how to proceed.

As the Agency evaluates a drug safety issue to determine whether regulatory action is warranted, we may communicate further information to the public at appropriate points in the decision-making process. Consistent with our public health mandate, we may advise the public of an emerging drug safety concern as well as the next steps the Agency may take regarding an important drug safety issue.

## **V. WHEN DOES FDA COMMUNICATE EMERGING DRUG SAFETY INFORMATION?**

We use the term *emerging drug safety information* to describe information FDA is monitoring or analyzing that may have the potential to alter the benefit/risk analysis for a drug in such a way as to affect decisions about prescribing or taking the drug (i.e., an important drug safety issue), but that has not yet been fully analyzed or confirmed. Emerging drug safety information may be derived from data from postmarketing surveillance (for example, reported serious adverse drug experiences), clinical studies, clinical pharmacology studies, epidemiological studies, or the scientific literature. Such information may relate to new risks or new information on known risks.

For years, FDA and sponsors have disseminated emerging drug safety information. The Agency currently disseminates emerging drug safety information after having completed an analysis of available data and, in some cases, before having reached a decision about the need for a regulatory action. Agency communications about emerging drug safety information may help achieve certain longstanding public health goals, including enhanced vigilance on the part of healthcare professionals who may be prompted by the information to increase their reporting of safety observations to FDA. We are mindful of the potential public health implications of providing emerging drug safety information and are particularly concerned about possible consequences, such as inappropriate modification or discontinuation of useful treatment. We attempt to anticipate and address these possible consequences through our risk communications by describing the nature of a safety concern and what is known about its relationship to a particular drug and making recommendations for healthcare professionals and patients about how to monitor for and manage the concern. There will always be some tension between the goal of having people informed about potentially important information as early as possible and the goal of having that information thoroughly substantiated. Our goal is to make emerging drug safety information available to the public in a balanced, impartial manner so that healthcare professionals and patients can consider the information when making decisions about medical treatment despite uncertainties in the data. The Agency is committed to providing accurate, clear, reliable, and useful drug safety information.

FDA considers many factors in the course of evaluating an emerging drug safety concern and deciding whether emerging drug safety information should be made available to the public. These factors include, but are not limited to, the following:

- Reliability of the data
- Magnitude of the risk
- Seriousness of the event (e.g., severity and reversibility) relative to the disease being treated
- Plausibility of a causal relationship between the use of a drug and the adverse event<sup>8</sup>
- Extent of patient exposure (e.g., how broadly is the drug used)
- Potential to prevent or mitigate the risk in the patient population (e.g., monitoring)
- Effect on clinical practice
- Disproportionate impact on particular populations (e.g., children or the elderly)

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<sup>8</sup> See, e.g., guidance for industry on *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment* at pages 6 to 7 and 17 to 18.

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Providing information about an emerging drug safety issue does not necessarily mean that FDA has concluded there is a causal relationship between the drug and the adverse events described. Communicating emerging drug safety information also does not necessarily mean that FDA is advising healthcare professionals to limit their prescribing of the drug at issue, rather it is intended to further inform such prescribing.

**VI. HOW DOES FDA COMMUNICATE IMPORTANT DRUG SAFETY INFORMATION?**

FDA uses a broad range of methods to communicate drug safety information to the public. Certain forms of communication are targeted to specific audiences (e.g., healthcare professionals or patients). Others are directed at more than one group to ensure widespread dissemination of information about important drug safety issues, including emerging drug safety issues. FDA is continuing to evaluate its communication efforts and will modify them to enhance their accessibility and effectiveness. We welcome public comment at any time suggesting ways to improve our safety communications. The table, below, summarizes the methods discussed in this section for FDA communication of drug safety information.

Table: Summary of Selected Methods for FDA Communication of Drug Safety Information

Type of Communication	Content	Target Audience
Professional labeling for prescription drugs	Summary of essential information needed for safe and effective use of the drug.	Healthcare providers
Patient-directed labeling for prescription drugs (patient package inserts and Medication Guides)	Summary of essential information needed for safe and effective use of the drug.	Patients
OTC “Drug Facts” labeling	Summary of essential information needed for safe and effective use of the drug.	Consumers
Public Health Advisory	Information and advice regarding an emerging drug safety issue or other important public health information.	General public
Patient Information Sheet	Concise summary in plain language of the most important information about a particular drug. Includes an Alert when appropriate to communicate an important, and often emerging, drug safety issue.	Patients and/or consumers, lay caregivers, and interested members of the general public
Healthcare Professional Sheet	Concise summary of an important, and often emerging, drug safety issue, with background information about the detection of the issue and points to consider for clinical decision making.	Healthcare professionals
Alerts on Patient Information and Healthcare Professional Sheets	Summary of an important, and often emerging, drug safety issue. Alerts are tailored to the needs of the primary target audience for each type of information sheet.	Healthcare professionals, patients and/or consumers, lay caregivers, and interested members of the general public

