



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

August 31, 2009

TO: The Secretary
Through: DS _____
COS _____
ES IS

FROM: Commissioner of Food and Drugs

SUBJECT: Report to Congress on Communicating to the Public on the Risks and Benefits of New Drugs, Required by Section 904 of the Food and Drug Administration Amendments Act of 2007 (FDAAA)

Attached for your consideration is the Food and Drug Administration's (FDA) Report to Congress entitled, Communicating to the Public on the Risks and Benefits of New Drugs. On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85), directing the FDA to report on the best ways to communicate to the public the risks and benefits of new drugs, the role of the Risk Evaluation and Mitigation Strategies in assessing risks and benefits, and the potential use of a unique symbol to indicate the newness of a newly approved drug and direct-to-consumer advertising.

The report provides an overview of the more longstanding approaches to communication, such as drug labeling and the use of patient package inserts. It outlines the merits of providing information to make patients and prescribers more aware that a drug product is newly approved. Finally, the report describes current communication vehicles, such as FDA's Web site, FDA-published safety alerts, and other targeted communications.

RECOMMENDATION

I recommend that you review and approve the report and forward it to Congress.


Margaret A. Hamburg, M.D.

Attachments (2)
Tab A – Transmittal Letters
Tab B – Report to Congress



THE SECRETARY OF HEALTH AND HUMAN SERVICES

WASHINGTON, D.C. 20201

October 8, 2009

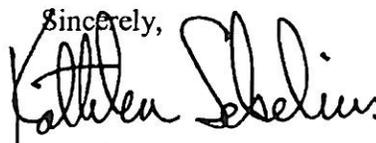
The Honorable Joseph Biden, Jr.
President of the Senate
United States Senate
Washington, DC 20510

Dear Mr. President:

Attached for your consideration is the Food and Drug Administration's (FDA) Report to Congress entitled *Communicating to the Public on the Risks and Benefits of New Drugs*. On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85), directing the FDA to report on the best ways to communicate to the public the risks and benefits of new drugs, the role of the Risk Evaluation and Mitigation Strategies in assessing risks and benefits, and the potential use of a unique symbol to indicate the newness of a newly approved drug and direct-to-consumer advertising.

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I hope you will find the report useful and informative.

Sincerely,


Kathleen Sebelius

Enclosure



THE SECRETARY OF HEALTH AND HUMAN SERVICES

WASHINGTON, D.C. 20201

October 8, 2009

The Honorable Joe Barton
Ranking Member
Committee on Energy and Commerce
House of Representatives
Washington, DC 20515

Dear Mr. Barton:

Attached for your consideration is the Food and Drug Administration's (FDA) Report to Congress entitled Communicating to the Public on the Risks and Benefits of New Drugs. On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85), directing the FDA to report on the best ways to communicate to the public the risks and benefits of new drugs, the role of the Risk Evaluation and Mitigation Strategies in assessing risks and benefits, and the potential use of a unique symbol to indicate the newness of a newly approved drug and direct-to-consumer advertising.

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Kathleen Sebelius

Enclosure



THE SECRETARY OF HEALTH AND HUMAN SERVICES

WASHINGTON, D.C. 20201

October 8, 2009

The Honorable Henry A. Waxman
Chairman
Committee on Energy and Commerce
House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

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THE SECRETARY OF HEALTH AND HUMAN SERVICES

WASHINGTON, D.C. 20201

October 8, 2009

The Honorable Nancy Pelosi
Speaker of the House of Representatives
Washington, DC 20515

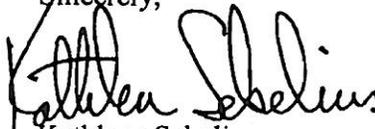
Dear Madam Speaker:

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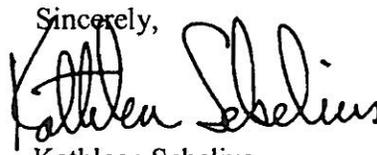
The Honorable Michael B. Enzi
Ranking Member
Committee on Health, Education, Labor, and Pensions
United States Senate
Washington, DC 20510

Dear Senator Enzi:

Attached for your consideration is the Food and Drug Administration's (FDA) Report to Congress entitled Communicating to the Public on the Risks and Benefits of New Drugs. On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85), directing the FDA to report on the best ways to communicate to the public the risks and benefits of new drugs, the role of the Risk Evaluation and Mitigation Strategies in assessing risks and benefits, and the potential use of a unique symbol to indicate the newness of a newly approved drug and direct-to-consumer advertising.

