Guidance
Drug Safety Information – FDA's Communication to the Public

DRAFT GUIDANCE

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For questions regarding this draft document contact (CDER) Edward Staffa 301-796-5301, or (CBER) Office of Communication, Outreach and Development at 301-827-1800 or 800-835-4709.

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

March 2012
Drug Safety

Revision 1

Guidance

Drug Safety Information – FDA's Communication to the Public

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Drug Safety Information – FDA's Communication to the Public

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

INTRODUCTION

This guidance explains how FDA develops and disseminates information to the public about important drug safety issues, including emerging drug safety information.[2] Timely communication of important drug safety information provides health care professionals, patients, consumers, and other interested persons with access to the most current information concerning the potential risks and benefits of a marketed drug, helping them to make more informed treatment choices.

This guidance revises the March 2007 guidance, *Drug Safety Information – FDA's Communication to the Public*[3] by providing updated information about FDA's approach to communicating important drug safety information. The revised guidance describes the Center for Drug Evaluation and Research's (CDER's) single, standardized format for electronic drug safety communications about marketed drugs and provides information about the Center for Biologics Evaluation and Research's (CBER's) safety communication activities. In addition, the revised guidance describes FDA's posting of other safety assessments on its Web site in accordance with the requirements of the Food and Drug Administration Amendments Act of 2007 (FDAAA) and to further our transparency objectives. When finalized, this guidance will replace the 2007 guidance.

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[1] This guidance has been prepared by the Office of Communications in the Center for Drug Evaluation and Research (CDER) in consultation with CDER's Safety First Steering Committee at the Food and Drug Administration and in cooperation with the Center for Biologics Evaluation and Research (CBER).

[2] For purposes of this guidance, all references to *drugs* include both human drugs and biological drug products. This guidance does not apply to human cells, tissues, and cellular and tissue-based products regulated solely under section 361 of the Public Health Service Act.

[3] We update guidance documents periodically. To make sure you have the most recent version of a guidance, check the Guidances (Drugs) page at http://www.fda.gov/RegulatoryInformation/Guidances/default.htm. Although this guidance addresses drug safety communications in general, it is not meant to be a comprehensive description of our communications for the wide range of products regulated by FDA (e.g., vaccines). FDA's Web site contains more specific information for certain classes of products.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

BACKGROUND

All drugs have risks, and health care professionals and patients must balance the risks and benefits of a drug therapy when making decisions about whether to use the drug. The general risks and benefits of a drug therapy are described in the product's prescribing information. In addition, however, FDA provides information on drug risks and benefits to health care professionals and patients when that information has generated a specific concern, usually waiting until that information has been fully evaluated and has prompted a regulatory action, such as a revision to the drug's prescribing information. In recent years, FDA has begun making information on potential drug risks available to the public earlier — often while the Agency is still evaluating the data and determining whether any regulatory action is warranted. FDA believes that timely communication of important drug safety information will give health care 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.

The following questions and answers provide general guidance on how FDA communicates important safety information to the public.

QUESTIONS AND ANSWERS

1. What Is This Guidance About?

This guidance describes how FDA develops and disseminates information to the public about important drug safety issues, including emerging drug safety information. 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. Examples of important drug safety issues include, but are not limited to:

- Serious adverse drug reactions identified after drug approval

- Medication errors, which include, but are not limited to, confusion between drug names and confusion regarding drug labeling. These may lead to improper use of the drug, to prescribing or administering an improper dose, or to a patient's taking another medication with which the drug interacts.

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 a way that would affect decisions about prescribing or taking the drug, but that has not yet been fully analyzed or confirmed. Such information may relate to new risks or new information about known risks.

FDA may disseminate important drug safety information by other methods and at other times than those described in this guidance. For example, FDA may decide to issue a Public Health Alert or a press release about a medical product or hold a media briefing to communicate important risk information.