**A. Labeling (including patient package inserts and Medication Guides)**

FDA-approved drug product labeling is the primary source of information about a drug's safety and effectiveness, and it summarizes the essential scientific information needed for the safe and effective use of the drug. Compliance with the recently issued physician labeling rule<sup>9</sup> for prescription drugs is expected to further enhance the usefulness of product labeling and further facilitate the safe and optimal use of prescription drugs.

Labeling for prescription drug products is directed to healthcare professionals, but may include sections that are intended for patients and that also must be FDA-approved. For some prescription drugs, such as oral contraceptives and estrogens, FDA long ago determined that the safe and effective use of the drug required additional labeling in nontechnical language to be distributed directly to patients by their healthcare provider or pharmacist (21 CFR 310.501 and 310.515). These *patient package inserts* also may be provided voluntarily by manufacturers for other drugs and are regulated by FDA as product labeling.

More recently, when patient-directed labeling was considered necessary for proper use of a drug, FDA has required patient labeling in nontechnical language in the form of Medication Guides (MedGuides). These have been required for certain prescription drugs that pose a serious and significant public health concern and for which FDA-approved patient information is necessary for a patient's safe and effective use of the product. MedGuides are required if FDA determines that one or more of the following circumstances exists:

- Patient labeling could help prevent serious adverse effects.
- A drug product has serious risk(s) (relative to benefits) of which patients should be made aware because information concerning the risk(s) could affect a patient's decision to use, or to continue to use, the product.
- A drug product is important to health, and patient adherence to directions for use is crucial to the drug's effectiveness.<sup>10</sup>

Finally, over-the-counter (OTC) drugs bear a *Drug Facts* label that conveys information in a clear, standardized format to enable patient self-selection of an appropriate drug and enhance the safe and effective use of the drug by consumers.<sup>11</sup>

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<sup>9</sup> Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 FR 3922 (January 24, 2006). For further information, see <http://www.fda.gov/cder/regulatory/physLabel/default.htm>.

<sup>10</sup> See 21 CFR 208.1.

<sup>11</sup> See 21 CFR 201.66 (format and content requirements for over-the-counter (OTC) drug product labeling).

## **B. Public Health Advisories**

FDA issues Public Health Advisories (PHAs) to provide information regarding important public health issues to the general public, including patients and healthcare professionals. For example, PHAs may:

- Highlight important safety information about a drug
- Inform the public about the status of FDA's evaluation of an emerging drug safety issue
- Announce the implementation of a RiskMAP for a drug
- Advise the public regarding a manufacturer's suspension of marketing of a drug due to safety concerns
- Provide other important public health information

Emerging drug safety information has been disseminated in PHAs for many years, and such PHAs may include recommendations to mitigate a potential risk. PHAs often are issued in conjunction with other drug safety communications, such as Alerts on Patient Information Sheets and Healthcare Professional Sheets (see next sections). PHAs are available through the CDER Web site and disseminated via the MedWatch Partners Program.

## **C. Patient Information Sheets**

In 1998, FDA began posting Information Sheets for consumers following approval of drugs that are new molecular entities (i.e., contain an active ingredient not previously marketed in the United States). These communications convey, in plain language, important information for consumers contained in a drug product's approved labeling about the safe and effective use of the drug. In 2005, FDA began posting Patient Information Sheets when important new information regarding the safety of a marketed drug came to the attention of the FDA.<sup>12</sup> Patient Information Sheets include an Alert (see section below on Alerts) when appropriate to communicate an emerging drug safety issue. These Information Sheets can be found on the FDA's Index to Drug-Specific Information, currently at <http://www.fda.gov/cder/drug/DrugSafety/DrugIndex.htm>.

Patient Information Sheets encourage patients to talk with their healthcare providers for further information. Patient Information Sheets also provide telephone and e-mail contact information for FDA's Drug Information line to address specific questions. FDA continues to collect input on the usefulness of these consumer communications through feedback mechanisms, such as focus groups, surveys, and public meetings, and anticipates that these consumer communications will continue to evolve.

