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OXYCONTIN: BALANCING RISKS AND BENEFITS

HEARING

OF THE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS UNITED STATES SENATE

ONE HUNDRED SEVENTH CONGRESS

SECOND SESSION

ON

EXAMINING THE EFFECTS OF THE PAINKILLER OXYCONTIN, FOCUSING ON FEDERAL, STATE AND LOCAL EFFORTS TO DECREASE ABUSE AND MISUSE OF THIS PRODUCT WHILE ASSURING AVAILABILITY FOR PATIENTS WHO SUFFER DAILY FROM CHRONIC MODERATE TO SEVERE PAIN

FEBRUARY 12, 2002

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C O N T E N T S

STATEMENTS

TUESDAY, FEBRUARY 12, 2002

Page

Reed, Hon. Jack, a U.S. Senator from the State of Rhode Island, opening statement 1

Warner, Hon. John W., a U.S. Senator from the State of Virginia, opening statement 4

Clinton, Hon. Hillary Rodham, a U.S. Senator from the State of New York, opening statement 6

Collins, Hon. Susan M., a U.S. Senator from the State of Maine, opening statement 8

Dodd, Hon. Christopher J., a U.S. Senator from the State of Connecticut, opening statement 10

Jenkins, Dr. John K., Director, Office of New Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, Rockville, MD; Dr. H. Westley Clark, M.P.H, J.D., Director, Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, Rockville, MD 13

Prepared statements of: .....

Dr. Jenkins 14

Dr. Clark 24

Payne, Dr. Richard, Chief, Pain and Palliative Care Service, Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, NY; Dr. Art Van Zee, Lee Coalition for Health, St. Charles, VA; Nancy Green, C.N.M., President, Neighbors Against Drug Abuse, Calais, ME; Lieutenant William R. Bess, J.D., Drug Enforcement Division, Virginia State Police, Wytheville, VA; and Dr. Paul D. Goldenheim, Vice President for Research, Purdue Pharma, L.P., Stamford, CT 40

Prepared statements of: .....

Dr. Payne 42

Dr. Van Zee 46

Ms. Green 61

Lt. Bess 66

Dr. Goldenheim 70

ADDITIONAL MATERIAL

Articles, publications, letters, etc.:

Response from the Department of Health & Human Services to questions asked of Dr. John Jenkins by Senator Reed 18

Response from the Department of Health & Human Services to a question asked of Dr. John Jenkins by Senator Collins 19

Response from Dr. Goldenheim to a question asked by Senator Reed 81

American Pharmaceutical Association (APhA) 96

Charlene Cowley (ASPMN) 97

National Association of Chain Drug Stores (NACDS) 98

National Institute on Drug Abuse (NIDA) 100

Carlos Ortiz on Behalf of CVS Pharmacy 101

American Academy of Family Physicians (AAFP) 103

Russell K. Portenoy, M.D. 105

OXYCONTIN: BALANCING RISKS AND BENEFITS

TUESDAY, FEBRUARY 12, 2002

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The committee met, pursuant to notice, at 2:34 p.m., in room SD–430, Dirksen Senate Office Building, Hon. Jack Reed, presiding.

Present: Senators Reed, Dodd, Clinton, Warner and Collins.

OPENING STATEMENT OF SENATOR REED

Senator REED. Good afternoon. Let me call this hearing to order and make an opening statement and recognize my colleagues prior to calling the first panel.

I am very pleased this afternoon to chair this full committee hearing of the Senate Health, Education, Labor, and Pensions Committee on OxyContin. OxyContin is a synthetic, time-release pain medication containing oxycodone, which is an opiod similar to morphine. OxyContin is manufactured by Purdue Pharma and was approved by the Food and Drug Administration in December 1995 to aid cancer patients and people with moderate to severe pain who require around-the-clock opiods for an extended time. While this medication has revolutionized pain management for thousands of Americans, OxyContin, like other Schedule II narcotics, has a high potential for abuse and sadly, that potential for abuse has become a reality in too many cases.

OxyContin abusers have discovered that if the tablets are broken, the time release mechanism of the drug is broken, enabling the abuser to achieve a euphoric, heroin-like high. In this form, and if taken with alcohol or other drugs, OxyContin is extremely dangerous. No one predicted the level of diversion and abuse that would become the legacy of this drug.

I would like to thank all of our witnesses who will be appearing this afternoon. This afternoon we will hear from Dr. John K. Jenkins, director, Office of New Drugs at the Food and Drug Administration, and Dr. H. Westley Clark, Director of the Center for Substance Abuse Treatment at SAMHSA.

On our second panel we will have Dr. Richard Payne, Chief of Pain and Palliative Care Services at Memorial Sloan-Kettering Cancer Center in New York; Dr. Art Van Zee of the Lee Coalition for Health in St. Charles, VA; Ms. Nancy Green, a Certified Nurse-Midwife and President of Neighbors Against Drug Abuse in Calais,

ME; Lieutenant William R. Bess of the Drug Enforcement Division of the Virginia State Police; and Dr. Paul D. Goldenheim, Vice President for Research, Purdue Pharma, L.P., the manufacturer of OxyContin.

Last October, a Drug Enforcement Agency report on autopsy data revealed that there was evidence to suggest that OxyContin played a role in the overdose deaths of 282 people over a 19-month period. Most of those deaths also involved other drugs and alcohol.

In addition, OxyContin has been associated with an increasing wave of pharmacy robberies and other violent crimes, particularly in rural areas. OxyContin diversion and abuse has become rampant in rural parts of Maine, Tennessee, Kentucky, Virginia and Massachusetts. While the trend in OxyContin abuse originated in more rural areas, it is now beginning to make its way to urban centers along the Eastern seaboard. Indeed, there have even been armed robberies of pharmacies in my home State of Rhode Island.

While these trends are certainly cause for alarm, we must also consider the importance of OxyContin for those who suffer moderate to severe chronic pain. For many Americans OxyContin has meant the difference between total incapacitation from pain and being able to return to a semblance of normal life. Numerous studies show that pain management in this country is far from ideal. Many physicians, in fact, tend to undertreat pain for many reasons. A 2000 end-of-life study by Brown University Associate Professor, Dr. Joan Teno, based on interviews with bereaved families of nursing home residents reported that half of those patients experienced pain at end-of-life while two-thirds of those families rated the pain as severe more than half the time. Indeed, we have a lot of work to do with respect to the management of pain and we have to recognize that OxyContin is an important part of that management regime in some cases.

During today's hearing I hope we can gain a better understanding of the promotion and marketing practices of OxyContin and whether or not these activities have contributed to the extensive abuse of this drug and whether or not Federal agencies responsible for approving narcotics require additional authority in light of these new challenges. We will gain an insight into the devastation that illegal use of this drug has caused in many rural parts of America and how those areas are working to fight back. I also hope we will learn why OxyContin is considered to be a significant advancement in the treatment of pain, as well.

I look forward to the testimony of all our witnesses and thank you again for attending this afternoon's hearing.

Prior to recognizing my colleagues, let me also submit for the record a statement from Senator Bunning, who could not be here but would like his statement included.

[The prepared statement of Senator Bunning follows:]

PREPARED STATEMENT OF SENATOR BUNNING

Good afternoon, Mr. Chairman and Members of the Committee. I appreciate the Committee's willingness to hold a hearing on this very important issue before us today.

OxyContin was approved by the Food and Drug Administration in 1995 and has been celebrated as a "miracle drug" for people who

suffer from chronic pain and patients with terminal cancer. OxyContin, is a controlled substance, like morphine and other intense pain relievers, and has been found to have a high potential for abuse. It is supplied in a controlled-release dosage form and is intended to provide up to 12 hours of relief from severe pain. The tablet must be taken whole and orally. However, when crushed in can be snorted or diluted to be injected where then the drug produces an intense high which many users say is equal to, or even better than, heroin. Therefore, it is as well, highly addictive.

The illegal use and sale of OxyContin has risen dramatically throughout the nation, but nowhere as prominently as in the rural areas of the eastern United States. While the problem has been most heavily documented in Appalachia, criminal cases are popping up at alarming rates all across the United States.