2. How Does FDA Evaluate Drug Safety Information?

FDA monitors and reviews safety information about a drug throughout the product's lifecycle, interacting with sponsors during product development and clinical investigation of the drug, closely reviewing safety issues during consideration of a marketing application, and, if the drug is approved, monitoring safety reports after the drug is marketed. Every approved drug has labeling (e.g., prescribing information) that contains, among other things, information about the benefits and risks of using the drug.

After drug approval, FDA may learn of new, or more serious or more frequent, adverse drug reactions from, for example, postapproval voluntary or mandatory reporting of adverse drug reactions during use of the drug, postapproval clinical trials exploring new uses of the drug, other postapproval studies including epidemiologic studies or active surveillance evaluations. For example, additional adverse drug reactions, some of them serious, may be identified once a drug is used more widely and under more diverse conditions (e.g., concurrent use with other drugs), or when the drug is prescribed for off-label uses. In some cases, medication errors can occur because of name confusion or other factors that influence safe use of the medication.

As new information related to a drug becomes available, the Agency reviews the data and evaluates whether there is an emerging drug safety concern. When such a concern arises, relevant medical and scientific experts within FDA engage in a prompt review and analysis of available data. Often, however, there is a period of uncertainty while FDA evaluates the emerging 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 and, if so, what type of action is necessary.[4]

[4] FDA recently issued a draft guidance to FDA staff for comment on *Classifying Significant Postmarket Drug Safety Issues.* This guidance describes the methodological framework by which FDA will classify significant postmarket drug safety issues as *priority*, *standard*, or *emergency*. This guidance is available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm. The draft, when finalized, will reflect the Agency's current thinking on this issue.

During this period, FDA also is actively engaged in scientific efforts to gather additional safety information. Drug sponsors[5] also gather and evaluate emerging safety information and provide the results of their analyses to FDA. As additional data relevant to an emerging drug safety issue become available (e.g., data from an ongoing study or trial, data from surveillance evaluations, or data from available clinical databases), these data are considered in the analysis and decision-making process. FDA may decide that, based on evaluation of additional data related to the drug, further regulatory action, such as requiring a revision to prescribing information or a Risk Evaluation and Mitigation Strategy (REMS), may be appropriate.

Interpreting postmarket safety data is complex, involving analysis of clinical data and detailed review of a wide range of potentially relevant information, including adverse drug experience spontaneous reports, pertinent controlled clinical trials and epidemiologic studies, active surveillance efforts, 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 and adequately informed persons with relevant expertise may disagree. We engage in robust and comprehensive discussions within the Agency regarding potential drug safety issues to ensure that all points of view are considered before making a decision on how to proceed.[6] We may consult the Drug Safety Oversight Board, established by FDA in February 2005, asking it to provide recommendations to the center director regarding the management and communication of an emerging drug safety issue.[7] We also may engage in external discussions by convening an Advisory Committee, or coordinating with other public health agencies, such as the Centers for Disease Control and Prevention, or the National Vaccine Program Office, regarding an emerging drug safety issue.

As the Agency evaluates a drug safety issue to determine whether regulatory action is warranted, we may decide to communicate further information to the public at appropriate points during 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, and there may be updates to this information.

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[5] The term *sponsor* is used broadly in this guidance to refer to the individual or entity that markets a drug or that takes responsibility for and initiates a clinical investigation of a drug. Usually, the sponsor is the owner of the application (*application holder*) for the drug. The *sponsor* also might be the manufacturer of the drug.

[6] See the Manual of Policies and Procedures (MAPP) 4151.1, *Scientific/Regulatory Dispute Resolution for Individuals Within a Management Chain*, Revision 1, effective September 16, 2010; MAPP 4151.2, *Resolution of Differing Professional Opinions: Review by Ad Hoc Panel and CDER Director*, Revision 1, effective September 16, 2010; and MAPP 4151.8, *Equal Voice: Discipline and Organizational Component Collaboration in Scientific and/or Regulatory Decisions*, effective September 16, 2010. These MAPPs can be accessed at http://www.fda.gov/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/default.htm. See also the CBER Standard Operating Procedure and Policy (SOPP) 8006: Resolution of Differences in Scientific Judgment in the Review Process, Version #2, effective January 15, 2009, available at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm109584.htm.