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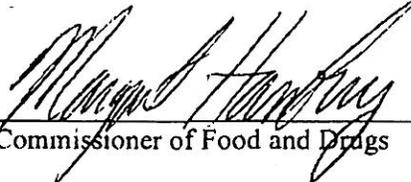
Sincerely,

Kathleen Sebelius

Enclosure

Report to Congress

**FDA Amendments Act of 2007
Section 904: Communicating to the Public on
the Risks and Benefits of New Drugs**

**Department of Health and Human Services
Food and Drug Administration
August 2009**



Commissioner of Food and Drugs

Date 08/31/09

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EXECUTIVE SUMMARY

This report to Congress fulfills the requirements of FDAAA Section 904, which directed FDA to report on the best ways to communicate to the public the risks and benefits of new drugs, the role of REMS in assessing risks and benefits, and the potential use of a unique symbol to indicate the newness of a newly approved drug. In this report, FDA provides an overview of the more long-standing approaches to communication, such as drug labeling and the use of patient package inserts, and describes how those long-used approaches continue to undergo changes to improve the effectiveness of what they provide and how they are used. As an example, FDA has revised the format of product labeling to include a Highlights section to facilitate prescriber access to the most pertinent information on risks and benefits. The agency has created special offices and used Web technology and targeted communication vehicles to more effectively communicate to particular patient and health professional audiences. To support continuous improvements in the ways it communicates drug risks and benefits to the public, FDA is also conducting a number of research efforts to better understand the information impact of variations in content and different communication formats.

The use of REMS, intended to educate and communicate to healthcare professionals and patients a drug's risks and benefits, gives FDA the opportunity to better manage drug risks after a product is marketed while learning more about which risk management strategies work best through regular sponsor assessments of a REMS' effectiveness in managing drug risks. REMS will help determine how FDA is doing and lead to continual gains in our knowledge base on how best to communicate the risks and benefits of new drugs.

Finally, this report discusses the merits of providing information to make patients and prescribers more aware that a drug product is newly approved. FDA strongly supports the concept and goals of a unique symbol that would remind prescribers and patients to use a product with particular care during its initial years of marketing and encourage prescribers to report suspected adverse events related to the use of newly approved drugs. For this reason, the Physician Labeling Rule requires that the approval year be placed in the Highlights section of healthcare professional labeling.

INTRODUCTION

On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85). Section 904 of Title IX of FDAAA, Benefit–Risk Assessments states the following:

Not later than 1 year after the date of the enactment of this Act, the Commissioner of Food and Drugs shall submit to the Congress a report on how best to communicate to the public the risks and benefits of new drugs and the role of the risk evaluation and mitigation strategy in assessing such risks and benefits. As part of such study, the Commissioner may consider the possibility of including in the labeling and any direct-to-consumer advertisements of a newly approved drug or indication a unique symbol indicating the newly approved status of the drug or indication for a period after approval.

The report that follows fulfills this statutory requirement. Section I addresses the role of current processes and methods, such as drug labeling and patient package inserts, special communications offices within FDA, and the role of FDA's Risk Communication Advisory Committee (RCAC). Section I also describes current communication vehicles, such as FDA's Web site, FDA-published safety alerts, and other targeted communications. Additionally, this Section reports on current FDA research to improve risk–benefit communication.

Section II of the report describes several new communication approaches FDA has implemented since the publication of the recommendations issued in 2006 by the Institute of Medicine (IOM)¹ and the enactment of FDAAA in September 2007. Section II also outlines the responsibilities of the RCAC and the goals of research underway at FDA on risk communication.

Section III details the role of FDAAA Section 901 Risk Evaluation and Mitigation Strategies (REMS) in assessing the risks and benefits of new drugs.

Section IV addresses the potential use of a unique symbol in new drug labeling and DTC advertising of newly approved drugs.

Section V concludes this report.

¹ The IOM made recommendations to FDA and others in its report, entitled *The Future of Drug Safety—Promoting and Protecting the Health of the Public*. FDA issued a response to that report in January 2007, explaining that it agreed with most of the recommendations to FDA. FDA's 2007 response is available at <http://www.fda.gov/oc/reports/iom013007.pdf>. Several of the IOM recommendations were codified in FDAAA, and FDA was asked to provide a status update on the activities reported on in its 2007 response. The status update report is available at www.fda.gov

I. FOOD AND DRUG ADMINISTRATION (FDA) APPROACHES FOR COMMUNICATING RISKS AND BENEFITS OF NEW DRUGS

Ensuring the safety and effectiveness of human drugs is a primary regulatory goal of the FDA. FDAAA gave FDA additional authority and resources to enhance the agency's ability to assess and ensure drug safety after marketing approval. FDA defines "safe" to mean that a drug's benefits outweigh its risks. FDA's current benefit-risk evaluation process utilizes the extensive evidence of clinical safety and effectiveness submitted by a drug sponsor in the new drug application, as well as a broader set of benefit-risk findings for other drugs approved for use in treating the same indication, and a complex array of other factors affecting the assessment of benefits and risks. The process involves quantitative analysis as well as a subjective weighing of evidence that leads to a regulatory decision on a new drug's benefit-risk profile. After a new drug is approved, FDA evaluates additional safety information to continually ensure that the drug's benefits outweigh its risks as it is prescribed to the broader population.