In Eastern Kentucky, the illegal use of the drug has risen to epidemic proportions. After nearly an eight-month investigation, details started to emerge in early February 2001 of an elaborate multi-state "pipeline" that ran from Greater Cincinnati to the mountain communities in Eastern Kentucky. During a raid in Eastern Kentucky, Federal agents and local police arrested over 200 people ranging in age from 20 to 65 for the abuse of OxyContin. This drug has torn families apart, ruined lives, and stretched the resources of law enforcement and social service agencies to its limit.

Using pharmacists and doctors in several states, suppliers are evading a computerized watchdog system in Kentucky known as KASPER (Kentucky All-Schedule Prescription Electronic Reporting system) and successfully slipping thousands of the pills into Eastern Kentucky where many residents are wrestling with OxyContin addictions. Data from the Kentucky Cabinet for Health Services shows there were 82,880 prescriptions filled for the drug in 1999. In 2000, the total prescriptions filled almost doubled and jumped to 156,660. This is not only amazing, but is frightening.

It has been alleged that Purdue Pharma, the producer of OxyContin, has marketed the drug excessively without stressing its addictive nature. In testimony before the House Appropriations Committee's Commerce, Justice, State and Judiciary Subcommittee, the Drug Enforcement Administration said that Purdue Pharma had contributed to its "disproportionate abuse" by aggressively marketing it as less prone to abuse than similar drugs.

My Kentucky colleague in the House of Representatives, Congressmen Hal Rogers recently requested that the General Accounting Office (GAO) investigate the marketing of the prescription drug OxyContin. I am anxiously awaiting GAO's study with the hopes that its findings will present Congress with some alternatives and justifications to help stem the abuse of this "miracle drug." While I certainly do not want to see this "miracle drug" prohibited from being manufactured, marketed and prescribed. I do, do however, want to ensure that if there are abusive marketing, distribution and prescription practices, that they be ended to make our families stronger and communities safer.

The abuse of this drug is literally ripping apart families and communities in Eastern Kentucky. The OxyContin addiction is so strong in some areas that some are beginning to prostitute them-

selves to pay for their addiction to the drug. Burglaries and robberies are up in Appalachian Kentucky, and law enforcement point the finger at OxyContin addiction. These problems are not just relative to Kentucky, but all across the nation the abuse of this addictive drug has turned good people into drug dealers and addicts, and some communities have been turned into places where neighbors and acquaintances are feared because of OxyContin.

I appreciate this Committee taking the time to take a look at this problem. It is not a problem that is going to go away quickly, but I hope from this and other hearings we can find some solutions to stem the abuse and addiction of OxyContin. Thank you, Mr. Chairman.

Senator REED. At this time, I would like to call upon Senator Warner for his opening comments.

Senator WARNER. I thank you, Mr. Chairman. Might I yield to my colleague?

Senator COLLINS. Go right ahead. Thank you.

OPENING STATEMENT OF SENATOR WARNER

Senator WARNER. Well, thank you, Mr. Chairman.

Mr. Chairman, may I commend you on a very thorough and carefully prepared opening statement. A great deal of the material that you have covered I had intended to use in my statement so I think I will just file my statement for the record.

[The prepared statement of Senator Warner follows:]

PREPARED STATEMENT OF SENATOR WARNER

Mr. Chairman and Senator Gregg, thank you for scheduling this important hearing today on the risks and benefits of OxyContin.

As you may recall, in July of last year, I wrote and spoke to you both about the emerging problem of OxyContin abuse, and I was the first United States Senator to ask for a Senate hearing on this matter.

Senator Kennedy and Senator Gregg—you both have been responsive in scheduling this hearing at my request, along with Senator Collins' request. Today's hearing had been previously scheduled a number of times but was repeatedly postponed due to the events of September 11th and the days that followed. I thank you both for your diligence in scheduling this hearing today.

I also would like to welcome two Virginians who are with us today to testify before the Committee.

First, I am pleased that we are joined today by Dr. Art Van Zee of Lee County, Virginia. Last year, I had the pleasure of meeting with Dr. Van Zee to hear his views about OxyContin during one of my visits to the St. Charles Community Health Center in St. Charles, Virginia. I look forward to hearing his testimony today.

In addition, I would like to welcome Lieutenant William Bess of the Virginia State Police. While I have not had the pleasure of meeting with Lieutenant Bess before today, I have had a number of discussions about OxyContin abuse with the Virginia State Police, and I look forward to receiving an update on law enforcement's experience with OxyContin in Virginia.

Given that southwest Virginia has been effected disproportionately by illegal use and abuse of OxyContin, I am particularly grateful that two Virginians who are so familiar with this issue are here to share their expertise with the Committee. I thank you both in advance for your testimony today.

The importance of the issues before this Committee today cannot be overstated.

In OxyContin, we have a prescription drug that was hailed as a miracle pain reliever for chronic pain when it first became available to patients in the mid 1990s. Indeed, OxyContin serves an important function for many Americans who are suffering from chronic pain.

On the other hand, the very fact that OxyContin is so effective at relieving pain also makes it a target for abuse. In Virginia alone, it is estimated that there have been over 55 deaths linked to OxyContin.

While OxyContin is a relatively new drug and OxyContin abuse is a newer phenomena, the issues surrounding OxyContin have been well documented in the media.

The New York Times Magazine did a feature article on its cover called, "The OxyContin Underground: How a Prescription Painkiller is Turning into a Pernicious Street Drug.

Newsweek's cover in April of 2001 contained a featured article highlighted on its cover called, "Painkillers: Vicodin and OxyContin: Hot Drugs That Offer Relief—And Danger."

And, the front page of the USA Today on August 9, 2001 , contained a cover story on opiods, including OxyContin.

These are just a few of the many articles that I have read about OxyContin.

In addition, I have taken the initiative to meet with experts all across Virginia to examine the benefits and risks of OxyContin.

The facts are simple, and I am sure we will hear them today. This drug has a lot of benefits when prescribed by a doctor and taken in accordance with the prescription. However, this miracle drug is also being abused, has led to increased crime, and has been linked to deaths not just in Virginia, but across the United States, particularly in rural Appalachia.

Accordingly, I look forward to the testimony today, particularly testimony about how this Committee can be helpful in curbing OxyContin abuse.

1 thank my Chairman once again for calling this hearing. After today's hearing, I imagine that some of us on this Committee will sit down and determine how the Federal Government can be more helpful in efforts to stem OxyContin abuse. I look forward to working on this issue with my colleagues.

Senator WARNER. Mr. Chairman, I am the son of a doctor. If I had had half the brains of my father, a distinguished serving gynecologist, I would have been in the medical profession but I came up a little short and here I am. But I have taken a particular interest throughout my now 24 years in the U.S. Senate regarding those issues which are related to medicine and also law enforcement. I spent my early years in life as an assistant U.S. Attorney and this, to me, is one of the most complex that I have ever seen.

We are privileged to have a number of people here from Virginia who will testify. There are others, like my good friend the Church family back here who have labored tirelessly with the United Mine Workers for many years and this problem is very prevalent in Southwest Virginia on up through the Roanoke Valley. But, as the chairman mentioned in his own State, here it is in Northern Virginia, four robberies here in the last few weeks.

Now I wish to say, speaking for myself, that we are not going to leap to legislation. What we have to do is to encourage the responsible partners—the medical profession where, as you say, this drug is essential to relieving pain. My father devoted much of his life to cancer and that is one of the primary uses of this product. Indeed, the law enforcement have got a major role, to explain what it is about this particular drug that has induced so many to perform crimes and then oftentimes become addicts themselves. The treatment of those who either legally or illegally get possession of this drug and use it without the careful guidance of the physician.

So there are many parties, in my judgment, that have to work with us before the Congress can move on the question of legislation.

So I thank the chair and my colleagues on this committee for joining with me today and I thank you. Yes, I was among the first to ask for this hearing. After traveling my State and holding a number of town meetings on this subject I felt it was urgent for the U.S. Senate to devote its attention and I thank the chair.

Senator REED. Thank you, Senator Warner.

Senator Clinton, do you have an opening statement?

OPENING STATEMENT OF SENATOR CLINTON

Senator CLINTON. Thank you very much, Senator Reed. I join my colleague, Senator Warner, in thanking you for holding this important hearing. And I think it is important not only because of the particular issues that have already been addressed and the particular drug that brings us here but also because we generally face a significant drug abuse problem and particularly a prescription drug abuse problem that does not quite get the attention that it deserves because of the human cost it entails.