[7] The DSB was subsequently established by statute as part of the Food and Drug Administration Amendments Act of 2007 (FDAAA), creating section 505-1(j) of the Federal Food, Drug, and Cosmetic Act.

3. When Does FDA Communicate Emerging Drug Safety Information to the Public?

FDA currently disseminates emerging drug safety information after having completed an analysis of available data and, in some cases, before having reached a decision about whether regulatory action is warranted. FDA communications about emerging drug safety information can help achieve certain long-standing public health goals, including enhanced vigilance on the part of health care professionals who also may be prompted to increase their reporting of safety observations to FDA.

FDA recognizes the potential public health implications of providing emerging drug safety information, and we are particularly concerned about possible unintended consequences, such as inappropriate modification or discontinuation of useful treatment. We attempt to anticipate and address these possible consequences through our risk communications by (1) describing the nature of a safety concern and what is known about its relationship to a particular drug and (2) making recommendations for health care professionals and patients about how to monitor for and manage the concern.

With respect to potentially important information, the dual goals of having people informed as early as possible and having that information thoroughly substantiated inevitably creates tension. Despite this tension, we lean toward early communication of emerging drug safety information unless, in our judgment, the information available is not reliable enough to be useful and could mislead the public. We recognize this means that, in some cases, we will have to say that a safety concern "has not yet been substantiated." Our goal is to make emerging drug safety information available to the public in a balanced, impartial manner so that health care professionals and patients can consider the information when making decisions about medical treatment, despite uncertainties in the data. FDA 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 issue and deciding whether emerging drug safety information should be made available to the public. These factors may include, but are not limited to, the following:

- Seriousness of the event (e.g., severity and reversibility) relative to the benefits of treatment
- Magnitude of the risk (e.g., likelihood of occurrence)
- Strength of the evidence of a causal relationship between the use of a drug and the adverse event[8]
- Extent of patient exposure (e.g., how broadly the drug is used)
- Disproportionate impact on particular populations (e.g., children or the elderly)

[8] See, for example, guidance for industry on *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment* at pages 6 to 7 and 17 to 18, available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

- Potential for preventing or mitigating the risk in the patient population (e.g., by monitoring patient selection or avoiding a concomitant treatment)
- Availability of alternative therapies

The decision to provide 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 event described. Nor does communicating emerging drug safety information necessarily mean that FDA is advising health care professionals to limit their prescribing of the drug at issue. Rather, the communications are intended to further inform prescribing and assist health care professionals in making individualized treatment decisions with their patients, based on the balance of potential benefits and risks of the drug for that patient.

At times, decisions to communicate about important drug safety issues are affected by information the public has received from sources other than FDA, such as the mainstream media. In these cases, the safety of a particular drug or drug class may be publicly questioned based on information provided by these other sources that may be incorrect, incomplete, or misleading. In such cases, FDA may issue a statement or engage in other methods of communication to clarify or correct information and respond to public interest.

FDA strives to keep all communications clear and understandable. We also consider elements of human behavior in our communications. We realize, for instance, that risk information provided without context may alarm patients, causing them to discontinue needed medication. With all drug safety communications, FDA now makes a concerted effort to communicate the benefits of a drug along with its risk. Whenever possible and appropriate, when we communicate drug safety information, we include specific advice to patients who use the drug on its safe and effective use to facilitate discussions with their health care practitioners.

4. How Does FDA Communicate Important Drug Safety Information to the Public?

FDA has created effective and ongoing relationships with a wide array of trade and professional associations, patient advocacy and consumer groups, safety organizations, media, and other entities. When drug safety issues arise, we reach out to these groups and work with them to communicate the safety issue to their constituencies.

