

Testimony on behalf of Purdue Pharma

By

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United States House of Representatives

Investigative Hearing:

To Do No Harm: Strategies for Preventing Prescription Drug Abuse

February 9, 2004
Winter Park, Florida

On behalf of Purdue Pharma, I am pleased to appear at this hearing today on strategies for preventing prescription drug abuse. I am Dr. Jack Henningfield, Professor of Behavioral Biology, Department of Psychiatry, The Johns Hopkins University School of Medicine, where I direct the Robert Wood Johnson Foundation, Innovators Combating Substance Abuse Awards Program. I am also Vice President, Research and Health Policy at Pinney Associates, a science and health policy consulting firm.

Pinney Associates is a science and health policy consulting firm specializing on issues emerging at the convergence of science, health and policy, always with a goal of contributing to the improvement of public health. In this capacity we serve many organizations and agencies, public and private, including pharmaceutical companies, large and small. These include Abbott Laboratories, Bayer, GlaxoSmithKline, Janssen, Pfizer, Purdue Pharma, Shire, and Women's Capital Corporation. Such companies seek the expertise of myself and my colleagues at Pinney associates to help to identify potential factors contributing to drug misuse, abuse, diversion, and addiction, and then to assist in the development of strategies for minimizing such unintended consequences while enabling appropriate medication use and access. Pinney Associates has assisted Purdue Pharma in its efforts to understand the factors that lead to abuse and diversion of OxyContin[®] (oxycodone HCl controlled-release) Tablets (hereinafter, "OxyContin") and similar drugs and to assist in developing more effective strategies for reducing abuse and diversion.

I was trained in behavioral science, pharmacology, and other disciplines relevant to understanding drug addiction and have been actively engaged in addiction research for more than 30 years. From 1980 to 1996, I was a scientist at the National Institute on Drug Abuse (NIDA), where I also headed the Biology of Dependence and Abuse Potential Assessment Laboratory and Clinical Pharmacology Research Branch. My studies at NIDA included assessment of a variety of prescription drugs for abuse potential and the development of treatments for addiction. I was also actively engaged in drug policy issues and public health, contributing to the first four of NIDA's Triennial Reports to Congress, serving on FDA and other governmental committees, and contributing addiction expertise to numerous reports to the Surgeon General on Smoking and Health. I have published over 300 scientific articles as well as several books and monographs pertaining to drug addiction.

I should also note that I am not a medical doctor and do not treat pain patients, rather I am here as an expert in addiction to provide information that I hope will be relevant to the consideration of policies to reduce prescription drug abuse and addiction, while ensuring access to these life saving drugs for those who need them. I have been invited by Purdue Pharma and the Subcommittee to offer my recommendations on the topic, "to do no harm: strategies for preventing prescription drug abuse." I recognize that there is a myriad of issues to address and recommendations to consider, however, my focus and recommendations will be on those pertaining to drug abuse and addiction. There are no simple solutions and in few areas of public health are the words of H.L. Mencken so apropos. He said: "*For every complex problem there is a solution that is simple, neat, and wrong.*"

Use of Terminology

Before I begin I would like to define a few of the terms that are key to my testimony, but that are often used inconsistently or inappropriately. The term “addiction” is generally used synonymously with “drug dependence,” “chemical dependence,” or “substance dependence” and refers to a chronic disease characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. See Exhibit A. In the case of opioid analgesics, that is, morphine-like pain medicines, the body will generally develop a level of “physical dependence,” such that abrupt abstinence will precipitate a ‘withdrawal syndrome,’ also called the ‘abstinence syndrome.’ Medically managed analgesic use includes strategies for gradual discontinuance, if the patient no longer needs a medicine, to avoid withdrawal. “Tolerance” describes the diminishing of some effect of a drug when a person has taken it repeatedly. In the case of opioid abuse, tolerance to the euphoria or “high” develops predictably and relative quickly, leading the abuser to consume more of the substance, or mix it with other substances, trying to achieve the same degree of euphoria. In the case of a patient taking an opioid analgesic in a proper manner, tolerance to the respiratory depression effects occurs quickly, adding a margin of safety that the occasional abuser may not have. Tolerance to the constipating effects of opioid analgesic virtually never occurs, however. Tolerance to the analgesia may occur, but clinical experience shows that what is initially thought to be tolerance to analgesia is often due to disease progression, in the case of pain from cancer, or causes other than analgesic tolerance in cases not related to cancer, such as disease progression, over-exertion in the face of deconditioning related to chronic pain, etc. In the setting of medical care, taking an opioid analgesic on a repeated basis can be expected to produce physical dependence. In the medical setting, neither physical dependence nor tolerance is synonymous with addiction.

The term “misuse” is generally employed when a drug is used to treat a symptom, but not under supervision of a health care professional. For example, a person with pain might take an extra dose of medication at bedtime hoping it will help them sleep better, or a person who did not obtain a prescription for an analgesic might use the prescribed analgesic of a spouse to self treat his or her acute back pain.

“Drug abuse” is nonmedical use of a drug, e.g., abusing a drug at a party. Abuse of opioid analgesics often leads to addiction and can be especially deadly because of the inexperience and low levels of tolerance to respiratory depression of the abusers. This risk is especially enhanced when drugs with different mechanisms of action are abused simultaneously, e.g., intoxication with alcoholic beverages followed by abuse of a prescription sedative or an opioid analgesic. The term “drug abuse” or its variant, “substance abuse” is often used as a broad umbrella term to cover both addiction and abuse, based on the notion that every active addict is, by definition, abusing drugs. Unfortunately, most national surveys provide little basis for distinguishing among these various categories of drug misuse, drug abuse and addiction. For example, misuse is generically identified as abuse (“nonmedical use”) in the National Household Survey of Drug Abuse because it does not distinguish between such medication misuse and abuse.

