

March 2009

**METHADONE-
ASSOCIATED
OVERDOSE DEATHS**

**Factors Contributing
to Increased Deaths
and Efforts to Prevent
Them**



GAO

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Highlights of [GAO-09-341](#), a report to congressional requesters

Why GAO Did This Study

Prescription drug abuse is a growing public health problem. In particular, methadone-associated overdose deaths—those in which methadone may have caused or contributed to the death—have risen sharply. Before the late 1990s, methadone was used mainly to treat opioid addiction but has since been increasingly prescribed to manage pain. Taken too often, in too high a dose, or with other drugs or alcohol, methadone can cause serious side effects and death. Methadone-associated overdose deaths can occur under several different scenarios, including improper dosing levels by practitioners, misuse by patients who may combine methadone with other drugs, or abuse—using the drug for nontherapeutic purposes.

This report examines the regulation of methadone, factors that have contributed to the increase in methadone-associated overdose deaths, and steps taken to prevent methadone-associated overdose deaths.

GAO reviewed documents, laws and regulations, data, and research from relevant state and federal agencies, including the Drug Enforcement Administration (DEA) and the Substance Abuse and Mental Health Services Administration (SAMHSA). GAO also interviewed federal officials, officials in five selected states, officials from professional associations and advocacy groups, and experts in pain management, addiction treatment, and forensic sciences.

[View GAO-09-341](#) or [key components](#). For more information, contact Kathleen King at (202) 512-7114 or kingk@gao.gov.

METHADONE-ASSOCIATED OVERDOSE DEATHS

Factors Contributing to Increased Deaths and Efforts to Prevent Them

What GAO Found

Methadone is regulated as a controlled substance, under federal and state laws and regulations, when used for pain management and addiction treatment. When methadone is used for pain management, it is regulated under federal and state laws and regulations that apply to controlled substances generally and that do not impose requirements unique to methadone. For addiction treatment, however, federal and state laws and regulations impose additional requirements that are specific to the use of methadone in opioid treatment programs (OTP), which treat and rehabilitate people addicted to heroin or other opioids. GAO, however, only reviewed relevant state laws and regulations for five selected states.

Although information on methadone-associated overdose deaths is limited, available data suggest that methadone's growing use for pain management has made more of the drug available, thus contributing to the rise in methadone-associated overdose deaths. Methadone prescriptions for pain management grew from about 531,000 in 1998 to about 4.1 million in 2006—nearly eightfold. Methadone has unique pharmacological properties that make it different from other opioids, and as a result, a lack of knowledge about methadone among practitioners and patients has been identified as a factor contributing to these deaths. DEA data suggest that abuse of methadone diverted from its intended purpose has also contributed to the rise in overdose deaths as the number of methadone drug items seized by law enforcement and analyzed in forensic laboratories increased 262 percent, from 2,865 in 2001 to 10,361 in 2007. Nonetheless, data and research from five states GAO reviewed suggest that the specific circumstances of these deaths are variable because of drug combinations and unknown sources of methadone.

GAO identified selected efforts to prevent methadone abuse and overdose deaths that focused on education, safety, and monitoring. For example, to educate practitioners about using methadone for pain management and addiction treatment, SAMHSA is establishing a physician clinical support system for methadone. To improve safety, in 2006, the Food and Drug Administration (FDA) approved a revised label for methadone tablets that included new safety information regarding the use of methadone for pain and modified dosage instructions for those beginning pain management treatment with methadone. Additionally, to prevent diversion and abuse of controlled substances such as methadone, DEA reports that as of February 2009, 31 states have established prescription monitoring programs. Some officials and experts cautioned that any prevention efforts focused on methadone alone might unintentionally shift similar problems to a different drug.

GAO received comments from the Department of Health and Human Services stating that FDA recently notified manufacturers of certain opioid drug products, such as methadone, that they must take certain steps to ensure that the benefits of these drugs continue to outweigh the risks. The Department of Justice provided GAO with technical comments.

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Abbreviations

AMA	American Medical Association
ARCOS	Automation of Reports and Consolidated Orders System
CDC	Centers for Disease Control and Prevention
CSAT	Center for Substance Abuse Treatment
DEA	Drug Enforcement Administration
FDA	Food and Drug Administration
HARMD	Helping America Reduce Methadone Deaths
HHS	Department of Health and Human Services
KASPER	Kentucky All-Schedule Prescription Electronic Reporting System
LAAM	levomethadyl acetate
NDIC	National Drug Intelligence Center
NFLIS	National Forensic Laboratory Information System
ONDCP	Office of National Drug Control Policy
OTP	opioid treatment program
SAMHSA	Substance Abuse and Mental Health Services Administration

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United States Government Accountability Office
Washington, DC 20548

March 26, 2009

The Honorable Edward M. Kennedy
Chairman
Committee on Health, Education, Labor, and Pensions
United States Senate

The Honorable John D. Rockefeller, IV
Chairman
Subcommittee on Health Care
Committee on Finance
United States Senate

Prescription drug abuse is a serious and growing public health problem. Drug overdoses, including those from prescription drugs, are the second leading cause of unintentional injury deaths in the United States, exceeded only by motor vehicle fatalities, according to the Centers for Disease Control and Prevention (CDC).¹ Of particular concern is the sharp rise in methadone-associated overdose deaths—in which methadone may have caused or contributed to the death.² CDC data show that from 1999 to 2005, the number of these deaths increased more than fivefold, from 786 to 4,462, a rate higher than overdose deaths associated with other prescription narcotics, such as oxycodone, hydrocodone, and fentanyl.³

Methadone has been approved by the Food and Drug Administration (FDA) for the treatment of opioid addiction and pain, and it is relatively inexpensive compared to other opioids.⁴ Methadone's unique

¹CDC data regarding overdose deaths include those resulting from accidental or intentional overdoses of a drug, being given the wrong drug, taking the wrong drug in error, or taking a drug inadvertently. The majority of overdose deaths are unintentional, according to CDC. CDC's data on overdose deaths do not include deaths in which drugs are present but the cause of death was determined to be something other than a drug overdose, such as cancer or motor vehicle traffic crashes.

²In this report we are using "methadone-associated overdose deaths" to refer to overdose deaths in which methadone was listed on a state death certificate as contributing to the death.

³Narcotics are drugs derived from opium or opium-like compounds, with potent pain relief effects and with the potential for dependence and tolerance following repeated administration.

⁴Opioids are synthetic drugs, such as methadone, possessing narcotic properties similar to opiates but not derived from opium.

pharmacologic properties make it different from other opioids, so it must be carefully administered. Particular vigilance is needed when starting treatment and increasing dosages, regardless of whether methadone is being used for addiction treatment or pain management. FDA reports that side effects can include slow or shallow breathing, dangerous changes in heartbeat, and death.

Until recently, methadone was primarily used in opioid treatment programs (OTP) to treat and rehabilitate people addicted to such opioids as heroin or certain prescription drugs.⁵ It works as a replacement for such drugs by preventing withdrawal symptoms. Its slow onset allows patients to be monitored as the drug takes effect, and its 24- to 36-hour duration of action suppresses opioid withdrawal symptoms with one daily dose. When used for addiction treatment, methadone cannot be dispensed by a practitioner outside of an OTP.

Since the late 1990s, methadone has been increasingly prescribed by practitioners⁶ to treat their patients' pain. However, while a single dose suppresses opioid withdrawal symptoms for a day or more, it generally relieves pain for 4 to 8 hours despite remaining in the body much longer. Further, it may take 3 to 5 days to achieve full pain relief, so dosage increases must be done more slowly than with other opioids. As a result, patients may feel the need to take more methadone before the previous dose has left the body. However, if taken too often, in too high a dose, or with certain other medicines or supplements, it may build up in the body to a toxic level. Variability in methadone's absorption, metabolism, and relative pain relief potency among patients requires a highly individualized approach to prescribing. When used for pain management, methadone may be prescribed by appropriately licensed and registered practitioners and obtained through licensed and registered retail pharmacies.

⁵For purposes of this report, OTPs refers to when practitioners dispense and administer narcotic drugs for maintenance or detoxification treatment, which also may be known as narcotic treatment programs.

⁶The types of practitioners who prescribe controlled substances such as methadone vary among states. The majority of prescribing practitioners are physicians, but nonphysicians may also prescribe, including physician assistants, dentists, and certain types of nurses, such as nurse practitioners and advanced practice nurses. For purposes of this report, "practitioner" includes persons such as physicians or nurse practitioners who may prescribe, administer, or dispense controlled substances, or pharmacists who dispense controlled substances.

Like many drugs, methadone can also be abused—that is, used for nontherapeutic purposes or for purposes other than those for which it was prescribed, and dangerous side effects or death can occur when methadone is combined with other drugs or alcohol. Because of its accepted medical use as well as its high potential for abuse and for severe psychological or physical dependence, methadone is classified as a Schedule II controlled substance under the Controlled Substances Act.⁷

Questions have been raised about the regulation of methadone for both pain management and addiction treatment, as well as the factors contributing to the increase in methadone-associated overdose deaths. Such deaths can occur in a number of ways, including intentional overdoses, or suicide, and accidental overdoses due to improper dosing levels, abuse, or patient misuse, such as by combining methadone with other drugs. While CDC collects limited information on overdose deaths from state death certificates, there is no standard, nationwide method to document detailed information about each death, such as the form or source of the drug, nor is there a standard definition for a methadone-associated overdose death, so state medical examiners and coroners investigating these deaths may define and report them differently. Defining methadone's role in a death is difficult because of inconsistencies in determining and reporting causes of death, the presence of other drugs in the deceased person's system, and a lack of information about the deceased person's level of opioid tolerance. CDC has also reported that it has been difficult to determine the extent to which increases in methadone-associated overdose deaths have resulted from specific prescribing practices, misuse by patients, diversion of the drug such as by illegal sale, or other means.⁸

⁷Under the Controlled Substances Act, drugs are classified as controlled substances and placed into one of five schedules based on the extent to which a drug has an accepted medical use, its potential for abuse, and the degree of psychological or physical dependence. Schedule I drugs have no accepted medical use and, along with Schedule II drugs, have a higher potential for abuse than drugs in Schedules III through V. Schedule II drugs have the highest potential for abuse of any schedule drugs that have an accepted medical use. See Pub. L. No. 91-513, Tit. II, § 202, 84 Stat. 1242, 1247-1252 (1970) (codified, as amended, at 21 U.S.C. § 812).

⁸Diversion can involve illegal sales of prescription drugs by physicians, patients, or pharmacists, as well as obtaining controlled substances from Internet pharmacies without a valid prescription. Diversion can also involve such activities as “doctor shopping” by individuals who visit numerous physicians to obtain multiple prescriptions, prescription forgery, and pharmacy theft.

To explore these issues, you asked that we further examine methadone-associated overdose deaths. Specifically, we examined (1) the regulation of methadone for pain management and addiction treatment, (2) the factors contributing to the increase in methadone-associated overdose deaths, and (3) the steps taken to prevent methadone-associated overdose deaths.

To examine the regulation of methadone for pain management and addiction treatment, we reviewed relevant provisions of the Controlled Substances Act, implementing regulations, and federal case law. We interviewed officials from the Drug Enforcement Administration (DEA) and the Substance Abuse and Mental Health Services Administration (SAMHSA), and we reviewed relevant agency policies. We also interviewed officials and examined relevant codified statutes and regulations in five selected states—Florida, Kentucky, Maine, New Mexico, and West Virginia—to determine how these states regulate the use of methadone for both pain management and addiction treatment. We chose these states based on their meeting four of five criteria we selected, including whether the state had one of the top 10 highest rates of increase in methadone-associated overdose deaths from 1999 through 2004 and whether there was research on methadone-associated overdose deaths in that state.⁹ The findings from our review of these five states cannot be generalized to any other state.

To determine the factors contributing to the increase in methadone-associated overdose deaths, we interviewed officials from CDC, DEA, FDA, the Office of National Drug Control Policy (ONDCP), and SAMHSA.¹⁰ We also interviewed officials from relevant professional associations and experts in pain management, addiction treatment, and forensic science. In addition, we interviewed researchers and officials in our five selected states regarding their views on what factors were contributing to the increases in methadone-associated overdose deaths in their states, and reviewed state data and studies. We reviewed methadone poisoning death data from CDC's National Vital Statistics System and relevant DEA data, including DEA data on methadone drug items seized by law enforcement

⁹When we made our state selection for this study, 2004 CDC data on methadone-associated overdose deaths were the most current data available. However, 2005 data have since been published.

¹⁰CDC, FDA, and SAMHSA are all part of the Department of Health and Human Services (HHS).

and analyzed in forensic laboratories. We interviewed CDC and DEA officials to obtain information about the reliability of their data, including quality control such as edit checks, and any limitations of these databases. We determined that these data were sufficiently reliable for use in this report, and identified any limitations.