I believe that you have put together an excellent series of witnesses. I am going to have to excuse myself. I am not going to be able to hear all the panels but I particularly wanted to thank Dr. Richard Payne, chief of Pain and Palliative Care Services at Memorial Sloan-Kettering Cancer Center in New York for being here because one of the purposes of this hearing is to educate the public about prescription drug abuse, to work with the medical professions represented to determine how best they can have more control over the prescription drugs that are so central to the legitimate purposes in medicine. For example, we should be looking at prescription monitoring programs, which constitute an information tool that doctors can use to protect themselves from drug-seekers and doctor-shoppers.

But I also think we have to take a hard look at what particular specific problems are arising out of OxyContin in and of itself. I agree completely with Senator Warner that we have to go at this in a very careful and thoughtful way because on the other side of

the ledger I worry about the people who do suffer from cancer and other very painful diseases and conditions for whom this drug is literally a life-saver because of the way that it can relieve their pain.

You know, the Institute of Medicine issued a June 2001 report concluding that people with cancer, including children, suffer great pain and much of that pain, even at the end of life, is often ignored or treated less than successfully and many, many people who are themselves patients feel concern about what they should or should not accept from their physicians in terms of relieving pain.

So this whole question of pain relief is one that I hope we will also get into more directly through this hearing and other hearings. I am concerned, for example, that one out of every 10 women undergoing radical mastectomies reported chronic pain but often that was just chalked up to psychological anguish. And finally, a study in the 1980s showed that the surgical technique for radical mastectomy was often severing a major thoracic nerve in women and the technique was reversed, but the fact that women had complained about this and the intense pain, even though it was in the context of an amputation, was not really understood for quite some time.

So I think we have to deal with the scourge of prescription drug abuse with the kind of break-ins and robberies that are unfortunately all too common, particularly in the rural areas of our State. At the same time we have to look for ways to provide the kind of palliative care that prescription drug developments certainly can do.

When New York developed a tracking system for tranquilizers, emergency rooms in New York and Buffalo reported 47 percent fewer tranquilizer overdose admissions. So there are some techniques that have been found to work and I would like to look at ways to minimize the adverse health consequences for legitimate patients.

Even in New York, though, where we saw a dramatic success, there were also reports that physicians, fearful of legal reprisals, substituted tranquilizers that were not tracked, often which had difficult and more complicated potential side effects, than the monitored drugs. So we clearly have a problem here and it goes beyond this particular drug.

I am also concerned about inappropriate prescription drug marketing and promotion. The other night watching the Olympics with my husband, a drug advertisement came on and it has beautiful pictures and the text referred to some side effects and then in little, little tiny print it had some additional information about some potential adverse effects. I do not think that that is appropriate. Advertising should provide accurate information, not misleading impressions. And I hope that we can also begin to address this issue.

And finally, Mr. Chairman, we need in general in our country more education about pain. It is a problem that leads to both underprescribing and overprescribing. And I think, in part, we have not paid enough attention. We have not done enough research. We have not educated ourselves adequately to really understand pain. We have a lot of people who are caught up in this OxyContin abuse who started out as legitimate users and then fell

into the abyss of being dependent and addicted and maybe if we understood pain better in the first place we could also avoid some of those questions.

So these are among the many issues that this excellent hearing raises for us, Mr. Chairman, and I thank you for convening us.

Senator REED. Thank you very much, Senator Clinton.

Senator Collins?

OPENING STATEMENT OF SENATOR COLLINS

Senator COLLINS. Thank you, Mr. Chairman.

I want to begin by thanking Senator Reed for agreeing to chair this hearing, which Senator Warner and I jointly requested a few months ago in response to extremely troubling developments in drug abuse in our States.

We are here today to examine the benefits and the risks of a legal but regulated narcotic pill marketed under the name of OxyContin. We will hear compelling testimony today that this drug, when used properly, has benefited thousands of individuals by relieving their suffering and improving the quality of their lives. There are many people who have a legitimate medical need for OxyContin and we cannot forget that in some cases this drug has made a real difference in the quality of their lives.

On the other hand, we will also learn today that OxyContin, diverted from its legitimate purpose to control pain, has instead created untold pain and suffering in communities like those in Washington County, Maine. I am very sad to say that the State of Maine was among the first places in the Nation to experience an epidemic of OxyContin abuse. It was not long after the first press report about OxyContin abuse in the Bangor Daily News in April of 2000 that other State and national media began documenting the effects of OxyContin on several other rural communities across the country.

One of the features that makes OxyContin so attractive to elicit users is that the time release mechanism can be defeated by simply crushing or dissolving the tablets, creating an effect similar to heroin. The drug can then be snorted or injected, with a number of tragic consequences, including addiction, criminal activity to support the addiction, involvement in other dangerous drugs such as heroin, hepatitis C and HIV infection, and, of course, overdose and even death.

It is important to acknowledge that the abuse of prescription drugs has long been a significant national problem. It is estimated that 4 million Americans abuse prescription drugs. The use and abuse of prescription medications have more than a $100 billion impact on our Nation's health care costs.

It would be disingenuous, however, to dismiss the current epidemic of OxyContin abuse as simply the latest drug of choice, no different from last year's or perhaps next year's popular drug. The testimony this afternoon will highlight how OxyContin has insinuated itself into communities and, as one Maine law enforcement officer has described it, spread like wildfire. Indeed, yesterday afternoon I was talking with our witness from Maine and we talked about the number of addicts living in Washington County, which

is a rural, beautiful but very economically disadvantaged part of my State.

Washington County has a population of only about 35,000 citizens. It is estimated by law enforcement officials that 1,000 of those citizens are addicted. That is just a startling statistic.

The first step toward any solution, of course, is to understand the problem and that is why I am so pleased that an outstanding community leader, Nancy Green, is here with us today to help us understand the problem in Washington County, Maine and, by extension, the problem that faces communities across the Nation. She serves on the front lines in her practice as a certified nurse-midwife helping pregnant women who are also OxyContin addicts. In another part of my conversation with her yesterday afternoon she described the addicted babies that she has been delivering.

In her testimony she will describe how the affliction of OxyContin abuse has affected her own community of Calais, ME. This affliction has been termed Maine's latest and newest epidemic. A brief recitation of some of the more appalling statistics about the situation in my State certainly supports that conclusion. For example, during the last 5 years Washington County has experienced an 800 percent increase in arrests related to the sale or possession of narcotics. The county sheriff attributes fully 50 percent of the increase in personal and property crimes to the abuse of OxyContin and other prescription drugs.

Admissions to substance abuse treatments for opiates, including OxyContin, have increased by 500 percent in the State of Maine since 1995, the year that OxyContin was first introduced. Admissions in Washington County alone have increased by 1,600 percent and I would tell you that it is not as if there are a lot of treatment facilities available to help people struggling with addiction.

A recent report issued last month by the Maine Substance Abuse Services Commission reported that opium addicts have gone from constituting 2 percent of the treatment population in 1995 to making up 12 percent of the treatment population in 2001. This is an unprecedented change.

Mr. Chairman, I would ask that a copy of this full report be included in the hearing record.

Senator REED. Without objection.

[The report follows:]

(The report was not available at press time, however, a copy is maintained in the Committee files.)

Senator COLLINS. These statistics, however shocking, do not fully convey the destruction of human lives caused by the abuse of OxyContin. When talking to people on the front lines in Maine I have heard stories of lost jobs, broken families, and young people who naively thought that a legal drug available at a local pharmacy could not possibly do them any real harm but who are now in a desperate fight to reclaim their lives.

The devastation spawned by OxyContin abuse in rural Maine, Virginia and other States has persuaded some people, including at least one of our witnesses, to call for the removal of the drug from the market. I respect their views but I have yet to be persuaded that the solution is that simple for removing OxyContin from the market would deprive some people of access to a drug that does in-

deed provide relief from severe pain. But in talking with people from Maine I have been convinced that we need a comprehensive approach that includes prevention, education, training for physicians, substance abuse treatment programs, and assistance to law enforcement and I look forward to exploring all of those issues with our witnesses.