The term “iatrogenic addiction” to opioids is addiction that develops in a person, without a prior history of substance abuse or addiction, who is using opioids as intended for a legitimate medical purpose – that is, the treatment of pain. It should not be confused with the development of tolerance or physical dependence, as described above. The development of addiction to opioid analgesics in properly managed patients with pain has been reported to be rare. However data

are not available to establish the true incidence of addiction in chronic pain patients. This phenomenon was reviewed in detail by a special taskforce of the College on Problems of Drug Dependence (CPDD) and at an FDA advisory committee meeting that occurred this past September.¹ Both the CPDD taskforce and the FDA advisory committee noted that there is a need for study of the rates of new onset, or iatrogenic addiction among patients treated for pain, in different clinical settings, with and without histories of substance abuse.

Prescription Drug Abuse: Brief History of an Evolving Problem

Prescription drug abuse is a complex and evolving public health problem in which life saving medicines are sometimes misused, abused, or associated with addiction. The modern history of analgesic abuse and addiction in America may be traced to the introduction of the hypodermic syringe used to deliver morphine as a means of providing effective pain relief to thousands of suffering soldiers during and following the Civil War. The treatment was considered by many to be a “Godsend” to many thousands who were injured and disabled with pain. While pain relief drugs such as morphine provided much needed relief to the injured, they also had downsides. For example, a new disease emerged, referred to by some as “soldiers’ disease.” This term referred to the use of pain relieving drugs by soldiers who did not appear to need them for medical purposes, as well as those who appeared to suffer psychologically and socially from taking such medication. Of course, at that time in our history, the concept of ongoing, chronic pain was just forming in the medical literature. In fact, one of the first treatises on a family of chronic pain conditions emerged from the medical experience of Dr. Silas Weir Mitchell during and immediately following the Civil War. In this era, the presence of physical dependence or tolerance alone was equated with addiction, unlike modern thinking. Thus, the questions that have never been fully answered about “soldiers’ disease” is this: How many were addicted, how many were merely physically dependent and using the morphine to stave off the withdrawal syndrome, and how many were, in fact, suffering from unrecognized chronic pain and using the morphine in a manner that would be considered appropriate today? It is interesting in the context of today’s hearing to remind ourselves that, at that time, morphine, heroin, and other drugs could be obtained over the counter and even ordered from the Sears, Roebuck and Company.

By the early 20th century, it was recognized that certain drugs warranted more stringent control with access sufficiently restricted to reduce inappropriate use, abuse, and addiction. One piece of legislation from the early 20th century worthy of noting is the **Harrison Narcotic Act of 1914**. This legislation was a well-intended effort to allow for medical access to “narcotic drugs,” predominately derivatives of coca and opium, through regulation of their distribution and dispensing via taxation. However, within a year of passage it was evident that serious problems were emerging, including the jailing of innocent doctors, which led to reluctance to use of opioids to treat patients suffering from debilitating pain. In addition, a black market of drugs was emerging to supply the needs and desires of abusers and addicted persons.

¹ Zacny J, Bigelow G, Compton P, et al. College on Problems of Drug Dependence taskforce on prescription opioid non-medical use and abuse: Position statement. Drug and Alcohol Dependence 2003;69:215-232; Meeting of the Anesthetic and Life Support Drugs Advisory Committee, September 9-10, 2003.

From a legislative perspective, the Harrison Narcotic Act was only the beginning, but it is important to note in light of today's hearing because it illustrates the problem that we are still struggling with today – a way to ensure that people with legitimate medical needs get the medicine they deserve, while curtailing diversion, trafficking, abuse and addiction. The regulatory struggles we are faced with today in terms of finding the right balance of access and control have been with us for over a century and most likely will be with us for the foreseeable future.

The **Controlled Substances Act (CSA)**, of the Comprehensive Drug Abuse Prevention and Control Act of 1970, laid the legal foundation for efforts by the Department of Justice to reduce drug abuse. The legislation placed restrictions on the manufacture and distribution of several categories of drugs with a potential to produce abuse and addiction, as well as certain chemicals used in the illicit production of controlled substances. Controlled substances are those drugs designated by the Drug Enforcement Administration (DEA) and the Food and Drug Administration (FDA) on the basis of definitions and criteria described in the Act.

Controlled substances are regulated into one of five schedules. Schedule I is reserved for highly addictive drugs with no recognized medicinal value and thus are not permitted for sale (e.g., heroin, LSD, marijuana). Schedules II through V are used to classify drugs that are approved for medicinal use and marketing, but also have addiction or abuse potential and, thus, have varying levels of control over manufacturing, distribution, and prescribing, depending on the schedule. Cough medicines requiring a prescription are placed in schedule V, many sedatives are placed in schedule IV or III, and schedule II is reserved for morphine-like opioid analgesics and amphetamine-based stimulants. Recommendations for drug scheduling are jointly developed by the FDA, DEA and NIDA.

Since passage of the CSA, new challenges have emerged that were not anticipated by the Act. For example, the Internet provides a virtually instantaneous means of enabling drug abusers to learn of new ways to obtain and abuse drugs as well as to purchase drugs without prescriptions. In addition, the way a drug is formulated can make it a target for abuse and diversion but virtually all morphine-like opioids are abused. These and other factors have required that the CSA be increasingly supplemented by what the FDA now terms risk management programs to provide additional controls on a drug specific basis. I will provide greater detail on this later in my testimony.

The struggle to find the right balance will unfortunately not end in the near term because the continuing push for ever more effective medicines will undoubtedly be matched by creative entrepreneurial illicit drug sellers whose interest is in creating and feeding abuse and addiction. In fact, it may be appropriate to view the problem in much the same way that the Centers for Disease Control and Prevention (CDC) views infectious diseases, such as influenza. From a public health perspective, there are many similarities in measuring, documenting, and responding to the challenges posed by potentially addictive drugs, both licit and illicit, as are posed by the endless cycles of influenza and other infectious diseases.

