

FDA's SAFE USE INITIATIVE

***Collaborating to
Reduce Preventable Harm from
Medications***



***U.S. Department of Health and Human Services
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Executive Summary

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, even death, as a result of preventable medication errors or misuse.

The approaches used today for managing medication risks in the United States were put in place over the last century, often in a piecemeal fashion and usually in response to various crises and specific needs. Although FDA and many other stakeholders have been working to improve how the healthcare system manages medication risks in the United States, it is widely recognized that more needs to be done to protect the public from preventable harm from medication use. All participants in the healthcare community at large—patients, consumers, caretakers, healthcare practitioners, pharmacists, healthcare systems, health insurers, drug manufacturers, FDA, and other Federal agencies—have a role to play in managing medication risks and reducing preventable harm from medication. We believe that much preventable harm from medications results from problems that can be addressed best in a more coordinated, systematic manner, with interventions across all sectors of the medication distribution and use system.

This report announces the launching of FDA's ***Safe Use Initiative***. Through this initiative, FDA seeks to partner and collaborate with relevant stakeholders to measurably reduce preventable harm from medications, thereby improving patient health. FDA proposes to identify, 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 preventable harm. Cases will be carefully 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 interested partners will develop appropriate activities and evaluation metrics. In the months ahead, FDA intends to:

- Develop a general list of candidate cases for collaborative analysis and intervention. The list will be developed through extensive consultation with all interested public and private stakeholders and may include one or more of the existing opportunities listed in the Proposal section of this report.
- Collaborate with Federal partners to develop population-based national estimates of preventable harm from medications, categorized by drug, drug classes, and therapeutic situations.
- Open a public docket to receive suggestions and comments related to this report, risk management issues, and proposed candidate cases.
- Hold a series of meetings to gather broad public feedback as the candidate list is being developed.
- Based on the public contribution just outlined and the best available population-based data, work with interested partners to select specific candidate cases for analysis, intervention proposals, and evaluation metrics.
- During the Initiative's first 12 months, implement a small number of interventions. Each intervention will have an explicit plan for measuring impact. Interventions may involve FDA regulatory actions in concert with actions by other stakeholders.

Through a coordinated effort, involving all interested stakeholders, we can work to minimize the risks associated with using medications and reduce preventable harm.

FDA’S SAFE USE INITIATIVE—

Collaborating to Reduce Preventable Harm from Medications

INTRODUCTION

This report presents FDA’s analysis of medication risks in the United States and proposes — through the ***Safe Use Initiative*** — to create collaborative, cross-sector projects to better manage specific risks and reduce preventable harm from medication use.

Medications offer great benefit, but they come with risks. Whenever medications are not used optimally, risks of harm can increase significantly. In the United States, responsibility for managing medication risks is shared by many parties including:

- Federal agencies, such as FDA, the Drug Enforcement Agency (DEA), the Agency for Health Care Research and Quality (AHRQ), the Centers for Disease Control and Prevention (CDC), and others
- Drug developers, manufacturers, and distributors
- Pharmacies, hospitals, and other healthcare entities (including those operated by the Federal government and the states)

- Healthcare professionals, including physicians and physician assistants, dentists, pharmacists, nurses, and their professional societies
- State regulatory bodies, including professional licensure and oversight boards
- Healthcare insurers
- Patients, caregivers, consumers, and organizations representing their interests

Despite efforts by all parties, each year medications cause hundreds of thousands of injuries and deaths. Adverse events from drug use result in more than 4 million visits to emergency departments, doctors' offices, or other outpatient settings annually¹ and 117,000 hospitalizations each year.² A report on long-term care facilities projected nearly 10 adverse drug events per month for every 100 residents.³ There is also a high incidence of adverse drug events in hospitals; reports range from just over 2 events per 100 admissions⁴ to more than 6 adverse drug events per 100 admissions.⁵

Many injuries associated with medication use — estimates range from 11 percent⁶ to 50 percent,⁷ depending on the population, the setting, and the terminology — could be prevented **with currently available knowledge**. The long-term care study previously mentioned estimated that 40 percent of the adverse events, and 60 percent of the serious, life-threatening and fatal adverse events, were preventable.⁸ The IOM estimates that 400,000 hospitalized patients experience a preventable adverse drug event annually.⁹ Adding in nursing home care and care in other ambulatory settings, at least 1.5 million preventable adverse drug events

¹ Zhan C, Arispe I, Kelley E, et al., Ambulatory Care Visits for Treating Adverse Drug Effects in the United States, 1995–2001, *Joint Commission Journal on Quality and Patient Safety*, July 2005, Vol 31, Nr 7, p. 372.

² Budnitz DA, Pollock DA, Weidenback, KN, et al., National Surveillance of Emergency Department Visits for Outpatient Adverse Drug Events, *Journal of the American Medical Association*, October 18, 2006, Vol 296, No 15, p. 1858.

³ Gurwitz JH, Field TS, Avorn J, et al., The Incidence of Adverse Drug Events in Two Large Academic Long-term Care Facilities, *The American Journal of Medicine*, 2005, 118, pp. 251.

⁴ Classen DC, Pestotnik SL, Evans RS, et al. Adverse Drug Events in Hospitalized Patients. *Journal of the American Medical Association*, January 22/29, 1997, Vol. 277, No. 4, p. 303.

⁵ Bates DW, Cullen DJ, Laird N, et al., Incidence of Adverse Drug Events and Potential Adverse Drug Events: Implications for Prevention. *Journal of the American Medical Association*, Vol. 274, July 5, 1995, pp. 31.

⁶ Gandhi, TK, Weingart, SN, Borus, J, et al., Adverse Drug Events in Ambulatory Care. *The New England Journal of Medicine*, 348;16, p. 1556.

⁷ Gurwitz JH, Field TS, Avorn J, et al., Incidence and Preventability of Adverse Drug Events in Nursing Homes, *The American Journal of Medicine*, August 25, 2000, Vol 109, p. 87.

⁸ Gurwitz JH, Field TS, Avorn J, et al., The incidence of Adverse Drug Events in Two Large Academic Long-term Care Facilities, *The American Journal of Medicine*, 2005, 118, pp. 253.

⁹ Institute of Medicine of the National Academies, *Preventing Medication Errors*, National Academies Press, 2007, p. 120.

... at least 1.5 million preventable adverse drug events occur within the healthcare system each year.

In 2007, 5.2 million Americans 12 years and older reported using a prescription pain reliever for a non-medical use in the last month.

occur within the healthcare system each year.^{10,11} The IOM estimates the costs of these preventable adverse drug events to exceed \$4 billion annually.¹² The amount of preventable harm from OTC medication use is not known.

Unintended exposure to medications causes a significant number of injuries and deaths, primarily in children. One study found that more than 9,000 children were accidentally exposed to prescription opioid drugs between 2003 and 2006.¹³ It is estimated that 60,000 emergency department visits occur each year as a result of unsupervised ingestion of medications by children under twelve.¹⁴

The amount of harm from non-medical use of drugs is difficult to estimate. We know that abuse of prescription drugs is an increasing problem in the United States. In 2007, 5.2 million Americans 12 years and older reported using a prescription pain reliever for a non-medical use in the last month¹⁵ — resulting in more than 165,000 emergency department visits related to non-medical use of hydrocodone, oxycodone, and methadone-containing products alone.¹⁶

The number of injuries and deaths resulting from attempts at self-harm are also difficult to quantify. An estimated 55,000 emergency department visits¹⁷ result from intentional overdose with acetaminophen-containing products annually. The Drug Abuse Warning Network (DAWN) estimates that 180,000 emergency department visits for drug-related suicide attempts occurred in 2006. More than half (58 percent) involved psychotherapeutic agents, such as benzodiazepines or antidepressants.¹⁸

¹⁰ Institute of Medicine of the National Academies, *Preventing Medication Errors*, National Academies Press, 2007, p. 124.