FDA has traditionally employed a wide range of tools and approaches to communicate the risks and benefits of new drugs. Information in medical product labeling is directed to health professionals, and patient package inserts are included to inform patients and guide safe use. However, FDA has a variety of additional processes and tools it uses to communicate drug safety information because it understands how important it is to ensure that benefit-risk information is easily available to patients and their healthcare practitioners when they are making important treatment decisions. For example, FDA makes extensive use of the Internet to communicate safety information. FDA has established special offices to support communication to particular patient populations. After products are approved and marketed, FDA continues to communicate safety information to the public, providing updated benefit-risk information. While employing these various approaches, FDA also seeks to continually improve on its communication of drug risks and benefits. These activities are discussed in more detail in the following sections.

Drug Labeling and Patient Package Inserts

I. Drug Labeling

Drug labeling is FDA's principal tool for educating healthcare practitioners and consumers about the risks and benefits of drugs to help ensure safe and effective use. Labeling may also provide patients with information to ensure safe and effective use. A critical part of FDA's mission is its review of the adequacy of labeling. FDA experts review the information submitted by the manufacturer on a new drug's risks and benefits, and they work to ensure that approved labeling contains all important benefit and risk information that patients and prescribers should consider when making healthcare decisions. FDA tries to ensure that less important risks are not presented in a way that detracts from important risk information. The agency also tries to ensure that risk information that is not adequately supported by scientific information is not included in labeling.

Once a medicine is approved and marketed, FDA continually evaluates the latest available scientific information to monitor the safety of the new medicine, incorporating new information into product labeling when appropriate. Under FDAAA, FDA may require labeling changes to

reflect new safety information that emerges postapproval. The phrase "new safety information," with respect to a drug, signifies information derived from a clinical trial; an adverse event report; a postapproval study, including a study under Section 505(o)(3); peer-reviewed biomedical literature; data derived from the postmarket risk identification and analysis system under Section 505(k); or other scientific data deemed appropriate.

FDA strives to promote a better understanding of the risks and benefits of new drugs through its drug labeling. In January 2006, FDA issued the Physician Labeling Rule, which contained a new requirement for the content and format of prescription drug labeling. To ensure appropriate use to maximize benefits, manage the risks of medication use, and reduce medical errors, the newly designed package insert provides the most up-to-date information in an easy-to-read format that draws physician and patient attention to the most important pieces of drug information before a product is prescribed. The changes include requirements for new and recently approved drugs to include highlights of the prescribing information (Highlights) and a table of contents (Contents) for the full prescribing information, reordering of currently required information and minor changes in its content, and the establishment of minimum graphical requirements.

To help inform healthcare professionals about the new labeling, the agency developed a new accredited health professional educational module available online entitled, "An Introduction to the Improved FDA Prescription Drug Labeling." This interactive training module, launched in December 2007, is designed to give physicians, nurses, pharmacists, and other healthcare practitioners a better understanding of the revised prescription drug labeling, the format changes that were made, and why they were necessary. The goal of this training module is to make information about the revised labeling more clearly and more easily understood. The program is well-regarded by external reviewers and received an award of excellence from the National Association of Government Communicators in May 2008.

2. Patient Package Inserts and Medication Guides

To increase the effectiveness of benefit-risk communication to patients, FDA encourages the use of patient labeling. Patient labeling is a type of informational insert for certain medications designed to be understood by patients. There are two types of patient labeling regulated by FDA: patient package inserts (PPI) and Medication Guides. PPIs serve as an extension of the healthcare practitioner labeling and can be distributed to patients when a drug is dispensed. Medication Guides are user-friendly handouts that are required to be distributed with certain prescription medicines that have a serious and significant public health concern. Medication Guides address issues that are specific to particular drugs and drug classes. Medication Guides are required when one or more of the following circumstances exist:

- The drug product is one for which patient labeling could help prevent serious adverse effects;
- The drug product is one that 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; and
- The drug product is important to health, and patient adherence to directions for use is crucial to the drug's effectiveness.

Communicating Risks and Benefits Through Dedicated Offices

FDA understands the unique challenges involved in effectively communicating risks and benefits while addressing certain health issues or when communicating with target patient populations. The agency has offices dedicated to communicating on certain predetermined special issues and with specific target populations, including the Office of Special Health Issues (OSHI) and the Office of Women's Health (OWH).