To identify steps taken to prevent methadone-associated overdose deaths, we interviewed officials from CDC, DEA, FDA, ONDCP, and SAMHSA. We also interviewed officials from relevant professional associations and experts in pain management, addiction treatment, and forensic science. We reviewed relevant studies and reports about efforts to prevent methadone and other prescription drug overdose deaths. To obtain additional information about prescription drug monitoring initiatives, we examined relevant codified statutes and regulations in our five selected states. We also interviewed officials in our five selected states to learn about initiatives in their states to prevent these deaths. However, we did not evaluate these efforts, and our findings are not representative of all such efforts nor can they be generalized to all states. (See app. I for a detailed discussion of our methodology.)

We conducted our work from November 2007 through February 2009 in accordance with all sections of GAO's Quality Assurance Framework that are relevant to our objectives. The framework requires that we plan and perform the engagement to obtain sufficient and appropriate evidence to meet our stated objectives and to discuss any limitations in our work. We believe that the information and data obtained, and the analysis conducted, provide a reasonable basis for any findings and conclusions.

Background

Methadone, a long-acting opioid medication, is available as a liquid, a solid tablet (5 and 10 mg), a rapidly dissolving wafer or diskette (40 mg), or a powder. Liquid methadone is most commonly used for addiction treatment, while the 5 and 10 mg tablets are most often prescribed for pain management. FDA considers methadone safe and effective for both pain management and addiction treatment, although not all forms of methadone are FDA approved for both of these purposes.

Use of Methadone for Addiction Treatment

OTPs offer methadone maintenance treatment, including counseling, for people addicted to heroin and certain prescription drugs. Daily doses of methadone help normalize the body's neurological and hormonal functions that have been impaired by the use of heroin or misuse or abuse of other short-acting opioids. When starting treatment, individuals go to an

OTP daily to take their methadone dose under observation, although patients may receive a single take-home dose for a day that the clinic is closed for business. After a few months, they may become eligible for unsupervised take-home doses. The National Institute on Drug Abuse notes that 1 year is generally the minimum for methadone maintenance treatment, and that some individuals will benefit from treatment over several years. Buprenorphine and levomethadyl acetate (LAAM) are also FDA-approved medications for treating opioid addiction.¹¹ When used for addiction treatment, methadone must be dispensed by an OTP that is certified by SAMHSA and registered with DEA.¹² As of February 2009, about 1,200 OTPs were operating nationwide, but not all states have OTPs.¹³ (See fig. 1.) OTPs are operated by private for-profit organizations, private nonprofit organizations, hospitals, or government agencies.

¹¹In October 2002, FDA approved certain forms of the drug buprenorphine for use in opioid addiction treatment. Given this approval and because buprenorphine is a Schedule III drug, the drug may be prescribed, dispensed, or administered by qualified physicians for the treatment of opioid addiction outside of an OTP. This means that these physicians are not required to obtain the federal registration and certification that are required for OTPs when they meet certain conditions, including obtaining required training, holding appropriate licensure and certifications, having the capacity to refer patients to appropriate counseling, and limiting the number of patients treated at any one time. LAAM is indicated as a second-line treatment for opioid addiction if patients fail to respond to methadone or buprenorphine. According to FDA officials, the manufacturer of LAAM discontinued marketing this drug in 2003 and it is currently not available.

¹²Practitioners dispensing or administering Schedule II drugs for opioid addiction treatment must register for this purpose with the Attorney General on an annual basis. One condition of this registration is being determined qualified by the Secretary of Health and Human Services for the treatment of opioid addiction. An OTP must obtain a valid certification from SAMHSA in order to be considered qualified by the Secretary. There are, however, a few exceptions. For example, OTP registration and certification is not required when a hospital provides maintenance or detoxification treatment to a patient who is admitted for a medical condition other than opioid addiction but who requires this treatment during his or her stay.

¹³According to SAMHSA, Montana, Wyoming, South Dakota, and North Dakota do not have federally certified OTPs.

Figure 1: Number of OTPs by State That Have Been Certified by SAMHSA, February 2009



Source: SAMHSA.

Note: The total number of OTPs includes seven programs in Puerto Rico and one in the Virgin Islands not listed on the figure.

Use of Methadone for Pain Management

FDA approved methadone for treating pain in 1947,¹⁴ but from the early 1970s until the late 1990s the drug was primarily used for treating addiction. In the mid-1990s, various national pain-related organizations began to issue guidelines for treating and managing pain, including using opioids to treat both cancer and noncancer pain. For example, the practice guidelines issued by the Agency for Health Care Policy and Research informed physicians and other health care professionals about the management of acute pain in 1992 and cancer pain in 1994.¹⁵ In 2001, health care providers and hospitals were required to ensure that their patients received appropriate pain treatment when the Joint Commission, a national health care facility standards-setting and accrediting body, implemented pain standards for hospital accreditation.¹⁶ At first, methadone was prescribed more for the treatment of cancer pain, but it has been increasingly prescribed for the treatment of chronic noncancer pain. Methadone's advantages include that it costs less than other opioids used to treat pain, and it comes in multiple forms.

Unlike methadone's use in addiction treatment where it generally must be dispensed by OTPs, when used to treat pain methadone may be prescribed by an appropriately licensed and registered practitioner and dispensed by licensed and registered retail pharmacies. Licensed and registered practitioners may also dispense methadone directly to patients for pain management, but DEA officials said that it is not a common practice.

Relevant Federal Agencies

DEA, on behalf of the Attorney General of the United States, is the agency primarily responsible for enforcing the Controlled Substances Act.¹⁷ Under the act, controlled substances are classified into five schedules based on

¹⁴In 1947, when federal law only required that new drugs be shown to be safe, FDA determined that methadone was safe for pain management. Subsequently in 1962, when the law was amended to impose additional requirements for the approval of new drugs, including the demonstration of their efficacy, FDA retrospectively evaluated methadone and determined that the drug was also effective for pain management.

¹⁵In 1999, the name of the Agency for Health Care Policy and Research was changed to the Agency for Healthcare Research and Quality. The agency, which is part of HHS, is responsible for supporting research designed to improve the quality of health care, reduce its costs, and broaden access to essential services.

¹⁶The Joint Commission was formerly known as the Joint Commission on Accreditation of Healthcare Organizations or JCAHO.

¹⁷See Pub. L. No. 91-513, Tit. II, 84 Stat. 1242 (1970) (codified, as amended, at 21 U.S.C. §§ 801, et seq.); see also 21 C.F.R. §§ 1300.01, et seq.

the extent to which the drug has an accepted medical use, and its potential for abuse and degree of psychological or physical dependence.¹⁸ Schedule II controlled substances—which include opioids such as morphine, oxycodone, and methadone—have a currently accepted medical use and a high potential for abuse, and may lead to severe psychological or physical dependence. DEA’s regulation of the manufacturing, distribution, dispensing, and prescribing of controlled substances, including Schedule II drugs, encompasses the following:

- *Manufacturing.* DEA limits the quantity of Schedule II controlled substances that may be produced by each manufacturer in the United States each year. DEA determines these quotas based on a variety of factors, including disposal and inventories. DEA also sets aggregate production quotas that limit the production of bulk raw materials used to manufacture Schedule II controlled substances.
- *Distribution.* DEA regulates transactions involving the sale and distribution of Schedule II controlled substances by manufacturers and wholesale distributors. Manufacturers and distributors are required to report their inventories of controlled substances to DEA, and these data are available for monitoring the distribution of controlled substances throughout the United States and identifying retail registrants that received unusual quantities of controlled substances.
- *Dispensing and prescribing.* Practitioners who dispense, administer, or prescribe controlled substances must obtain a valid registration.

SAMHSA is the lead federal agency addressing substance abuse and mental health services. Its mission is to build resilience and facilitate recovery for people with or at risk for substance abuse and mental illness. SAMHSA’s resources and programs are designed to expand service capacity and improve service and infrastructure to address prevention and treatment gaps. SAMHSA directly supports state and local service systems

¹⁸As Schedule II controlled substances have a high potential for abuse and the potential for severe psychological or physical dependence, these drugs are subject to certain federal requirements including storage security and a quota on manufacturing. In addition, Schedule II drugs may only be dispensed by pharmacists with nonrefillable written prescriptions except in emergency situations when the drugs may be dispensed upon an oral prescription. When used for opioid addiction treatment, however, Schedule II drugs may only be dispensed or administered but not prescribed by registered practitioners. This means that for addiction treatment, patients cannot obtain prescriptions from their physicians for Schedule II drugs.

and funds activities to improve practice through grants and contracts. SAMHSA's Center for Substance Abuse Treatment provides national leadership to expand the availability of effective treatment and recovery services for alcohol and drug problems, and to improve access, reduce barriers, and promote high-quality, effective treatment and recovery services for people with substance abuse problems and their families and communities.

Under federal law and regulations, drugs must be approved by FDA before they can be marketed in the United States.¹⁹ The agency reviews new drug applications to determine whether they provide sufficient evidence that the drug is safe and effective for the proposed use. In approving a drug, FDA may require that the drug be dispensed only by a prescription by a licensed practitioner. Because some risks may not become known until after a drug's approval and use in a wider segment of the population, FDA has certain postmarket oversight responsibilities once a drug is approved, such as assessing sponsors' compliance with requirements for adverse event reporting. The agency compiles data from sponsor reports on adverse events, and voluntary reports submitted to its MedWatch program, a voluntary reporting program through which health professionals and consumers can report adverse reactions and other problems related to FDA-approved drugs. In addition, as of 2008, if FDA identifies postmarket safety concerns, the agency may take specific actions such as requiring drug manufacturers to make safety-related changes to a drug's labeling and requiring drug manufacturers to implement a Risk Evaluation and Mitigation Strategy when necessary to ensure that the benefits of a particular drug outweigh the risks.

Overdose Death Investigation and Reporting

Death investigations in the United States are typically conducted by a county, district, or state coroner system or a medical examiner system. These systems investigate deaths due to external causes, such as injury or poisoning; sudden and unexplained deaths; and deaths that occur under medical care.²⁰ Most coroners are elected, and they may not be physicians. In contrast, medical examiners are usually appointed and are, with few

¹⁹See 21 U.S.C. §§ 353, 355, 355-1; see also 21 C.F.R. Part 310.

²⁰CDC reports that a poison is any substance that is harmful to your body when ingested, inhaled, injected, or absorbed through the skin. Any substance taken in excess, including a prescription drug, can be a poison. Therefore, CDC categorizes drug overdoses as drug poisonings. In this report, we refer to CDC poisoning data as drug overdose data.

exceptions, required to be physicians and are often pathologists or forensic pathologists.²¹

The registration of deaths varies by state. Death certificates can be completed by funeral directors, attending physicians, medical examiners, or coroners and contain such information as the deceased person's age, sex, and race; the circumstances and cause of death; and the signature of the physician, medical examiner, or coroner. Each disease, abnormality, injury, or poisoning that the medical examiner or coroner believes contributed to the death generally is reported. The original records are filed in state registration offices. Statistical information is compiled in a national database through the National Vital Statistics System by CDC's National Center for Health Statistics. From these data, monthly, annual, and special statistical reports are prepared for the United States and for cities, counties, states, and regions by various characteristics, such as sex, race, and cause of death. However, statistical data derived from death certificates can be no more accurate than the information provided on the certificate. For example, causes of death on the death certificate reflect a medical opinion that might vary among the individuals completing the certificates.

²¹According to a 2007 article in the *American Journal of Forensic Medicine and Pathology*, about 31 percent of counties in the United States are served by a medical examiner at the county, district, or state level. R. Hanzlick, "The Conversion of Coroner Systems to Medical Examiner Systems in the United States: A Lull in the Action," *American Journal of Forensic Medicine and Pathology*, vol. 28, no. 4 (2007).

Methadone Is Regulated as a Controlled Substance and Subject to Additional Requirements When Used for Addiction Treatment

Methadone is regulated as a controlled substance, under federal and state laws and regulations, when used for pain management and addiction treatment.²² When methadone is used for pain management, it is regulated under federal and state laws and regulations that apply to controlled substances generally and that do not impose requirements unique to methadone. For addiction treatment, however, federal and state laws and regulations impose additional requirements that are specific to the use of methadone.

When Used for Pain Management, Methadone Is Regulated as a Controlled Substance under Federal and State Laws and Regulations

The use of methadone for pain management is regulated under federal and state laws and regulations that apply to controlled substances generally and that do not impose requirements unique to methadone. DEA has certain authorities, under the Controlled Substances Act, to regulate the use of methadone for pain management, as part of its oversight for controlled substances.²³ For example, practitioners must register with DEA in order to dispense, administer, or prescribe Schedule II through V controlled substances.^{24,25} The Controlled Substances Act and implementing regulations also require that Schedule II controlled substances, including methadone, only be dispensed by pharmacists upon

²²For purposes of this report, we only reviewed relevant state laws and regulations from five states, Florida, Kentucky, Maine, New Mexico, and West Virginia. Accordingly, references to state laws and regulations in the report are limited to our findings in these five states and cannot be generalized to include any other state.