One final point that I want to explore includes the circumstances surrounding the marketing of OxyContin by its manufacturer and its rise to becoming the 18th best selling prescription drug in the country and the number one opiate painkiller. Serious questions have been raised about Purdue Pharma's marketing of OxyContin and its education of physicians and thus the ability of some physicians to properly prescribe the drug. This issue prompts still further questions about whether additional Federal and State regulation and monitoring is needed.

The answers to these questions cannot erase the damage already done by OxyContin abuse to far too many people in my State and throughout the country but let us not forget that other powerful drugs, some of them in development now, may become the OxyContin of the future if we do not learn from the lessons of the past couple of years and act on them today.

Again I look forward to hearing our witnesses and thank you again, Senator Reed, for chairing this important hearing.

Senator REED. Thank you, Senator Collins.

Senator Dodd, do you have an opening statement?

OPENING STATEMENT OF SENATOR DODD

Senator DODD. Thank you, Mr. Chairman. I apologize for arriving a few minutes late for the hearing but I want to thank you, as well, for holding it and I am looking forward to hearing the testimony today. The drug OxyContin, by so many accounts, has become vital to people suffering from chronic and debilitating pain and stories of addiction and devastation obviously in States like Maine and other places are obviously very real and deserve our attention.

As the director of Helen and Harry Gray Cancer Center at Hartford Hospital in Connecticut has pointed out, drugs like OxyContin have allowed patients, and I quote, "patients suffering from chronic pain to have their lives back." So this is both a drug that causes problems but also has been the source of some real relief for people.

We are here today because of the growing number of individuals suffering from the addiction to powerful painkillers like OxyContin and the rising number of those preying upon this tragedy by diverting and selling prescription medications for illegal use. We are here today because of the millions of Americans suffering from debilitating pain who deserve the right, in my view, to have access to the most effective treatment. The abuse and diversion of OxyContin has tragically led to fatalities among abusers and it has also deterred patients who could truly benefit from the drug from taking it because of a fear that is not unfounded.

All of us agree that the alarming stories of abuse of OxyContin and the resulting addiction and destruction demand an immediate and aggressive response and, Mr. Chairman, you are holding this hearing in response to that. Because the response must be a coordi-

nated effort between targeted law enforcement and comprehensive substance abuse treatment, I am glad that we will hear from both Dr. Clark from the Substance Abuse and Mental Health Services Administration and Lieutenant Bess of the Drug Enforcement Division of the Virginia State Police, and our colleague from Virginia I am sure has already made reference to that.

Addiction destroys lives. We all know that. It destroys families, destroys neighborhoods. There is no doubt that the tragedy of drug addiction is exacerbated in communities across our country by poverty and a lack of opportunity and, as many have pointed out, our work to stem the tide of addiction must be accompanied by economic revitalization in these communities.

I am glad that we will also have a chance to hear from Purdue Pharma, the manufacturer of OxyContin, which is based in my home State of Connecticut. The company has taken some important steps since reports of abuse problems from OxyContin first began to surface to battle the misuse and diversion of their product. They are educating doctors and pharmacists in abuse and diversion prevention in coordination with the DEA, providing placebos and law enforcement sting operations, working with the FDA to craft stronger warnings on the drug's label, and pursuing development of a new abuse-resistant dosage form.

Purdue is clearly willing to participate in an effort to curtail the diversion and misuse of their product and I urge them to continue to do so. I hope that today's hearing and subsequent discussions will generate even more strategies, Mr. Chairman, for all the interested parties here to implement.

Some have suggested that the abuse of OxyContin is related to the aggressive marketing and promotion by the company. Last December Representative Frank Wolf, who chaired a hearing on this topic before a House Appropriations subcommittee requested a General Accounting Office study of Purdue's marketing techniques. Because the Federal Government has an important responsibility to monitor drug advertising and promotion in the interest of public health, we should carefully consider the quality and effect of Purdue's marketing.

In addition, we should look at the relationships between marketing and the abuse or misuse of a drug. While the prescribed and legal use of OxyContin has increased significantly since its introduction in the marketplace in 1996 as a result of manufacturer promotion and the effectiveness of the medicine, questions remain about the link between marketing and illicit use or diversion of the drug. In fact, in January of 2002 a Federal judge in Kentucky wrote that the plaintiffs in a motion to impose restrictions on the access to OxyContin had "failed to produce any evidence showing that the defendant's marketing, promotional or distributional practices have ever caused even one tablet of OxyContin to be inappropriately prescribed or diverted."

Because this issue is so critical to developing strategies for preventing abuse of a highly addictive prescription medication, I intend to ask the General Accounting Office to broaden their study to look at the entire class of medicines subject to abuse and diversion and to report on whether there is evidence of a link between marketing practices of a manufacturer and increased misuse and

diversion. I think that information, Mr. Chairman, could be of value to this committee, so we are not just looking at one product but a variety of them, as well.

So I appreciate the participation of all the witnesses and am anxious to hear what they have to say and raise some questions at the appropriate time. I thank you for holding the hearing.

Senator REED. Thank you, Senator Dodd.

I would now like to call Dr. John Jenkins and Dr. H. Westley Clark to please come forward.

Senator WARNER. Mr. Chairman, if I could——

Senator REED. Senator Warner?

Senator WARNER. I think we have had very good opening statements and what strikes me is the localization of this problem in just certain areas within my State, within your State, yet how serious they are in those localities. And if we do not get a responsible response to this issue that could spread like wildfire across the United States and become a national catastrophe. So I think it is important that we have this landmark hearing here in the Senate.

Senator REED. Thank you very much, Senator Warner. I want to also thank you and Senator Collins for your efforts. Without your insistence, this hearing would not be taking place and we appreciate that effort and commitment.

Let me introduce our first panel. Dr. John Jenkins is currently the director of the Office of New Drugs, Center for Drug Evaluation and Research at the Food and Drug Administration. Dr. Jenkins began his distinguished medical career in 1983, training in internal medicine, pulmonary and critical care at Virginia Commonwealth University and the Medical College of Virginia, where he subsequently served as an assistant professor of pulmonary and critical care medicine. He later served as medical director of the lung transplant program at the McGuire VA Medical Center and medical officer of the Division of Oncology and Pulmonary Drug Products at FDA. He has also served as a pulmonary medical group leader and director of pulmonary drug products and director of the Office of Drug Evaluation II before being appointed to his current position. Thank you very much, Dr. Jenkins, for joining us today.

Dr. H. Westley Clark, welcome. Dr. Clark is someone who has enjoyed a long and esteemed career in the field of substance abuse. He currently serves as the director of the Center for Substance Abuse Treatment at the Substance Abuse and Mental Health Services Administration under the United States Department of Health and Human Services.

In addition to obtaining his medical degree, he has a masters in public health, as well as his juris doctorate. Dr. Clark completed a two-year substance abuse fellowship at the Department of Veterans Affairs Medical Center in San Francisco, where he later served as the chief of Associated Substance Abuse Programs.

He was a senior program consultant to the Robert Wood Johnson Substance Abuse Policy Program, as well as co-investigator on a number of National Institute on Drug Abuse-funded research grants and has served as associate clinical professor of psychiatry at the University of California at San Francisco. Dr. Clark, welcome.

Dr. Jenkins and Dr. Clark, your full statements will be made part of the record so feel free to summarize your comments, as you consider appropriate. We want to go ahead and make sure that all the witnesses have ample time to present their testimony this afternoon.

Dr. Jenkins, if you would begin, please.

STATEMENTS OF JOHN K. JENKINS, M.D., DIRECTOR, OFFICE OF NEW DRUGS, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, ROCKVILLE, MD; AND WESTLEY H. CLARK, M.D., M.P.H, J.D., DIRECTOR, CENTER FOR SUBSTANCE ABUSE TREATMENT, SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION, ROCKVILLE, MD

Dr. JENKINS. Thank you, Mr. Chairman. And I will try to be brief, since many of the things I had planned to say have already been said by members of the panel.

Senator REED. Now you know how we feel.

Dr. JENKINS. I appreciate the opportunity to meet with you today to talk about the drug OxyContin and to explain FDA's actions in response to the recent reports of abuse, misuse and illegal diversion of this drug. I can assure you, Mr. Chairman, that FDA has taken these reports very seriously and we have responded to these reports with aggressive actions.

