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STATEMENT

OF

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UNITED STATES SENATE

"PROTECTING SENIORS FROM MEDICATION LABELING MISTAKES"

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INTRODUCTION

Madam Chairwoman and members of the Subcommittee, I am Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss safe use of prescription medications and the steps FDA is taking to help reduce medication errors through labeling. My testimony will describe what FDA is doing to improve the quality of information being provided to patients about their medication.

FDA is charged with protecting and enhancing the public health by ensuring the safety, efficacy and quality of medicines. Helping all Americans make better informed decisions concerning their health care is a top priority of the Agency.

FDA's goal is for consumers to be provided with current, easy-to-understand information in a standardized format with an approved drug product. This is an important step in educating all patients, particularly vulnerable populations like seniors, about their medications and how to use them safely.

The current system for ensuring that patients receive essential medication information needed to use a drug safely requires improvement. In keeping with recommendations from FDA's Risk Communication Advisory Committee and input from stakeholders, FDA sees merit in adopting the use of a single document, standardized with respect to content and format, which we refer to as the Patient Medication Information (PMI). As I will discuss, FDA has been

working on a new framework for the development and distribution of PMIs to patients in consultation with stakeholders, including patients, providers, and drug manufacturers, among others.

Statutory and Regulatory Authority

FDA regulates the manufacture, sale, and distribution of drugs in the United States under authority of the Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act), which includes approval of prescription drug labeling that provides information about the use of a drug. The term "labeling" is generally defined by section 201(m) of the FD&C Act as "all labels and other written, printed, or graphic matter: (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." Prescription drug labeling, as defined in the Federal regulations, specifically, 21 CFR 201.56, must meet certain requirements, including:

- Contain a summary of essential scientific information for the safe and effective use of the drug
- Be informative and accurate
- Not be promotional in tone, false, or misleading
- Not make claims or suggest uses for drugs when there is not sufficient evidence of safety and substantial evidence of effectiveness
- Contain information based, whenever possible, on data derived from human experience

The labeling also must be updated when new information becomes available that causes it to become inaccurate, false, or misleading.

In short, drug labeling contains important information essential to safe use of the drug. I will provide a brief overview of the history of prescription drug labeling and FDA's efforts in this area.

Providing Effective Information to Consumers about Prescription Drugs

FDA is developing a new framework to provide patients with quality, up-to-date prescription product information that will promote the safe use of prescribed medication. The goal of the new PMI is to provide patient-oriented information for each prescription product. Currently, when a prescription is dispensed, a patient may receive any, all, or none of the following: Patient Package Insert (PPI), Medication Guide (MG), or Consumer Medication Information (CMI). These types of prescription information are developed by different sources and may be duplicative, incomplete, or not appropriately written for patient comprehension. FDA sees merit in adopting a single, standardized PMI document to accompany dispensed prescriptions.

Use of a standardized format for prescription product patient information is prevalent internationally. In the European Union (EU), Canada, Japan, Australia, and New Zealand, manufacturers provide patient information for prescription products based on regional regulations,[1] and distribution of this information generally occurs when the medication is dispensed to the patient. Almost all of these countries take steps to make the information consumer friendly; some require consumer testing with patient groups to ensure the information is legible, clear, and easy to use, and others simply stipulate that the documents should be simple, non-technical, easy to read, legible, and clearly written at a predefined reading level. Depending on regional regulatory requirements, disclosure of risks ranges from complete disclosure of all major risks and side effects to disclosure of only common and severe side effects.

[1] Raynor DK, Svarstad B, Knapp P, et al. *Consumer medication information in the United States, Europe, and Australia: a comparative evaluation. J Am Pharm Assoc. 2007;47(6):717–724*

Patient Package Inserts (PPIs)

PPIs are developed by the manufacturer, approved by FDA, and required to be dispensed with specific products or classes of products (*e.g.*, estrogen-containing products). Since 1968, FDA regulations have required that PPIs written specifically for patients be distributed when certain prescription drugs, or classes of prescription drugs, are dispensed. The first FDA regulation requiring a PPI was published in 1968, mandating that isoproterenol inhalation medication contain a short warning that excessive use could cause breathing difficulties. Other PPIs are submitted to FDA voluntarily by the manufacturer and approved by FDA, but their distribution is not mandated. In the 1970s, FDA began evaluating the general usefulness of patient labeling for prescription drugs, resulting in a series of regulatory steps to help ensure the availability of useful written consumer information.