²³See 21 U.S.C. §§ 801, et seq.; see also 21 C.F.R. §§ 1300.01, et seq. In guidance, DEA has also clarified that the legal standard for prescribing controlled substances, including methadone, to treat pain is the same as that for prescribing controlled substances generally. See 71 Fed. Reg. 52,716 (2006).

²⁴21 U.S.C. §§ 822(a)(2), 823(f). The Attorney General may register a practitioner to dispense, administer, or prescribe controlled substances in Schedules II through V if the applicant meets certain criteria, including being authorized to dispense, administer, or prescribe controlled substances under the laws of the states in which they practice. Practitioners must reapply for this registration every 3 years. 21 C.F.R. §1301.13.

²⁵For purposes of this requirement, “practitioner” refers to any person or entity that dispenses a controlled substance, including physicians, hospitals, pharmacists, and pharmacies.

a written prescription,²⁶ which must be issued for a legitimate medical purpose by registered practitioners acting in the usual course of professional practice.²⁷ In addition, DEA uses its data on the distribution of methadone and other controlled substances to identify retail-level registrants, such as pharmacies, that receive and dispense unusual quantities of these drugs. Under these authorities, DEA may take action against practitioners that fail to prescribe or dispense controlled substances, including methadone, for legitimate medical purposes, one sanction of which is suspension or revocation of DEA registration.²⁸

The use of methadone for pain management is also regulated under state law and regulations that apply to controlled substances generally. In the states we reviewed, some of these requirements were similar to provisions of the federal Controlled Substances Act. For example, these states require, in general, that Schedule II controlled substances may only be dispensed by pharmacists upon a written prescription of a practitioner.²⁹ States also may impose requirements beyond what is required under the federal Controlled Substances Act. For example, officials in Maine said that they require the use of tamperproof prescription notepads when writing prescriptions for Schedule II drugs. However, none of the laws and regulations in the five states we reviewed had any provisions specific to methadone when used for pain management other than provisions that generally apply to all Schedule II controlled substances.

²⁶21 U.S.C. § 829(a), 21 C.F.R. § 1306.11. Pharmacists, however, may dispense Schedule II drugs upon an oral prescription in emergency situations, with the prescribing practitioner providing a written prescription within 7 days of the oral prescription.

²⁷21 U.S.C. § 829(a), 21 C.F.R. § 1306.04(a). The Supreme Court has stated that under the Controlled Substances Act, Congress regulates medical practice insofar as it bars doctors from using prescription-writing powers as a means to engage in illicit drug dealing and trafficking. Beyond this, however, the act manifests no intent to regulate the practice of medicine. This silence is understandable given the structure and limits of federalism, which allow the states' great latitude to legislate as to the protection of the health of their citizens. See *Gonzales vs. Oregon*, 546 U.S. 243, 269-70 (2006).

²⁸As discussed previously, as of 2008, if FDA identifies postmarket safety concerns for drugs, the agency may take specific actions such as requiring drug manufacturers to make safety-related changes to a drug's labeling or to implement a Risk Evaluation and Mitigation Strategy. Such oversight could have an impact on the dispensing, administering, or prescribing of certain controlled substances, including methadone.

²⁹There are certain exceptions to this requirement. For example, in Florida, Maine, New Mexico, and West Virginia, pharmacists may dispense Schedule II controlled substances upon an oral prescription of a practitioner in an emergency situation.

Because states regulate the practice of medicine and pharmacy, controlled substances that are prescribed, administered, or dispensed by state-licensed practitioners are also generally regulated under these state laws and regulations. For example, in the states we reviewed, physicians must be licensed by their state boards of medicine in order to engage in the practice of medicine, which includes the prescribing of drugs.^{30,31} Similarly, pharmacists must be licensed by their state boards of pharmacy in order to engage in the practice of pharmacy, which includes the dispensing of prescription drugs.³² Under this authority, the state medical boards and state boards of pharmacy oversee the regulation of the practice of medicine and pharmacy, respectively. As part of this oversight, these boards or other related state agencies may investigate complaints about practitioners, discipline practitioners that violate applicable laws or regulations, and facilitate rehabilitation of practitioners when appropriate.

States and professional licensing boards may further regulate the prescribing or dispensing of controlled substances for the treatment of pain. According to the Federation of State Medical Boards, a number of states have implemented standards for the use of controlled substances for pain, including the five states we reviewed. Some of these states have based these standards on the model policy for use of controlled substances for the treatment of pain published by the Federation of State Medical Boards. For example, Florida law expressly provides that physicians may prescribe or administer controlled substances for the treatment of intractable pain.³³ Under its regulations, Florida's Board of Medicine and Board of Osteopathic Medicine also impose standards that

³⁰In Florida, the Department of Health issues a license to medical doctors upon certification by Florida's Board of Medicine and also issues a license to osteopathic physicians upon certification by Florida's Board of Osteopathic Medicine.

³¹Oversight of nonphysicians, such as nurse practitioners who may be licensed to prescribe controlled substances, may be provided by other state agencies, such as boards of nursing.

³²In Florida, the Department of Health issues a license to pharmacists upon certification by Florida's Board of Pharmacy.

³³Florida law defines intractable pain as pain for which, in the generally accepted course of medical practice, the cause cannot be removed and otherwise treated. Practitioners may prescribe controlled substances for this pain provided that they do so in accordance with that level of care, skill, and treatment recognized by a reasonably prudent physician under similar circumstances. Fla. Stat. Ann. § 458.326.

include steps physicians must take prior to prescribing controlled substances for pain.³⁴

When Used for Addiction Treatment, Methadone Is Subject to Additional Requirements under Federal and State Laws and Regulations

Although methadone is subject to federal and state requirements that apply to controlled substances, there are additional requirements specific to methadone when used for addiction treatment.^{35,36} For example, as part of its enforcement responsibilities under the Controlled Substances Act, DEA has the authority to regulate the use of methadone for addiction treatment. Under the act, OTPs must register with DEA in order to dispense or administer methadone for addiction treatment, and there are three conditions for this registration.³⁷ Under the first condition of this registration, DEA must determine that the OTPs will appropriately secure stocks of methadone and maintain appropriate records.³⁸ DEA officials informed us that they also inspect OTPs in order to ensure that OTPs are maintaining proper security, safety, and storage of methadone and other narcotic drugs used for addiction treatment. DEA officials said that inspections are conducted every 3 years, and there are a series of graduated penalties if OTPs are not in compliance, including suspension or revocation of OTP registration. If DEA suspends or revokes a registration, that OTP would be unable to purchase, administer, or dispense methadone to OTP patients for addiction treatment.

³⁴These steps include patient evaluations; establishment of a written treatment plan; obtaining informed consent from the patient; reviewing the course of treatment periodically; referring the patient for additional evaluation, when necessary; and treatment and maintaining complete records. Fla. Admin. Code Ann. § 64B8-9.013.

³⁵There are certain distinctions in requirements that apply to methadone as a controlled substance when used for different purposes. For example, under federal law, prescriptions may not be issued for Schedule II drugs, including methadone, when used for opioid addiction treatment. Accordingly, federal requirements described previously, which address prescriptions for Schedule II controlled substances, do not apply to OTPs.

³⁶These requirements also apply to buprenorphine, which is another FDA-approved medication for treating opioid addiction.

³⁷21 U.S.C. § 823(g). Practitioners that dispense or administer narcotic drugs to individuals for maintenance or detoxification treatment must obtain a separate registration for that purpose from the Attorney General on an annual basis. This registration is distinct from the registration required for any practitioner that dispenses, administers, or prescribes controlled substances in Schedules II through V described previously.

³⁸21 U.S.C. § 823(g)(1)(B). In order for the Attorney General to register an applicant to dispense or administer narcotic drugs for maintenance or detoxification treatment, the Attorney General must determine that the applicant will comply with federal standards for securing stocks of narcotic drugs and maintaining records on such drugs.

As a second condition of DEA registration for OTPs, SAMHSA must determine that OTPs are qualified to engage in methadone maintenance treatment for addiction.³⁹ Federal opioid treatment regulations define SAMHSA's standards for determining whether OTPs are qualified.⁴⁰ Specifically, such standards include requiring OTPs to obtain a current, valid certification from SAMHSA to dispense methadone for addiction treatment. To obtain certification, an OTP must have a current, valid accreditation by an accreditation body, such as the Joint Commission or other entity designated by SAMHSA. An OTP also must comply with a number of other requirements for certification established by SAMHSA. These other requirements include maintaining a diversion control plan that contains specific measures to reduce the possibility of diversion of methadone from legitimate treatment to illicit use and ensuring that all licensed professional care providers comply with the credentialing requirements of their respective professions.

The third condition of DEA registration for OTPs requires SAMHSA to determine that OTPs will comply with standards regarding unsupervised take-home doses of methadone.⁴¹ SAMHSA has established specific criteria for unsupervised take-home doses of methadone under federal regulations for OTPs.⁴² (See table 1.) These criteria were established to limit the potential for diversion of methadone to illicit uses. OTPs are also required

³⁹21 U.S.C. § 823(g)(1)(A). In order for the Attorney General to register an applicant to dispense narcotic drugs for maintenance or detoxification treatment, the Secretary of Health and Human Services must determine that the practitioner is qualified to engage in the treatment for which the registration is sought.

⁴⁰Previously FDA, on behalf of the Secretary of Health and Human Services, determined whether OTPs were qualified in accordance with the agency's regulations. As part of its oversight role, FDA was required to periodically inspect OTPs to determine whether they were in compliance with regulations and therefore qualified for purposes of registration with the Attorney General. In 2001, these federal regulations were modified, replacing FDA with SAMHSA as the primary agency responsible for implementation of OTP standards. The modified regulations also introduced an accreditation and certification process for OTPs. See 66 Fed. Reg. 4076 (2001).

⁴¹21 U.S.C. § 823(g)(1)(C). In order for the Attorney General to register an applicant to dispense narcotic drugs for maintenance or detoxification treatment, the Secretary of Health and Human Services must determine that the applicant will comply with the Secretary's standards for quantities of narcotic drugs, which may be provided for unsupervised use by individuals in such treatment.

⁴²Any patient in comprehensive maintenance treatment may receive a single take-home dose for the day that the OTP is closed. Beyond this, however, the medical director of the OTP must determine which patients may qualify for unsupervised use of methadone by considering the criteria identified in table 1.

to maintain procedures for take-home doses of methadone that will allow identification of the theft or diversion of these doses, such as by labeling containers with the OTP's name, address, and telephone number. For additional information on select aspects of the federal regulations relating to OTPs, see appendix II.

Table 1: Criteria for Take-Home Doses of Methadone

Criteria used to determine whether a patient is responsible in handling opioid drugs for unsupervised use

1. Absence of recent abuse of drugs, including alcohol.
 2. Regularity of OTP clinic attendance.
 3. Absence of serious behavioral problems at OTP.
 4. Absence of known recent criminal activity (e.g., drug dealing).
 5. Stability of the patient's home environment and social relationships.
 6. Length of time in comprehensive methadone maintenance treatment.
 7. Assurance that take-home medication can be safely stored within the patient's home.
 8. Whether the rehabilitative benefit derived from decreasing the frequency of OTP attendance outweighs the potential risks of diversion.
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Source: SAMHSA regulations at 42 C.F.R. 8.12 (h)(4)(i)(2).

States may also regulate the use of methadone for opioid addiction treatment under state laws and regulations, which may be equal to or stricter than federal standards.⁴³ For example, while federal regulations do not specify the days or hours that OTPs must be open, regulations in three of the states we reviewed—Kentucky, Maine, and West Virginia—require that OTPs be open 7 days a week.⁴⁴ Further, states may implement drug testing requirements that are stricter than the federal standard of at least eight random drug abuse tests per year for each patient in maintenance treatment. For example, in Maine, drug tests on OTP patients must be conducted at least every 30 days unless the individual treatment plan indicates that drug testing should be done more frequently. Appendix II compares OTP regulations in the five states we reviewed.

⁴³One of the requirements for SAMHSA's certification for OTPs is the OTPs' compliance with all applicable state laws and regulations.

⁴⁴In Kentucky, OTPs may close for nine specified holidays. In West Virginia, OTPs may close for eight holidays and two training days per year.