FDA uses various tools and methods to communicate drug safety information to the public. Important tools used in this effort include, but are not limited to, FDA-approved prescribing information (i.e., drug labeling) and a postmarket communication tool called a *Drug Safety Communication* (DSC), both discussed in the following questions, along with other important tools and methods we use to communicate drug safety information to the public.

5. What is FDA-Approved Labeling?

FDA-approved prescribing information for health care professionals — and patient package inserts and Medication Guides for patients — is the primary source of established information about a drug's safety and efficacy; it summarizes the essential scientific information needed for

the safe and effective use of the drug. The prescribing information for prescription drugs contains sections directed to health care professionals, and may also include sections that are intended for patients.[9]

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 information in nontechnical language to be distributed directly to patients by their health care practitioner 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 labeling.

When patient-directed information is considered necessary for proper use of a drug, FDA requires patient-oriented information 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 safe and effective use of the drug. MedGuides are required if FDA determines that one or more of the following circumstances exist:

- Patient-focused information (*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.[10]

In addition, over-the-counter (OTC) drugs bear a *Drug Facts* label that conveys information in a clear, standardized format to enable consumer self-selection of an appropriate drug and enhance the safe and effective use of the drug by consumers.[11]

FDA-approved prescribing information for CDER-regulated drug products is available on the FDA Web site at *Drugs@FDA*. FDA-approved prescribing information for CBER-regulated products is available on the FDA Web site.[12] In addition, FDA facilitates the availability of up-to-date drug prescribing information in an easily accessible electronic format on the National Library of Medicine Web site at *DailyMed*.[13] See also question 10.

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[9] In the *Federal Register* of January 24, 2006 (71 FR 3922), FDA published a final rule, "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products," designed to improve the usefulness of prescribing information for prescription drugs approved after June 30, 2001 (for further information, see http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm). Labeling for these drugs is currently being converted to the new content and format according to a schedule determined at the time of publication of the final rule, and is expected to facilitate the safe and optimal use of prescription drugs.

[10] See 21 CFR 208.1.

[11] See 21 CFR 201.66 (format and content requirements for over-the-counter (OTC) drug product labeling).

[12] See http://www.fda.gov/BiologicsBloodVaccines/ucm121134.htm.

[13] See http://dailymed.nlm.nih.gov/dailymed/about.cfm.

6. What is a CDER Drug Safety Communications (DSC)?

A *Drug Safety Communication* (DSC) is a specific tool used by FDA to communicate to the public important information about safety issues, including emerging safety information, about marketed drugs. DSCs are standardized electronic communications posted on the FDA Web site.[14] Written as clearly as possible, DSCs are targeted to both health care professionals and patients. DSCs generally communicate the following information:

- A summary of the safety issue and the nature of the risk being communicated
- The established benefit or benefits of the drug being discussed
- Recommended actions for health care professionals and patients, when appropriate
- A summary of the data reviewed or being reviewed by FDA

The DSC is FDA's primary safety communication tool for important postmarket drug safety issues. In the past, and at the time our March 2007 guidance was released on this topic, safety communications were issued by FDA in a variety of formats. They were issued under different titles and targeted to different audiences. For instance, in August 2007, FDA began issuing *Early Communications about Ongoing Safety Reviews* (ECs) to keep health care professionals and the general public informed of postmarket safety issues under evaluation by FDA. Safety communications have also been issued under the titles *Public Health Advisory*, *Patient Information Sheet*, *Healthcare Professional Sheet*, and *Alerts on Patient Information and Healthcare Professional Sheets*, and, as these titles suggest, have targeted different audiences. To improve the clarity of our communications, FDA began using a single communication vehicle — the *Drug Safety Communication* — in early 2010.

Some DSCs are related to drug safety issues that continue to develop as more information is obtained. FDA disseminates follow-up DSCs to keep the public informed of new information pertaining to a previously communicated DSC. In addition, some emerging safety information may take a long time to evaluate (if, for example, there is a need for additional clinical trial or epidemiological data to further assess the risk). During the evaluation period, FDA may issue a follow-up DSC as a public reminder, even if no additional information is available since the original DSC was issued.