OSHI serves as an important interface with patients and their families, healthcare professionals, the media, and other components of FDA to respond to questions about FDA's activities related to HIV/AIDS, cancer, and other serious disease and health issues. The staff works with patients and their advocates to encourage patient community input and support their participation in formulating

FDA regulatory policy. The staff also provides information about clinical trials and about FDA's drug approval process.

OWH serves as a champion of women's health both within FDA and externally. To achieve its goals, OWH ensures that FDA regulatory and oversight functions remain gender-sensitive and responsive. OWH works to correct any identified gender disparities in drug, device, and biologics testing and regulation policy. OWH monitors progress of priority women's health initiatives within FDA and promotes an integrative and interactive approach regarding women's health issues across all the organizational components of FDA. OWH forms partnerships with governmental and non-governmental entities, including consumer groups, health advocates, professional organizations, and industry. For example, OWH partnered with the National Association of Chain Drug Stores to provide literature about safe medicine use and sponsored educational sessions on this topic. The brochure "My Medicines" was translated into 14 languages, including Spanish, Cantonese, Russian, and Hmong.

Communicating Risks and Benefits through the Web Site

FDA has expanded the role of Internet-based forms of communication during the past decade in its efforts to communicate the risks and benefits of new drugs with these rapidly-emerging types of media. Recently, FDA has been redesigning its Web site to ensure a more user-friendly site containing complete, unambiguous, and accessible information. An effort is also under way to modernize MedWatch, FDA's system for voluntary reporting of individual adverse reactions.

1. Redesigning of the FDA Web Site

FDA's Web site² represents a primary mechanism for communication of information regarding FDA-regulated products. During the past year, FDA has initiated a number of improvements in the site's accessibility and usefulness for all of its constituents, especially for the general public. In March, FDA unveiled its new home page, a design based on extensive constituent research and usability testing. The new home page enables viewers to easily locate and access both new drug approval and drug risk information. It also provides viewers the option of identifying themselves as consumers versus healthcare professionals and routes them appropriately to information specifically designed and displayed for them. FDA has also redesigned its Consumer Health

² See <http://www.fda.gov>.

Information page, which provides convenient access to a variety of other information designed to aid patients in using their prescription and nonprescription drugs.³

In a related effort, FDA recently launched a consumer education Web site⁴, produced in cooperation with EthicAd.org.⁵ This site provides the public with useful information about DTC drug advertising. FDA will continue to assess customer needs to determine how best to improve these communication tools.

2. Modernizing MedWatch

MedWatch is FDA's safety information and adverse event reporting system for voluntary reporting of individual adverse reactions. An adverse reaction is any undesirable effect reasonably associated with the use of a drug that may occur as part of the pharmacological action of the drug or may be unpredictable in its occurrence. The MedWatch system stores voluntary reports of adverse reactions and product quality problems, and product use errors reported by healthcare professionals, consumers, and patients. The reports can be submitted online, through surface mail, by fax, or by phone. In addition to providing a mechanism for FDA to receive new safety information, the MedWatch staff prepares monthly summaries of changes to drug products, including safety labeling changes, and makes those available via the MedWatch Web site.⁶ MedWatch helps ensure the timely dissemination of safety information for FDA-regulated drugs to healthcare professionals and consumers.

FDA is in the process of modernizing the way it collects, reviews, analyzes, and communicates adverse event reports and other safety information for all FDA-regulated products, through the MedWatch^{Plus} effort. MedWatch^{Plus} will expand the current MedWatch system and create a unified data repository, enabling the agency's eight existing safety reporting systems for the range of different FDA-regulated products (i.e., foods, drugs, biologics, and medical devices) to use a common system. Additionally, the agency is developing a single Web-based portal, or entryway, for submitting reports to and from all reporters for all products. This new portal will feature a logical, user-friendly Web questionnaire that will help users complete and submit their reports easily and consistently. Making voluntary reporting easier should encourage more consumers to take the time to submit suspected adverse events and product problems to FDA.

Having adverse events and product problem information readily accessible in one data repository will also enable FDA staff to efficiently analyze thousands of safety reports and quickly identify potential safety problems. FDA is partnering with the National Institutes of Health to develop the Web portal and user-friendly questionnaire.

On May 22, 2008, FDA launched the Sentinel Initiative with the ultimate goal of creating and implementing the Sentinel System – a national, integrated, electronic system for monitoring medical product safety. This system will enable FDA to query multiple, existing data sources, such as electronic health record systems and medical claims databases, for information about medical products. The system will enable FDA to query data sources at remote locations, consistent with

³ See <http://www.fda.gov/consumer/default.htm>.

⁴ See <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/default.htm>

⁵ See <http://ethicad.org/>.

⁶ See <http://www.fda.gov/medwatch/index.html>.

strong privacy and security safeguards. Data sources will continue to be maintained by their owners.