¹¹ *Ibid*, p. 4. The IOM defines ADE as any injury due to medication. Examples include a wrong dosage leading to injury (e.g., rash, confusion, or loss of function) or an allergic reaction occurring in a patient not known to be allergic to a given medication.

¹² *Ibid*, p. 132.

¹³ Bailey JE, Campagna E, Dart RC, The Underrecognized Toll of Prescription Opioid Abuse on Young Children, *Annals of Emergency Medicine*, April 2009;53:419-424.

¹⁴ Substance Abuse and Mental Health Services Administration, Office of Applied Studies. Drug Abuse Warning Network, 2006: *National Estimates of Drug-Related Emergency Department Visits*. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2008. (DAWN Series D-30, DHHS Publication No. (SMA) 08-4339.

¹⁵ Substance Abuse and Mental Health Services Administration, Office of Applied Studies. *The NSDUH Report: Trends in Nonmedical Use of Prescription Pain Relievers: 2002 to 2007*. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2009, p. 143.

¹⁶ Substance Abuse and Mental Health Services Administration, Office of Applied Studies. *Drug Abuse Warning Network, 2006: National Estimates of Drug-Related Emergency Department Visits*. Rockville, MD: Substance Abuse and Mental Health Services Administration.

¹⁷ Budnitz, DS, Joint Meeting of the Drug Safety and Risk Management Advisory Committee with the Anesthetic and Life Support Drugs Advisory Committee and the Nonprescription Drugs Advisory Committee June 29. See Guest Speakers, Budnitz, Slide 10. (<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm171562.htm>).

¹⁸ Department of Health and Human Services, *Drug Abuse Warning Network (DAWN), 2006: National Estimates of Drug-Related Emergency Department Visits*, pp. 10-11.

...coordinated cross-system efforts would have the greatest effect on reducing preventable harm.

These potentially avoidable injuries and deaths, resulting from medication errors, unintentional exposures, drug abuse, misuse, or self harm, represent a collective failure of society to adequately manage medication risks. These shortcomings have been widely recognized, and many healthcare system participants, including FDA, have taken steps to improve the parts of the system in which they participate. However, it is clear that coordinated cross-system efforts would have the greatest effect on reducing preventable harm.

Accordingly, FDA is proposing the Safe Use Initiative, with the goal of creating collaborations among relevant stakeholders to identify specific, preventable problems related to medication use, develop cross-sector interventions to reduce harm, and identify metrics by which to measure the success of these interventions.

WHAT ARE THE RISKS OF USING MEDICATIONS?

When a person decides to use a medication, he or she is agreeing to take certain risks.

When a person decides to use a medication, he or she is agreeing to take certain risks. To understand what the risks of using medications are and how they are managed — and could be better managed — it is important to understand the various sources, or origins, of these risks. The following sections describe the sources of both unavoidable and manageable risks, including the risks from medication errors, unintentional exposures, medication misuse, abuse, and self-harm.

Note: We use the term *risk* in this document to mean the probability (likelihood) of harm and the severity (consequences) of harm. This follows usage in the field of risk management. Box 1 presents a formal definition of *risk* and also contains consensus definitions of medical error, medication error, and other associated terms as defined by researchers in the field and by the IOM report *Preventing Medication Errors*.¹⁹ In this report, we use *adverse drug reaction*, *side effect*, and *drug-related harm/injury* interchangeably to describe injuries that result from the use of medications.

¹⁹ Institute of Medicine of the National Academies, *Preventing Medication Errors*, National Academies Press, 2007, p. 4.

Box 1: Key Terminology

Risk – The potential for an unwanted outcome resulting from an incident, event, or occurrence, as determined by its likelihood and the associated consequences.

Error* (or **Medical Error, QIC Task Force,** 2000**) – The failure of a planned action to be completed as intended (error of execution) or the use of a wrong plan to achieve an aim (error of planning). An error may be an act of commission or an act of omission. (IOM 2004)

Medication error

– Any error occurring in the medication use process (Bates et al., 1995¹⁴). Examples include wrong dosage prescribed, wrong dosage administered for a prescribed medication, or failure to give (by the provider) or take (by the patient) a medication.

– Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use. (National Coordinating Council for Medication Reporting and Prevention (NCCMERP))

Drug-related adverse event (ADE)* – Any injury due to medication (Bates et al. 1995). Examples include a wrong dosage leading to injury (e.g., rash, confusion, or loss of function) or an allergic reaction occurring in a patient not known to be allergic to a given medication.

Adverse reaction – Any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of safety reporting to FDA during the investigational stage, *reasonable possibility* means there is evidence to suggest a causal relationship between the drug and the adverse event.

Preventable Harm/injury – For purposes of this report, any injury or adverse drug event that occurs because of a medication error, drug quality problem, unintended exposure, intentional abuse or misuse, or attempts at self-harm.

* IOM, *Preventing Medication Errors* (2007)

** *Quality Interagency Coordination Task Force* (2000)

Unavoidable Risks

There are two key sources of unavoidable risk from using medications: gaps in current knowledge about a medication, and unpreventable known side effects (see Box 2).

Box 2: Key Sources of Unavoidable Risks from Medications

Gaps in current knowledge – Risks from taking a medication that are not known to the medical scientific community.

Unpreventable known side effects – Risks from taking a medication that cannot be avoided, even when all parts of the medication use process are executed optimally.

Risks associated with ***gaps in current knowledge*** are, by definition, unavoidable. As new products enter the market, for example, the potential for interactions with other drugs, biologics, medical devices, dietary supplements, and foods increases. *Off-label*²⁰ use may also lead to new risks that are not understood. Rare side effects may not be detected in clinical trials. And increases in the frequency of common events can be hard to detect: although nonsteroidal antiinflammatory drugs (NSAIDs) were first approved in the 1970s, it was not until 2000 that their risk of exacerbating ischemic heart disease was uncovered — and this risk is still not well understood. FDA operates programs intended to fill in these knowledge gaps (e.g., required postmarket trials and registries, adverse event surveillance programs, and pharmacoepidemiologic studies). However, it is likely that knowledge about any given drug will always be incomplete.

Unpreventable known side effects are a second, common source of unavoidable risks associated with taking medications. The probability of any given side effect occurring is evaluated during medical product development and described in the drug label, but often there is no way to predict who, of the many people taking a medication, will experience it. Known drug side effects can be mild and manageable (e.g., nausea, headache, mild dizziness) as well as serious and life-threatening (e.g., seizures, blood disorders, liver failure, heart problems). A known side effect that occurs even when all parts of the medication use process are executed optimally is considered *unavoidable*.

Some known side effects are avoidable, however. Many times a known side effect can be prevented by more judicious prescribing, more attention to the potential for

²⁰ *Off-label use* involves using a medication for a condition that was not evaluated during clinical trials and for which use information has not been provided in product labels.

drug–drug interactions, better communication with a patient, or optimal monitoring. In these cases, the side effect is considered *preventable and its occurrence is attributable to a medication error*.

Manageable Risks

. . . reducing the incidence of preventable injury . . . [from medication use] is the target of the Safe Use Initiative.