Note: Although a DSC communicates important safety issues about marketed drugs, it is ***not*** a crisis communication document. If a drug product is defective or tainted, or poses some other form of immediate danger, FDA uses other communication tools, such as *Public Health Alerts*, press releases, stakeholder calls, and media briefings, to inform the public rapidly and protect public health.

7. How Does CBER Communicate Safety Information?

FDA's Center for Biologics Evaluation and Research (CBER) communicates important postmarket safety information regarding biological products to the public using the most

[14] See at http://www.fda.gov/Drugs/DrugSafety/ucm199082.htm.

appropriately targeted communication, taking into consideration the type of product (e.g., vaccine, blood product, or cell therapy), safety issue, and audience. Examples of communication tools include Public Health Notifications, press releases, and safety information updates. These safety communications, like DSCs noted above, include the following important information: (1) a summary of the safety issue and FDA's current understanding of the risk; (2) a summary of information, including the source of the information, reviewed by FDA; (3) information on the benefits and risks of the product involved; and (4) when available and appropriate, recommendations for health care professionals and/or patients and caregivers. Follow-up information is disseminated to keep the public informed of new information pertaining to a previously communicated safety issue. CBER may issue a follow-up as a public reminder, even if no additional information is available since the original communication was issued.

As with CDER-regulated products, if a CBER-regulated biological product is defective or tainted, or poses some other form of immediate danger, FDA may choose from a variety of other communication tools and channels to rapidly inform the public and protect public health.

8. What Other Safety Information Does FDA Post on Its Web Site?

In accordance with requirements of the Food and Drug Administration Amendments Act of 2007 (FDAAA) and to further our transparency objectives, FDA posts various other types of drug safety information, in addition to DSCs, on its Web site, including the following:[15]

- Since 2008, as required by section 921 of FDAAA, FDA has posted on its Web site reports of potential safety issues with drugs[16] identified as a result of our reviews of reports to FDA's Adverse Event Reporting System (AERS). The appearance of a drug on this list, which is updated quarterly, means that FDA has identified a potential safety issue (i.e., new safety information or a potential signal of a serious risk), but it does not mean that FDA has concluded there is a causal relationship between the drug and the risk described.[17]

- Since June 16, 2010, FDA has been posting the results of evaluations performed in accordance with section 915 of FDAAA. Section 915 requires FDA to evaluate marketed drugs 18 months after approval or after 10,000 individuals have used the drug, whichever is later. These evaluations are conducted using various sources of available safety information about marketed drugs to determine whether there are any new serious adverse events not previously identified during development, known side effects reported

[15] This is not an all inclusive list but highlights some new categories of drug safety information we have begun to post as required by FDAAA.

[16] See http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/UCM082196.

[17] FDA has used the term *safety signal* to refer to a concern about an excess of adverse events compared to what would be expected to be associated with a product's use. See FDA guidance for industry, *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment*, available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

in an unusual number of patients, or potential new safety concerns now that the drugs are being used in the general population.[18]

- In accordance with section 915 of FDAAA, FDA maintains a list of drugs that have been approved with Risk Evaluation and Mitigation Strategies (REMS) and copies of those REMS on its Web site.[19]

9. What Other Methods Are Used to Communicate Drug Safety Information?

In addition to written communications, FDA uses other communication tools, including webinars, broadcasts, and conference calls, to disseminate drug safety information. FDA uses various forms of electronic social media to communicate some safety issues and is continuing to assess additional ways to communicate effectively with the public using these vehicles.

Consistent with FDA's commitment to the expansion of existing communication channels to provide targeted drug safety information to the public, FDA is exploring additional methods of communication, including concise advisories and other Internet postings; more detailed short articles; articles in trade and professional journals; a standardized, one-document solution for patient medication information (PMI); and background papers. If new communication tools are adopted, we intend to update this guidance.