Each state with OTPs also has a state agency or official designated to oversee opioid treatment in that state. Each of the five states we reviewed had an official designated as the state methadone authority or state opioid treatment authority, although responsibilities for this position varied and these officials had other duties in addition to responsibilities in overseeing the state's OTPs. For example, a state official told us that the primary responsibilities of the State Methadone Authority in West Virginia were to approve or disapprove OTP patients' requests for exceptions to methadone take-home policies and to receive and refer patient appeals and grievances to the designated state oversight agency. In contrast, in addition to approving or disapproving take-home exception requests, a state official explained that the State Opioid Treatment Authority in New Mexico has initiated activities such as site audits of the eight existing OTPs in the state to ensure compliance with state regulations. These officials also have quarterly conference calls with SAMHSA and their counterparts from other states to discuss issues regarding OTPs and best practices.

Increased Availability Combined with Lack of Knowledge and Abuse of Diverted Methadone Have Contributed to Increasing Methadone-Associated Overdose Deaths

Although information on methadone-associated overdose deaths is limited, available data suggest that methadone's growing use for pain management has increased availability of the drug, therefore contributing to the rise in methadone-associated overdose deaths. Lack of knowledge about the drug's unique pharmacological properties among practitioners and patients as well as abuse of diverted methadone also appear to have contributed to these deaths. State data and research support the idea that lack of knowledge and abuse of diverted methadone contributed to deaths, but also suggest that the specific circumstances of these deaths are variable.

Methadone’s Growing Use for Pain Management Has Increased the Drug’s Availability, Contributing to an Increase in Overdose Deaths

The growing availability of methadone through its increased use for pain management is a contributing factor to the rise in methadone-associated overdose deaths. DEA data show that from 2002 to 2007, distribution of methadone to business types associated with pain management—pharmacies and practitioners—almost tripled, rising from about 2.3 million grams to about 6.5 million grams. In contrast, distribution to OTPs increased more slowly, from about 5.3 million grams to about 6.5 million grams. See table 2 for the numbers for methadone distribution to four business types from 2002 through 2007. Similarly, data from IMS Health, a private company that tracks prescription drug trends, showed that from 1998 through 2006 the number of annual prescriptions of methadone for pain increased by about 700 percent, from about 531,000 in 1998 to about 4.1 million in 2006.

Table 2: Methadone Distribution by Type of Business, 2002 to 2007

	2002	2003	2004	2005	2006	2007
OTPs	5,262,052	5,743,272	6,584,721	6,892,025	7,345,623	6,451,288
Hospitals ^a	309,315	393,685	466,352	521,216	584,144	590,649
Pharmacies	2,329,083	3,274,331	4,246,007	4,863,736	5,986,488	6,442,516
Other practitioners ^b	10,381	15,113	35,492	43,260	51,046	49,503

Source: GAO analysis of DEA methadone distribution data.

Notes: Methadone distribution numbers are in grams. Prior to 2002 DEA’s methadone distribution data did not track sales to OTPs, therefore, we did not include data prior to 2002 in our analysis.

^aDEA reports that in hospitals methadone may be dispensed or administered for pain management. Hospitals may also dispense or administer methadone for addiction treatment when patients are admitted to the hospital for another condition but require treatment for opiate addiction during their stay.

^bIn addition to issuing prescriptions for controlled substances that patients can have filled in retail pharmacies, appropriately licensed practitioners may also dispense controlled substances directly to patients. DEA officials said that while practitioners may dispense methadone directly in their offices for pain management purposes, it is not a common practice. Officials did not have information on the specific types of practitioners who are dispensing methadone directly.

Most officials from federal and state agencies, as well as experts in addiction treatment and pain management that we spoke with, cited the increased availability of methadone due to its use for pain management as a key factor in the rise in deaths, while some added that addiction treatment in OTPs was not related to increased deaths. Federal officials and experts in epidemiology, pain management, and addiction treatment at SAMHSA’s National Assessment of Methadone-Associated Mortality in 2003 also acknowledged a correlation between the increased distribution of methadone through pharmacies for pain management with the increase in methadone-associated overdose deaths and reached consensus that the

increase in these deaths was not associated with addiction treatment in OTPs. Additionally, in 2006 CDC researchers suggested that the increase in deaths involving methadone was related to physicians increasingly prescribing the drug for pain. The researchers reported that the increase in deaths tracked the increase in methadone used for pain management rather than its use in OTPs.

To explain the increasing prescribing of methadone for pain management, many officials and experts we spoke with mentioned the publicity surrounding the increased abuse and diversion of the drug OxyContin in the early 2000s as a reason for the increased prescribing of methadone for pain.⁴⁵ A November 2007 report by the National Drug Intelligence Center (NDIC) also noted that following increases in OxyContin addiction and death rates, many practitioners began using methadone instead to manage pain.

Lack of Knowledge about Methadone by Practitioners and Patients Has Also Contributed to Methadone-Associated Overdose Deaths

Lack of knowledge about the unique pharmacological properties of methadone by both practitioners and patients has also been identified as a factor contributing to methadone-associated overdose deaths. Background information prepared for SAMHSA's 2007 Methadone Mortality Reassessment meeting noted that physicians need to understand methadone's pharmacology as well as specific indications and cautions before using it to treat pain or addiction. FDA has issued similar statements, adding that practitioners should closely monitor patients when starting treatment with methadone or converting patients to methadone from other opioids. Some experts we spoke with advocated a "start low and go slow" approach with methadone. Additionally, some pain management specialists we interviewed warned that practitioners following conversion tables, which are commonly used to switch patients to methadone from other drugs, may start some patients on too high a dose. The specialists explained that using these conversion tables for patients who have already developed a tolerance for other opioids may be lethal, because tolerance for other opioids is not equivalent to tolerance for methadone.

⁴⁵For additional information regarding OxyContin abuse and diversion, see GAO, *Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem*, [GAO-04-110](#) (Washington, D.C.: Dec. 23, 2003).

Several sources have also cited inadequate training among some practitioners. NDIC reported in 2007 that some general practitioners and novice pain management specialists may lack the training to adequately monitor patients to whom they prescribe methadone. A 2005 survey by the National Center on Addiction and Substance Abuse found less than half of surveyed physicians (48 percent) received instruction in pain management while in medical school. DEA also noted that several of the top prescribers of methadone have been practitioners with specialties not generally associated with extensive training in pain management. Reports based on SAMHSA's 2003 National Assessment of Methadone-Associated Mortality and 2007 Reassessment recommended that practitioners needed better training in how to manage pain and addiction. Many experts, representatives of national associations, and state officials we spoke with agreed that more training in both pain and addiction treatment and about methadone's unique properties is needed for medical professionals. However, opinions varied about whether such training should be optional (e.g., offered for continuing education credit) or mandatory (e.g., required for license renewal).

Insufficient patient education has also been cited as contributing to methadone-associated overdose deaths. Patients may not understand how methadone works, including that it can stay in the body long after the pain returns. As a result, these patients might take methadone more frequently than prescribed to manage their recurring pain, risking overdose as the drug builds to toxic levels in their bodies. Unaware of potentially lethal drug combinations, patients might also take methadone with other drugs, including antianxiety drugs and other opioids, or alcohol.

Abuse of Diverted Methadone Is an Additional Contributing Factor to Methadone-Associated Overdose Deaths

Data suggest that abuse of diverted methadone is also contributing to the rise in methadone-associated overdose deaths. Increased thefts as well as seizures of methadone by law enforcement indicate that more diverted methadone is available for potential abuse. DEA tracks drug abuse, including the diversion of legally manufactured drugs such as methadone into the illegal market, through its National Forensic Laboratory Information System, which collects the results of state and local forensic laboratories' analyses of drugs seized as evidence by law enforcement agencies. The DEA data on national estimates of the most frequently analyzed drugs seized by law enforcement from 2001 through 2007 showed that the number of methadone drug items analyzed by state and local labs

increased 262 percent, though the estimated number was smaller than that of some of the other drugs (see table 3).⁴⁶ In 2007, DEA reported that per prescription, methadone was more likely to be diverted and abused than either hydrocodone or oxycodone based on its analysis of data from the National Forensic Laboratory Information System and IMS Health.

Table 3: Top Five Drugs with Highest Percentage Increases in Analyzed Drug Items Seized by Law Enforcement, 2001 to 2007

Drugs/substances	2001	2002	2003	2004	2005	2006	2007	Percentage change, 2001 to 2007
Methadone	2,865	3,867	4,967	6,397	7,302	9,822	10,361	262
Morphine	1,842	2,424	2,534	2,827	3,619	4,672	5,343	190
Hydrocodone	12,847	16,869	16,903	18,608	23,549	30,480	36,803	186
Oxycodone	12,013	17,619	16,520	18,962	19,274	25,041	29,487	145
Carisoprodol ^a	1,890	2,946	3,297	2,757	3,020	3,558	4,420	134

Source: GAO analysis of data from DEA's National Forensic Laboratory Information System.

Note: The numbers included in this table are national estimates calculated each year by DEA based on a national sample model of state and local laboratories. Therefore, DEA reports that the national estimates should not be affected by the number of participating laboratories in any given year. According to DEA officials, DEA did not produce national estimates prior to 2001; therefore, we did not include data prior to 2001 in our analysis.

^aCarisoprodol is a centrally acting muscle relaxant.

Likewise, DEA data on drug theft and loss showed that methadone thefts nationwide more than doubled, from 176 in 2000 to 393 in 2007. For the five states we reviewed, the data showed that most thefts were reported from pharmacies, while no thefts were reported from OTPs in four of these states during the same time period.

Federal and state officials told us that abuse of prescription drugs, including methadone, has become more of a problem in recent years than abuse of illicit drugs, such as heroin or cocaine. Officials from ONDCP said that overall opioid drugs are being increasingly diverted and abused, while abuse of illicit drugs is decreasing. SAMHSA's National Survey on Drug Use and Health provides some additional information about where those who are abusing prescription pain relievers, such as methadone,

⁴⁶DEA defines a drug item as an exhibit that is an integral component of physical evidence within a submission or case that is examined and individually specified in a laboratory analysis report. For example, a drug item could be a bottle of pills or a bottle of liquid methadone.

obtain their drugs. According to the 2007 survey, among the estimated 5.2 million persons aged 12 or older who reported using prescription pain relievers nonmedically in the past 12 months, 56.5 percent said they got the drugs from a friend or relative, another 18.1 percent reported that they got the drug from just one doctor, 4.1 percent reported that they got the pain relievers from a drug dealer or other stranger, and 0.5 percent reported buying the drug on the Internet.

State Data and Research Support That Lack of Knowledge and Abuse of Diverted Methadone Contribute to Deaths, but Death Circumstances Are Variable

Data and research regarding methadone-associated overdose deaths in the five states we reviewed support the idea that lack of knowledge and abuse of diverted methadone contributed to deaths, but also suggest that the circumstances under which people are dying are variable. Specifically, state data and research show that death circumstances, such as the source of the drug and the most commonly detected other drugs, may vary by state. Furthermore, participants at SAMHSA's 2007 Methadone-Associated Mortality Reassessment concurred that the circumstances of methadone-associated overdose deaths vary by state. While research suggests that the source of methadone for those who die from overdose deaths is often unknown, available information indicates that there are three distinct populations who are dying: individuals with a prescription for methadone; individuals undergoing methadone maintenance treatment in OTPs; and individuals who obtained methadone from some other source, such as diversion. However, generally more of those who died had a prescription for methadone or obtained it through diversion rather than receiving methadone for addiction treatment in an OTP.⁴⁷ For example, a Kentucky study of deaths from 2000 to 2004 found that of the 95 deaths for which coroners documented methadone use, 48 percent of those who died had a physician's prescription for methadone, 20 percent obtained methadone through illicit means, 22 percent obtained methadone through unknown means, and 10 percent had received treatment in OTPs. Coroners' investigations also documented that one-third of the victims had been undergoing pain management. A New Mexico study of unintentional methadone-associated overdose deaths from 1998 to 2002 found that although a much larger percentage of deaths were related to methadone maintenance treatment than in the other states we reviewed, more deaths overall were linked with prescriptions for methadone. Specifically, of the

⁴⁷Data available from Florida do not include information on the source of methadone for those who died, and research from Maine did not contain information regarding the source of methadone for most deaths.

79 methadone-associated overdose deaths for which a source of methadone was available, 39 percent had methadone because they were undergoing methadone maintenance treatment, while 47 percent had a prescription for methadone. See appendix III for a summary of the findings of research studies in the five states we reviewed.

In addition, data and research from the five states we reviewed show that methadone is often found in combination with other drugs or alcohol, suggesting a lack of knowledge about the dangers of combining methadone with other drugs or that people are abusing methadone. In Florida, for example, of the 1,095 methadone-associated overdose deaths in 2007, 124 deaths were caused by methadone alone, while 971 deaths, or about 89 percent, were caused by methadone in combination with other drugs. The Kentucky study found that only 6 percent of the 176 methadone-associated overdose deaths were caused by methadone alone; other frequently detected drugs included antidepressants, benzodiazepines, and other opioids.⁴⁸ The New Mexico study showed somewhat different results, and found that of the 143 methadone-associated overdose deaths, 22 percent were due to methadone alone, 24 percent were due to methadone and prescription drugs (no illicit drugs), 50 percent were due to methadone and illicit drugs, and 4 percent were due to methadone and alcohol.