FDA believes that many drug-related risks can be managed, reducing the incidence of preventable injury. This type of harm is the target of the Safe Use Initiative.

The four broad sources of preventable injury are *medication errors (including informational errors and procedure and process errors)*; unintended exposures; *intentional drug misuse, abuse, and self harm*; and *drug quality defects* (see Box 3). Of these, medication errors and unintentional exposures result in the vast majority of preventable harm in the United States.

Box 3: Sources of Manageable Risks From Medicines

Medication Error – A mistake that occurs anywhere in the medication use process. Broad categories of medication errors include:

- **Informational errors in prescribing** – Introduction of risk by failing to incorporate current knowledge when prescribing a drug
- **Informational errors by patients and consumers** – Introduction of risk by failing to use currently available knowledge about how to use a medication safely
- **Procedure and process errors** – mistake or mix-up during processes associated with use

Unintended, or accidental, exposures – These occur when an individual, often a child, is exposed to a medication accidentally.

Intentional misuse, abuse, and self-harm – Using a medication in a non-medical context introduces a variety of potential risks and can result in significant harm.

Drug Quality Defect – Risks introduced by drug quality problems. These risks are very small.

Medication Errors

The Institute of Medicine (IOM) report, *Preventing Medication Errors*, uses²¹ the definition **medication error** as coined by Bates et al.: a mistake that occurs anywhere in the *medication use process*.²² *Complex medication use processes and*

²¹ Institute of Medicine of the National Academies, *Preventing Medication Errors*, National Academies Press, 2007, p 37.

²² Bates, DW, Boyle, DL, Vander Vliet, MB, et al., Relationship between medication errors and adverse drug events. *Journal of General Internal Medicine* 10(4):100-205, 1995. This is in contrast to errors such as “wrong-side surgery.”

procedures exist in the United States, having evolved, largely, as attempts to manage risks known at the time. For example, prescription drugs require the supervision of a healthcare professional; OTC drugs undergo extensive FDA evaluation to make sure they are suitable for consumer self-use. Figures 2-2, 2-3, and 2-4 in Attachment A illustrate the complexity of the medication use processes for inpatient and long-term care, care in the community (i.e., prescription), and self care (i.e., OTC or nonprescription) settings, respectively, as laid out by the IOM. Errors are frequently made at each step along the process and may be exacerbated or caught and corrected at later steps. Although many errors do not lead to harm, medication errors are frequent enough that substantial harm results each year.

Lack of access to, or understanding of, currently available information needed for safe use causes informational errors by healthcare practitioners, patients, and consumers.

Much of the public debate and discussion about medication errors has focused on procedural and process errors — that is, drug mix-ups, administration of wrong strengths, mistaken handwriting. This focus is understandable since these types of errors are comparatively easy to identify and understand. However, studies show that another type of medication error, sometimes referred to as an *informational error* can lead to significantly more harm.²³ Lack of access to, or understanding of, currently available information needed for safe use causes informational errors by healthcare practitioners, patients, and consumers. For the purposes of this document, we discuss *informational errors* separately from procedural or process errors because preventing informational errors will be a major focus of the Safe Use Initiative.

Informational Errors

Prescribers, patients, and consumers often inadvertently increase the risk of harm from medication use. Informational errors *in prescribing* happen when additional risk is introduced because a prescriber has incomplete access to or does not effectively use existing information about the drug, the patient, or the condition. Examples of informational errors in prescribing include:

- Prescribing a very high-potency opioid analgesic, indicated for use only in opioid-tolerant individuals, to a patient who is not opioid tolerant, possibly leading to respiratory depression or even death.
- Prescribing a drug known to cause birth defects to a woman of child-bearing age without doing a prior pregnancy test.
- Prescribing a drug that can cause dizziness to an elderly patient, who may be at high risk for falls, when an alternative medication would suffice. (A fall and resultant hip fracture can lead to complications, loss of independence, even death.)

²³ Woolf, SH, Kuzel, AJ, Doherty, SM, and Phillips, RL, A String of Mistakes: The Importance of Cascade Analysis in Describing, Counting, and Preventing Medical Errors, *Annals of Family Medicine*, Vol.2., No 4, July/August 2004. See also Larson, EB, Ne Comer, LN, Brennan, RA, Jencks, S, et al. *First Do No Harm — To Err Is Human*, American College of Physicians, American Society of Internal Medicine, 2000, pp. 294–304.

- Prescribing a drug that interacts significantly with a drug the patient is already taking, potentially leading to serious side effects.
- Failure to institute appropriate patient monitoring needed for the drug being prescribed.

... of 70% of tested patients with low literacy who could correctly state the instructions "take two tablets by mouth twice daily," only 34% could demonstrate the number to be taken daily.

Patients and consumers can also increase medication risks through informational errors. For example, an individual may increase the dose in an attempt to improve the beneficial effect of a medication, or may unknowingly take multiple versions of the same drug at the same time.²⁴ Each year, an estimated 5,000 emergency department visits are due to patients knowingly taking additional doses of acetaminophen in a misguided attempt to obtain additional symptom relief.²⁵ Similar to prescriber errors noted above, harm could be prevented if the end user had access to and fully understood up-to-date information about how to use the medication safely.

Drug labels and accompanying information can be confusing, contributing to informational errors. A recent FDA-commissioned evaluation found that only 75% of written consumer medication information provided to patients at the time a new prescription is filled meets minimal criteria for usefulness.²⁶ And certain patient groups may need additional informational support. One study found that of 70 percent of tested patients with low literacy who could correctly state the instructions "take two tablets by mouth twice daily," only 34 percent could demonstrate the number to be taken daily.²⁷

²⁴ A 2002 survey of Americans found that one-third of respondents took more than the recommended dose of an OTC product and 91% of these respondents did so because they thought it would improve the medication's efficacy. See Harris Interactive, Inc., *Attitudes and Beliefs About the Use of Over-the-Counter Medicines: A Dose of Reality, 2002*, p. 27: http://www.bemedwise.org/survey/final_survey.pdf.

²⁵ Budnitz D, at APAP Advisory Committee Meeting June 29, Guest Speakers, Slide #27. (<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm171562.htm>).

²⁶ Kimberlin, CL, Winterstein, AG, Expert and Consumer Evaluation of Consumer Medication Information – 2008, Final Report to the U.S. Department of Health and Human Services and the Food and Drug Administration, November 4, 2008. (<http://www.fda.gov/AboutFDA/CentersOffices/CDER/ReportsBudgets/ucm163777.htm>).

²⁷ Davis, TC, Wolf, MS, Bass, PF, et al. Literacy and Misunderstanding Prescription Drug Labels, *Annals of Internal Medicine*, December 19, 2006; 145(12): p. 887. Epub 2006 Nov. 29. (http://www.ncbi.nlm.nih.gov/pubmed/17135578?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DiscoveryPanel.Pubmed_RVAbstractPlus).

Procedural or Process Errors

A multitude of procedural or process errors increase risks from medication use. For example, if a prescriber's handwriting is hard to read or if information is omitted from the prescription (e.g., drug name suffix), a pharmacist may dispense the wrong drug. Specific patient monitoring may be ordered by a prescriber, but not occur. A healthcare worker may administer the wrong drug or dose for a number of reasons, including:

- Mistakes in transcription
- Misinterpreting the instructions for use
- Confusing two products that have similar names
- Selecting the wrong product because of similar appearance (either of two different strengths of the same drug or between different drugs)

Although these errors have been discussed extensively elsewhere,²⁸ numerous opportunities remain for additional FDA collaboration with external organizations to improve risk management for specific process-related problems.