Over the past year FDA has worked closely with Purdue Pharma to strengthen the warnings and precautions sections of the product labeling regarding the serious and potentially fatal risk of abuse and misuse of this product. The labeling has also been changed to emphasize that OxyContin is only approved by FDA for treatment of moderate to severe pain in patients who require around-the-clock narcotics for an extended period of time. Finally, FDA has been working closely in partnership with the Drug Enforcement Administration, SAMHSA and other Federal agencies to address this problem of abuse, misuse and illegal diversion.

In the next few minutes I would like to give you a brief overview of OxyContin and summarize FDA's activities in response to the reports of abuse of this drug. I would also like to briefly touch on FDA's activities related to regulation of the promotion and marketing of OxyContin.

As has been noted already, OxyContin is a narcotic drug that was approved by FDA in 1995 for treatment of moderate to severe pain. It contains oxycodone, which is a narcotic that has an abuse and addiction potential similar to that of morphine. OxyContin is formulated in a sustained release mechanism that allows release of oxycodone in a slow and steady manner following oral ingestion to provide up to 12 hours of relief from pain. If the tablet is crushed, however, as has been noted already, the controlled release mechanism is defeated, resulting in the immediate release of the entire OxyContin dose. Ingestion, snorting or intravenous injection of the resulting powder can result in a fatal overdose in some situations.

At the time of approval, FDA determined that the benefits of OxyContin outweighed its risk when used to treat moderate to severe pain. At the time of approval, FDA also considered the abuse potential of OxyContin and determined that its abuse potential was

similar to that of other Schedule II narcotics and we did not foresee the widespread abuse and misuse of OxyContin that has been reported in the past few years. Despite these troubling reports, however, FDA continues to believe that the benefits of OxyContin outweigh its risks when the drug is used according to the approved labeling.

In July of last year Purdue Pharma, working in cooperation with FDA, significantly strengthened the warnings and precautions in the labeling for OxyContin. The labeling for OxyContin now includes a black box warning, which is the strongest warning for an FDA-approved product. This boxed warning alerts patients and physicians to the potentially lethal consequences of crushing the controlled release tablets. Purdue Pharma sent a "Dear Health Care Professional" letter to thousands of physicians and other health care professionals to alert them to these important new warnings.

Furthermore, the labeling for OxyContin now makes clear that it is only approved by FDA for treatment of moderate to severe pain in patients who require around-the-clock narcotics for an extended period of time. And finally, a patient instruction sheet which provides information to assist patients in the proper use of OxyContin was recently added to the labeling.

Now let me briefly discuss issues related to the advertising and promotion of OxyContin, an issue that several of you have raised in your opening statements.

First, FDA is not aware of any direct-to-the-consumer marketing or advertising of OxyContin. As far as FDA is aware, all advertising and marketing for OxyContin has been directed only to health care professionals and has generally been in compliance with FDA regulations.

In May of 2000, however, FDA did send a letter to Purdue Pharma regarding a medical journal advertisement that promoted OxyContin in a manner that FDA considered to be inappropriate. Purdue Pharma agreed to cease dissemination of that advertisement and the matter was considered to be resolved.

In conclusion, Mr. Chairman, FDA believes that OxyContin is a valuable product for the treatment of moderate to severe pain when it is used according to the approved labeling. FDA is continuing to work closely with Purdue Pharma to take appropriate actions to curb the abuse and misuse of OxyContin and we are committed to continuing to work with SAMHSA and our other Federal agency partners in an effort to address this serious public health issue. Thank you and I would be happy to take any questions.

Senator REED. Thank you very much, Dr. Jenkins.

[The prepared statement of Dr. Jenkins follows:]

PREPARED STATEMENT OF JOHN K. JENKINS, M.D.

Introduction

Mr. Chairman and Members of the Committee, I am John K. Jenkins, M.D., Director, Office of New Drugs, Center for Drug Evaluation and Research (CDER), Food and Drug Administration (FDA or the Agency). I appreciate the opportunity to talk about the drug OxyContin and the steps that FDA has taken in an effort to decrease abuse and misuse of this product while assuring that this drug is used properly and remains available for patients who suffer daily from chronic moderate to severe pain.

Let me assure you that the Agency has taken reports of abuse and misuse of OxyContin very seriously and we have implemented aggressive steps in response to these reports. FDA has worked closely with the manufacturer of OxyContin, Purdue Pharma L.P., to strengthen the warnings and precautions sections of the approved labeling for OxyContin in order to educate physicians, other healthcare professionals, and patients regarding the serious, and potentially fatal, risks of abuse and misuse of this product. FDA has also worked with Purdue Pharma to modify the approved labeling for OxyContin to emphasize that it is approved for the treatment of moderate to severe pain in patients who require around-the-clock narcotics for an extended period of time. FDA also has worked closely with the Drug Enforcement Administration (DEA) to address their concerns regarding abuse, misuse, and illegal diversion of OxyContin.

In order to help you to better understand FDA's actions, I would like to give you a brief overview of the process FDA followed in approving OxyContin and FDA's activities related to regulation of the promotion and marketing of OxyContin.

Background

OxyContin is a narcotic drug that was approved by FDA for the treatment of moderate to severe pain on December 12, 1995. OxyContin contains oxycodone HCI, an opioid agonist with an addiction potential similar to that of morphine. Opioid agonists are substances that act by attaching to specific proteins called opioid receptors, which are found in the brain, spinal cord, and gastrointestinal tract. When these drugs attach to certain opioid receptors in the brain and spinal cord they can effectively block the transmission of pain messages to the brain. OxyContin is formulated to release oxycodone HCI in a slow and steady manner following oral ingestion. OxyContin is the only currently marketed FDA approved controlled-release formulation of oxycodone. The drug substance oxycodone, however, has been marketed in the U.S. for many decades and is available in a wide variety of immediate release and combination dosage forms.

Oxycodone, like morphine and other opioid agonists, has a high potential for abuse. OxyContin was specifically developed as a controlled release formulation by Purdue Pharma to allow for up to 12 hours of relief from moderate to severe pain. This dosage form allows patients with chronic moderate to severe pain to have their pain controlled for long periods of time without the need for another dose of medication and significantly reduces the number of tablets the patient must take each day.

When used properly, the OxyContin tablet must be taken whole and only by mouth. If the tablet is crushed, the controlled-release mechanism is defeated and the oxycodone contained in the tablet is all released at once. If the contents of an OxyContin tablet are injected intravenously or snorted into the nostrils a potentially lethal dose of oxycodone is released immediately. The risk of death due to abuse of OxyContin in this manner is particularly high in individuals who are not tolerant to opioids.

Oxycodone, the active ingredient in OxyContin, is a controlled substance in Schedule II of the Controlled Substances Act (CSA), 21 U.S.C. § 801 et seq., which is administered by the DEA. Schedule II provides the maximum amount of control possible under the CSA for approved drug products. Schedule I drugs are considered to have no recognized medical purpose and are illegal in the U.S. outside of FDA approved research.

FDA Drug Approval Process

Before any drug is approved for marketing in the U.S., FDA must decide—as quickly as a thorough evaluation allows—whether the studies submitted by the drug's sponsor (usually the manufacturer) have adequately demonstrated that the drug is safe and effective under the conditions of use in the drug's labeling. It is important to realize; however, that no drug is absolutely safe. There is always some risk of adverse reactions with drugs. FDA's approval decisions, therefore, always involve an assessment of the benefits and the risks for a particular product. When the benefits of a drug are thought to outweigh the risks, and if the labeling instructions allow for safe and effective use, FDA considers a drug safe for approval and marketing.

OxyContin was reviewed by FDA and was approved for treatment of moderate to severe pain based on two clinical trials that demonstrated that it was safe and effective for this use. Prior to approval, FDA evaluated the benefits and risks of use of OxyContin for treatment of moderate to severe pain and determined that the drug was appropriate for use in this population when used according to the approved labeling.