Trends in Substance Abuse

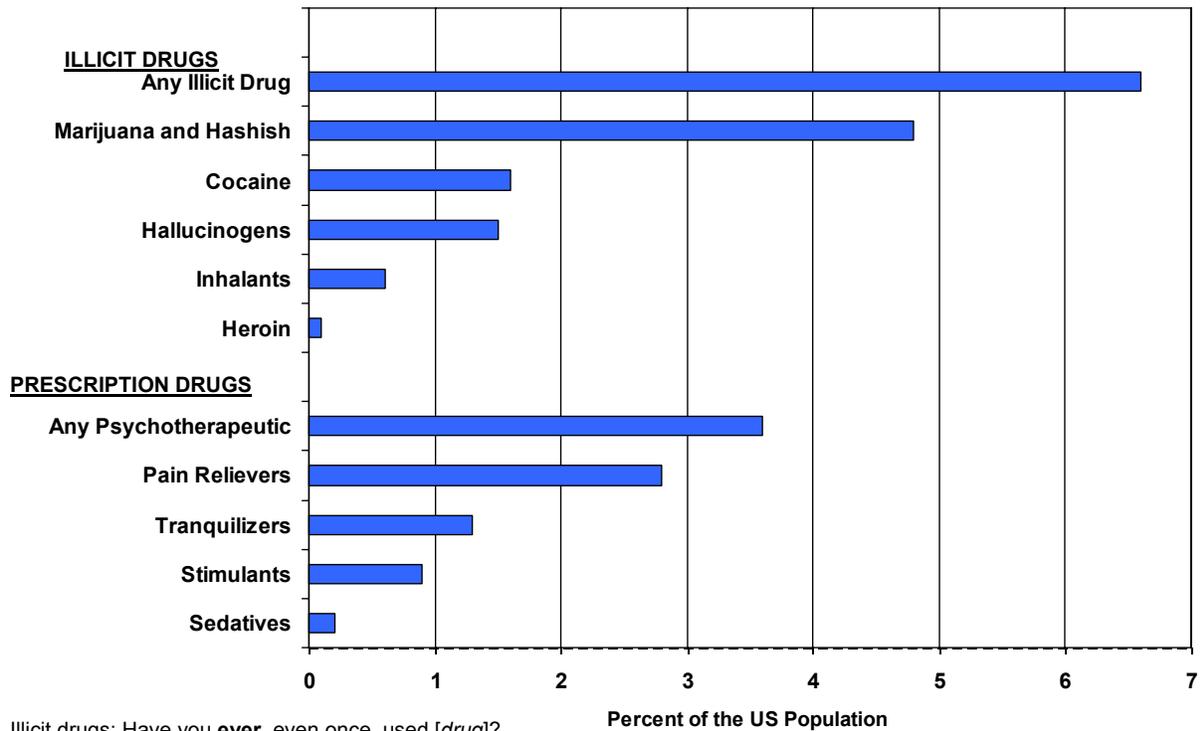
The various cycles of substance abuse are not entirely controllable nor readily anticipated. For example, cocaine went from a small blip on the tracking surveys to our nation's major drug of concern from the 1970s to the 1980s; and that was before the advent of the crack formulation in the mid-1980s that fostered further expansion of the illicit market. Opioids including heroin also saw resurgence in the 1980s as depicted in a 1981 Newsweek article entitled, "Middle-Class Junkies."

The 1990s witnessed an increase in prescription opioid abuse as these drugs were considered to be identifiable, purer, and, erroneously, safer and less addictive when abused. This may have been further fostered by widely reported interviews with popular icons such as Courtney Love who claimed she didn't abuse "street narcotics," but did abuse prescription opioids. The ability of the Internet to enable drug abusers and sellers to share information has undoubtedly complicated efforts to control abuse and to limit "outbreaks."

Increased prescription drug abuse in the 1990s has been particularly noteworthy among the stimulants and opioid analgesics as well as anabolic steroids. Among opioid analgesics, national figures indicate that the hydrocodone-containing cough and analgesic medicines are abused most frequently, with the oxycodone drugs currently in second place.

The chart below shows rates of non-medical use for a number of drugs and drug classes, including illicit drugs and prescription medications, for the year 2002. It is important to keep the overall substance abuse problem, illicit and prescription, in perspective.

Past Year Abuse and Non-Medical Use of Drugs, Reported by SAMHSA: NSDUH, 2002

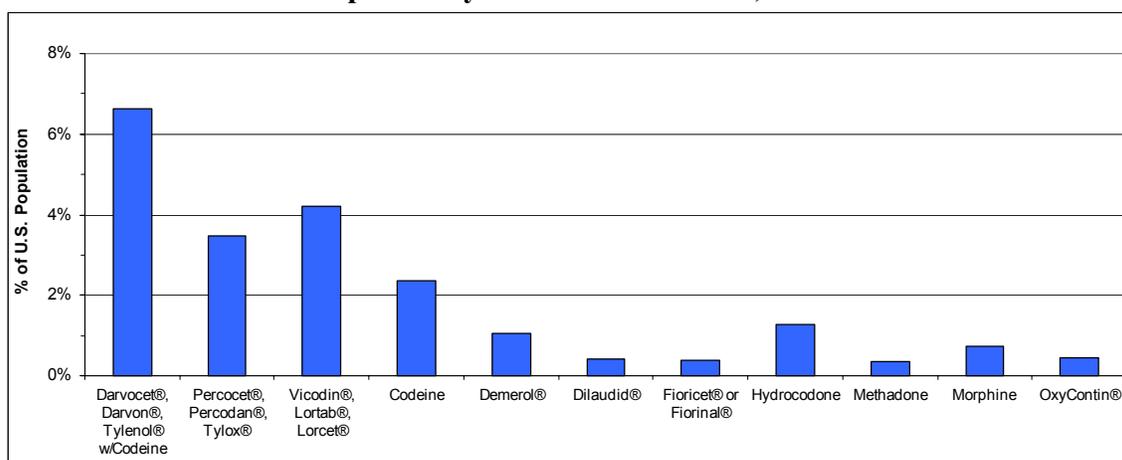


Illicit drugs: Have you **ever**, even once, used [drug]?