Unintentional exposures most commonly result from failure to keep medications out of the reach of children.

Of note: Failure to prescribe or take an indicated medication (error of omission) can also place patients at risk; this situation is included in the definition of *medication error*. However, since omission of therapy does not constitute harm from medication use, it is not discussed in this document.

Unintended Exposure

Harm from unintentional exposure to medications is not a rare problem. In 2007, 23,783 cases of accidental exposure to another person's medication were reported to Poison Control Centers (the percentage that caused harm is unknown).²⁹ In principle, harm from accidental exposure is entirely preventable. Unintentional exposures most commonly result from failure to keep medications out of the reach of children. Each year, many thousands of children are accidentally exposed to prescription or OTC drugs, and some die as a result.³⁰ Toddler-age children are often able to open and drink liquid medications. Approximately 4,600 emergency department visits yearly result from unsupervised pediatric ingestion of OTC cough and cold remedies (other risks involve mix-ups among various medications used by

²⁸ Institute of Medicine of the National Academies, *Preventing Medication Errors*, National Academies Press, 2007, see especially pp. 74 – 88 .

²⁹ Bronstein, AC et al. *2007 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 25th Annual Report*, Alexandria, VA., p.938.

³⁰ Schillie, SF, Shehab, N, Thomas, KE, and Budnitz, DS, Medication Overdoses Leading to Emergency Department Visits Among Children, *American Journal of Preventive Medicine*, 2009;37(3), Elsevier Inc., p. 181.

Intentional misuse and abuse of medications, as well as attempts at self-harm, are significant sources of drug-related risks in the United States.

family members).³¹ Based on related studies, an estimated 71,224 emergency department visits for medication overdoses are made annually by children aged 18 and under (approximately 68 percent of overall emergency department visits are for unintentional pediatric poisonings).³²

Intentional Misuse, Abuse, and Self Harm

Intentional misuse and abuse of medications, as well as attempts at self-harm, are significant sources of drug-related risks in the United States.³³ Although such acts are not 100 percent preventable, concerted risk management efforts across stakeholder communities could help reduce these risks. Traditionally, these sources of drug-related risks have not been a primary focus of FDA regulation. With the passage of the Food and Drug Administration Amendments Act of 2007 (FDAAA), FDA is now better able to address this problem.³⁴ Collaborations among Federal agencies and the broad healthcare community can improve risk management approaches for this major and growing problem.

Risk of Drug Quality Defects

The risk of injury from drug quality defects is very small in the United States, where great attention is paid to product quality during manufacturing and distribution. Managing risks from drug quality is the responsibility of drug manufacturers and the drug distribution chain, as overseen by FDA, and is not discussed further in this report.

³¹ Schaefer, MK, Shehab, N, Cohen, AL, and Budnitz, DS, Adverse Events From Cough and Cold Medications in Children, *Pediatrics*, Official Journal of the American Academy of Pediatrics, April 2008, p. 785.

³² Schillie, SF, Shehab, N, Thomas, KE, and Budnitz, DS, Medication Overdoses Leading to Emergency Department Visits Among Children, *American Journal of Preventive Medicine*, 2009;37(3), Elsevier Inc., p. 181.

³³ *National Hospital Ambulatory Medical Care Survey 2000-2006* (http://www.cdc.gov/nchs/ahcd/ahcd_questionnaires.htm).

³⁴ See, for example, discussion of Risk Evaluation and Mitigation Strategies (REMS) in the section on FDA efforts to manage risk.

HOW ARE MEDICATION RISKS MANAGED?

... processes for managing medication risks have been put into place ... often in a piecemeal fashion and usually in response to various crises ...

Numerous processes for managing medication risks have been put into place over the last century, often in a piecemeal fashion and usually in response to various crises and specific needs of the time. It is widely recognized that additional steps need to be taken, in a more coordinated, systematic fashion, to protect the public from preventable harm from medication use.

Fig. 2-1 (see Attachment A) from the IOM publication *Preventing Medication Errors* diagrams the overall drug development and use process. The first three phases of this elaborate process — drug research and development, regulatory review, and manufacturing, distribution and marketing — are primarily the responsibility of FDA and regulated industry, although the National Institutes of Health (NIH) and academic groups also engage in drug research. The drug research and development phase has many steps — including animal and human safety testing — intended to identify risks associated with the medications. A large proportion of drugs are eliminated during the development phase because of safety problems. During the regulatory review phase, FDA evaluates applications to ensure that the benefits from a drug outweigh the risks in the intended population. Distribution and marketing of approved drugs are also overseen by FDA to maintain the quality of drugs as they move along the drug supply chain and to ensure that related information about them remains accurate. The fourth phase of the drug development and use process — medication use — occurs within the healthcare system or in the community. Within this last phase, three key medication use processes are described (see Figs 2-2, 2-3, and 2-4, in Attachment A). These medication use processes are in large part intended to ensure safe use. FDA standards and requirements for the first three phases of the risk management system (research through marketing) have significant impact on the medication use phase, and information from the medication use phase may be used to modify FDA's approach to the first three phases.

Although detailed descriptions of FDA's risk management activities can be found both in the FDA publication *Managing the Risk of Medical Product Use*³⁵ and in the IOM's *Preventing Medication Errors*, they are described very briefly here, with a focus on how risk management activities have evolved, primarily, during the past decade.

FDA's Drug Risk Management Activities

Historically, FDA regulation has focused on maintaining drug quality; premarket evaluation of drug safety and effectiveness; appropriate drug labeling; drug

³⁵ FDA, *Managing the Risks from Medical Product Use, Report to the FDA Commissioner from the Task Force on Risk Management*, 1999, (<http://www.fda.gov/Safety/SafetyofSpecificProducts/ucm180325.htm>).

advertising and promotion; and postmarket surveillance for unexpected side effects. In addition, FDA, along with NIH, has helped manage the risks related to controlled substances (e.g., opioids, barbituates) by providing scientific recommendations to the Drug Enforcement Administration on scheduling a new drug under the Controlled Substance Act. All of these activities are part of FDA's broad medication risk management effort.

Beginning in the early 1990s, however, FDA determined that these regulatory programs were not sufficient to manage all the risks associated with using medications. To address other types of errors, such as the informational errors described in the previous sections of this report, FDA took on additional activities to further reduce preventable harm during the medication use phases.

Because informational errors by prescribers and medication users cause a large share of preventable harm, FDA began to standardize medication labels and target communication of key information on medication use to consumers, patients, and the healthcare community. In addition, steps were taken to improve the management of specific medical product safety risks. Important efforts of the last several decades are highlighted here.³⁶

Efforts to Improve Communication

In 1999, FDA published regulations for a new standardized format for OTC drug labels, intended to relay the most important use information in an organized fashion. Almost all OTC drugs are now required to follow these regulations. Important information for safe and effective use is identified in the Drug Facts box on the package or container. Information is presented in an organized fashion, using easy-to-read standardized headings that enable users to locate the active ingredients, uses, warnings, directions for use, inactive ingredients, and other information. Important safety warnings are given prominence. The information is presented in a bulleted format for easier reading. There are minimum standards for type size, font, contrast, bullets, alignment, and punctuation, all of which make the label easier to read. All OTC drug products have similar formats so consumers can find information more easily. These changes were intended to improve consumers' ability to use OTC medications safely and effectively.