During the approval process of OxyContin, as with all drugs that are active in the brain, FDA assessed its potential for abuse and misuse. Abuse liability assess-

ments are based on a composite profile of the drug's chemistry, pharmacology, clinical manifestations, similarity to other drugs in a class, and the potential for public health risks following introduction of the drug to the general population. At the time of approval, the abuse potential for OxyContin was considered by FDA to be no greater than for other Schedule II opioid analgesics that were already marketed in the U.S. Based on. the information available to FDA at the time of its approval, including the record of other modified release Schedule II opioids, the widespread abuse and misuse of OxyContin that has been reported over the past few years was not predicted. In fact, at the time of its approval, FDA believed that the controlled-release characteristics of the OxyContin formulation would result in less abuse potential since, when taken properly, the drug would be absorbed slowly and there would not be an immediate "rush" or high that would promote abuse. In part, FDA based its judgment of the abuse potential for OxyContin on the prior marketing history of MS-Contin, a controlled-release formulation of morphine that had been marketed in the U.S. by Purdue Pharma without significant reports of abuse and misuse for many years. At the time of OxyContin's approval, FDA was aware that crushing the controlled-release tablet followed by intravenous injection of the tablet's contents could result in a lethal overdose. A warning against such practice was included in the approved labeling. FDA did not anticipate, however, nor did anyone suggest, that crushing the controlled-release capsule followed by intravenous injection or snorting would become widespread and lead to a high level of abuse.

FDA Actions

Labeling Changes

In July 2001, Purdue Pharma, working in cooperation with FDA, significantly strengthened the warnings and precautions sections in the labeling for OxyContin. The labeling for Oxycontin now includes a "black box" warning, the strongest warning for an FDA approved product, which warns patients and physicians of the potentially lethal consequences of crushing the controlled release tablets and injecting or snorting the contents. The indication for use was clarified to reflect that it is approved for the treatment of moderate to severe pain in patients who require around the clock narcotics for an extended period of time.

To help in the effort to curb abuse and misuse of OxyContin, FDA has worked with Purdue Pharma to implement other specific changes in the OxyContin labeling. The new labeling is intended to highlight to physicians, other health care professionals, and patients that OxyContin should be used for the treatment of moderate to severe pain in patients who require around the clock narcotics for an extended period of time. As part of the labeling changes, a patient instruction sheet was added, which contains information to assist patients in the proper use of OxyContin. These labeling changes are an effort to educate pharmacists, other health professionals, and the general public regarding just how important it is to use this drug properly. The new warnings are intended to lessen the chance that OxyContin will be prescribed inappropriately for pain of lesser severity than the approved use or for other disorders or conditions inappropriate for a Schedule II narcotic.

FDA has developed a patient-information page on its website www.fda.gov/cder/drug/infopage/oxycontin/default.htm). This site provides important information to patients regarding how to safely use OxyContin, urges patients to keep their supply of OxyContin in a secure location, and instructs patients to destroy unneeded tablets.

As part of a longer-term strategy to address the current reports of abuse and misuse of OxyContin, Purdue Pharma has informed FDA that the company is working to reformulate OxyContin. The reformulation would add an opioid antagonist that would counteract the effects of oxycodone, the active ingredient in OxyContin, if the OxyContin tablet were crushed into a powder and injected or snorted. FDA is working actively with Purdue Pharma to evaluate the safety and effectiveness of such a reformulated product. It must be noted that such a reformulation is not a simple task and it could be several years before any new combination product is developed, tested in clinical trials, and approved by FDA. It also must be noted that the addition of the opioid antagonist to OxyContin to deter abuse means that legitimate patients would be exposed to a drug substance that they do not need. This could result in adverse reactions in such legitimate patients. These potential safety issues, and assurance that the combination tablet retains its effectiveness in treating moderate to severe pain, must be a part of FDA's review of a reformulated OxyContin product.

Letters to Health Care Professionals

There have been numerous reports of OxyContin diversion and abuse in several states. Some of these reported cases have been associated with serious consequences including death. In an effort to educate health care providers about these risks, Pur-

due Pharma has issued a warning in the form of a "Dear Healthcare Professional" letter. The "Dear Healthcare Professional" letter was distributed widely to physicians, pharmacists, and other health professionals. The letter explains the changes to the labeling, including proper prescribing information and highlights the problems associated with the abuse and diversion of OxyContin.

FDA approved indication for OxyContin is for the treatment of patients with moderate to severe pain who require around-the-clock opioids for an extended time. An important factor that must be considered in prescribing OxyContin is the severity of the pain that is being treated, not simply the disease causing the painful symptoms.

FDA continues to recommend that appropriate pain control be provided to patients who are living with moderate to severe pain. Although abuse, misuse, and diversion are potential problems for all opioids, including OxyContin, they are a very important part of the medical armamentarium for the management of pain when used appropriately under the careful supervision of a physician.

Meeting With Other Government Agencies and Industry

FDA has met with DEA, the Substance Abuse and Mental Health Services Administration, the National Institute on Drug Abuse, the Office of National Drug Control Policy, the Centers for Disease Control and Prevention and Purdue Pharma, and continue to work collaboratively sharing information and insights needed to address the problem of OxyContin abuse and diversion.

Millions of Americans suffer from some form of chronic pain. The pain can be debilitating and often prevents those afflicted from working or even leaving their home. Many medications, including opioids, play an important role in the treatment of chronic pain. Opioids, however, often have their use limited by concerns regarding misuse, addiction, and possible diversion for non-medical uses. The use of opioid therapy in some patients has shown extraordinary promise, enabling some to return to work and to lead a normal life again. FDA is committed to continuing to work with other government agencies and sponsors to insure that options are available to patients with chronic moderate to severe pain, so that in consultation with their personal physician they can achieve as normal a life as possible.

Advisory Committee Meetings

An FDA advisory committee, a group of non-Agency experts, held a meeting on January 30–31, 2002, to discuss the medical use of opioid analgesics, appropriate drug development plans to support approval of opioid analgesics, and strategies to communicate and manage the risks associated with opioid analgesics, particularly the risks of abuse of these drugs. Committee members agreed that opioids are essential for relieving pain and that a great deal of progress has been made within the last few years to remove the stigma associated with opioid treatment. Members suggested that a balanced approach should be taken to relieve pain for patients and to prevent diversion. They noted that imposing restrictions on use of opioids could have substantial likelihood of hurting legitimate patients and reversing the tremendous progress that has been achieved in the appropriate treatment of pain.

FDA will continue to monitor reports of abuse, misuse, and diversion of OxyContin and other opioids and will work with other Federal agencies and drug manufacturers to help ensure that these important drugs remain available to appropriate patients.

Drug Advertising

FDA has regulated the advertising of prescription drugs since 1962, under the Food, Drug, and Cosmetic (FD&C) Act and its implementing regulations. The Division of Drug Marketing, Advertising, and Communications (DDMAC), in CDER, is responsible for regulating prescription drug advertising and promotion. DDMAC's mission is to protect the public health by insuring that prescription drug information is truthful, balanced, and accurately communicated. This is accomplished through a comprehensive surveillance, enforcement, and education program, and by fostering optimal communication of labeling and promotional information to both health care professionals and consumers.

FDA regulates prescription drug advertisements and other promotional materials (called "promotional labeling") disseminated by or on behalf of the advertised product's manufacturer, packer or distributor to health care professionals and consumers.

Title 21 of the Code of Federal Regulations (21 CFR § 314.81(b)(3)(i)) requires that advertisements and promotional labeling be submitted to FDA at the time of initial dissemination (labeling) and initial publication (advertisements); a post-marketing submission requirement. The FD&C Act generally prohibits FDA from requiring that advertisements be approved prior to their use (see § 502(n)). In other words,

FDA's review of promotional materials is generally intended to occur *post hoc*—once the materials have already appeared in public. Accordingly, any FDA enforcement action that FDA takes is *post hoc* as well. Most of FDA's enforcement actions request that sponsors stop using the violative materials. In some cases, FDA also asks sponsors to run corrective advertisements or issue corrective letters to remedy inaccurate product impressions created by false or misleading materials.