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<sup>12</sup> Information Sheets for consumers developed to communicate information about drugs that are new molecular entities previously have been titled "Consumer Information Sheets" and are transitioning to the Patient Information Sheet format. References to Patient Information Sheets in this Guidance should be interpreted to include Consumer Information Sheets, as appropriate.

#### **D. Healthcare Professional Sheets**

Healthcare Professional Sheets provide a summary of important, and often emerging, drug safety information for a particular drug or drug class and also can be found on the FDA's Index to Drug-Specific Information. Healthcare Professional Sheets begin with a summary Alert paragraph (see section below on Alerts) followed by more detailed sections explaining the Alert, including clinical considerations or recommendations for the healthcare professional, a summary of the data, and, when applicable, implications of the Alert.

Healthcare Professional Sheets are intended to provide adequate factual information to address potential questions from patients and facilitate a healthcare professional's consideration of the drug safety issue. As with the Patient Information Sheets, FDA continues to collect input on the usefulness of these communications through a variety of feedback mechanisms and anticipates that healthcare professional communications will continue to evolve.

#### **E. Alerts on Patient Information and Healthcare Professional Sheets**

When FDA becomes aware of emerging information on a potentially important drug safety issue and we determine patients and healthcare professionals should know about the information while we continue our evaluation, we currently provide this information in Patient Information Sheets and Healthcare Professional Sheets as an *Alert*. Alerts also may be used to highlight important new information in product labeling or an important change in a risk management program. For example, an Alert may describe:

- Newly observed, serious adverse events that may be associated with use of a drug
- Information about how such serious adverse events might be prevented by appropriate patient selection, monitoring of patients, or use or avoidance of the therapy
- Information regarding a serious adverse event that FDA believes may be associated with use of a drug in populations in whom the drug was not previously studied

In some cases, an Alert and/or other safety communication may comment on an international regulatory agency action with respect to a drug also marketed in the United States or on published literature reporting a new safety-related finding regarding a marketed drug.

The essential information in the Alert should not differ between the Patient Information Sheets and Healthcare Professional Sheets, although we may clarify technical terms on the Patient Information Sheets to enhance consumer understanding and provide more detailed information for healthcare professionals in the Healthcare Professional Sheets.

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An Alert is clearly identified along with a statement that reflects the stage of the analysis with respect to regulatory decision making or other potential limitations on the interpretation of the safety information. For example, a statement regarding emerging drug safety information may advise the following:

This information reflects FDA's current analysis of available data concerning this drug. Posting this information does not mean that FDA has concluded there is a causal relationship between the drug product and the emerging drug safety issue. Nor does it mean that FDA is advising practitioners to discontinue prescribing the product. FDA is considering, but has not reached a conclusion about, whether this information warrants any regulatory action. FDA intends to provide updated information when it becomes available.

As noted in section V above, our goal is to make emerging drug safety information available to the public in a balanced, impartial manner so that healthcare professionals and patients can consider the information when making decisions about medical treatment despite uncertainties in the data. The Agency is committed to providing accurate, clear, reliable, and useful drug safety information.

#### **F. Other Methods of Communication**

Consistent with the Agency's commitment to the expansion of existing communication channels to provide targeted drug safety information to the public, FDA is exploring various methods of communication, including concise advisories and other Internet postings, more detailed short articles, and background papers. In addition to written communications, FDA is assessing other communication tools, including broadcasts and conference calls to disseminate drug safety information. If new communication tools are adopted, we intend to update this guidance, if appropriate.

Sponsors also use various methods to communicate drug safety information. For example, a sponsor may distribute a "Dear Healthcare Professional" letter (sometimes referred to as a "Dear Doctor" letter) to convey important information regarding a marketed drug. A sponsor may issue a Dear Healthcare Professional letter on its own initiative or following a request by FDA. Dear Healthcare Professional letters may be used to disseminate information regarding a significant hazard to health, to announce important changes in product labeling, or to emphasize corrections to prescription drug advertising or labeling.