II. NEW APPROACHES FOR COMMUNICATING RISK AND BENEFIT INFORMATION

FDA has expanded and improved its approaches to communicating drug safety information since the publication of the 2006 IOM report and the enactment of FDAAA in the fall of 2007. In several cases, new approaches have been developed. The internet is key to many of the agency's new approaches for disseminating postmarket risk–benefit information. Recent changes to FDA's Web site will make risk and benefit information easily available to the public. In addition, the creation of a risk management advisory committee, and research that is under way to evaluate how best to communicate risk and benefit information, will help the agency continue to adjust its communication approaches.

A. Drug-Specific Risk–Benefit Communications

FDA has expanded the methods it uses to communicate risk and benefit information about medicines; and a variety of new tools have been developed to communicate important, sometimes emerging, drug safety issues related to medicines marketed in the United States. FDA communications are designed to help healthcare professionals, patients, and other consumers in making decisions about the safe and appropriate prescribing and use of medicines.

To enhance timely and effective communication of significant new information to health professionals, FDA has created a number of listservs on a range of topics for a variety of audiences.⁷ A new listserv, FDA Updates for Health Care Professionals, sends announcements particularly related to safety. Announcements may also include updates on medical product approvals, opportunities to comment on proposed rules, information about upcoming public meetings, and other information of interest to health professionals.

The agency is also developing a new health professional Web page that will serve as a portal for FDA information, particularly safety-related information of interest to healthcare professionals. Usability testing has been completed, and launch of the new Web page is expected in 2009.

FDA uses Public Health Advisories, Information for Healthcare Professionals sheets, and Early Communications about ongoing safety reviews to disseminate information important to consider when weighing the benefits and risks of medicines. These drug safety communications contain information that can help minimize risks and help prevent adverse events. Communications are distributed electronically to more than 110,000 members of FDA's MedWatch listserv and to approximately 140 healthcare partner organizations, who, in turn, distribute this information to their members and constituents. FDA seeks to provide practical, timely, balanced, and accurate information about medicines and their use that will lead to both the safe and appropriate use of these products.

⁷ FDA listservs can be accessed at <http://www.fda.gov/emaillist.html>.

B. Drug Safety Newsletter

FDA's quarterly Drug Safety Newsletter provides healthcare professionals with information about the findings of selected postmarket drug safety reviews from FDA's Center for Drug Evaluation and Research. This newsletter, launched in the fall of 2007, provides information on important emerging drug safety issues and recently approved new molecular entities (drugs that are approved for the first time). The intent of the Drug Safety Newsletter is to provide information useful to physicians and other healthcare professionals in making decisions about the use of medicines in their practice and to encourage reporting of serious adverse events to FDA. The newsletter is distributed electronically to U.S. healthcare professionals and consumers who subscribe to the Drug Safety Newsletter or to the MedWatch listserv. The newsletter can also be downloaded from FDA's Web site.⁸

C. Patient Safety News

FDA's Patient Safety News is a monthly televised series for healthcare personnel, carried on satellite broadcast networks aimed at hospitals and other medical facilities across the country. For almost a decade, this series has featured up-to-date information about drugs, biologics, and medical devices, including FDA safety notifications and product recalls and about ways to protect patients when using medical products. The Patient Safety News can also be viewed and downloaded directly from FDA's Web site.⁹

D. Consolidated Drug Safety Information for Practitioners and Patients

Under FDAAA Section 915, FDA is required to consolidate drug safety information for patients and providers. The CDER Web Page¹⁰ which was launched in October 2008, also provides links to safety information at other external sites, such as the National Library of Medicine and Medline Plus. FDA has improved public access to its approved labeling (both professional labeling and patient labeling), Medication Guides, safety alerts, and safety-related guidance and regulations, among other safety-related information of interest, such as REMS, and summaries of adverse reaction data. The site also enables voluntary submission of adverse drug reactions and product problems.

E. Posting of Adverse Drug Reaction Reports and Postmarket Safety

FDAAA Section 921 requires that FDA conduct a biweekly screening of the Adverse Event Reporting System (AERS) database and post quarterly reports of new safety information and/or potential signals of serious risks identified during the indicated quarter, using data from AERS. However, the listing of a product **does not mean** that FDA has determined the drug has a serious new risk. It means that FDA has identified a potential signal of a risk that may be associated with the product and is evaluating this potential signal. Based on that evaluation, the agency may decide to take regulatory action, such as requiring changes to product information (labeling), developing a REMS, or gathering additional data to better characterize the risk.

⁸ See <http://www.fda.gov/cder/dsn/default.htm>.

⁹ See <http://www.fda.gov/psn>.

¹⁰ See <http://www.fda.gov/cder/drugSafety.htm>.