In 2006, FDA issued a regulation that revised the content and format of prescription drug package inserts. The goal was to better manage the risks of medication use, reduce errors, and prevent side effects. The final rule required that new and recently approved products include (1) highlights of the prescribing information (*Highlights*) and (2) a table of contents (*Contents*). The rule also

³⁶ FDA had long considered the drug label to be its primary means to communicate with health practitioners, but the Internet has enabled FDA to provide safety communications that target all audiences. FDA posts a variety of safety information on its Web site, including Public Health Advisories, Early Communications about ongoing safety reviews, Information for Healthcare Professionals (HCP), press releases, and media briefing, among others.

provides for a reordering of content and minor content changes and minimum graphical requirements. The revisions make it easier for healthcare professionals to access and use the information. Drug labels in the new format are now available online through DailyMed, a health information clearinghouse created by FDA and the National Library of Medicine. Drug labels accessed through DailyMed are up-to-date, without the time lag associated with paper-based information. DailyMed makes current information about FDA-regulated products readily available, free of charge, to physicians, other healthcare professionals, and patients.

On December 16, 2008, FDA released the results of a study that found that printed consumer medication information (CMI) voluntarily provided with new prescriptions by retail pharmacies does not consistently offer easy-to-read, understandable information about the use and risks of medications. CMI is information developed by the private sector intended for distribution with every prescription dispensed at a pharmacy. Public Law 104-180, enacted in 1996, established CMI as a private sector process. This law required that, by the year 2000, 75 percent, and by the year 2006, 95 percent of people receiving new prescriptions would receive useful written patient information with their prescriptions. Following enactment of PL 104-180, a steering committee of stakeholders delineated criteria for evaluating whether written medication information was useful and developed a long-range comprehensive action plan to achieve the goals specified in the statute. FDA was charged with evaluating the private sector's progress in meeting the goals. PL 104-180 prohibited FDA from taking regulatory action if the goals were met, but instructed the Agency to seek public comment on next steps if the goals were missed.

Two separate studies conducted in 2001 and in 2008 found that much of the written patient information provided at U.S. pharmacies failed to provide consistently easy-to-read and understandable information about the use and risks of medications. The 2008 study showed that although 94 percent of consumers received CMI with new prescriptions, only 75 percent of this information met minimum criteria for usefulness.

FDA's Risk Communication Advisory Committee met in February 2009 to share research and explore approaches to improving the communication of prescription drug information to patients, specifically with regard to CMI, Medication Guides (MedGuides), and patient package inserts (PPIs). One key recommendation was that FDA should adopt a *single standard document* for communicating essential information about prescription drugs, which would replace PPIs, CMI, and MedGuides. The Committee also recommended that this document be FDA approved and be subject to rigorous empirical evaluation of its effectiveness.

FDA held a public workshop in September 2009 including multiple stakeholders to discuss the challenge of developing a one-document solution to consumer medication information.

Efforts to Mitigate Process Errors

Beginning in the 1990s, FDA intensified efforts to prevent process errors, such as confusing one drug for another because of similar drug names, use of the wrong strength or dosage form because of similarities in appearance of container labels and carton labeling, and errors relating to the overall product design. The Agency has continued to strengthen its programs in this area and now has a specific division devoted to evaluation and prevention of these sorts of medication errors — for example, by decreasing confusion caused by similar trade names or packaging.

Efforts to Mitigate the Risks of Unintended Exposure

Recently, FDA announced a new effort, Disposal by Flushing of Certain Unused Medicines: What You Should Know,³⁷ directed at preventing serious harm and death caused by exposure of children to certain drugs, including opioid drugs, used in the home. Unused portions of these medications must be disposed of properly to avoid harm.

Efforts to Mitigate Drug-Specific Safety Risks

In 1992, FDA published a regulation that formalized FDA's ability to approve a drug for a serious or life-threatening disease or condition with a restricted distribution program to better manage a particular safety risk. The Agency has required various restrictions for particular drugs, depending on the safety issue being managed. Although restricted distribution systems have a direct effect on the medication use process within the healthcare system and must be implemented by healthcare practitioners and patients, the programs are established by drug manufacturers.³⁸

Additional FDA-Related Risk Management Efforts

In September 2006, the IOM issued a report titled *The Future of Drug Safety—Promoting and Protecting the Health of the Public*.³⁹ The report, a product of a drug safety study requested by FDA, made 25 recommendations about how FDA could improve its drug safety program and what actions other parts of government should take to create a robust and comprehensive system for ensuring the safe use of medical products. Since the report's publication, FDA has significantly strengthened its internal drug safety infrastructure by establishing the Drug Safety Board, improving communication to consumers, and launching the Risk Communication Advisory Committee, among other efforts. Details are provided in

³⁷ See FDA's Web page at <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm>.

³⁸ See discussion of the Food and Drug Administration Amendments (FDAAA) Act of 2007, below.

³⁹ Institute of Medicine of the National Academies, *The Future of Drug Safety, Promoting and Protecting the Health of the Public*, National Academy of Sciences, 2007.

FDA's January 2007, response to the IOM recommendations. A second FDA response, issued in July 2009, updated Congress on FDA's drug safety efforts and the status of FDA activities related to implementing the IOM recommendations.⁴⁰

In 2007, FDA created the Risk Communication Advisory Committee, which advises the Commissioner on strategies and programs designed to communicate with the public about the risks and benefits of FDA-regulated products so as to facilitate optimal use of these products.

In 2007, FDAAA⁴¹ gave FDA new drug safety authorities, including the ability to require safety labeling changes, postmarket studies,⁴² and Risk Evaluation and Mitigation Strategies (REMS) The Agency can require a REMS for drugs with particular safety issues before approving a product if FDA determines that a REMS is necessary to ensure the benefits of a medication outweigh the risks — a REMS may be required after marketing approval if FDA becomes aware of new safety information and determines that a REMS is necessary to ensure the benefits of the medication outweigh the risks.

A REMS may be required . . . to ensure that the benefits of a medication outweigh the risks of the medication.

A REMS can include a MedGuide or patient package insert, a communication plan to healthcare practitioners, and “elements to assure safe use,” such as requirements for education or experience for those who prescribe or dispense the drug. These elements incorporate many of the restricted distribution provisions of FDA's 1992 regulation. In addition, in conjunction with FDAAA, Congress appropriated additional resources for FDA's drug safety programs.

The steps just outlined have created a stronger risk management program for medications. But it is clear that to have maximum effect on reducing preventable harm, FDA must work in a more formalized manner with the many stakeholders in the broad healthcare community. Many of these organizations have extensive experience, resulting from the large number of initiatives they have started in the last decade. Some initiatives are highlighted in the following section.

Risk Management in the Broad Healthcare Community

Current medication use processes (see Figures 2-2, 2-3, and 2-4, Attachment A) were instituted in large part to help better manage medication risks. For example, in the out-patient setting, pharmacies regulated by state boards dispense drugs to patients in response to prescriptions written by a health professionals. This process — in which access to prescription drugs is controlled by highly trained professionals — is intended to ensure that patients receive a medical evaluation prior to treatment, that a health professional is involved in the choice of therapy, and that drugs are properly dispensed to a patient with directions for use and availability of

⁴⁰ See FDA's safety-related reports on the FDA Web page at <http://www.fda.gov/Safety/>.

⁴¹ Pub. Law 110-85, September 27, 2007 (<http://prsinfo.clinicaltrials.gov/fdaaa.html>).