Prescription drugs: Have you ever, even once, used [drug] that was **not** prescribed for you or that you took only for the experience or feeling it caused?

The next chart focuses specifically on prescription analgesics, showing rates of non-medical use for a number of different medication brands. I show it to illustrate the diversity of analgesics that are abused and the complexity of the challenges facing us: drug abusers have lots of choices and history tells us that if they are denied one source they will turn to another, particularly when they have not been thoroughly educated regarding the dangers of abusing prescription medications.

Lifetime Non-Medical Use of Specific Prescription Analgesics in the U.S. population, Reported by SAMHSA: NHSDA, 2001



Source: SAMHSA, Office of Applied Studies, National Household Survey on Drug Abuse, 2001.

Limitations of Available Data

While hindsight provides a clear picture of trends in substance abuse, current limitations on tracking such trends is a problem that warrants greater attention. Tracking prescription drug abuse raises challenges that go beyond those that exist for tracking illicit drug abuse trends. For example, while any use of an illicit drug might be considered abuse in a general sense, it appears likely that at least some nonmedical use of prescription analgesics is more appropriately termed misuse. However, available surveys do not always distinguish between use by a person for whom the medication was not prescribed, even if it were taken only once and for a reasonable medical need, and a pattern that might more accurately be considered “abuse,” such as “recreational” abuse of an illicitly procured medication. In addition, with respect to prescription drug abuse and diversion, brand names can be highly relevant. In fact, various brands of oxycodone-containing medications differ widely in their content and formulation, which can alter their affect and appeal. However, the surveys were not designed to collect valid brand-specific data. Rather, they were developed with a focus on illicit drugs, in which various types are identified in some surveys (e.g., injection cocaine versus smoked cocaine), but there has been no apparent historical need for the equivalent of “brand” specific information. The December 2003 General Accounting Office (GAO) report on prescription drugs, entitled “Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem”, acknowledged these limitations

concluding that current federal surveys do not provide reliable, complete, or timely information that could be used to identify abuse and diversion of a specific drug.²

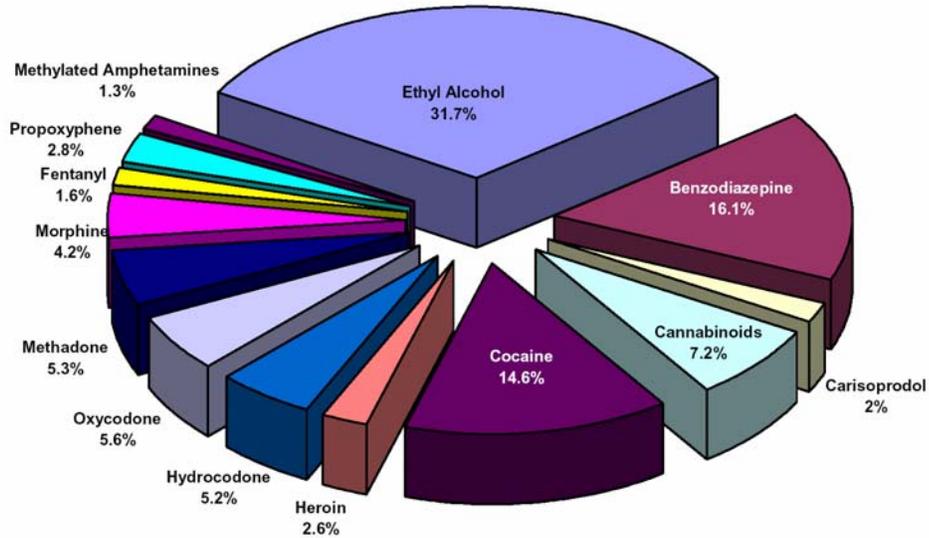
This represents an important gap in our nation's drug abuse surveillance infrastructure that needs to be remedied in order to provide the data needed to guide effective responses to trends and apparent "outbreaks." To put it into perspective, imagine if the CDC did not receive reliable data until 1-2 years after an outbreak began of an infectious disease, such as SARS, West Nile Virus, or a new influenza, and if the data provided little specific information as to the nature of the newly emergent strain. Although hard to imagine, this is the current situation in terms of surveillance data for prescription drug abuse. A more timely, reliable and efficient means for tracking such abuse is warranted.

Another important aspect of any public health effort is accurately estimating the numbers of deaths and correctly attributing their cause. This is critical in the development of efforts to prevent future deaths; otherwise, time, effort, and resources can be diverted into ineffective efforts. While this may seem basic, in the area of substance abuse, the science of estimating and attributing deaths has lagged far behind that in other areas of public health. This was starkly evident at SAMHSA's important hearing last May to address the rising deaths attributed to methadone, which I will discuss in greater detail shortly. That hearing made clear that the numbers of deaths appropriately attributed to methadone has probably been greatly overestimated because it appears that most of the deaths involved the simultaneous abuse of more than one drug, often including alcohol, so-called "polydrug abuse." Second, although some news stories attributed the rise to lax procedures in methadone treatment clinics for heroin addicted persons, in fact, it appeared that increased use of methadone as a analgesic – its original indication -- was a major factor. The need for substantial improvements in our ability to estimate and appropriately attribute cause of death was also discussed in detail.