#### **VII. WHERE CAN I FIND FDA'S DRUG SAFETY INFORMATION?**

All of the various forms of drug safety communications described in the preceding section currently are available via links found on the FDA Web site (e.g., links to the Index to Drug-Specific Information Web page, Drugs@FDA, and MedWatch Web pages). FDA's Web site provides an easily accessible link to the Index to Drug-Specific Information Web page (currently at <http://www.fda.gov/cder/drug/DrugSafety/DrugIndex.htm>) from which the public may access information about drugs that are the subject of a Public Health Advisory and/or an Alert regarding an important, and often emerging, drug safety issue, as well as established drug safety information. This

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Index contains links to available Drug Information Pages for specific drugs (identified by both trade name and nonproprietary name), which contain approved drug product labeling, consumer-friendly Information Sheets, and other drug information. Drug Information Pages generally are available for drugs that (1) are new molecular entities; (2) have existing Consumer or Patient Information Sheets, Healthcare Professional Sheets, or other consumer information materials; or (3) have been the subject of recent safety communications. Drugs that have an active FDA safety alert are identified by an asterisk. For drugs without a Drug Information Page, the Web page links consumers to Drugs@FDA, which contains drug product labeling and other regulatory information related to approved drugs (see <http://www.accessdata.fda.gov/scripts/cder/drugsatfda>).

Safety information regarding medical products (including drugs, biologics, devices, and dietary supplements), such as Dear Healthcare Professional letters, Public Health Advisories, Press Releases, and market withdrawals, also is available through MedWatch Safety Alerts. The MedWatch program augments FDA and manufacturer communication of drug safety information by distributing MedWatch Safety Alerts to individual subscribers and through its MedWatch Partners Program. This information is available to the general public on the MedWatch Web site (<http://www.fda.gov/medwatch/safety>), which contains archived information dating back to 1996.

## **VIII. HOW WILL FDA HANDLE CONFIDENTIAL INFORMATION?**

Most of the information currently posted on the Index to Drug-Specific Information Web page is information that is now made available to the public pursuant to Freedom of Information Act (FOIA) requests. Because of the importance of emerging drug safety information to healthcare professionals and patients, FDA has decided to take steps to make such information available, after proper redaction of confidential commercial and personal privacy information, without waiting for a FOIA request. Information will be posted in accordance with applicable disclosure laws and FDA regulations.

## **IX. HOW WILL DRUG SAFETY INFORMATION BE UPDATED?**

As already explained, we have established a Drug Safety Oversight Board (DSB) which is responsible for making recommendations to the Director of the Center for Drug Evaluation and Research (CDER) about the management of emerging drug safety issues. The DSB is supported by a staff that coordinates CDER's communication efforts regarding emerging drug safety information.

The public can access the most current safety information about a drug through the Index to Drug-Specific Information Web page. FDA intends to update the information available on this Web page on a periodic basis to reflect new information that becomes available.

Emerging drug safety information presented as Alerts is identified by the month and year in which the information is posted on the Index to Drug-Specific Information Web page. We intend to update Alerts on Patient Information Sheets and Healthcare Professional Sheets to describe important new information relevant to the emerging drug safety issue, or remove Alerts after the

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emerging drug safety issue is addressed through revision of product labeling, restricted distribution, request for voluntary withdrawal from the market, or other regulatory action. Once an emerging safety issue has been addressed through regulatory action or a decision that the emerging safety concern is not an important drug safety issue, we intend to modify and/or archive the Patient Information Sheet, Healthcare Professional Sheet, and other communications on our Web site. We intend to make this information available via a link to historical information as follows:

*Patient Information Sheets:* If the emerging drug safety issue has been addressed by a revision to product labeling, we intend to remove the Alert and incorporate the updated labeling information into the Patient Information Sheet.

*Healthcare Professional Sheets:* To ensure continuity following resolution of an Alert that results in a revision to product labeling, we intend to keep the Healthcare Professional Sheets available on the Drug Safety Web site until the revised product labeling is widely available. Thereafter, we intend to archive the Healthcare Professional Sheets on our Web site.

*Public Health Advisories:* Following a determination of whether regulatory action is appropriate to address the emerging drug safety issue, we intend to archive on our Web site the Public Health Advisories related to the safety concern.

Some important drug safety information may have utility independent of any regulatory action. For example, sometimes a sponsor may agree to conduct a long-term study related to an emerging drug safety issue. In such instances, the drug safety information may remain posted until the issue is resolved.