FDA is not aware of any direct-to-consumer advertising for OxyContin. There is nothing in the FD&C Act to prohibit such advertising. The advertising and marketing for OxyContin has been directed only to health care professionals. It should be noted that the current approved product labeling for OxyContin contains a "black box" warning. Boxed warnings are used in labeling to convey serious risks associated with the use of the drug product. The promotional materials of drug products with boxed warnings must present these serious risks in a prominent manner. DDMAC sent a letter to Purdue Pharma dated May 11, 2000, regarding a journal advertisement that appeared in the *New England Journal of Medicine* that promoted OxyContin in a manner that was false or misleading. Specifically, the advertisement implied OxyContin had been studied in all types of arthritis and can be used as first-line therapy for the treatment of osteoarthritis, failed to include important limitations to claims presented from an osteoarthritis study; and promoted OxyContin in a selected class of patients without presenting risk information especially applicable to that selected class of patients. Purdue Pharma agreed to cease dissemination of this advertisement and this matter was resolved with the cooperation of the sponsor.

Conclusion

The Agency recognizes OxyContin as a valuable product when used properly. We need to do all we can to ensure that the prescriptions get to the appropriate patients and that labeling and promotion are appropriate for the product. FDA is working closely with the manufacturer to take appropriate action to curb the misuse and abuse of OxyContin. In addition, FDA is involved in the strong interagency effort to address this issue and we are aware we cannot solve this problem by ourselves.

We share the Committee's interest and concerns regarding this drug and would be happy to answer any questions.

RESPONSE FROM THE DEPARTMENT OF HEALTH AND HUMAN SERVICES TO QUESTIONS ASKED OF DR. JOHN JENKINS BY SENATOR REED

DEPARTMENT OF HEALTH AND HUMAN SERVICES,
ROCKVILLE, MD 20857,
March 7, 2002.

Hon. EDWARD M. KENNEDY,
U.S. Senate,
Washington, D.C. 20510-6300.

DEAR MR. CHAIRMAN: This letter is in follow-up to the Committee's February 12, 2002, hearing on balancing the risks and benefits of the drug OxyContin. Senator Jack Reed posed two questions to Dr. John Jenkins, Director, Office of New Drugs, Center for Drug Evaluation and Research, Food and Drug Administration (FDA or the Agency) for the public record. We have restated the questions and provided answers below.

Question 1. Would the abuse potential of a drug that is the subject of an investigational drug application ever be a reason for FDA's deciding that the drug is not safe and effective? That is, would the abuse potential of a drug, and the level of harm that the drug can do when it is abused, ever outweigh the benefits provided by proper use of the drug?

Answer 1. The decision to approve or not approve a drug is based on the demonstration of efficacy and safety of the drug in the population intended for use of the drug. In the situation where an investigational drug has been shown to be safe and effective for the intended use but is considered to have a significant potential for misuse, FDA would consider implementing a strategy, in cooperation with the sponsor, to effectively manage this risk. Such a risk management strategy could be put into place in the form of a voluntary agreement with the sponsor regarding the distribution and/or marketing of the product, or may be required by FDA as a condition of approval. The Agency has used this approach to manage the risk of misuse of opiates and would consider utilizing similar strategies in the future for other drugs that are subject to misuse.

Question 2. It seemed that all of the panelists agreed that patients who use OxyContin appropriately rarely become addicted to the drug. How many times

would someone need to use or how much OxyContin would someone have to use to start on the way to becoming addicted?

Answer 2. There is an important distinction to be made between physical dependence and addiction to an opioid drug. In the case of physical dependence, with regular dosing over the course of several weeks, evidence of physical dependence can be seen. This is a natural phenomenon, which in general leads to no untoward consequences. In fact, once these individuals no longer require treatment with the opioid, they suffer no residual physical effects and do not crave the effects of the drug. Along with physical dependence, comes tolerance to the effects of the drug, so that the patient may require higher doses over time to achieve the same level of pain control. These natural effects, however, also occur in the addicted patient.

Addiction, as distinguished from physical dependence, is not a normal condition, but rather one with a complex set of contributing etiologies that leads to abnormal craving for the drug to the extent that the addict is willing to commit crimes and engage in self-destructive behaviors in order to obtain the drug. The contribution of physical dependence and tolerance add to the exaggerated drug craving from which the addict is unable to break free. In the case of an addict, it may take only one or two doses to launch back into the cycle of addictive behavior. Whereas in the case of a patient who does not have this addictive propensity, addiction will not occur even after years of treatment.

Thank you again for your interest in this matter. If you have further questions, please let us know.

Sincerely,

MELINDA K. PLAISIER,
Associate Commissioner for Legislation.

RESPONSE FROM THE DEPARTMENT OF HEALTH AND HUMAN SERVICES TO A QUESTION ASKED OF DR. JOHN JENKINS BY SENATOR COLLINS

DEPARTMENT OF HEALTH & HUMAN SERVICES,
ROCKVILLE, MD 20857,
March 12, 2002.

Hon. EDWARD M. KENNEDY,
U.S. Senate,
Washington, D.C. 20510–6300.

DEAR MR. CHAIRMAN: Thank you for the opportunity that was provided to Dr. John Jenkins, Director, Office of New Drugs, Center for Drug Evaluation and Research, Food and Drug Administration (FDA or the Agency), to testify before your committee on February 12, 2002, regarding balancing the risks and benefits of the drug OxyContin.

During the hearing, Senator Susan M. Collins asked if FDA had ever sent a warning letter to Purdue Pharma, the manufacturer of OxyContin, for the drug MS Contin. Dr. Jenkins offered to provide that information for the record.

FDA's Division of Drug Marketing, Advertising, and Communications did issue a warning letter to Purdue Pharma on its promotion of MS Contin on November 20, 1996, for making unsubstantiated comparative claims for MS Contin over other opioid products for cancer pain. Although it was a warning letter, the violations did not raise serious health concerns. A copy of the warning letter is enclosed.

Thank you for making this a part of the public record. If you have further questions, please let us know.

Sincerely,

MELINDA K. PLAISIER,
Associate Commissioner for Legislation.

ATTACHMENT

DEPARTMENT OF HEALTH & HUMAN SERVICES,
ROCKVILLE, MD 20857,
November 20, 1996.

RAYMOND R. SACKLER, M.D.,
President, The Purdue Frederick Company,
100 Connecticut Avenue,
Norwalk, CT 06850–3590.

RE: NDA# 19–516,
MS Contin (morphine sulfate controlled release) Tablets,

MACMIS ID #4247

WARNING LETTER

DEAR DR. SACKLER: This Warning Letter concerns The Purdue Frederick Company's (Purdue) promotional materials for the marketing of MS Contin (morphine sulfate controlled release) Tablets. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed these materials as part of its monitoring and surveillance program. We have concluded that Purdue is disseminating promotional materials for MS Contin that contain statements, suggestions, of implications that are false or misleading in violation of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. §§ 352(a) and 331(a) and applicable regulations. This violation is occurring despite repeated notification to Purdue by DDMAC that claims of product superiority were unsupported and were false and/or misleading and in violation of the Act.

The promotional materials disseminated by Purdue that are the subject of this letter are represented to be "reprints" of an article by Michael H. Levy entitled *Pharmacologic Management of Cancer Pain* that appeared in *Seminars in Oncology* (Vol. 21, No. 6, pages 718–739), December 1994.[1] These materials were submitted to FDA by Purdue pursuant to the post-marketing reporting requirements for promotional labeling and advertising, 21 CFR 314.81(b)(3).

This Warning Letter does not concern Dr. Levy's published article. It does concern the use of reprints and promotional materials derived from the article that were disseminated by Purdue in its promotion of MS Contin.

Violations

These promotional materials contain false and/or misleading statements and suggestions that MS Contin is superior to other analgesics, either in effectiveness, safety, or other parameters, in the management of cancer pain. Specifically, the article states or suggests that controlled-release morphine (MS Contin) is superior to other opioid analgesics for chronic cancer pain. According to the modified reprint of the Levy article,[2]

- "Controlled-release morphine (MS Contin) is the best opioid analgesic for pain prevention in patients with chronic cancer pain." (See page 724).
- "MS Contin is recommended over Oramorph based on the smaller size and the color-coding of its tablets and the availability of its 15-mg and 200-mg dosage forms." (See page 724).
- "Because of its 12-hour dosing interval, MS Contin is the preferred opioid analgesic for these patients along with PRN supplements of MSIR for breakthrough pain." (See page 727).