The chart below is reproduced *in toto* from the 2003 Interim Report of Drugs Identified in Deceased Persons by Florida Medical Examiners. The chart shows the frequency of association of various drugs with deceased persons. Cases in which multiple drugs were in evidence were multiply counted, and the specific cause of death may not have been clear, or may have been accurately attributed to a lethal cocktail of several drugs, each one of which is counted as a causative agent in the tally. Nonetheless, the chart reflects the many drugs that are associated with drug deaths and thus indicates the scope and complexity of preventing deaths from drug abuse. Alcohol was associated with the greatest number of deaths at 31.7%, then benzodiazepines, cocaine and so forth. All oxycodone medications were associated with 5.6%, although I remind you that in some of these cases other drugs were also found and considered causative by the originating medical examiner.

² United States General Accounting Office (GAO). Report to Congressional Requesters. Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem. GAO-04-110. December, 2003.

Frequency of Occurrence of Drugs in Decedents January – June 2003



Note: GHB, Ketamine, Freon, N2O, Hydromorphone, Meperidine, and Tramadol constituted less than 1% of the drug frequencies.

Source: Interim Report by Florida Medical Examiners Commission on Drugs Identified in Deceased Person, October 2003.

While this chart appears to illustrate a simple, straightforward story, in reality, the story is not so simple. A recent study, done at the request of Purdue Pharma, sheds further light on this issue. The study was conducted by two of our nation's leading forensic experts, Dr. Edward Cone, former chief of the chemistry laboratory at the NIDA and presently at Pinney Associates, and Dr. Yale Caplan, former chief toxicologist of the Maryland Medical Examiner's Office. The purpose of the study was to help better understand actual causes of death involving one oxycodone drug, OxyContin. This analysis was published last year as the lead article in the March edition of the *Journal of Analytical Toxicology*.³ One of the major findings of the study was that the vast majority of deaths that were attributed to OxyContin were, in fact, polydrug abuse deaths, frequently involving alcohol.

In pointing out these statistics, I must state that any death from drug abuse is tragic. But in order to seek solutions, one must first understand the problems.

³ Cone EJ, Fant RV, Rohay JM, et al. Oxycodone involvement in drug abuse deaths: A DAWN-based classification scheme applied to an oxycodone postmortem database containing over 1000 cases. *Journal of Analytical Toxicology* 2003;27:57-67.

Single Entity Drug Abuse is Rare

A further complication in identifying and understanding prescription drug abuse trends is that single entity abuse (i.e., abuse involving just one drug) is rare. At a general level this has been well understood for decades. With respect to prescription drug abuse, the relationships appear even more complex as brands within a category and across categories are interchanged as a function of such factors as availability, price, current media hype, and what, in the realm of product marketing, is termed “buzz” marketing. That is to say, the “buzz” or “hype” or reputation developed for a particular product may be short or long lived and may have little to do with its actual physical performance.

In the case of analgesics, Pinney Associates has analyzed data from the 1999, 2000, and 2001 National Survey on Drug Use and Health (NSDUH, which was formerly known as the National Household Survey on Drug Abuse or NHSDA) to examine rates of non-medical drug use in the U.S. population (12 years of age and older) and examine the demographic and drug abuse profiles of those reporting such use.

Although the focus of our analysis was specific to OxyContin, the findings are not unique to oxycodone drugs but certainly apply to other classes of analgesics, as well as other categories of prescription drugs. Specifically, the analysis shows that the overwhelming majority of persons who had abused OxyContin non-medically during their lifetime had abused at least two other analgesics and/or nonprescription drugs of abuse such as heroin, cocaine and marijuana. Alcohol and marijuana abuse, along with cigarette smoking, are prominent in this survey and generally precede abuse of opioid analgesics.

For each of the three years examined, non-medical OxyContin users were, on average, approximately twice as likely to report non-medical use of at least two additional prescription analgesics, 1.7 times as likely to report having abused cocaine, 2.8 times as likely to report having abused heroin, and 3.6 times as likely to report having used needles to inject drugs of abuse as compared to non-medical users of other prescription analgesics. Furthermore, the initial non-medical use of prescription analgesics was typically preceded by abuse of other drugs: over 80% of those reporting non-medical use of OxyContin reported having abused illicit drugs or engaged in non-medical use of other prescription medications (i.e., tranquilizers, sedatives, stimulants) prior to their first non-medical use of prescription analgesics. These data are also consistent with those from a NIDA-supported Kentucky Youth Survey in 2001 that found that most youth who had abused OxyContin had prior experience with several drugs of abuse.

Such findings are consistent with decades of data indicating that abusers of drugs within a given class (e.g., sedatives, stimulants, or opioids) are very likely to try new drugs that come along and that their actual abuse patterns will be substantially influenced by a range of factors including cost, availability, and reputation. The challenge to reducing drug diversion, abuse, and addiction is to respond appropriately to the “drug of the day” without simply shifting abusers to other drugs, which in some cases may be even more risky.

The complexity of the problem is made even more difficult by the fact that the solution to one problem may precipitate or exacerbate another. For example, concerns about overdose led the

FDA to approve the following warning for inclusion in the OxyContin labeling: “OxyContin TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OxyContin TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.” As noted in the GAO Report discussed above, this “safety warning... may have also contributed to the drug’s potential for abuse and diversion, by inadvertently providing abusers with information on how the drug could be misused.”

None of the examples provided are intended to fully explain prescription drug abuse trends and consequences. Rather, they are an attempt to illustrate the complexity of the challenges before us and the need to minimize unintended consequences. For example, as a result of media attention on the dangers of oxycodone drugs, some doctors are turning to alternative analgesics to treat their patients with pain. One such analgesic is methadone, a strong analgesic also used to treat opioid addicted persons, such as those addicted to heroin. However, methadone requires close monitoring of dosing, particularly when it is used in the treatment of pain, as the doses that are effective for relieving pain can produce severe respiratory depression for many people if it is not dosed and titrated appropriately. Unlike most other opioid analgesics, methadone demonstrates great variability between patients with regard to duration of action, accumulation and excretion, making its safe use more challenging than other opioid analgesics.