In 1979, FDA proposed regulations that would have required written patient information for all prescription drugs[2] and, in 1980, finalized those regulations, establishing requirements and procedures for the preparation and distribution of manufacturer-prepared and FDA-approved patient labeling for a limited number of prescription drugs.[3] However, FDA revoked those regulations in 1982 based on assurances, in part, by health care professional associations, private-sector providers of written information for patients, and pharmaceutical manufacturers that the goals of the final rule could be met more effectively without regulation.[4]

[2] 44 FR 40016, July 6, 1979.
[3] 45 FR 60754, September 12, 1980
[4] 47 FR 39147, September 7, 1982

Medication Guides (MGs)

MGs come with many prescription medicines and address issues specific to particular drugs and drug classes. They contain FDA-approved information that can help patients avoid serious adverse events by underscoring significant safety concerns that can be weighed against the benefits of the drug. MGs are developed by the manufacturers, reviewed by FDA, considered to be part of the product's approved labeling, and required to be distributed by pharmacies with each prescription.

FDA is committed to monitoring the progress of this voluntary private-sector effort. FDA surveys showed that, although the distribution of written prescription drug information increased, the usefulness of the information was highly variable. As a result, FDA proposed a regulation entitled "Prescription Drug Product Labeling: Medication Guide Requirements,"[5] which was designed to set specific distribution and quality goals, and time frames, for distributing written information. Goals of the proposed rule were: by 2000, 75 percent of people receiving new prescriptions would receive useful written patient information with their prescriptions, increasing to 95 percent in 2006. The proposed rule would have required manufacturers to prepare and distribute MGs for a limited number of prescription drug products that posed a serious and significant public health concern.

As FDA was reviewing the comments received in response to the proposed rule, in August 1996, legislation was enacted[6] regarding patient labeling that adopted the goals and time frames of the 1995 proposed rule. The legislation established a voluntary private-sector

[5] 60 FR 44182, August 24, 1995

[6]Section 601 of the Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act, for the fiscal year ending September 30, 1997, Public Law 104-180, August 6, 1996.

process through which a committee (Steering Committee) of interested stakeholders (national organizations representing health care professionals, consumer organizations, voluntary health agencies, the pharmaceutical industry, drug wholesalers, and patient drug information database companies, among others) would develop a long-range, comprehensive action plan to achieve the goals of FDA's proposed rule concerning patient labeling, and required the Secretary of HHS to evaluate the private sector's progress toward meeting the goals.

Though the law prohibited FDA from taking further regulatory action if private-sector initiatives met the goals of the plan within specified time frames, legislative history makes it clear that this law did not preclude FDA from using its existing authority to "require as part of the manufacturer's approved product labeling the dispensing of written information inserts to consumers…to meet certain patient safety requirements."[7]

In 1998, FDA published a Final Rule[8] that established a program under which MGs would be required for a small number of drugs considered to pose a serious and significant public health concern. The Final Rule did not deal with the private-sector voluntary program but only applied to the mandatory program covering products of "serious and significant concern."

In September 2007, the FD&C Act was amended to include MGs as one potential element of a Risk Evaluation and Mitigation Strategy (REMS). FDA may require a sponsor to develop a REMS, if it determines a REMS is necessary to ensure that the benefits of a drug outweigh the risks. The use of MGs as part of REMS, particularly as part of REMS that affect whole

[7] S. Rept. 104-317, 104th Cong., 2d sess., p. 132-33, July 11, 1996.
[8] 63 FR 66378, December 1, 1998

classes of drugs, has provided further impetus to evaluate different approaches to providing the type of prescription drug information that is normally provided in an MG to consumers.

Recognizing that many consumers rely on technology, the National Institutes of Health's Web site, DailyMed, provides quality information about marketed drugs, including medical product labeling that is currently in use and distributed by manufacturers as package inserts. This site provides health information for providers and the public with a standard, comprehensive, up-to-date, look-up-and-download resource of medical product labeling, including MGs. In addition, FDA posts updated information on MGs on its website.

Consumer Medication Information (CMIs)

CMI is information developed by the private sector intended for distribution with every prescription dispensed at a pharmacy. CMI information is not FDA-reviewed or approved.