Drug sponsors also use various methods to communicate drug safety information. For example, a sponsor might distribute a Dear Health Care Provider Letter (sometimes referred to as a *Dear Doctor* letter) to convey important information about a marketed drug. A sponsor can issue a Dear Health Care Provider Letter on its own initiative or following a request or requirement by FDA. A sponsor can be required to issue a Dear Health Care Provider Letter or other communication that is approved as part of a communication plan of a REMS. Dear Health Care Provider letters can be used to disseminate information regarding a significant hazard to health, to announce important changes in prescribing information, or to emphasize corrections to prescription drug advertising or prescribing information. Depending on the issue and whether the communication is tied to a regulatory action, FDA may notify the public when sponsors issue a Dear Health Care Provider Letter.

10. Where Is FDA's Drug Safety Information Located?

All of the drug safety information FDA communicates is available via links found on FDA's Web site (e.g., links to the Index to Drug-Specific Information Web page, Drugs@FDA, Safety and Availability [Biologics] and MedWatch Web pages), as described below.

FDA's Web site provides an easily accessible link to the Index to Drug-Specific Information Web page (http://www.fda.gov/cder/drug/DrugSafety/DrugIndex.htm) from which the public can access information about drugs that are the subject of a DSC regarding an important, and often

[18] See http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/ucm204091.htm.

[19] See http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm.

emerging, drug safety issue, as well as established drug safety information. This Index contains links to available Drug Information Pages for specific drugs (identified by both trade name and nonproprietary name) that contain approved drug prescribing information, consumer-friendly information sheets, when available, and other drug information. Drug Information Pages generally are available for drugs that are new molecular entities, or that have been the subject of recent safety communications.

For drugs without a Drug Information Page, the Web page links consumers to Drugs@FDA, which contains drug prescribing information and other regulatory information related to approved drugs (see http://www.accessdata.fda.gov/scripts/cder/drugsatfda).

FDA's Web site contains the Safety & Availability [Biologics] page from which the public can access information about CBER-regulated drugs that are the subject of an important safety communication. (http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/default.htm). In addition, product information pages for licensed biological products include links to related safety information.

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. Safety information about medical products (including drugs, biologics, devices, and dietary supplements), such as selected information that is the subject of Drug Safety Communications, Dear Health Care Provider Letters, press releases, and market withdrawals, also is available through MedWatch Safety Alerts. 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.

MedWatch, in addition to sending out individual medical product alerts, posts Monthly Safety Labeling Changes on the Web and also distributes them via an alert.[20] This posting includes clinically important prescribing information updates to the following sections of the prescribing information:

- Boxed Warnings
- Contraindications
- Warnings and Precautions
- Adverse Reactions
- Patient Package Insert & Medication Guide

11. How Is Drug Safety Information Updated?

The public can access the most current safety information about a drug through the Index to Drug-Specific Information and Safety & Availability [Biologics] Web pages. FDA intends to update the information available on these Web pages on a periodic basis to reflect new information that becomes available.

[20] See http://www.fda.gov/Safety/MedWatch/SafetyInformation/Safety-RelatedDrugLabelingChanges/default.htm.

Emerging drug safety information presented as a DSC 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 DSCs to describe important new information relevant to the emerging drug safety issue after the emerging drug safety issue is addressed through revision of prescribing information, approval of a REMS, request for voluntary withdrawal from the market, or other regulatory action. 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. After an emerging safety issue has been addressed through regulatory action, it is permanently archived (as are all DSCs) on the FDA Web site.

If data become available that provide sufficient evidence that a drug is not associated with the safety concern previously described by FDA as an emerging drug safety issue, FDA intends to update the information accordingly. In these instances, we plan to issue a new update of comparable prominence to the DSC to reflect this new information. Updated DSCs, like all DSCs, are permanently archived on the Web site.