The posting of safety information in accordance with Section 921 is not intended to suggest that healthcare practitioners should stop prescribing products included in the reports or that patients should stop taking these products. As FDA completes its evaluation of a particular drug, it will issue further public communications about these safety issues and actions.

F. The Risk Communication Advisory Committee (RCAC)

Effective communication to patients and health professionals requires careful planning and evaluation of effectiveness. Recognizing the value of expert advice in designing and implementing the most effective communication strategies, the FDA Commissioner determined that it was in the public interest to establish an external expert advisory group. Established in 2007 under the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), the RCAC advises the Commissioner and the Agency on strategies and programs designed to communicate with the public about both the risks and benefits of FDA-regulated products so as to facilitate optimal use of these products. The Committee also reviews and evaluates research by both FDA and other entities relevant to such communication to the public. The RCAC also facilitates interactive sharing of risk and benefit information with the public to enable individuals to make informed, independent judgments about the use of FDA-regulated products. Establishment of the RCAC was recommended by IOM in its September 2006 report on drug safety and was codified in FDAAA.

The RCAC has met three times as of September 2008. On February 28 and 29, 2008, the Committee met for the first time for presentations and discussion about FDA's risk communication programs and responsibilities. This meeting included discussion about FDA's proposed template for press releases announcing product recalls. On May 15 and 16, 2008, the Committee met for presentations and discussion of communication issues related to DTC advertising, including how DTC advertising relates to communicating to subsets of the general population, such as the elderly, children, and racial and ethnic minority communities and whether it increases access to health information and decreases health disparities for these populations. The Committee also discussed studying the appropriateness of including, in televised DTC ads, a statement encouraging consumers to report negative side effects of prescription drugs to MedWatch, as is currently required for print DTC prescription drug ads. On August 14 and 15, 2008, the Committee met and focused on non-persuasive versus persuasive communication in the context of FDA-regulated products—what knowledge is needed and, from a public perspective, what people should know and how they should find out about it.

G. Research on Improving Risk and Benefit Communication

Section 1701(a)(4) of the Public Health Service Act (42 U.S.C. 300u(a)(4)) authorizes FDA to conduct research relating to health information. Section 903(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 393(b)) authorizes FDA to conduct research relating to drugs and other FDA-regulated products in carrying out the provisions of the Act. The discussion that follows provides an overview of ongoing FDA research to improve agency understanding of public perceptions of risk and benefit information, and support improved communication of risks and benefits.

1. Current Studies

FDA is undertaking three studies that will provide information about how best to communicate with healthcare professionals and the general public about new drugs:

- A national survey of physician primary care and specialty providers on their use of and perceptions of emerging risk information about medical products (drugs and medical devices). FDA completed the preliminary analyses of the study data in December 2008, and is discussing how to communicate the data most effectively.
- A study of physicians' and midwives' cognitive models concerning treatment decisions for pregnant and nursing women—specifically women taking medicines for chronic illnesses—to determine what information they use to make decisions, how they value that information, and how they weigh the benefits and risks of recommending that their patients continue to use their drugs versus changing to different drugs versus completely stopping drug use.
- A study to examine models of consumers' cognitive understanding of the benefits and risks of prescription drugs and then allow preliminary testing of draft messages designed to address the gaps in their understanding of drugs' relative risks and benefits.

2. Conveying Effective Information in Direct-to-Consumer (DTC) Advertising

FDA regulations require that advertisements that make claims about a prescription drug include a fair balance of information about the benefits and risks of advertised products, in terms of both content and presentation. Healthcare professionals and consumers have expressed concern to FDA about the effectiveness of FDA regulation of DTC prescription drug advertising, especially as it relates to ensuring balanced communication of risks compared with benefits.

Advertisements can present information in ways that can optimize or skew the relative balance of risks and benefits. For example, many critics assert that the visuals shown during DTC television advertisement of medical products are virtually always positive in tone and often depict only product benefits.¹¹ Such compelling visuals during the audio risk presentation of advertisements have the potential to lead a consumer to form a positive opinion of a drug for no other reason than that it is presented in the same context as positive images. A consistently raised question is whether showing visuals of benefits interferes with consumer understanding and processing of the risk information in an advertisement's audio or text.

The manner in which required risk information is presented in DTC ads has been recently addressed in FDAAA. Section 901(d)(3) requires that the major statement¹² in DTC broadcast advertisements "shall be presented in a clear, conspicuous and neutral manner." Furthermore, the Secretary shall establish standards for determining whether the major statement is presented in such

¹¹ See, for example, Wolfe, Sidney (2002), Direct-to-consumer advertising: Education or emotion promotion? *New England Journal of Medicine*, 346(7), 524-526.