⁴² FDA launched the Sentinel Initiative in 2008, in part, to address the requirements of Section 905 of FDAAA (<http://www.fda.gov/Safety/FDAsSentinelInitiative/default.htm>).

pharmacist advice. Within healthcare settings — hospitals, out-patient surgery centers, long-term care facilities, dialysis centers — drugs are managed by healthcare practitioners during the entire use process and administered to the patient by a healthcare practitioner. In contrast, an OTC drug is available from a pharmacy or drug store at the complete discretion of an individual. OTC status is permitted in situations when self-diagnosis of a condition is possible (e.g., headache, sunburn), self-selection of treatment is possible, the directions for use can be made understandable to consumers, and the drug is very safe under ordinary use conditions.

. . . numerous groups within and outside the healthcare community have been spearheading healthcare quality and patient safety initiatives.

During the 1990s, it became clear that these long-established medication use processes were not doing the intended job of keeping patients and consumers safe. In its publication *To Err is Human*, the IOM cited a 10-year study that estimated that approximately 7,000 deaths occur annually as a result of medication errors.⁴³ Errors in the medication use process were seen as part of a larger patient safety problem in healthcare. It was estimated that more than 100,000 deaths per year result from various types of medical errors. The IOM called for a healthcare system that is transparent and patient-centered, and that uses the principles of quality and risk management to maximize safety.⁴⁴

Engineering controls, warnings, administrative controls, and behavioral controls. . . promote safe use and reduce preventable harm.

Catalyzed by IOM's call to action, numerous groups within and outside the healthcare community have been spearheading healthcare quality and patient safety initiatives. A number of organizations have begun to seek and evaluate interventions intended to reduce the incidence of specific errors. These organizations are working on many fronts. Among their efforts are educational campaigns, data-gathering, research, the setting of safety standards, and political advocacy. Steps such as creation and use of a surgical checklist⁴⁵ and use of information technologies,⁴⁶ are having an impact on patient safety, especially in hospitals. Additional efforts are under way to design interventions, including engineering controls, administrative controls, and behavioral controls and warnings. Although patient safety and healthcare quality initiatives seek to improve all aspects of healthcare, some of their activities are directed specifically at medication errors. See Attachment B for an overview of some of the organizations working in this area.

In addition to these efforts, a number of organizations concentrate *exclusively* on medication safety. The ***Institute for Safe Medication Practices (ISMP)***, a 30-year-old nonprofit organization, is dedicated to medication error prevention and safe

⁴³ See Phillips, DP, Christenfeld, H, and Glynn, LM, Increase in US medication-error deaths between 1983 and 1993, *The Lancet*, 351:643-644, February 28, 1998.

⁴⁴ Institute of Medicine, *Crossing the Quality Chasm, A New Health System for the 21st Century*, 2001 pp 48-51.

⁴⁵ See Haynes, A.B, T.G. Weiser, W.R. Berry, et al. A Surgical Safety Checklist to Reduce Morbidity and Mortality in a Global Population, *The New England Journal of Medicine*, 360;5, January 29, 2009, p. 493.

⁴⁶ Bates, D.W, and A.A. Gawande, Improving Safety with Information Technology, *The New England Journal of Medicine*, 348;25, June 19, 2003, p. 2526.

FDA believes that through a coordinated effort involving . . . other[s]. . . even more can be achieved.

medication use. ISMP operates a medication error reporting system focused on process errors. The **National Council on Patient Information and Education (NCPPIE)** seeks to advance the safe, appropriate use of medications through enhanced communications. The Council is an umbrella coalition comprising a large number of health-related organizations. The **National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP)**, which is made up of healthcare professional groups, develops recommendations to prevent medication errors.

All of these important efforts have helped to improve medication use and reduce preventable harm. FDA believes that through a coordinated effort involving these groups and others, as part of the Safe Use Initiative, even more can be achieved.

The Safe Use Initiative Proposal

FDA proposes to identify, using a transparent and collaborative process, specific candidate cases — drugs, drug classes, and/or therapeutic situations — that are associated with significant and measurable amounts of preventable harm. Cases will be carefully 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 intervention, FDA and interested partners will develop appropriate activities and evaluation metrics to measure an intervention’s success.

FDA believes that in many cases, interventions to prevent harm may consist of a regulatory component and non-regulatory components, highlighting the need for collaborative action. For example, FDA may require that manufacturers of a specific drug class implement a REMS while FDA works closely with relevant stakeholders to develop complementary, voluntary, collaborative actions that will improve the medication use process for these medications. Or FDA may participate in the design and implementation of a broad public education effort. FDA also believes that those affected by any intervention must be able to contribute to the design of interventions and development of evaluation metrics, including determining how relevant information will be collected.

FDA’s **Safe Use Initiative** will be the sum of these efforts, working toward the overall goal of improving patient health by ensuring that medications are used as safely as possible.

Opportunities for Collaboration

FDA has already launched (or is planning) several medication risk reduction projects that could benefit from collaboration with relevant stakeholders. The following efforts are only a small sampling of the types of problems that could benefit from Safe Use Initiative support. In some cases, collaborative activities already are being considered.

Consumer medication information (CMI). Many stakeholders have asked FDA to modify the current system for CMI to ensure that all patients receive a single, brief, standardized leaflet about their medications, as is the practice in many other countries.⁴⁷ However, this step would significantly affect established medication use processes in the out-patient setting. It is clear that any new approach to CMI will require a collaborative effort across most of the stakeholders in the ambulatory medication use process.

Medication dosing devices. There have been numerous reports of accidental overdoses attributed to the measuring devices that are provided with OTC liquid drug products. These reports are of special concern because OTC liquid drug products are frequently intended to be used in young children, where dosing errors can be more serious. FDA is developing guidance for industry with the goal of making these measuring devices easier to use. We believe a broad collaborative effort to make the public aware of the importance of correct dosing for OTC products would complement FDA's efforts and reduce the risk of accidental overdosing. In addition, FDA should engage with the Consumer Product Safety Commission, the CDC, industry, and others to discuss changes to the packages of OTC liquid drug products to reduce the risk of accidental ingestion.

Acetaminophen toxicity. FDA recently held an Advisory Committee meeting on mitigating the risks of acetaminophen liver toxicity. Although it may rarely occur with appropriate use, most toxicity is linked to either unintended or deliberate overdose. FDA is considering a variety of steps from a regulatory perspective. To complement the agency's actions, much will need to be done, in collaboration with various healthcare stakeholders, to improve communication about inadvertent overexposure and discourage intentional overdose.

Alcohol-based surgical preps. Topical surgical skin preparations are essential during in-patient and out-patient surgeries to reduce microbial skin contamination, thereby reducing the risk of surgical site infections, but the alcohol-based preps have been associated with surgical room fires. These fires would be entirely preventable if procedures were in place and followed, yet an estimated 100 to 600 fires occur per year in surgical settings.⁴⁸ Although the number is small, the risk to the patient — of serious burns and even death, can be great. It is possible that FDA can collaborate with relevant stakeholders — from oversight groups to direct patient care staff — to identify and implement activities to further reduce surgical fires.

⁴⁷ Among many presenters, Dr. Theo Raynor, PhD, MRPharmS, University of Leeds, UK, described European practices regarding consumer medication information. Standardized patient leaflets that are user-tested are provided with all medications (<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/RiskCommunicationAdvisoryCommittee/ucm150189.htm>,

⁴⁸ See International Academy of Cosmetic Dermatology, *Fire in the Operating Room* (<http://www.iacdworld.org/legal/fire.htm>; and ECRI Institute, (http://www.ecri.org/Products/Pages/Surgical_Fires.aspx.