Some important drug safety information may have utility independent of any regulatory action. For example, sometimes a sponsor may be required to conduct a long-term study or clinical trial related to an emerging drug safety issue.[21] This is one reason why DSCs remain permanently archived.

FDA recognizes that evaluation of some emerging drug safety issues may not be accomplished quickly. This may be because of the complexity of an issue or the need for studies or clinical trials of adequate duration to evaluate a potential risk with a long latency period.[22] In these cases, archived DSCs create a permanent record of the continued evaluation of the issue. This will help ensure that important information about ongoing safety issues that may affect a health care professional's decision to prescribe, or a patient's or consumer's decision to use, a medication will continue to be communicated.

For CBER-regulated products, emerging drug safety information is presented on FDA's Web page Safety & Availability [Biologics] by the year in which the information is posted. Updates are provided as new information becomes available.

12. How Does FDA Handle Confidential Information About a Drug Safety Issue?

Most of the information currently posted on the Index to Drug-Specific Information Web page is information that is prepared for public disclosure and contains no confidential information. FDA may publish related information on the Web page that was not specifically prepared for public disclosure, such as FDA scientific reviews. This information is reviewed before publication to ensure that disclosure of this information is in accordance with applicable disclosure laws and FDA regulations.

[21] See 21 U.S.C. 355(o)(3).

[22] See draft guidance, *Classifying Significant Postmarket Drug Safety Issues*.

13. Does FDA Involve Sponsors Before Making Emerging Drug Safety Information Public?

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. FDA strives to notify the relevant sponsor at least 24 hours before the first public communication that emerging safety information about its drug will be posted on the FDA Web site.

For purposes of this guidance, the relevant sponsor generally is the new drug application (NDA), biologics license application (BLA), or abbreviated new drug application (ANDA) holder(s) for the drug or drug class that is the subject of a DSC containing an important drug safety issue. We recognize that over-the-counter (OTC) drugs subject to one or more final OTC monographs, rather than approved under 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.

Note: Sponsors are required to report certain adverse drug experience information to FDA in accordance with the U.S. Food, Drug, and Cosmetic Act (FDCA) and our regulations[23] and may provide FDA 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.[24]

14. Can FDA Risk Communication Be Used in Prescription Drug Promotion?

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 FDA. We remind sponsors that all safety and effectiveness claims made in prescription drug promotion,[25] 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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[23] Sponsors of approved NDAs or ANDAs, manufacturers of marketed prescription drugs for human use without approved NDAs or ANDAs, and licensed manufacturers of approved BLAs are required to report adverse experiences to the FDA under 21 CFR 310.305, 314.80, 314.98, and 600.80. Manufacturers of OTC products subject to monographs are required to report serious adverse experiences to the FDA under FDCA section 760.

[24] Any such request should be made in accordance with standard procedures for submitting information concerning a particular drug to FDA (e.g., directed to the appropriate division within the Office of New Drugs, the Office Generic Drugs, or the Office of Nonprescription Products, as appropriate).

[25] The Federal Trade Commission (FTC) has primary responsibility for regulating the advertising of nonprescription drug products.

Neither the fact that FDA 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 FDA 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 FDA also may be considered false or misleading. For those seeking to explain to health care 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.

SUMMARY

FDA plays a critical role in detecting and managing safety issues that are identified after a drug is approved for marketing, including a critical role in communicating information to the public. The actions we take depend on many factors, including the characteristics of the adverse events, the frequency of the reports, the seriousness of the diseases or conditions for which the drug provides a benefit, the availability of alternative therapies, and the consequences of not treating the disease. Despite working toward systematic methods of identifying and disseminating information about drug safety issues, communicating about drug safety issues will always require a significant amount of judgment about whether to communicate in a given case and, if so, what to communicate.

It is our goal is to make the most up-to-date drug safety information available to the public in a timely manner so that health care professionals and patients can consider the information when making decisions about medical treatment, yet be aware of uncertainties in the data. FDA is committed to providing accurate, clear, reliable, and useful drug safety information.