This issue is generally well understood by health care professionals with experience in treating addiction and pain with methadone. However, for doctors without such experience, turning to methadone as an alternative to oxycodone and hydrocodone medicines could prove dangerous to their patients. According to Dr. Edward C. Covington of Ohio’s Cleveland Clinic, who was quoted in the *New York Times* (February 9, 2003), “Methadone is probably one of the very few drugs that I’ve seen doctors almost kill patients with. It’s that hard to use when you first start to use it.”

Use of methadone as an alternate analgesic is being increasingly viewed as a major contributor to the sharp increase in methadone related deaths over the past few years. Unfortunately, the media portrayal of the increase in methadone use has often been attributed to other things, such as liberal use of methadone and methadone dosing take home privileges in heroin treatment clinics.⁴ As a result, some states took actions to restrict how methadone is used in the treatment of heroin addiction.

Last May, the U.S. Substance Abuse and Mental Health Services Administration’s Center for Substance Abuse Treatment (SAMHSA, CSAT) convened the conference referenced previously to examine the extent, nature, and cause of methadone-related deaths in the US. Specifically, deaths initially attributed to methadone had increased substantially in Washington D.C., Maine, and Florida. The conference included representatives of the CDC, DEA, FDA, NIDA, other organizations, and many experts. Although not intended as a consensus conference per se, strong agreement emerged around several points. First, the increase in deaths attributable to methadone were largely polydrug related and included many people apparently medicated for

⁴ “Methadone, Once the Way Out, Suddenly Grows as a Killer Drug”, *The New York Times*, February 9, 2003.

pain. Second, there is little evidence that there has been an increase in appropriate use of methadone treatment for addiction nor is there a basis for new national restrictions on the use of methadone in substance abuse treatment clinics. Third, concern was expressed that fear of prescribing oxycodone, in particular OxyContin, and other opioid analgesics among health care professionals, along with the substantially lower cost of methadone, was driving physicians, managed care plans, or state Medicaid programs to switch to methadone as an alternative analgesic. This was considered a potentially dangerous switch for doctors without extensive experience with methadone dosing for analgesia.

The methadone example is important because it illustrates a larger point. As we consider policies to reduce abuse and diversion of any given class of drugs, or any specific drug, it is important to study all potential consequences and make every effort to avoid harmful unintended consequences.

Potential Solutions

If there was a simple straightforward solution to the issue of prescription drug abuse, there would be no need for this hearing. If you took the extreme action to ban the top 10 prescription opioids that are associated with the highest rates of diversion and abuse, they would be quickly replaced by 10 other drugs. In addition, you would disrupt the lives of the many patients with pain whose well-being depends upon those drugs.

Although there remain many unknowns, there are many things that can be done to reduce prescription drug abuse without discouraging legitimate and medically appropriate use of medications by patients. However, severely limiting access of analgesics with new burdens on doctors and pharmacists would surely result in reduced utilization by patients and almost certainly increase pain and suffering in our country. It is also not clear that such action would have any effect on opioid abuse and addiction because there are so many alternatives to opioids that could be obtained on the street and through the Internet. It is important that in our zeal to reduce abuse and diversion, we do not forget that we continue to have a significant problem of under treatment of pain and its attendant suffering, in part due to fears surrounding the use of opioid analgesics. Ideally, in our efforts to devise strategies to reduce abuse and addiction, we should be simultaneously devising strategies to improve the treatment of pain.

Surveillance. There are deficits in our nation’s infrastructure for understanding prescription drug abuse and diversion that need to be remedied. We need a surveillance system that is geographically sensitive, responsive to emerging trends and timely. Our system for identifying drug abuse outbreaks and trends should be no less effective or comprehensive than is our nation’s system for tracking infectious disease such as influenza by the CDC. Many of our current surveys will continue to have an important place and have been undergoing improvements in recent years, yet GAO’s conclusion that “data on abuse and diversion are not reliable, comprehensive, or timely” is a sad reminder of the challenge that lies ahead in this area.

Education. Among the many challenges our nation faces in reducing prescription drug abuse is the need to better educate our children. The concept that abuse of an opioid analgesic can be as deadly as the abuse of street heroin is apparently not a readily known fact. It is plausible that by

focusing anti-drug messages on illicit drugs, we have created the impression that prescription drugs are not a major concern. Yet, most children have far easier access to potentially harmful medicines than they do street drugs – in the family medicine cabinet. We clearly need better balance in education and anti-drug information to teach our young about the dangers of prescription drug abuse, while helping them to understand the vast difference in safety between appropriately supervised medical use and the abuse of the same medicine. While children today receive more education about the dangers of illicit drug abuse, smoking and drinking, than in decades gone by, prescription drug abuse has not received the equivalent degree of attention.

Education also needs to include health care professionals (doctors, pharmacists, nurses, etc.), policy makers, medical licensing boards, other regulators, law enforcement and the public on the appropriate use of pain medications and what constitutes misuse, abuse and addiction. Education needs to include such basics as proper disposal of prescription medicines that are no longer needed. The educational needs are broad, real, and important.

Community Partnerships. During his State of the Union address, President Bush emphasized the importance of community-based strategies in preventing drug abuse and other problems of our young. Substance abuse community partnerships are recognized as a cornerstone of building awareness, providing guidance, and fostering alternatives to destructive behaviors, yet they are too often underappreciated, underutilized and under-funded.

NIDA, other federal agencies, and private organizations, have supported many of these efforts and helped to develop their science base so that we are learning more and more about what works, what doesn't work, and the important considerations in transferring success from one community to another. This is vital if we are to reduce prescription drug abuse in both the short and long-term.