In 1998, FDA contracted with the National Association of Boards of Pharmacy (NABP) to perform a pilot study to test the usefulness of the consumer medication information being developed. The standard for determining whether a particular piece of written medication information was useful to consumers came from a 1996 report entitled "Action Plan for the Provision of Useful Prescription Medicine Information,[9] drafted by the Steering Committee established by the 1996 legislation. This plan, known as the Keystone Action Plan, delineated

[9] Steering Committee for the Collaborative Development of a Long-Range Action Plan for the Provision of Useful Prescription Medicine Information, unpublished report submitted to The Honorable Donna E. Shalala, HHS Secretary, December 1996, available at *http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/reportsbudgets/ucm163793.pdf*

the following criteria for evaluating whether a particular piece of written medication information is useful to consumers, stating that materials should be:

- Scientifically accurate
- Unbiased in content and tone
- Sufficiently specific and comprehensive
- Presented in an understandable and legible format that is readily comprehensible to consumers
- Timely and up to date
- Useful, in that it enables consumers to use the medicine properly and appropriately, receive the maximum benefit, and avoid harm

The results of the pilot study found that much of the CMI that were assessed failed to provide sufficiently clear or specific information.[10] More than 90 percent of the CMI was judged to be unacceptable in terms of comprehensibility or readability. Virtually none of the information met acceptable levels of legibility. The study's conclusion noted that existing CMI "falls short of the information quality level required in the 1996 federal legislation."

In July 2002, FDA's Drug Safety and Risk Management Advisory Committee (Advisory Committee) met to review the study results and public comments.[11] The Advisory Committee recommended that FDA take a more active role in advising and encouraging the private sector to meet the next target goal set for 2006.

A final report issued in 2008 concluded that the CMI distribution method through pharmacies appears effective but that the content and format for this information had various shortcomings, including lack of critical information about the management of medications,

[10] Bonnie L. Svarstad, Ph.D. and Jeanine K. Mount, Ph.D., "Evaluation of Written Prescription Information Provided in Community Pharmacies (December 21, 2001)
http://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm169753.htm
[11] *http://www.fda.gov/ohrms/dockets/ac/cder02.htm#DrugSafetyRiskManagement*

significant redundancy of information resulting in long leaflets, poor formatting, and inadequate legibility and reading level.[12] The 2008 report also noted that it was unclear what quantity, presentation, and format of CMI will result in adequate patient comprehension and appropriate actions to improve patient safety.

Evolution of Patient Medication Information (PMIs)

In June 2008, FDA received a Citizen Petition from a large group representing pharmacy practice, medical consumers, and medical communications companies, requesting FDA adopt a "one-document solution" or PMI to replace CMIs, PPIs, and MGs.[13] In February 2009, the Advisory Committee also recommended adopting a single standard document for communicating essential information about prescription drugs, as a replacement for CMIs, PPIs, and MGs.[14] In September 2009, FDA held a public workshop to discuss optimal content and format of written prescription drug information. Input was sought on four draft patient information prototypes, which were developed through review of scientific literature, current labeling practices, and guidance. In response to the feedback provided during these meetings, FDA developed three draft patient information prototypes. In May 2010, FDA announced the design of an evaluation strategy to test different ways of presenting information about prescription drugs to patients, asking for comments by July 2010.

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[12]Carole L. Kimberlin, Ph.D., Almnut G. Winterstein, Ph.D., "Expert and Consumer Evaluation of Consumer Medication Information (November 4, 2008) *http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ReportsBudgets/UCM163783.pdf*

[13] National Consumers League, et al. – Citizen Petition Requesting FDA Action on a "One Document Solution: for all Pharmacy-Based Communications, June 30, 2008, *http://www.regulations.gov/#!documentDetail;D=FDA-2008-P-0380-0001*

[14]*http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/riskcommunicationadvisorycommittee/ucm152593.pdf*

During 2010 and 2011, FDA convened a series of expert meetings and public workshops, through a cooperative arrangement with the Engelberg Center for Health Care Reform at the Brookings Institution, to obtain broad stakeholder input on the design, content, format, and distribution of PMIs. There was agreement among the expert participants that providing patients with clear, concise, and consistent information about their medication is an important and feasible goal, and that achieving this goal requires broad-based collaboration among key stakeholders, including health care professionals, pharmacies, academia, and technology vendors. Areas for further exploration were highlighted, such as evaluation metrics, stakeholder cooperation for PMI distribution, and potential pilot studies. Since the last Brookings Institution meeting in February 2011, FDA has held approximately 18 meetings with a variety of stakeholders on various aspects of PMI, such as labeling content, patient comprehension, and distribution studies. FDA is continuing these discussions with Brookings and others so that the many benefits of useful and effective PMI may be realized.

Safe Use Initiative

FDA is also taking additional steps to foster safe use of drugs and help prevent medication errors through our "Safe Use Initiative" program, established in November 2009, to help reduce the likelihood of preventable harm from medication use. Today, tens of millions of people in the United States depend on prescription and over-the-counter (OTC) medications to sustain their health—as many as 3 billion prescriptions are written annually. Too many people, however, suffer unnecessary injuries, and some die, as a result of preventable medication errors. We believe that many of these medication-related risks are manageable, if parties committed to the safe use of medications work together. Through this initiative, FDA

seeks to partner and collaborate with relevant stakeholders to measurably reduce preventable harms from medications, thereby improving patient health.