Medications in vials. Many injectable medications come packaged in vials of various sizes and strengths. Anyone drawing up and administering these medications must follow appropriate injection practices to minimize preventable harm, such as infectious outbreaks associated with vial contamination. Partnerships, such as with the professionals who use the products, infection control personnel, and standard setting organizations can identify the problems leading to unsafe use of these medications, and devise strategies to reduce risks.

Next Steps

In the months ahead, FDA intends to:

- Develop a general list of candidate cases for collaborative analysis and intervention. The list will be developed through extensive consultation with all interested public and private stakeholders and may include one or more of the existing opportunities listed in the previous section.
- Collaborate with Federal partners to develop population-based national estimates of preventable harm from medications, categorized by drug, drug classes, and therapeutic situations.
- Open a public docket to receive suggestions and comments related to this report, risk management issues, and proposed candidate cases.
- Hold a series of meetings to gather broad public feedback as the candidate list is being developed.
- Based on the public contribution just outlined and the best available population-based data, work with interested partners to select specific candidate cases for analysis, intervention proposals, and evaluation metrics.
- During the Initiative's first 12 months, implement a small number of interventions. Each intervention will have an explicit plan for measuring impact. Interventions may involve FDA regulatory actions in concert with actions by other stakeholders.

Conclusion

Today, tens of millions of people in the United States depend on prescription and OTC medications to sustain their health — as many as 3 billion prescriptions are written annually. But too many people suffer unnecessary injuries and some die as a result of errors or misuse that could have been prevented. FDA and many other stakeholders have been working to improve how the healthcare system manages medication risks in the United States. However, much preventable harm results

from problems that can be addressed only through coordinated interventions across all sectors of the system. All participants in the broad healthcare community — patients, consumers, caretakers, healthcare practitioners, pharmacists, healthcare systems, health insurers, drug manufacturers, FDA, and other Federal agencies — have a role to play in managing medication risks and reducing preventable harm from medication use. As part of its role, FDA is launching the ***Safe Use Initiative***, through which FDA seeks to join in partnership and collaboration with relevant stakeholders to measurably reduce preventable harm from medications and improve patient health.

Attachment A: The Medication Use Processes for Hospital and Long-Term Care; in Community Care; and for OTC Use; The Four Stages of the Drug System

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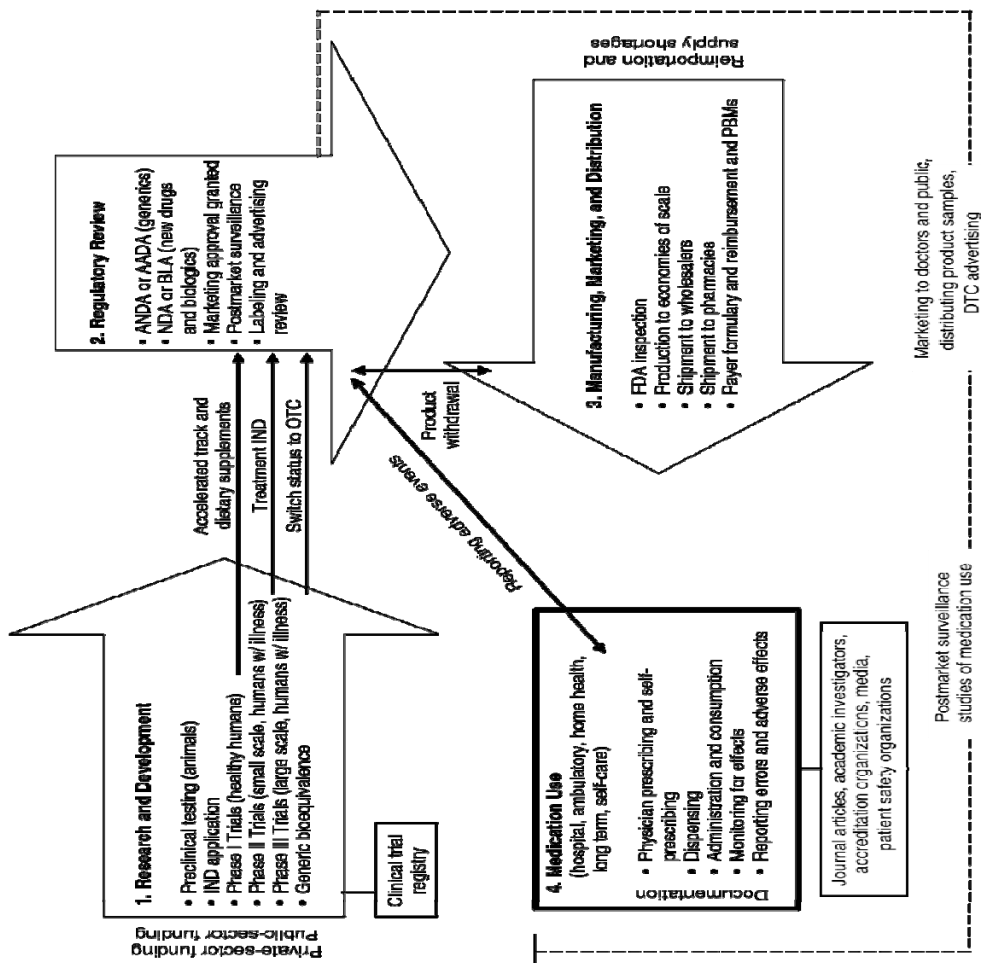


FIGURE 2-1 Four stages of the drug system.
 NOTE: AADA = Abbreviated Antibiotic Drug Application; ANDA = Abbreviated New Drug Application; BLA = Biologic Licensing Application; DTC = direct to consumer; FDA = U.S. Food and Drug Administration; IND = Investigational New Drug Application; NDA = New Drug Application; OTC = over-the-counter; PBM = Pharmacy Benefits Manager.

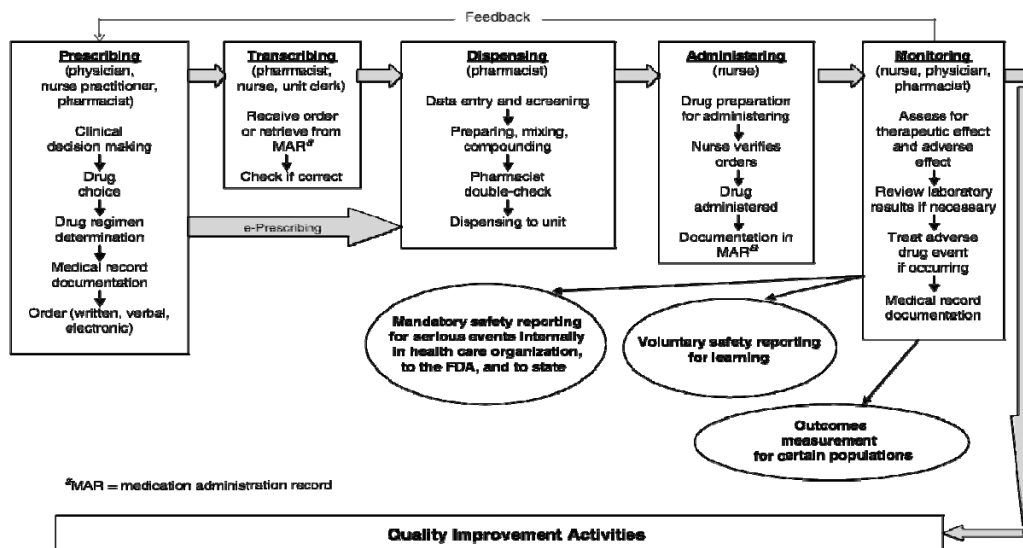


FIGURE 2-2 Medication-use process for hospital and long-term care.