One such program is the **Communities That Care**[®] (CTC) program, which emerged in part with funding from the NIDA, and is sponsored in 10 communities in seven states by Purdue Pharma. CTC is a community mobilization and prevention effort that is based on over 20 years of careful social science research. Program professionals collaborate with local community leaders to develop long-term strategies to reduce the occurrence of a number of different problems facing youth in communities today. One of the important nurturing grounds for CTC was the State of Pennsylvania, where the program had strong support from then Governor Tom Ridge and benefited from the active involvement of Mrs. Ridge, who is today a national spokesperson for CTC. Today, the program is in place in over 500 communities in the U.S. and is also in place in the United Kingdom, Australia and the Netherlands. Such partnerships of government, community, and corporate America should be encouraged. All have a stake; all stand to benefit.

Drug Addiction Treatment Needs. There is also a considerable need to strengthen our treatment infrastructure. More treatment is needed today and will undoubtedly be needed in the future, despite our many efforts to curb addiction. Former Surgeon General, Dr. C. Everett Koop, has summarized the treatment situation most elegantly. He said, "It is easy to get the drugs, hard to get treatment. Our challenge as a nation is to reverse this."

It is evident from the streets of America to the White House that formidable challenges must be overcome to achieve Dr. Koop's vision. According to the Office of National Drug Control Policy (www.whitehousedrugpolicy.gov/publications/factsht/methadone), less than 165,000 methadone treatment slots are available for the more than 800,000 heroin users in apparent need of such treatment. Moreover, while heroin abuse is dispersed throughout the nation, most treatment centers are concentrated in major cities.

Today, those abusers who become addicted to prescription drugs are in much the same situation as those who become addicted to illicit drugs. The addictive drugs are accessible through channels that they know how to use. If they seek treatment, they typically face a discouraging patchwork quilt system that would challenge many of us to negotiate. In some respects, the plight of many prescription drug abusers is even worse, in that many of them live in regions of the country without opioid addiction treatment clinics. They may have to travel hours to reach one. Only a few clinics are prepared to address the needs of adolescents who become addicted to opioids, a growing trend according to the NSDUH. Our nation has taken some steps to address this. The Drug Abuse Treatment Act of 2000 was an important one. This Act enables certified doctors to offer certain treatments to opioid addicts in a general medical office setting. However, many barriers to the success of this Act exist and it needs refinement to have a significant impact on the national problem of opioid addiction.

Risk Management. We have a system of categorizing and regulating drugs based on their addictive potential, and that system is codified by the Controlled Substances Act (CSA). Although developed in a simpler day, when drug formulation was not so prominently on the radar screen of concern, the CSA and its provisions are the backbone of the system for regulating drugs with a potential for abuse and addiction. The CSA primarily addresses the pharmacology of the chemical entity, providing a basis for differentially scheduling and regulating drugs based on their pharmacology. This is a science-based mechanism of fundamental importance. For a number of years it was my honor to head the laboratory at NIDA that developed many of the scientific methods used to categorize drugs and I am well aware of the strengths and weaknesses of the methods. I have worked with the College on Problems of Drug Dependence and other organizations to continue to refine these methods. Refinement of the methods and evolution of strategies is critical and with continuing support from NIDA and other federal agencies this important area of science will continue to progress and keep pace. Again, one can think of this as the equivalent to what we expect of CDC in its ability to refine its methods and keep pace with evolution of disease types and the surprise emergence of new diseases.

On the other hand, the CSA has limitations, in that abuse and diversion are modulated by factors that go far beyond the chemistry and pharmacology of the drug. Such factors include the formulation of the drug, its dosing characteristics and capability, its liability to tampering, its indication, the nature of the intended patient population, how it is labeled and advertised, "buzz" about it in the media and on the street, and potential effects that are incidental to its intended effects. These factors and more can influence how a drug is properly used, its liability for abuse and diversion, and the consequences of abuse and diversion. Attempting to address this broad range of complex factors with any simple strategy will not work. It would be like attempting to manage a computer software glitch with a hammer – not that that isn't tempting at times. Here

the answer may be best summarized by another GAO conclusion that bolsters one of FDA's major strategic initiatives, namely, risk management.

Risk management is both a concept and a process. The concept is simple: On a drug by drug basis, identify all plausible risks of marketing the drug and take actions to mitigate those risks while fostering beneficial drug use. The process is more complex and is as varied as the drugs themselves, the indications, and other factors. Nonetheless, it is this process, which has enabled the approval and marketing of drugs for which there were serious concerns by providing mechanisms to mitigate risks [examples include Acutane[®], thalidomide, OTC nicotine, tramadol, Actiq[®]]. The process, with respect to drugs with potential for abuse and controlled substances, is largely guided by FDA, but in practice has input from DEA. This makes sense and continued collaboration should be encouraged. For these types of drugs, risk management programs contemplate not only the intended patient class, but exposure to people who would voluntarily abuse them. I would be remiss, however, if I did not encourage a third party in controlled substance scheduling issues to be given a more active role and that is the National Institute on Drug Abuse or NIDA. NIDA is not a regulatory agency and should not be turned into one, but NIDA is the closest thing our nation has to being the keeper of science in this field and NIDA's role in helping to keep the process guided to the greatest possible extent by science is important.

Implementation of the risk management process occurs via what is now referred to as the Risk Management Program. The GAO report concluded as follows: "FDA's risk management plan guidance should encourage pharmaceutical manufacturers with new drug applications to submit plans that contain a strategy for identifying potential problems with abuse and diversion." Risk management plans can be relatively simple or they can be very complex. In some cases they may include mechanisms for supplementing federal surveillance efforts with surveillance to address potential concerns that appear specific to the drug [examples include Tramadol, OTC nicotine gum, Purdue's RADARS[®] System]. In virtually all cases, they include attention to labeling, marketing, and formulation.