FDA's Safe Use Initiative identifies, using a transparent and collaborative process, specific candidate cases (*e.g.*, drugs, drug classes, and/or therapeutic situations) that are associated with significant amounts of harm. Cases are analyzed for their potential for coordinated FDA/stakeholder actions to better manage related risks and reduce harm. If the analysis suggests a potential benefit from an intervention, FDA and its collaborators will develop appropriate activities and evaluation metrics.

In September 2010, CDER's Safe Use Initiative team convened a roundtable of more than 40 experts from academia, health care management, consumer advocacy, and government to address the safe use of pain medications in older adults. The goal of the roundtable was to seek and bring into voluntary collaboration key stakeholders from the health care community to develop and implement interventions aimed at quantifiably reducing preventable harm from the use of pain medications in older patients. This roundtable was an important first step in stimulating collaboration and an exchange of information about appropriate approaches in safe pain management for older adults.

FDA is currently engaged in three collaborative activities focused on patient labeling and geriatric inclusion issues. First, as a direct outgrowth of the roundtable, in collaboration with Dr. Joseph Pergolizzi, M.D., a Florida pain practitioner and adjunct assistant professor at Johns Hopkins University, FDA has developed a collaboration of greater than 30

professionals with expertise in geriatrics and non-steroidal anti-inflammatory drugs (NSAIDs). Their goal is to increase awareness in health care providers about age-related factors and adverse events in patients using NSAIDs. The collaboration will highlight the "Best Practices in Safe NSAID Use in Geriatric Patients," and that information will be shared with pain specialists through a series of open-access electronic publications.

The Safe Use Initiative is also working on a project with the National Council for Prescription Drug Programs that includes representatives from McNeil Consumer Healthcare, a Division of McNeil-PPC, Inc., whose objective is to ensure that when there are two-ingredient prescription medications for pain, acetaminophen and a second active ingredient, both are clearly labeled on the prescription vial. Instead of the abbreviation "APAP" from the active ingredient acetyl-para-aminophenol for acetaminophen, it is recommended that acetaminophen be spelled out along with the name of the second ingredient on the vial label so that patients taking these two-ingredient products are aware of the existence of acetaminophen in their prescription drug, can compare active ingredients in the prescription and OTC drugs, and can avoid an acetaminophen overdose by taking two or more drugs that contain acetaminophen. Another objective of this project is to have the overdose and liver toxicity warnings consistently displayed on prescription vials in language that is patient-centered and simple to understand. We have found that these warnings are also being voluntarily and consistently affixed to vials for prescriptions containing acetaminophen.

Finally, we are collaborating with the Institute for Safe Medication Practices (ISMP), which developed several information sheets on "high alert" prescription medicines such as warfarin,

insulin analogs, methotrexate, and opioids. These information sheets provide a tool for the pharmacist to use to point out a few selected important points for counseling, and provide an information sheet for the patient to use as reference. ISMP piloted the information and found that both pharmacists and consumers appreciate the information. Through FDA, ISMP has connected to Pharmacy Quality Alliance to determine how to best display and use these information sheets in retail pharmacy settings. Pharmacy Quality Alliance is a non-profit, consensus-based, multi-stakeholder membership organization committed to improving health care quality and patient safety with a focus on the appropriate use of medications.

Generic Drugs

FDA understands that generic drugs play an important role in granting access to safe, effective, and affordable products that will benefit the health of consumers, and especially seniors—who often are on fixed incomes. All drug manufacturers, whether brand or generic, have an ongoing obligation to patient safety and to ensure that their product labeling is accurate and up to date. Just last month, FDA issued a proposed rule that would allow generic drug manufacturers to independently update product labeling with certain newly acquired, safety-related information and promptly distribute the revised labeling before FDA's review of the change, just as brand manufacturers are currently allowed to do. If finalized, this proposed rule would help ensure that health care professionals and consumers have quicker access to the latest safety information for the medications they use. This proposed regulatory change would benefit the public health by improving communication of important drug safety information to health care professionals and consumers.

CONCLUSION

FDA recognizes that the current system used to ensure patients receive the essential medication information needed to use a drug safely can be improved. We share the views of our stakeholders that to use prescription medications safely, patients need to receive clear, actionable information. Through our PMI initiative, FDA is striving to reduce the harm caused by inappropriate drug use and enhance the benefits of drugs by facilitating their proper use. We will keep the Congress informed of our progress as we conclude this comprehensive effort. I am happy to answer questions you may have.