¹² "Advertisements broadcast through media such as radio, television, or telephone communications systems shall include information relating to the major side effects and contraindications of the advertised drugs in the audio or audio and visual parts of the presentation..." 21 CFR 202.1(e)(1).

a manner. FDAAA does not define how the objective of “clear, conspicuous, and neutral” is to be achieved.

FDA is planning to examine these issues through an experimental study to investigate the effect of visual distraction and the interplay of different sensory modalities used to communicate risk and benefit information during a DTC television prescription drug advertisement. This study will serve multiple purposes: (1) to help determine whether the use of competing, compelling visual information about potential drug benefits interferes with viewers' processing and comprehension of risk information about drugs in DTC advertising or with their cognitive representations of the drugs, (2) to examine the role of textual elements in the processing of risk information, and (3) to provide FDA with information on defining the presentation of the major statement as “clear, conspicuous, and neutral” as required by Section 901(d)(3) of FDAAA.

Data from these studies will provide useful information for FDA as it considers whether it is appropriate to develop guidance to help improve how broadcast advertisements present a prescription drug's risks and benefits. The studies will also provide preliminary data on how FDA may interpret the “clear, conspicuous, and neutral” standard, as well as help the agency plan whether additional research is needed to develop the standards called for in FDAAA.

3. Improving the Communication of Effectiveness Claims in DTC Advertising

The FD&C Act requires that manufacturers, packers, and distributors (sponsors) who advertise prescription human and animal drugs, including biological products for humans, disclose in advertisements certain information about the advertised product's uses and risks.¹³ By its nature, the presentation of this risk information is likely to evoke active trade-offs by consumers (i.e., comparisons with the perceived risks of not taking treatment and comparisons with the perceived benefits of taking a treatment).¹⁴ Because FDA has an interest in fostering safe and proper use of prescription drugs, an activity that engages both risks and benefits, an in-depth understanding of how consumers process this information is central to this regulatory task.

As described in the previous section, FDA regulations require that prescription drug advertisements that make claims about a product also include risk information in a balanced manner (21 CFR 202.1(e)(5)(ii)), both in terms of the content and presentation of the information. In print advertisements, this balance applies to both the front (display) page of an advertisement, as well as the brief summary page. However, beyond the balance requirement, there is limited guidance to direct or encourage sponsors to present benefit claims that are informative, specific, and reflect clinical effectiveness data.

Furthermore, although there is research on the difficulties of communicating mathematical concepts and numerical information to consumers, specific research on how to most **effectively** present benefit and efficacy information in prescription drug advertisements is limited. For example, benefit claims, broadly defined, appearing in advertisements are often presented in general

¹³ For prescription drugs and biologics, the Act requires advertisements to contain “information in brief summary relating to side effects, contraindications, and effectiveness” (21 U.S.C. 352(n)).

¹⁴ See Schwartz, L, Woloshin, S, Black, W, and Welch, HG (1997). The role of numeracy in understanding the benefit of screening mammography. *Annals of Internal Medicine*, 127(11), 966-72.

language that does not inform patients of the likelihood of efficacy and are often simply variants of an intended use statement.¹⁵

To investigate this question, FDA is planning to conduct a three-part study to (1) understand how practicing physicians acquire and communicate clinical efficacy information to their patients; (2) understand how physicians interpret clinical efficacy information from the approved product labeling; and (3) use this understanding to test alternative designs that will inform FDA's thinking regarding how manufacturers can provide useful and non-misleading efficacy information to consumers in DTC print advertisements. Specifically, FDA is interested in how physicians and consumers form risk-benefit tradeoffs and, particularly, how consumers make such judgments in response to variations in the efficacy presentations in the display page of a DTC print advertisement. A concern is whether consumers form accurate perceptions and accurate risk-benefit tradeoffs. In other words, when provided with efficacy information of various styles, do consumer perceptions correspond with those of clinically based physician assessments of the benefits, risks, and benefit-risk tradeoffs of the same drugs?

III. USE OF RISK EVALUATION AND MITIGATION STRATEGIES (REMS) IN ASSESSING DRUG RISKS AND BENEFITS

FDAAA provides FDA with greatly increased authority to monitor, manage, and communicate new drug risks and benefits following approval for marketing. Section 901 of Title IX of FDAAA creates a new Section 505-1 of the FD&C Act that authorizes FDA to require manufacturers submitting certain new drug applications to provide a proposed REMS as part of their application if FDA determines that a REMS is necessary to ensure that the benefits of a drug outweigh the risks of the drug. This section of FDAAA also authorizes FDA to require REMS postapproval if FDA becomes aware of new safety information as defined in 505-1(b)(3) and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks. A REMS will always include a timetable for submitting assessments of the REMS. FDAAA specifies that the timetable for assessments must include an assessment at 18 months, 3 years, and 7 years after the strategy is approved. The applicant may voluntarily submit an assessment of an approved REMS at any time.