Moreover, risk management plans provide a mechanism to address the limitations of provisions of the Controlled Substance Act (CSA) on a drug-by-drug basis, taking into account the diverse range of factors that can contribute to benefit and risk.

Risk management plans enable drugs to realize their potential to provide benefits while endeavoring to address all plausible risks with strategies to reduce those risks. This concept inherently recognizes the importance of finding the right balance in drug access to enable realization of benefits, with controls to minimize risks. The concept makes sense for virtually all categories of drugs, but I believe it is particularly useful with respect to all controlled substances, which, by definition, have abuse and addiction potential.

Of course, risk management plans are no panacea or simple road to reducing abuse and diversion, and important issues remain to be addressed in the nature and process of risk management program development. For example, should the process be systematically extended to all drugs in a category or just to new drugs? Should the marketing and promotion of generic equivalents of a branded drug be accompanied by a risk management program similar to that of the branded medicine? How does the process of risk management interact with the scheduling

process? In other words, might the scheduling of a drug be influenced by its risk management program? It will also be helpful for FDA to develop further guidance on risk management program development procedures and expectations. By nature, the risk management program process will be evolutionary. My main plea for the process is that it strives to maintain the balance necessary to maximizing the benefits of drugs while minimizing their risks. That is the way to optimize the risk benefit ratio of a drug. That is the course to improving medicine, patient care, public health, and the lives of individuals in need of care.

Drug Monitoring and Internet Sales Restrictions. An apparently growing problem that needs to be addressed is that of distribution and sales that escapes regulation such as Internet sales. Some of you may have read the *Washington Post* series that began October 19, 2003. This series highlighted an investigation undertaken by *Post* reporters into the growing shadow market of prescription drugs. The yearlong investigation by the *Post* revealed networks of “middlemen, felons and opportunists” operating out of storefronts and garages, and rogue merchants setting up Internet pharmacies that serve as “pipelines for narcotics.” While the U.S. system for the distribution of prescription medicines has been arguably the best in the world for a half century or more, that system, according to the *Post* investigation, is being undercut by a growing illegal trade in pharmaceuticals. Increasing recalls of tainted medicines and cross-border pharmaceutical trade are all a part of a larger pattern according to *Post* investigators. This larger pattern is threatening public health, and leaving victims in its wake. The result of this growing trade is “pharmaceutical roulette for millions of unsuspecting Americans.”⁵

The *Post*'s analysis of one Internet pharmacy, prescriptiononline.com, showed that nearly 90 percent of the orders were for controlled substances, including hydrocodone. In some cases, orders went to multiple customers using the same address. For example, over the course of five months, 2,030 pills were shipped to five customers at one home in Baileyton, Alabama. Of those pills, 80 percent were for hydrocodone. When confronted with the *Post* analysis, the physician who wrote the prescriptions stated, “I didn't have that data at that time.” The physician called the information “very disturbing. You've presented some information that certainly gives me some pause how this whole system can be blatantly abused and easily abused.”

While some have argued that there have been no deaths related to importation, unfortunately they are wrong. The *Post* series identified multiple victims, including: James Lewis, 47, a former triathlete who suffered from aches and pains. Lewis turned to the Internet pharmacies in South Africa, Thailand and Spain to purchase painkillers. Lewis' wife found her husband dead of an overdose from a drug he bought online. Ryan Haight was an 18-year old who died in his bedroom from an overdose after taking narcotics obtained on the Internet. Todd Rode, 38, was a skilled musician and computer whiz, who battled depression from the time he was a teenager. As an adult, he had bouts of drinking and argued with his doctors about his treatment. In 1999, Rode overdosed on medications he bought from a South African online pharmacy. These stories illustrate the real dangers that exist from online “consultations” and Internet sales of controlled substances. No matter what restrictions we put in place in the U.S., to the extent that we allow

⁵ See Washington Post Five-Part Series, “U.S. Prescription Drug System Under Attack” (October 19-23, 2003).

this practice to continue, it will undoubtedly impact our ability to curb abuse and diversion of prescription medicines in the U.S.

Now my expertise is not on prescription monitoring and controlling Internet sales, but as a drug abuse expert it is clear to me that these unregulated sales are a hemorrhage in our system. For the record, I would like to append the testimony of Dr. J. David Haddox, Vice President, Health Policy, Purdue Pharma, as Exhibit B. On behalf of Purdue Pharma, Dr. Haddox recommended the following:

Additionally, Purdue supports the concepts in federal legislation that it understands is being considered by Members of Congress that, among other things, would promote the development of effective state prescription monitoring programs to identify and reduce “doctor shopping”; regulate Internet pharmacies in an effort to curb diversion and abuse of controlled substances; establish a working group to address pharmaceutical counterfeiting; and call for baseline research on prescription drug abuse, more comprehensive and accurate reporting, and grants for drug abuse education programs for healthcare professionals, teachers, and parents. Purdue also strongly supports efforts like the Dime Out a Dealer program being sponsored by Congressman Weldon from Pennsylvania. This program is aimed at finding and arresting “dealers” who are illegally selling prescription drugs on the streets and campuses.

Although this is not my area of expertise, the concepts he espoused make sense as strategies for addressing important gaps in our system of drug control.

Conclusion

Prescription drug abuse and diversion are an important public health problem and warrant increased attention. Unfortunately, there are no easy answers. As I stated earlier, H.L. Mencken once said, “For every complex problem there is a solution that is simple, neat, and wrong.” As we move forward in search for solutions to deter abuse and reduce diversion, we should be cognizant of the needs of pain patients, as well as the healthcare professionals who care for them. We need to recognize that efforts to reduce abuse and addiction by nonmedical users, and reduce diversion require finely tuned efforts as part of the risk management process to supplement national policies. Better surveillance is vital to enable responsive and appropriate actions and community partnerships need to be companions in the process.

Thank you for the opportunity to testify. I will be pleased to contribute to this important process in any way.