Education, Safety, and Monitoring Efforts to Prevent Methadone-Associated Overdose Deaths Have Been Implemented by Government Agencies and Other Organizations

Education, safety, and monitoring efforts have been implemented to prevent methadone abuse and methadone-associated overdose deaths—either specifically or as part of broader efforts to prevent prescription drug abuse and deaths—by various federal agencies, states, and other organizations. Educational efforts include physician training on the appropriate use of methadone to treat pain and opioid addiction, and public education campaigns about the dangers of methadone and other prescription drugs. Steps taken to improve the safety of using methadone include limiting the distribution of a high-dosage methadone tablet intended only for use in addiction treatment. In addition, states may monitor prescriptions of controlled substances as well as OTP patient enrollment through statewide registries.

⁴⁸The benzodiazepine family of depressants is used therapeutically to produce sedation, induce sleep, relieve anxiety and muscle spasms, and prevent seizures. It includes drugs such as Xanax and Valium.

Efforts to Educate Practitioners and the Public about Methadone and Other Prescription Drugs Have Been Initiated by Federal Agencies, States, and Other Organizations

Because lack of knowledge of methadone's unique properties has contributed to overdose deaths, federal and state officials and other experts agreed that more education is needed for practitioners and the public about how to safely use methadone and avoid its potential dangers. A number of efforts to educate practitioners and the public about how to use methadone and other prescription drugs safely have been initiated by federal agencies, states, and other organizations. Some of these efforts target methadone specifically while others are more broadly focused on using opioids to treat pain and preventing prescription drug abuse. Some officials and experts we spoke with cautioned that methadone is part of a larger problem of prescription drug abuse, and that prevention efforts focused on methadone alone might have the unintended consequence of shifting similar problems to a different drug—much like what occurred with methadone following reports of abuse and diversion of OxyContin.

Educational Efforts Targeted at Methadone

In August 2008, SAMHSA announced a 3-year grant of \$1.5 million to the American Society of Addiction Medicine to educate physicians and other practitioners on the appropriate use of methadone to treat pain and opioid addiction. The grant is to establish the Physician Clinical Support System for methadone, offering free support to prescribing physicians and other practitioners. SAMHSA reported that this system would include mentoring support, observation of practice, and consultative services by phone and e-mail. The system would also inform prospective practitioners through a Web site and published resources about science-based best practice guidelines for treating opioid addiction. According to SAMHSA, this initiative would aim to address the rise in methadone-associated overdose deaths spurred by misuse and abuse.

SAMHSA also has several current or planned educational initiatives focusing on OTPs. A risk management course for practitioners will focus on the safe use of methadone in OTPs, with a special emphasis on the beginning of treatment. The course will also educate OTP practitioners about using other drugs in conjunction with methadone, including benzodiazepines. In addition, SAMHSA is working with two work groups that include experts from academia, medical associations, medical researchers, and other federal agencies, such as FDA, to develop additional methadone-specific guidelines. One work group is reviewing available information to develop best practices on methadone and cardiac issues. The guidance will help practitioners identify patients at risk for cardiac arrhythmias that may be exacerbated by methadone, and provide information on how to monitor those patients for ongoing risks. Another work group is reviewing methadone interactions with other common

drugs, including HIV drugs. The ensuing guidelines will help practitioners safely treat patients who may be receiving several drugs simultaneously.

SAMHSA is also collaborating with FDA on a consumer education campaign designed to increase awareness of the potential for serious, life-threatening side effects in patients taking methadone for pain management or addiction treatment. FDA reports that the multimedia educational campaign would target OTPs and patients, pharmacies dispensing methadone, practitioners, and the public. According to FDA, materials developed for the campaign would include a brochure or flyer, fact sheets, podcasts, and online information. SAMHSA reported that the materials were scheduled to be finished by April 2009.

Educational Efforts Targeted at Opioids and Other Prescription Drugs

SAMHSA, along with the American Academy of Pain Medicine, the American Academy of Family Practitioners, and other medical organizations, has developed a continuing medical education course on how to safely use prescription pain relievers to treat pain. As of February 2009, 20 courses had been taught in 16 states. SAMHSA reported that 12 courses would be taught in 2009 and that priority would be given to states or regions with high per capita rates of opioid-associated overdoses and deaths. A brief Web-based version of the course has been developed in collaboration with MedScape, an online medical education company. Further, a five-module online version of the course will be posted on SAMHSA's Web site and disseminated through medical organizations and medical schools that offer continuing education credits.⁴⁹

The Federation of State Medical Boards developed a book, *Responsible Opioid Prescribing: A Physician's Guide*, in collaboration with a national pain expert.⁵⁰ The book includes strategies for treating chronic pain and reducing the risk of addiction, abuse, and diversion. The federation intends to distribute the book through state medical boards, and reports that medical boards can customize the book to include state-specific statutes, regulations, and guidelines. The federation reported that more than 60,000 copies of the book had been distributed in 13 states as of

⁴⁹The American Medical Association (AMA) reports that many state medical boards require continuing medical education for license re-registration. The AMA also reports that some states mandate content topics, such as HIV/AIDS, pain management, or prescribing controlled substances. However, according to the AMA, none of the five states we reviewed had continuing education requirements specific to prescribing methadone.

⁵⁰Scott M. Fishman, *Responsible Opioid Prescribing: A Physician's Guide* (Washington, D.C.: Waterford Life Sciences, 2007).

October 2008, and it intends to expand distribution in 2009 as more funds are raised.

Officials in the five states we reviewed told us about their states' efforts to educate practitioners and the public about controlled substances and drug abuse. For example, Kentucky's Operation UNITE (Unlawful Narcotics Investigations, Treatment, and Education) works to rid communities of illegal drug use, coordinate treatment and support for substance abusers, and educate the public on the dangers of drug use. New Mexico's Board of Pharmacy participates in the New Mexico Pain Policy Initiative, which educates practitioners on requirements for prescribing controlled substances and for New Mexico's Prescription Drug Monitoring Program. In West Virginia, law enforcement officials, physicians, and others have formed a controlled substance advisory board to address prescription drug abuse. One of its projects is to educate patients on the dangers of diversion by providing them with information when they pick up their prescriptions from pharmacies and to educate physicians about how to reduce doctor shopping. In addition to the five states we reviewed, Utah has also experienced rising prescription drug overdose deaths and has implemented two notable campaigns intended to reduce deaths and other harm from prescription drugs. The Use Only as Directed campaign educates the public about protecting themselves from unintentional overdose deaths. The Zero Unintentional Deaths campaign educates physicians, chronic pain sufferers, and communities about unintentional overdose deaths from prescription drugs.

Federal agencies have also begun educating the public about prescription drug abuse. For example, in January 2008, the ONDCP through its National Youth Anti-Drug Media Campaign launched a national television, print, and online advertising campaign to educate parents about teen prescription drug abuse. The campaign includes tips for preventing teen prescription drug abuse, such as safeguarding all drugs at home, monitoring drug quantities, and properly concealing and disposing of old or unused medicines in the trash. SAMHSA also piloted a public education program called SMART Rx in which participating pharmacies inform customers about controlled substances when they fill prescriptions. The information provided covers the risks and dangers associated with the opioid or benzodiazepine medication, steps to keep the medication from adolescents, and safe disposal of unused medications. SAMHSA reported that evaluations suggested that consumers found the content useful and kept the information for future reference or shared it with someone else.

DEA and FDA Have Taken Steps to Improve the Safety of Using Methadone

Both DEA and FDA have taken steps to improve the safety of using methadone. DEA officials told us that the agency formed a methadone mortality working group in 2006 to review information related to the increases in methadone-associated overdose deaths, including DEA methadone distribution data and data from other federal agencies, such as FDA and CDC. The data showed that methadone 40 mg diskettes had been increasingly prescribed for pain, despite only being FDA approved for addiction treatment in OTPs—a practice described as off-label prescribing.⁵¹ Some experts said that if prescribed for pain to a person without a tolerance to opioid drugs, an initial dose of 40 mg could potentially be deadly. DEA data show that distribution of the methadone 40 mg diskettes to retail pharmacies increased almost sixfold from about 350,000 grams in 2002 to about 2 million grams in 2007. At the same time, distribution to OTPs fell slightly from about 1.4 million grams to 1.2 million grams. Following their review, DEA officials told us that they became concerned about the diskette's increased use for pain management. DEA then worked with methadone manufacturers, which agreed to voluntarily restrict distribution of the diskettes to only OTPs and hospitals. Because the restriction began January 1, 2008, it is too soon to determine any effect on methadone-associated overdose deaths. DEA reported that it would continue monitoring methadone distribution and prescription data to evaluate the impact of the initiative.

In November 2006, FDA approved a revised label for methadone 5 mg and 10 mg tablets that included new safety information regarding using methadone for pain, such as warnings about life-threatening adverse events and modified dosage instructions. The revised label states that methadone can cause slow or shallow breathing and dangerous changes in heartbeat that may not be felt by the patient. The new dosage instructions for methadone prescribed for pain state that the usual initial dose should be 2.5 mg to 10 mg taken every 8 to 12 hours, or a maximum daily dose of 30 mg, slowly adjusted for effect. The previous instructions allowed initial total daily doses up to 80 mg a day, which several experts said could be hazardous or even deadly. As FDA approved the revised methadone label, it also issued a public health advisory for health care professionals and patients, stating that prescribing methadone is complex and that it should only be prescribed for patients with moderate to severe pain when their pain is not improved with other non-narcotic pain relievers. The advisory

⁵¹According to FDA, the prescribing of a drug product for an off-label use by a physician in the course of the practice of medicine is not a violation of federal requirements.

noted that FDA had received reports of life-threatening side effects and death in patients taking methadone, both those newly starting methadone for pain control and those who have switched to methadone after being treated for pain with other strong narcotic pain relievers.

Additionally, in February 2009, FDA sent letters to manufacturers of certain opioid drugs, including methadone, indicating that these drugs will be required to have a Risk Evaluation and Mitigation Strategy to ensure that the benefits of the drugs continue to outweigh the risks. In the first of a series of meetings, FDA invited those companies that market the affected opioid drugs to a meeting with the agency in March to discuss strategy development. Additional steps will include discussions with other federal agencies, patient and consumer advocates, representatives of the pain and addiction treatment communities, health care professionals, and other interested parties. FDA is planning a public meeting in late spring or early summer to allow for broader public input and participation in this process.

States May Monitor Prescriptions for Controlled Substances and OTP Patient Enrollment to Prevent Abuse and Diversion

States may monitor prescriptions for controlled substances and OTP patient enrollment to prevent abuse and diversion. Prescription drug monitoring programs facilitate the collection, analysis, and reporting of information about the prescribing, dispensing, and use of controlled substances such as methadone. DEA reported that as of February 2009, 31 states had operational prescription drug monitoring programs to help prevent abuse and diversion of controlled substances, including methadone, and 4 of the 5 states we reviewed had operational programs. These programs may provide information to practitioners on patients and to other entities, such as licensing boards, on prescribing and dispensing practices of practitioners, or state law enforcement and regulatory agencies, to assist in identifying and investigating activities potentially related to the illegal prescribing, dispensing, and procuring of controlled substances. According to the Alliance of States with Prescription Monitoring Programs, states have found that these programs are among the most effective tools to identify and prevent drug diversion at the practitioner, pharmacy, and patient levels. CDC officials told us that they have a study under way to evaluate the impact of state prescription drug monitoring programs on drug overdose deaths.

Prescription drug monitoring programs may vary in ways such as what data must be submitted and who has access to the information. For example, with respect to access to prescription monitoring data, West Virginia allows authorized agents of the state police and federal law

enforcement agencies to have access to prescription monitoring data. In contrast, in Maine, access by law enforcement is more limited as law enforcement officials can access prescription monitoring data only by grand jury subpoena for cases they are currently investigating. See appendix IV for a comparison of some of the characteristics of the four prescription drug monitoring programs we reviewed.⁵²

However, prescription drug monitoring programs have limitations. Their usefulness depends on practitioners using the programs, and in the four states we reviewed with prescription drug monitoring programs, practitioners' use was not widespread, according to state officials. In addition, not every state has a prescription drug monitoring program, and state officials we spoke with said that people would sometimes cross state borders to obtain prescription drugs in a state without a program. Furthermore, while DEA reports that several states' programs have the capability of generating reports on out-of-state prescribers or patients, they do not routinely disseminate this information to other states.⁵³ Another limitation of prescription drug monitoring programs mentioned by state officials was the lack of patient data on methadone dispensed in OTPs and from federal facilities such as Department of Veterans Affairs' hospitals or Indian Health Service facilities. Therefore, in the four states we reviewed with a prescription drug monitoring program, data on any prescription drugs received by patients at these types of facilities would not be captured by the program.