A. The Role of REMS

The role of a REMS is not to assess the risks and benefits of a new drug, but to provide a useful tool to help manage the risks and benefits of the drug once it is on the market. In making the determination of whether a REMS is needed, FDAAA requires FDA to take a variety of factors into consideration, including:

- The estimated size of the population likely to use the drug involved;
- The seriousness of the disease or condition to be treated with the drug;
- The expected benefit of the drug with respect to such disease or condition;

¹⁵ Woloshin, S. and Schwartz, L. (2001). Direct to consumer advertisements for prescription drugs: what are Americans being told. *Lancet*, 358, 1141-46.

- The expected duration of the treatment with the drug;
- The seriousness of potential adverse events related to the drug; and
- Whether the drug is a new molecular entity.

Based on these considerations, FDA will determine whether a REMS is necessary to ensure that the benefits outweigh the risks of a drug in the context of actual use once the product is on the market.

Possible elements of a REMS include Medication Guides or PPI's as discussed in Section I of this document. A communication plan targeted to healthcare practitioners and other elements to ensure safe use as described below can also be implemented to ensure that a drug's benefit-risk profile remains favorable. The communication plan may include sending letters to healthcare providers, disseminating information about the REMS to encourage implementation by healthcare providers, or disseminating information to healthcare providers through professional societies about any serious risks of the drug and any protocol to ensure safe use.

B. Elements to Assure Safe Use

Elements to assure safe use could be required as part of a REMS if the drug has been shown to be effective, but is associated with a serious adverse drug experience and FDA determines that it can be approved only if (or would be withdrawn unless) such elements are part of a strategy to mitigate the specific serious risk listed in the labeling of the product. Elements to assure safe use could also be required for a drug initially approved without elements to assure safe use if FDA determined that the other elements of a REMS are insufficient to mitigate the serious risk. The elements to assure safe use may require that:

- Healthcare practitioners who prescribe the drug have particular training or experience, or are specially certified;
- Pharmacists or other dispensing practitioners, and healthcare settings where the drug is dispensed are specially certified;
- The drug is dispensed to patients only in certain healthcare settings, such as hospitals;
- The drug is dispensed to patients with evidence or other documentation of safe-use conditions, such as laboratory test results;
- Each patient using the drug is subject to certain monitoring; and
- Each patient using the drug is enrolled in a registry.

In addition, the elements to assure safe use may include a system through which an applicant is able to take reasonable steps to monitor and evaluate implementation of those elements by healthcare practitioners in the healthcare system who are responsible for implementing those elements and work to improve their implementation.

IV. USE OF A UNIQUE SYMBOL / EDUCATIONAL CAMPAIGN FOR NEW DRUGS

The provisions of Section 904 specify that FDA's Commissioner consider the possibility of including a unique symbol in the labeling and DTC advertising of a newly approved drug or new use indicating the newly approved status of the drug or new use for a period after approval. The agency strongly supports the goals of this proposal to help ensure that prescribers use a product

with particular care during its initial years of marketing and to make prescribers more diligent in reporting suspected adverse events. However, as part of the Physician Labeling Rule, FDA concluded that the use of the initial year of approval would be a better mechanism to call attention to the relative newness of a product. The rule requires that the approval year be placed in the Highlights section of healthcare professional labeling.

FDA is also considering working with the producers of the Consumer Medication Information (CMI), which is distributed to patients with their prescriptions, to encourage them to voluntarily include the product approval date, as this information is currently not required to be in any patient or consumer-directed materials. CMI is the written medication information that is provided to patients or caregivers when a prescription medicine is dispensed. Private companies develop the CMI and sell the information to pharmacies to include with patient prescriptions. CMI is not written by pharmaceutical companies, and is not reviewed or approved by FDA. FDA is in the process of evaluating the usefulness of current CMI materials as required by Public Law 104-180, Title VI, Section 601 (Effective Medication Guides).¹⁶

V. CONCLUSION

Overall, FDA recognizes multiple opportunities for continual improvement in the approaches it uses to communicate drug risks and benefits. FDA will continue to take advantage of those opportunities through its ongoing evaluation and research and using the tools provided under FDAAA. The agency will strengthen the processes it uses to gather and analyze risk-benefit information while making the best use of new information technologies to maximize communication effectiveness. FDA's ultimate goal will be to yield increased benefits in patient health and safety.

¹⁶ This section in PL 104-180, passed on August 6, 1996, specifies the following goals for the distribution of useful written information: By the year 2000, distribution of useful written information to 75 percent of individuals receiving new prescriptions; and by the year 2006, distribution of useful written information to 95 percent of individuals receiving new prescriptions