FDA recognizes that resolution of some emerging drug safety issues may not be accomplished in the short term. This may be attributable to the complexity of an issue or the need for clinical studies of adequate duration to evaluate a potential risk with a long latency period. In such cases, we intend to maintain the emerging drug safety information on safety communications such as Patient Information Sheets and Healthcare Professional Sheets pending resolution of the safety issue, and plan to update them as appropriate to reflect continuing evaluation of the issue. This will ensure that important unresolved safety issues that may affect a healthcare professional's decision to prescribe, or a patient's or consumer's decision to use, a medication continue to be communicated. We plan to identify updated information with the month and year in which it was added to the Web site or communicated by other methods.

If data become available that provide sufficient evidence that a drug is not associated with the safety concern previously described by the Agency as an emerging drug safety issue, FDA intends to update the Alert accordingly. In such instances, FDA plans to revise safety communications such as Patient Information Sheets and Healthcare Professional Sheets to provide an update of comparable prominence to reflect this new information. We intend to keep this revised information on the Web site for an appropriate period following publication of the update resolving the safety issue.

## **X. WHAT INTERACTIONS WILL FDA HAVE WITH SPONSORS BEFORE COMMUNICATING EMERGING DRUG SAFETY INFORMATION TO THE PUBLIC?**

FDA intends to notify the relevant sponsor that emerging drug safety information about its drug will be posted on the FDA Web site at least 24 hours before the first instance in which emerging information about that drug is communicated. Our communication of emerging drug safety information is intended to represent FDA's independent analysis of emerging information and FDA's scientific judgment as to the appropriate communication of this emerging drug safety information to the public. FDA may solicit sponsor input when appropriate; for example, to confirm the accuracy of factual information.

For purposes of this guidance, the relevant sponsor generally is the NDA or ANDA holder for the drug that is the subject of a Patient Information Sheet or Healthcare Professional Sheet containing an Alert or a Public Health Advisory regarding an important drug safety issue. We recognize that OTC drugs subject to one or more final OTC monographs, rather than approved pursuant to an NDA or ANDA, may be manufactured by multiple entities and, thus, have multiple relevant sponsors. FDA continues to consider appropriate mechanisms to facilitate timely notification of affected entities marketing OTC drugs and welcomes comment on this issue.

Sponsors are required to report certain adverse drug experience information to FDA in accordance with our regulations<sup>13</sup> and may provide the Agency with additional information relevant to a drug safety issue at any time. A sponsor also may request that the Agency update its communication of emerging drug safety information if the sponsor provides additional information supporting the request.<sup>14</sup>

## **XI. HOW WILL THE COMMUNICATION OF DRUG SAFETY INFORMATION AFFECT THE PROMOTION OF PRESCRIPTION DRUGS?**

FDA recognizes that some sponsors may consider making promotional comparisons between their drugs and drugs for which emerging drug safety information has been provided by the Agency. We remind sponsors that all safety and effectiveness claims made in prescription drug promotion,<sup>15</sup> including claims based on government materials available from the Index to Drug-Specific Information, must be supported by substantial evidence or substantial clinical experience and must not be otherwise false or misleading (21 U.S.C. 355 and 352; 21 CFR 202.1(e)).

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<sup>13</sup> Sponsors of approved NDAs or ANDAs, manufacturers of marketed prescription drugs for human use without approved NDAs or ANDAs, and licensed manufacturers of approved biologic product license applications are required to report adverse experiences to the FDA under 21 CFR 310.305, 314.80, 314.98, and 600.80.

<sup>14</sup> Any such request should be made in accordance with standard procedures for submitting information concerning a particular drug to the Agency (e.g., directed to the appropriate division within the Office of New Drugs, the Office of Generic Drugs, or the Office of Nonprescription Products, as appropriate).

<sup>15</sup> The Federal Trade Commission (FTC) has primary responsibility for regulating the advertising of nonprescription drug products.

*Contains Non-binding Recommendations*

Neither the fact that the Agency has communicated emerging drug safety information for a drug nor the specific information posted about that drug will generally constitute (either separately or collectively) substantial evidence or substantial clinical experience that would support a comparative safety or effectiveness claim. Therefore, comparative claims made in prescription drug promotion based on an Agency communication of emerging drug safety information (e.g., “Our drug is safer because of the emerging drug safety information posted by the FDA about a competitor’s drug”) may be considered false or misleading.

Representations that minimize the implications of emerging drug safety information communicated by the Agency also may be considered false or misleading. For those seeking to explain to healthcare professionals what emerging drug safety information means, we refer to the sections of this guidance that discuss the purpose of disseminating emerging drug safety information and the nature of the information to be posted on the Index to Drug-Specific Information Web page.