States may also create systems to monitor the population of patients enrolled in OTPs. To monitor their patients, OTPs in Florida created a central registry designed to ensure that patients do not enroll in multiple OTPs within the state, thus preventing patients from receiving unsafe levels of methadone or additional methadone that could be diverted. Officials said that each OTP patient is given a unique identifier and a picture is taken and entered into the registry. All Florida OTPs, both nonprofit and for-profit, use the registry, according to state officials.

⁵²Florida does not have a prescription drug monitoring program.

⁵³DEA officials told us that states may not routinely disseminate information to other states due to concerns such as patient privacy, or technical difficulties in sharing data between different data systems.

Agency Comments

We provided a draft of this report to HHS and the Department of Justice for their review. We received general comments from HHS. (See app. V.) HHS provided clarification that in 1947 when federal law only required that new drugs be shown to be safe, FDA approved methadone as safe for pain management. When the law was amended in 1962 to impose additional requirements for the approval of new drugs, FDA retrospectively reviewed the efficacy of methadone for the treatment of pain. In addition, HHS stated that an attempt by FDA to restrict the distribution of methadone for pain was struck down by a court in the 1970s. HHS also reiterated that FDA recently sent letters to the manufacturers of certain opioid drug products, including methadone, indicating that these drugs will be required to have a Risk Evaluation and Mitigation Strategy to ensure that the benefits of the drug continue to outweigh the risks. Both HHS and the Department of Justice provided technical comments on a draft of this report, which we incorporated as appropriate.

As agreed with your offices, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies to the Acting Secretary of Health and Human Services, the Attorney General, and others. The report also will be available at no charge on GAO's Web site at <http://www.gao.gov>.

If you or your staffs have any questions about this report, please contact me at (202) 512-7114 or kingk@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made major contributions to this report are listed in appendix VI.



Kathleen King
Director, Health Care

Appendix I: Scope and Methodology

To examine the regulation of methadone for pain management and addiction treatment, we reviewed relevant codified federal statutes and regulations pertaining to the prescribing, administering, or dispensing of methadone for pain management and addiction treatment. Our review was limited to relevant provisions of the Controlled Substances Act and implementing regulations, including Department of Justice, Drug Enforcement Administration (DEA), and Substance Abuse and Mental Health Services Administration (SAMHSA) regulations. We also examined federal case law and relevant federal agency policies, including DEA's policy statement on dispensing controlled substances for the treatment of pain. We interviewed officials at relevant federal agencies, including SAMHSA and DEA. We also interviewed officials and reviewed information from relevant national associations, including the Federation of State Medical Boards.

In addition, we interviewed officials and examined relevant codified statutes and regulations in five selected states. The states we reviewed were Florida, Kentucky, Maine, New Mexico, and West Virginia. Each of the states met four or more of the following criteria:

- a top 10 rate of increase in methadone-associated overdose deaths from 1999 through 2004,¹
- a top 10 number of methadone-associated overdose deaths per 1,000,000 people in 2004,
- a state or district medical examiner system,²
- an operational prescription drug monitoring program,³ and

¹When we made our state selection for this study and interviewed officials and collected data from these states, 2004 Centers for Disease Control and Prevention data on methadone-associated overdose deaths were the most current available; however, 2005 data have since been published.

²We selected this criterion because these medical examiners would be likely to have access to all the death records for the entire state. Therefore, a broad perspective on what is occurring with methadone-associated overdoses in the state is more likely.

³We selected this criterion because prescription drug monitoring programs have been cited as a tool to prevent methadone abuse and diversion. In addition, if a state has an operational prescription drug monitoring program, researchers can often determine whether someone who died from a methadone overdose had a prescription.

- state-focused, methadone-specific research.

We examined how the prescribing, administering, or dispensing of methadone for pain management and addiction treatment were regulated in our five selected states. We only examined codified state statutes and regulations containing requirements relating to the administering or dispensing of methadone in opioid treatment programs (OTP) and the prescribing, administering, or dispensing of controlled substances to individuals for medical purposes, including pain management.⁴ In each state we interviewed officials from the state agency with oversight of OTPs, state boards of medicine and pharmacy, and law enforcement officials. The findings from our review of these five states cannot be generalized to all states.

To determine the factors contributing to the increase in methadone-associated overdose deaths in recent years, we interviewed officials from the Centers for Disease Control and Prevention (CDC), DEA, the Food and Drug Administration (FDA), the National Drug Intelligence Center (NDIC), the National Institutes of Health, the Office of National Drug Control Policy (ONDCP), and SAMHSA. We also interviewed professional association officials from the American Association for the Treatment of Opioid Dependence, the Federation of State Medical Boards, HARMD (Helping America Reduce Methadone Deaths), the National Alliance of Methadone Advocates, the National Association of Boards of Pharmacy, the National Association of Medical Examiners, the National Association of State Alcohol and Drug Abuse Directors, and the National Association of State Controlled Substances Authorities. In addition, we interviewed pain management, addiction treatment, and forensic science experts.

We reviewed national reports, including reports based on the 2003 SAMHSA Methadone Mortality Assessment and 2007 Reassessment and a November 2007 NDIC report on methadone mortality. We reviewed CDC methadone poisoning death data from the National Vital Statistics System, which tabulates information reported on death certificates. We interviewed CDC officials to obtain information about the reliability of their methadone mortality data, including how CDC ensures the quality of the data and any data limitations. In addition, we interviewed officials in

⁴For purposes of this report, OTPs refers to when practitioners dispense and administer narcotic drugs for maintenance or detoxification treatment, which also may be known as narcotic treatment programs.

our five selected states' medical examiners' offices about the factors contributing to the increase in methadone-associated overdose deaths in their states. We also reviewed state data and studies from our five selected states and interviewed researchers about their efforts to investigate methadone-associated overdose deaths in their states. However, because there is no standard definition for what constitutes a methadone-associated overdose death, there may be some variation in how states define this term and how they report these numbers. For example, data from Florida distinguish whether methadone was simply present or was the cause of death, but not all states make this distinction. Defining methadone's role in a death can also be complicated by inconsistencies in determining and reporting causes of death, by the presence of other drugs, and by the absence of information about the source of methadone and the deceased person's level of opioid tolerance. Results from these five state studies cannot be generalized to other states.

We reviewed relevant DEA data, including Automation of Reports and Consolidated Orders System (ARCOS) data, DEA National Forensic Laboratory Information System (NFLIS) data, and DEA Theft and Loss data.

- ARCOS is an automated drug reporting system that monitors the flow of DEA controlled substances from the point of manufacture through commercial distribution channels to the point of retail sale or distribution, including hospitals, retail pharmacies, practitioners, midlevel practitioners, and teaching institutions. ARCOS summarizes these transactions into reports, which give federal and state government investigators information that can then be used to identify the diversion of controlled substances into illicit channels of distribution.
- NFLIS systematically collects results from solid dosage drug analyses conducted by state and local forensic labs across the country. NFLIS provides information for monitoring and understanding drug abuse and trafficking involving both controlled and noncontrolled substances in the United States, including the diversion of legally manufactured drugs into illegal markets. As of March 2007, 44 state lab systems and 94 local lab systems, comprising 274 individual labs, were participating. Because NFLIS is a voluntary reporting system and the number of participating state and local laboratories has changed over time, DEA officials recommended that we report the NFLIS national estimates of analyzed drug items, instead of the actual numbers, to show trends over time, which they said would not be affected by the number of labs participating each year. DEA's national estimates are calculated every year based on a

national sample model of state and local laboratories. DEA officials told us they began producing national estimates in 2001.

- DEA's Theft and Loss database collects data on theft and loss of controlled substances by number of thefts; drug and dosage forms; business type, including pharmacies, hospitals, and manufacturers; and type of theft, such as night break-in or armed robbery. DEA registrants are required to report theft and loss of controlled substances to DEA. Although the database contains information on the forms of controlled substances lost or stolen, DEA officials told us there is no standard liquid dosage unit that would allow us to provide the total volume of liquid methadone stolen; therefore, we did not report thefts by form of methadone.

We interviewed DEA officials to learn about data collection; quality control, such as edit checks; and any limitations of these databases. We determined that these three sources of data were sufficiently reliable for use in this report, and included any limitations identified.

To determine steps taken to prevent methadone-associated overdose deaths, we interviewed officials at relevant federal agencies, including CDC, DEA, FDA, ONDCP, and SAMHSA. We also interviewed officials from relevant national associations, including the Federation of State Medical Boards, National Association of Medical Examiners, and National Association of State Controlled Substances Authorities, and experts in pain management, addiction treatment, and forensic science. In addition, we reviewed relevant studies and reports about efforts to prevent methadone and other prescription drug overdose deaths and interviewed officials in our five selected states to learn about initiatives in their states. To obtain additional information about prescription drug monitoring initiatives, we examined relevant codified statutes and regulations in our five selected states. We only reviewed codified state statutes or regulations relating to systems that monitor the prescribing of controlled substances. The findings from our review of these five states cannot be generalized to all states.

Because many efforts under way to prevent methadone-associated overdose deaths are new, their effectiveness has not yet been evaluated. Also, because we interviewed experts, officials from select organizations, and state officials, our findings do not represent all efforts to prevent these deaths. Finally, because methadone is part of a larger problem of prescription drug abuse and overdose deaths, many of the efforts are not focused on methadone alone.

We conducted our work from November 2007 through February 2009 in accordance with all sections of GAO's Quality Assurance Framework that are relevant to our objectives. The framework requires that we plan and perform the engagement to obtain sufficient and appropriate evidence to meet our stated objectives and to discuss any limitations in our work. We believe that the information and data obtained, and the analysis conducted, provide a reasonable basis for any findings and conclusions.

Appendix II: Comparison of Federal and Selected States' OTP Regulations

The following table describes selected requirements of the federal OTP regulations, as well as selected requirements of the OTP regulations in Florida, Kentucky, Maine, New Mexico, and West Virginia.¹

¹For purposes of this table, we refer to federal and state programs when practitioners dispense and administer methadone for maintenance or detoxification treatment as OTPs. However, Florida designates these programs as medication and methadone maintenance treatment and New Mexico designates these programs as narcotic treatment programs.

Appendix II: Comparison of Federal and Selected States' OTP Regulations

	Federal	Florida	Kentucky	Maine	New Mexico	West Virginia^a
Authority	42 C.F.R. pts. 2, 8	Fla. Admin. Code Ann. §§ 65D-30.004, 30.014	908 Ky. Admin. Regs. § 1:340	Code Me. R. 14-188 Ch. 5 §§ 1–19	N.M. Admin. Code tit. 7, § 32.8	W. Va. Code St. R. §§ 64-90-1 – 64-90-47
Dosing ^b	<p>-Oral form only; must be formulated so as to reduce its potential for parenteral abuse. (§ 8.12(h)(3)(i))</p> <p>-For each new patient, initial dose shall not exceed 30 mg and the total dose for the first day shall not exceed 40 mg unless the program physician documents in the patient's record that 40 mg did not work. (§ 8.12(h)(3)(ii))</p>	<p>Before a client receives an initial dose of methadone or other medication, physician must document current physiological addiction, history of addiction and exemptions from criteria for admission. (§ 65D-30.014(4)(e)(1))</p>	<p>-Dose means a 1-day quantity of an approved controlled substance, administered on site, in not less than 1 fluid ounce of an oral solution, formulated to minimize misuse by injection. (1:340.1(7))</p> <p>-Proposed programs must include in their applications initial and daily dosage levels and daily dosage levels. (1:340.4(3)(x), (y))</p> <p>-Medical record must indicate reason for dose changes and must be signed by the medical director or program physician. (1:340.6(5))</p>	<p>Initial doses of methadone must not exceed 30 mg unless the physician documents the need for a higher dose. (§ 19.8.6.5)</p>	<p>-Initial dose must not exceed 30 mg.</p> <p>-If 30 mg does not reduce withdrawal symptoms, may provide additional 10 mg only if documented.</p> <p>-If 40 mg does not reduce withdrawal symptoms, may provide additional dose only if documented.</p> <p>-Subsequent doses are based on the patient's needs. (§ 7.32.8.21(D))</p>	<p>-The initial full-day dose of medication shall be based on the physician's evaluation of the history and condition of the patient.</p> <p>-Usual initial dose of methadone should be 20 to 30 mg. Reasons for exceeding an initial dose of 30 mg must be documented.</p> <p>-Initial dose should not exceed 40 mg unless physician or prescribing professional documents that symptoms were not suppressed after a 3-hour period of observation.</p> <p>-Justification for daily doses above 100 mg must be documented. (§ 64-90-35)</p>
Take home conditions	<p>Decision made by medical director who must consider the following criteria:</p> <p>-Absence of recent drug abuse, including alcohol abuse.</p>	<p>Permitted only for clients participating in a methadone maintenance regimen under following conditions:</p> <p>-No evidence of recent drug abuse.</p>	<p>Conditions for entering each of the phases:</p> <p>-Phase 1: No program infractions for 90 consecutive days.</p> <p>-Phase 2: No program</p>	<p>-Results of drug tests must be reviewed and considered as part of the treatment planning process and decisions for take-home</p>	<p>Decision to be made by program medical director based on the following criteria:</p> <p>-Absence of recent drug abuse, including alcohol abuse.</p>	<p>Must consider the following criteria in determining patient eligibility:</p> <p>-Cessation of illicit drug use.</p> <p>-Regularity of program attendance.</p>