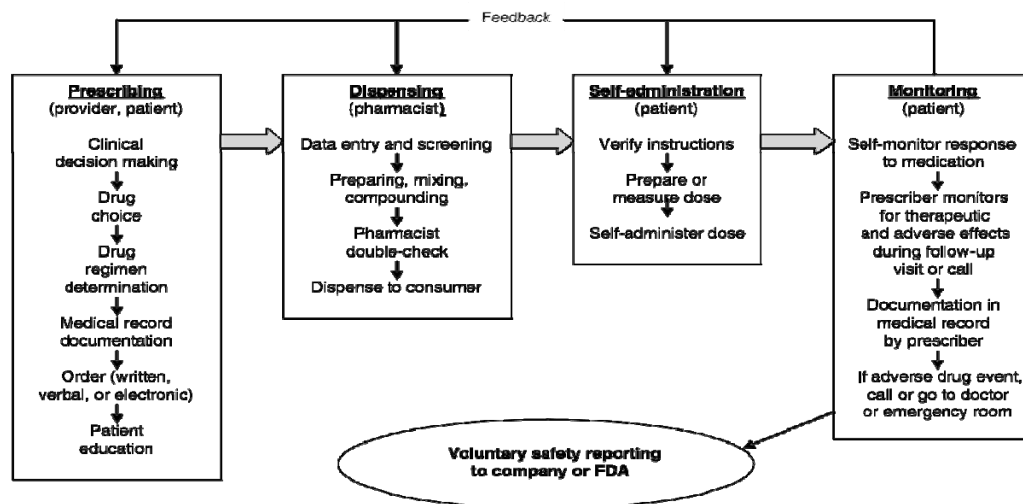


FIGURE 2-3 Medication-use process in community care.

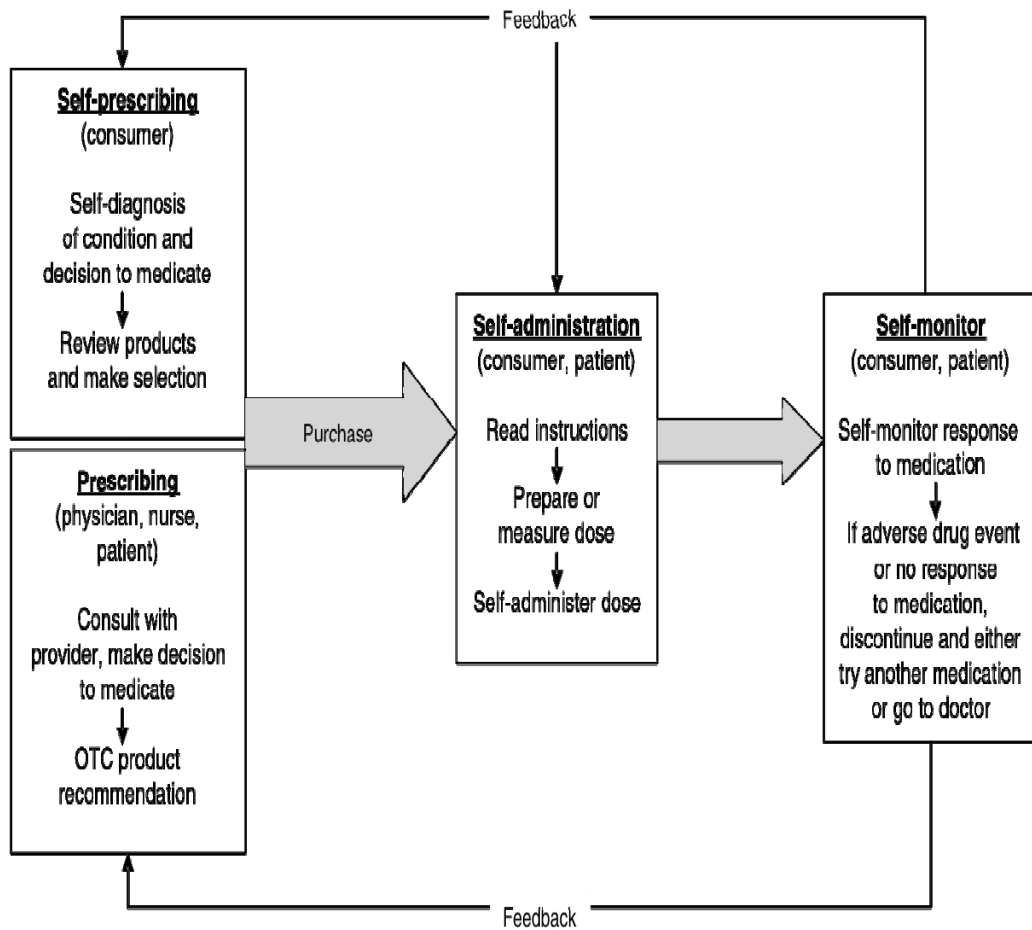


FIGURE 2-4 Medication-use process for over-the-counter drugs.

Attachment B: Key Agencies Involved in Healthcare Quality and Patient Safety Efforts

A number of Federal agencies are involved in efforts to improve patient safety and ensure the quality of healthcare. The following list highlights key efforts and some of the agencies that are involved.

The **Agency for Healthcare Research and Quality (AHRQ)** is the lead Federal agency for research on healthcare quality, costs, outcomes, and patient safety. AHRQ has designated Patient Safety Organizations to which participants in the healthcare system can confidentially submit medical error data in a standardized format that is easily shared. These data are aggregated and analyzed. As a result, over time, the healthcare community is gaining a better understanding of issues related to medical errors and their prevention.

Other Federal agencies (e.g., the **Center for Medicare & Medicaid Services, the Centers for Disease Control and Prevention, the Substance Abuse and Mental Health Services Administration**) are involved in researching and regulating healthcare and have made headway in developing national research efforts to examine issues of quality and patient safety.

The **Veteran's Health Administration (VHA)** has been a pioneer in patient safety programs. VHA's National Center for Patient Safety, launched in 1998, operates internal and external safety reporting systems, performs computer-aided root cause analysis, and uses systems engineering tools to identify critical system vulnerabilities and assess the effectiveness of system improvements.

A number of nonprofit organizations are dedicated to improving healthcare quality and patient safety.

The mission of the **National Quality Forum (NQF)** includes setting national priorities and goals for performance improvements; endorsing national consensus standards for measuring and publicly reporting on performance; and promoting attainment of goals through education and outreach programs.

The **National Patient Safety Foundation (NPSF)** is working to improve patient safety in all settings. NPSF supports the development of scientific data on safety and holds conferences to disseminate key safety findings, including medication safety findings.

Healthcare and health-related professional organizations such as the **American Medical Association (AMA), the Association Society of Health-System Pharmacists (ASHP), and the American Nurses Association** are developing and implementing programs to keep their members informed on safety-related issues.

America's Health Insurance Plans (AHIP), an association of health insurance providers, has set a goal of reducing healthcare costs while improving quality.

The Leapfrog Group, comprising corporations and public agencies that buy health benefits on behalf of their enrollees, is working to initiate breakthrough improvements in the safety, quality, and affordability of healthcare for Americans. Leapfrog's Hospital Quality and Safety Survey provides information on healthcare quality to enable consumers to compare hospitals. Leapfrog recognizes and rewards hospitals that achieve set safety goals.