Appendix II: Comparison of Federal and Selected States' OTP Regulations

Federal	Florida	Kentucky	Maine	New Mexico	West Virginia^a
<ul style="list-style-type: none"> -Regularity of clinic attendance. -Absence of serious behavioral problems at the clinic. -Absence of known recent criminal activity. -Stability of patient's home environment and social relationships. -Length of time in comprehensive maintenance treatment. -Assurances of safe storage at patient's home. -Rehabilitative benefit outweighs the potential risks of diversion. (§ 8.12(i)(2)) 	<ul style="list-style-type: none"> -Regular attendance at OTP. -No serious behavioral problems at the OTP. -No recent criminal activity. -Stable home environment and social relationships. -Sufficient length of time in treatment. -Assurances that take-home medication can be stored safely. -Satisfactory progress in treatment to warrant decreasing the frequency of attendance. -Verifiable source of legitimate income. (§ 65D-30.014(5)(d)) 	<ul style="list-style-type: none"> infractions for 180 consecutive days; pursuing one of the following: gainful employment, vocational training, higher education, volunteer opportunities, or parenting classes if a stay-at-home parent. -Phase 3: No program infractions for 270 consecutive days; same entry requirements as for phase 2. -Phase 4: Successful completion of phase 3 and adhered to program requirements for 2 consecutive years. (1:340.11) 	<ul style="list-style-type: none"> dosing. (§ 19.8.6.6) -All decisions regarding take-home privileges shall be documented in the client record and shall comply with the requirements cited in 42 C.F.R. pt. 8. (§ 19.8.10.1) 	<ul style="list-style-type: none"> -Regularity of program attendance -Length of time in comprehensive maintenance treatment. -Absence of known criminal activity. -Absence of serious behavioral problems at the program. -Special needs such as physical health needs. -Assurance that medication can be safely stored in patient's home. -Stability of patient's home environment and social relationships. -Patient's work, school, and daily activity schedule. -Hardship traveling to and from the program. -Rehabilitative benefit outweighs the potential risk of diversion. (§ 7.32.8.23(B)) 	<ul style="list-style-type: none"> -Length of time and level of treatment in medication therapy (ability to self-medicate). -Absence of recent criminal activity. -Absence of serious behavioral problems. -Absence of abuse of drugs, including excessive use of alcohol. -Other special needs of the patient, such as split dosing, physical health needs, pain treatment, etc. -Capacity to safely store take-home medication. -Stability of the home environment and social relationships. -Patient's work, school, or other daily life activity schedule. -Hardship in traveling to and from the program. Program physician may approve temporary unsupervised take-home doses for documented emergencies or other exceptional circumstances. (§ 64-90-41)

Appendix II: Comparison of Federal and Selected States' OTP Regulations

	Federal	Florida	Kentucky	Maine	New Mexico	West Virginia^a
Take-home dosing	<p>-Any patient may receive a single take-home dose for days clinic is closed. (§ 8.12(i)(1))</p> <p>-First 90 days of treatment – one single dose each week.</p> <p>-91-180 days – Two doses per week.</p> <p>-181-270 days – Three doses per week.</p> <p>-271 days to 1 year–maximum 6-day supply.</p> <p>-After 1 year of continuous treatment – 2-week supply.</p> <p>-After 2 years of continuous treatment – 1-month supply, but must make monthly visits. (§ 8.12(i)(3))</p> <p>-No medications may be dispensed to patients in short-term detoxification treatment or interim maintenance treatment for unsupervised or take-home use. (§ 8.12(i)(4))</p>	<p>-Must be available to all methadone clients during holidays, but only if clinically advisable. (§ 65D-30.014(4)(g))</p> <p>-No take-home doses permitted during the first 30 days in treatment unless approved by the state authority.</p> <p>-Clients in continuous treatment may qualify with negative drug screens as follows:</p> <p>-Phase I: Days 31-90 – one take-home dose per week.</p> <p>-Phase II: Days 91-180 – two take-home doses per week.</p> <p>-Phase III: Days 181-1 year – three take-home doses per week with no more than a 2-day supply at any one time.</p> <p>-Phase IV: After 1 year – four take-home doses per week with no more than a 2-day supply at a time.</p> <p>-Phase V: After 2 years – five take-home doses per week with no more than a 3-day supply at a time.</p>	<p>-Days 1-90: No take-home doses.</p> <p>-Phase 1: One take-home dose per week.</p> <p>-Phase 2 and 3: Up to two take-home doses per week.</p> <p>-Phase 4: Up to three take-home doses per week.</p> <p>-Under emergency conditions, a program may issue 14 consecutive days of take-home doses without notification of Center for Substance Abuse Treatment (CSAT); must notify state narcotic authority and request an exception to dosing procedures.</p> <p>-Medical director or program physician may grant an exception, subject to written approval from state narcotic authority for clients with serious physical disabilities or subject to exceptional hardship.</p>	<p>-Take-home methadone shall be dispensed in liquid form only in single dose containers, or in dry form only in multiple dose containers.</p> <p>-No take-home privileges during the first 90 continuous days of treatment.</p> <p>-91-180 days: One take-home dose per week.</p> <p>-181-270 days: Two take-home doses per week.</p> <p>-271-360 days: Three take-home doses per week.</p> <p>-361 days onward: Six take-home doses per week. (§ 19.8.10)</p> <p>-Certain exceptions for emergencies. (§ 19.8.12)</p>	<p>-A patient in comprehensive maintenance treatment may receive a single dose of take-home medication for each day that a provider is closed.</p> <p>-During the first 90 days, One take-home dose per week maximum.</p> <p>-91-180 days: Two take-home doses per week maximum.</p> <p>-181-270 days: Three take-home doses per week maximum.</p> <p>-For the remaining months of the year, 6 days of medication maximum per week.</p> <p>-After 1 year of continuous treatment, maximum 2-week take-home supply.</p> <p>-After 2 years, maximum of 1-month take-home supply, but must make monthly visits.</p> <p>-Exceptions made only as provided by federal OTP regulations and as approved by the state methadone</p>	<p>-For the first 90 days of treatment: A single take-home dose for the week of each holiday that the clinic is closed.</p> <p>-First 30 days of treatment: No take-home doses except the holiday dose.</p> <p>-31-90 days: One take-home dose per week plus the holiday dose.</p> <p>-91-180 days: Two take-home doses per week.</p> <p>-181-270 days: Three take-home doses per week.</p> <p>-Remainder of the first year: Maximum 6-day supply.</p> <p>-Second year of treatment: Maximum 13-day supply.</p> <p>-After 2 years of continuous treatment: Maximum 1-month supply with monthly visits.</p> <p>-State authority may approve exceptional unsupervised doses on a case-by-case basis if the program physician applies. (§ 64-90-41.6, 41.7)</p>

Appendix II: Comparison of Federal and Selected States' OTP Regulations

	Federal	Florida	Kentucky	Maine	New Mexico	West Virginia^a
		-Phase VI: After 3 years in treatment – six take-home doses per week. (§ 65D-30.014(5)(e))	-State narcotic authority may grant additional exceptions for medical emergency or natural disaster. (1:340.11, 1:340.16)		authority. (§ 7.32.8.23(C), (D))	
Hours of operation	No requirements specified.	-Must be open Monday through Saturday. -Must have medicating hours and counseling hours that accommodate clients, including 2 hours of medicating time daily outside of 9:00 a.m. to 5:00 p.m. -Must medicate on Sundays according to client needs. -Must give a minimum of a 7-day notice for observed holidays. -No two holidays can occur in immediate succession unless provider is granted an exemption by the federal authority. -On days when provider is closed, services must be accessible to clients for whom take-out methadone is not clinically advisable. (§ 65D-30.014(4)(g))	Must be open 7 days a week with the optional exception of nine specified holidays. (1:340.6(16))	Must be open 7 days weekly, including all holidays. (§ 19.8.4.2)	Must be open every day of the week except for federal and state holidays, and Sundays, and be closed only as allowed in advance in writing by CSAT and the state methadone authority. (§ 7.32.8.18(C))	-Must provide 24-hour, 7-day a week access to designated program staff so that patient emergencies may be addressed and dosage levels verified. (§ 64-90-20.1.c) -Must be open 7 days per week, but may close for eight holidays and two training days per year. (§ 64-90-41.6.a)

Appendix II: Comparison of Federal and Selected States' OTP Regulations

	Federal	Florida	Kentucky	Maine	New Mexico	West Virginia^a
Recordkeeping (for purposes of enrollment in other OTPs)	<p>Must document that OTP made a good faith effort to determine if patient is enrolled in any other OTP. (§ 8.12(g)(2))</p> <p>May disclose patient records to a central registry or to any detoxification or maintenance treatment program not more than 200 miles away for the purpose of preventing the multiple enrollment of a patient only if specified conditions are met:</p> <ul style="list-style-type: none"> -when disclosure is allowed, -what information may be disclosed, and -written patient consent.(§ 2.34) 	<p>-Must participate in regional registry activities for the purpose of sharing client identifying information with other providers located within a 100-mile radius, to prevent the multiple enrollment of clients at more than one provider.</p> <p>-A record of violations by individual clients shall become part of the record maintained in an automated system that may be accessed by all participating providers. (§ 65D-30.014(4)(f)(1), (7))</p>	<p>Proposed programs must include in their applications a system to prevent client's multiple program registration. (1:340.4(3)(k))</p>	<p>Prior to admitting a client, must confirm using the Office of Substance Abuse's system that client is not currently enrolled in another OTP. If system is unavailable, must check with all OTPs within 3 calendar days of admission. (§ 19.8.4.4-5)</p>	<p>-Must make and document good faith efforts to determine that a patient seeking admission is not receiving opioid dependency treatment medication from any other source, within the bounds of all applicable patient confidentiality laws and regulations.</p> <p>-Must confirm that the patient is not receiving treatment from any other OTP, except under exceptional circumstances, within a 50-mile radius of its location, by contacting any such program or by using the central registry, when established.</p> <p>-The Department of Health may establish an Internet-based registry of all current patients of a New Mexico OTP for the purpose of creating a system that prevents patients from receiving medication from more than one OTP. Each OTP as a condition of</p>	<p>-Must have a procedure for ensuring that patients are not enrolled in more than one OTP.</p> <p>-When practicable, must obtain a release of information from the patient in order to check the records by telephone or fax of every OTP within 100 miles to ensure that the patient is not currently enrolled in other programs.</p> <p>-The release must state that only prior admissions may be the subject of inquiry, not contacts without admission.</p> <p>-Results of the check must be placed in the clinical record.</p> <p>-The check shall be duplicated if the patient is discharged and readmitted at any time. (§ 64-90-30)</p>

Appendix II: Comparison of Federal and Selected States' OTP Regulations

Federal	Florida	Kentucky	Maine	New Mexico	West Virginia ^a
				approval to operate shall participate in the central registry as directed by the Department of Health. (§ 7.32.8.19(F), (G))	

Source: GAO analysis of federal OTP regulations and selected requirements of OTP regulations in Florida, Kentucky, Maine, New Mexico, and West Virginia.

^aWest Virginia has adopted 42 C.F.R. pt. 8 in its entirety by reference and provides that to the extent there is a conflict between federal regulations or standards and the standards set forth in this rule, the more stringent standard applies. W. Va. Code St. R. § 64-90-2.3.

^bDosing refers to standards for doses of methadone.

Appendix III: Data and Research regarding Methadone-Associated Overdose Deaths in Five States

The following information on methadone-associated overdose deaths in Florida, Kentucky, Maine, New Mexico, and West Virginia was taken from data and research in these states.

State	Years studied	Number of methadone-associated overdose deaths	Decedent characteristics	Drugs detected	Sources of methadone
Florida ^a	2007	1,095	Ages of decedents: <18: 2% 18-25: 21% 26-34: 23% 35-50: 38% >50: 17% n=785 ^b	Methadone only: 11% Drugs in combination with methadone: 89% n=1,095	No data available
Kentucky ^c	2000-2004	176 ^d	Caucasian: 100% Male: 60% Mean age: 38 years	Methadone only: 6% Drugs in combination with methadone:^e Antidepressants: 40% Benzodiazepines: 32% Additional opioids: 28%	Private physician: 48% Illicit means: 20% OTP: 10% Unknown: 22% n=95 ^f
Maine ^g	1997-2002	88 ^h	All drug-related deaths: Caucasian: 96% Male: 62% Mean age: 40 years Other known health conditions: Mental illness: 55% Drug abuse: 50%	Methadone deaths: Methadone primary or secondary causal factor: 88% Methadone a significant contributing factor: 12% n=66 ⁱ	Limited data available
New Mexico ^j	1998-2002	143 ^k	White non-Hispanic: 55% Male: 75% Median age: 40 years Other known health conditions: Mental illness: 24% Drug abuse: 25%	Methadone only: 22% Drugs in combination with methadone:^e Prescription drugs (no illicit drugs): 24% Illicit drugs: 50%	Methadone maintenance treatment: 39% Prescription for chronic pain: 34% Prescription for unknown reason: 13% Diversion: 14% n=79 ^l

**Appendix III: Data and Research regarding
Methadone-Associated Overdose Deaths in
Five States**

State	Years studied	Number of methadone-associated overdose deaths	Decedent characteristics	Drugs detected	Sources of methadone
West Virginia ^l	2006	112 ^m	All drug-related deaths:ⁿ Male: 67% Mean age: 39 years Substance abuse indicators, all drug-related deaths:ⁿ History of substance abuse: 78% Used diverted pharmaceuticals: 63% Doctor shopped (Five or more prescribing clinicians in the year before death): 21%	Methadone only: 26% Drugs in combination with methadone:^e Other prescription drugs: 63% Illicit drugs: 13% Alcohol: 10%	Diversion: 68% Prescription: 21% OTP: 11%

Source: GAO summary of data and research from Florida, Maine, and published manuscripts.

Note: Percentages may not total 100 percent because of rounding.

^aFlorida Department of Law Enforcement, Medical Examiners Commission, *Drugs Identified in Deceased Persons by Florida Medical Examiners: 2007 Report* (June 2008).

^bOf the total 1,095 deaths, methadone was determined to be the cause of death in 785 cases.

^cL.B.E. Shields et al., "Methadone Toxicity Fatalities: A Review of Medical Examiner Cases in a Large Metropolitan Area," *Journal of Forensic Sciences*, vol. 52, no. 6 (2007).

^dDeaths ascribed to methadone toxicity by the state of Kentucky's Office of the Chief Medical Examiner.

^eMany overdose deaths were found to have several drugs present; therefore, these percentages should not be totaled.

^fNumber of methadone-associated overdose deaths for which information was available about the source of methadone.

^gMarcella H. Sorg and Margaret Greenwald, *Maine Drug-Related Mortality Patterns: 1997-2002*, a special report prepared in cooperation with the Maine Office of the Attorney General and Maine Office of Substance Abuse, December 2002.

^hMedical examiner cases in which a drug or toxic substance caused the death; specifically, deaths in which methadone was found in toxicology results.

ⁱMethadone-associated overdose deaths in which methadone was listed on the death certificate.

^jN. Shah, S. L. Lathrop, and M. G. Landen, "Unintentional Methadone-Related Overdose Death in New Mexico (USA) and Implications for Surveillance, 1998–2002," *Addiction*, vol. 100, no. 2 (2005).

^kUnintentional drug overdose deaths in which methadone was cited as a cause of death, alone or in combination with another drug.

^lA. J. Hall et al., "Patterns of Abuse Among Unintentional Pharmaceutical Overdose Fatalities," *JAMA*, vol. 300, no. 22 (2008).

^mUnintentional drug overdose deaths for which an autopsy was performed that determined that methadone contributed to the death.

ⁿThis research was focused more broadly on overdose deaths rather than methadone alone; therefore, the decedent characteristic statistics apply to all drug overdose deaths studied.

Appendix IV: Comparison of Prescription Drug Monitoring Programs in Four Selected States

Program information	Kentucky	Maine	New Mexico	West Virginia
Name of program	Kentucky All-Schedule Prescription Electronic Reporting System (KASPER)	Controlled Substances Prescription Monitoring Program	Controlled Substance Prescription Monitoring Program	West Virginia Controlled Substances Monitoring Program
Year established ^a	1998	2003	2004	2002 ^b
Oversight agency	Drug Enforcement and Professional Practices Branch, Office of Inspector General, Cabinet for Health and Family Services	Office of Substance Abuse, Department of Health and Human Services	Board of Pharmacy	Board of Pharmacy
Controlled substances covered	Schedule II, III, IV, and V	Schedule II, III, and IV	Schedule II, III, and IV	Schedule II, III, and IV
Who must provide information	Authorized dispensers of controlled substances Includes dispensers located outside Kentucky but authorized by Kentucky's Board of Pharmacy to dispense controlled substances ^c	Individuals authorized to dispense or administer controlled substances	Authorized dispensers Does not include licensed hospital pharmacies that distribute controlled substances for inpatient hospital care	Individuals authorized to dispense or administer controlled substances ^d Includes pharmacists or pharmacies located outside the state but licensed by the Board of Pharmacy for delivery to a person residing in the state
Who may have access	Practitioners or pharmacists for current patients Board representatives involved in a specific investigation of licensees who are authorized to prescribe, administer, or dispense controlled substances Kentucky boards of medical licensure and nursing, regarding reviews of improper prescribing practices related to geographic area or business relationship State Medicaid program for a Medicaid recipient or provider Certified peace officer engaged in a specific investigation	Prescribers for current patients Pharmacists for customers filling prescriptions Patients Board representatives for an investigation of a licensed prescriber with reasonable cause Office personnel or personnel of any vendor or contractor, to establish and maintain the program's electronic system For public research purposes if identifying information has been removed Law enforcement for limited purposes ^e	Authorized prescribers and dispensers Patients Boards for licensees Professional licensing authorities of other states if their licensees practice in the state or prescriptions issued by their licensees are dispensed in the state State Medicaid program Public or private entities for research purposes, without identifying information Pharmacy board for oversight of this program Law enforcement or prosecutorial officials	Prescribing practitioners and pharmacists ^g Inspectors and agents of the Board of Pharmacy Authorized agents of licensing boards of practitioners in West Virginia and other states Authorized agents of the Bureau for Medical Services and the Workers' Compensation Commission Any person engaged in receiving, processing, or storing the information received by the central repository For educational, scholarly, or statistical purposes, without identifying information

**Appendix IV: Comparison of Prescription
Drug Monitoring Programs in Four Selected
States**

Program information	Kentucky	Maine	New Mexico	West Virginia
	Grand jury pursuant to a subpoena		engaged in an ongoing investigation	Authorized members of the state police
	Judge or probation or parole officer regarding a criminal defendant eligible for a court-ordered drug addiction program		Courts under grand jury subpoena or criminal court order	Authorized local and federal law enforcement agents who are members of a drug task force
	Civil actions and criminal proceedings ^e			Persons with a court order or administrative subpoena
	Another state program via reciprocal agreement			
Authorities	Ky. Rev. Stat. Ann. §§ 218A.202; 218A.245; 902 Ky. Admin. Regs. 55:110	Me. Rev. Stat. Ann. Tit. 22, §§ 7245-7252; 14-118 Code Me. R. ch. 11, §§ 1–9	N.M. Stat. Ann. § 30-31-16; N.M. Admin. Code tit. 16, §§ 19.29.1–13	W. Va. Code Ann. §§ 60A-9-1 -60A-9-7; W. Va. Code St. R. §§ 15-8-1 – 15-8-7

Source: GAO analysis of state prescription drug monitoring program laws and regulations in Kentucky, Maine, New Mexico, and West Virginia.

Note: GAO selected five states to review for this study: Florida, Kentucky, Maine, New Mexico, and West Virginia. However, Florida does not have a prescription monitoring program.

^aThis references the effective year of the state law or regulation that provided the authority to establish the state’s prescription drug monitoring program.

^bWest Virginia first established a monitoring program in 1995. The current version of the program dates to 2002.

^cIn Kentucky, reporting is not required for drugs administered directly to patients or drugs dispensed by practitioners at licensed facilities if the quantity dispensed is limited to an amount adequate for 48 hours of treatment.

^dIn West Virginia, reporting is not required for a drug administered directly to a patient or dispensed by a practitioner at a state-licensed facility, provided that the quantity dispensed is limited to an amount adequate for up to 72 hours with no more than two 72-hour cycles in any 15-day period.

^eA Kentucky court recently determined that the state law prohibiting disclosure of KASPER data for purposes of a civil action was unconstitutional and therefore cannot be enforced. The court further determined that such disclosures can be made for civil actions if a court conducts a review prior to requiring disclosure. *See Commonwealth, Cabinet for Health & Family Services v. Chauvin*, No. 2008-CA-000027-OA, 2008 WL 2388671 (Ky. Ct. App. June 13, 2008). A Kentucky court also recently determined that a criminal defendant had the right to obtain KASPER data for discovery purposes during a criminal proceeding. The court found that the defendant’s right to due and compulsory process took precedence over any limitations in access authority under state law. *See Commonwealth, Cabinet for Health & Family Services v. Bartlett*, No. 2008-CA-000046-OA, 2008 WL 2388690 (Ky. Ct. App. June 13, 2008).

^fAccording to a Maine official, law enforcement officials also have access to prescription monitoring data, but only by grand jury subpoena for cases they are currently investigating.

^gIn West Virginia, information released must be related to a specific patient for the purpose of providing treatment or a specific individual or entity under investigation by any party that has access. Prescribing practitioners may also request data related to their federal registration for controlled substances.

Appendix V: Comments from the Department of Health and Human Services



DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

MAR 30 2009

Kathleen King
Director, Health Care
U.S. Government Accountability Office
441 G Street, NW
Washington, DC 20548

Dear Ms. King:

Enclosed are the Department's comments on the U.S. Government Accountability Office's (GAO) draft report entitled: "METHADONE-ASSOCIATED OVERDOSE DEATHS: Factors Contributing to Increased Deaths and Efforts to Prevent Them (GAO-09-341).

The Department appreciates the opportunity to comment on this draft report before its publication.

Sincerely,

A handwritten signature in cursive script that reads "Barbara Pisaro Clark".

Barbara Pisaro Clark
Acting Assistant Secretary for Legislation

Attachment

GENERAL COMMENT FOR THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) TO THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, METHADONE-ASSOCIATED OVERDOSE DEATHS – FACTORS CONTRIBUTING TO INCREASED DEATHS AND EFFORTS TO PREVENT THEM (GAO-09-341)

In the report, GAO provides a description of options available to FDA to restrict distribution of a drug product, or to require other risk management strategies. It must be clarified that methadone was originally approved in 1947, when the prevailing laws and regulations required only that a drug be shown to be safe. Subsequently, when the law was amended in 1962 to require demonstration of efficacy, the efficacy of methadone for the treatment of pain and the appropriate labeling for the product was reviewed under the Drug Efficacy Study Implementation process, which retrospectively evaluated the efficacy of all drugs approved prior to the efficacy requirement.

When the use of methadone for the treatment of opioid dependence was approved, FDA attempted to implement restriction of distribution of methadone for pain, but this effort was struck down in court in the 1970s.

On February 6, 2009, FDA sent letters to manufacturers of certain opioid drug products, including brand name and generic drugs formulated with the active ingredient, methadone, indicating that these drugs will be required to have a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of the drugs continue to outweigh the risks. (See http://www.fda.gov/cder/drug/infopage/opioids/Opioid_Products_chart.htm) FDA has determined that a REMS is necessary to help reduce the occurrence of serious adverse events, abuse, diversion and addiction, to facilitate safe and appropriate use of these drugs. FDA has begun to hold a series of stakeholder meetings with those companies that market the affected opioid drugs to discuss REMS development. Additional steps will include discussions with other federal agencies and non-government institutions, including patient and consumer advocates, representatives of the pain and addiction treatment communities, other health care professionals and other interested parties. FDA is planning a public meeting in late spring or early summer to allow for broader public input and participation.

Appendix VI: GAO Contact and Staff Acknowledgments

GAO Contact

Kathleen King, (202) 512-7114 or kingk@gao.gov

Acknowledgments

In addition to the contact named above, key contributors to this report were Bonnie Anderson, Assistant Director; Lisa A. Lusk; Lisa Motley; Christina Ritchie; Hemi Tewarson; and Timothy Walker.

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