As you know, there are a variety of analgesic products, including other opioid products, other morphine products and other analgesic products for chronic cancer pain. Purdue has not demonstrated that MS Contin is superior in safety or effectiveness to either other morphine products, other opioid products, or other products used for pain control in cancer patients.

Repetitive Conduct

The dissemination of these materials represents a repetitive course of violative conduct by Purdue in the promotion of MS Contin. Purdue has repeatedly disseminated materials that contain unsupported claims that MS Contin is superior to other analgesics including Oramorph. Such unsupported superiority claims have also appeared in brochures that targeted patients with cancer pain. DDMAC determined that these claims were false and/or misleading on several occasions and communicated this to Purdue in letters dated October 15, 1993, March 25, 1994, June 7, 1994, July 7, 1994, and October 3, 1994, and at a meeting between FDA and Purdue on March 24, 1994. Each of these instances involved Purdue's dissemination of promotional materials containing unsupported claims that MS Contin is, in some way, superior to its competitors' products.

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[1] The materials Purdue represents to be reprints of the Levy article are identified as # OORM64 and # B4715. The OORM64 document appears to be a reprint of the original article that was published in *Seminars in Oncology*. Although portions of the article were deleted, these deletions are not relevant to the issues in this letter. The promotional material identified as B4715 is a booklet entitled *Pharmacologic Management of Cancer Pain* by Michael H. Levy states that it was "reprinted with permission" citing to the original Levy article and was disseminated by Purdue. However, the content of the booklet is substantially different than the Levy article.

[2] The page numbers cited above refer to the modified reprint of the *Seminars in Oncology* article identified as # OORM64. The booklet, # B4715, does not have the identical content, but also contains suggestions that MS Contin is superior to other analgesics.

Conclusion and Requested Actions

The materials and promotional messages Purdue disseminated contain false and/or misleading information about the safety and effectiveness of MS Contin. Accordingly, Purdue should propose a corrective action plan, including the mailing and publication of a "Dear Healthcare Professional" letter to disseminate corrective messages about the issues discussed in this letter to all healthcare providers, administrators at institutions, and organizations who received the violative messages.

This corrective action plan should also include:

A. Immediately ceasing the dissemination of all materials that contain false, misleading, or unbalanced claims that state, suggest, or imply that MS Contin is better than other opioid analgesics, including other controlled release morphine products, for the control and management of cancer pain.

B. A complete listing of all advertising and promotional materials that will remain in use and those that will be discontinued. Also, provide two copies of all promotional materials for MS Contin that Purdue intends to continue to distribute.

C. Within 15 days of the date of this letter, disseminating a message to all Purdue sales representatives and marketing personnel involved in the marketing and sales of MS Contin, instructing them to immediately cease dissemination of all promotional materials and messages discussed in this letter and providing each person a copy of this letter.

The Dear Healthcare Professional letter and Purdue's corrective action plan should be submitted to DDMAC for approval. After such approval, the letter should be disseminated by both direct mail and through a paid advertisement in all journals that contained advertisements for MS Contin during the 12 months prior to the date of this letter.

The violations discussed in this letter do not necessarily constitute an exhaustive list. We are continuing to evaluate other aspects of Purdue's campaign for MS Contin and we may determine that additional remedial measures will be necessary to fully correct the false and/or misleading messages resulting from Purdue's violative conduct.

Purdue should respond to this letter no later than December 6, 1996. If Purdue has any questions or comments, please contact Thomas Abrams or Norman A. Drezin, Esq. by facsimile at (301) 827–2831, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD40, Rm 17B–20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds Purdue that only written communications are considered official.

Failure to respond to this letter may result in regulatory action, including seizure and/or injunction, without further notice.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #4247 in addition to the NDA number.

Sincerely,

MINNIE BAYLOR-HENRY, R.PH., J.D.,
Director, Division of Drug Marketing, Advertising and Communications.

Senator REED. Dr. Clark?

Dr. CLARK. Thank you, Mr. Chairman. I am grateful for the opportunity to address this committee on the issue of treatment, substance abuse treatment and prevention associated with OxyContin abuse and addiction.

To begin with, I would like to agree with the members of this committee on the scope of the issue, the current problem of OxyContin. This is merely the newest part of a prescription opiod diversion and abuse problem that has been rising since the mid-1980s. If you will look at this chart here, it shows from SAMHSA's national household survey on drug abuse data that the incidence of new prescription opiod abuse and the number of new prescription opiod abusers has been rising steadily since well before the introduction of OxyContin.

The emergency room data from SAMHSA's Drug Abuse Warning Network in the next figure shows that the total number of OxyContin mentions is about half that of hydrocodone mentions.

OxyContin, of course, is only one of the marketed forms of oxycodone, which also includes other well known brands such as Percodan and Percoset.

So it is clear, as was stated by others, that we are dealing with a larger global issue of prescription drug abuse and it is important that we keep this in mind as we develop strategies of prevention, treatment, law enforcement strategies to deal with the issue of prescription drug abuse.

Of course, rural States have been seeing abuse and addiction with prescription opiods for some time. For instance, Alaska has reported that there are about 15,000 prescription opiod abusers in the State and that most methadone patients are not heroin-addicted but addicted to those prescription opiods. Even back when Arkansas was opening its first methadone clinic in December of 1993, the vast majority of its patients were not admitted for heroin addiction but for addiction to prescription opiods. When seeking treatment previously, these patients had to travel to other States because methadone treatment was not available at that time in Arkansas.

This continues to be the case today, for example, in the State of Mississippi. Our colleagues at the American Association for the Treatment of Opiod Dependence report that they have documented at least 500 Mississippi residents needing opiod agonist treatment that must travel to one of the adjacent States that do not allow for this life-saving medical therapy.

For patients who do not run into addictive problems with their medications or persons who do not start with a pain problem at all but who obtain diverted prescription opiods to further an existing drug abuse or addiction, we have several treatment strategies and we have been working with ONDCP, the FDA, NIDA, NIAAA, DEA and other Federal agencies so that we can have a rational strategy.

I would like to note that the president's new budget addresses the important general problem associated with the treatment gap. The president proposes in fiscal year' 03 a $127 million increase as the next installment of a five-year drug treatment initiative to reduce the difference between the number of Americans who need treatment for addictive disorders and the number that receive treatment. The president's proposal is, I think, a positive step. This will give us for our new fiscal year $60 million for the substance abuse block grant to the States and an additional $67 million for competitive drug treatment grants, which can be specifically targeted to urgent local needs, such as the one that we are talking about.

The treatment gap for opiod addiction is extremely important because it is estimated that there are over 1 million Americans addicted to illicit or licit opiods and only about 200,000 officially enrolled in medication-assisted treatment programs and this is an important thing because it is most difficult to find treatment for opiod addiction, especially in rural areas of our country, but that is exactly the location of the most urgent new reports of abuse and addiction with opiod drugs.

Substance abuse treatment providers, of course, as you have already mentioned, tell us that OxyContin addiction is so strong that people will go to great lengths to get the drug, including robbing

pharmacies and writing false prescriptions. A recently opened methadone treatment facility in Southwest Virginia began receiving telephone calls from people seeking treatment for OxyContin addiction even before it opened. Eighty percent of the patients entering this now-functioning out-patient treatment program name OxyContin as their primary drug of abuse. The new continuing reports of rural OxyContin tragedies have brought the rural opiod treatment gap into sharper contrast.

In September 2000 we at CSAT initiated a small project with Dr. Steven Savage of the Dartmouth Medical School and the New Hampshire Medical Society. The New Hampshire Regional Medical Opiod Treatment and Education Project is designed to be a groundbreaking planning strategy to reach out to primary care docs and other docs within the State so that opiod treatment will be more readily available.

Following that effort we have at SAMHSA allocated as a result of appropriations $500,000 for a CSAT community action grant targeted for planning for local communities, rural communities, and that effort is to involve State and local communities in developing opiod treatment services to meet the unique needs of rural communities and to address new and emerging treatment needs related to increased availability of prescription opiod medications and heroin so that we can begin to address this problem.

We have worked with the State of Connecticut since 1997 to fund demonstrations of office space opiod treatment and we believe that this may serve as one appropriate model for treatment that could help rural physicians. And we have had similar projects working with the National Institute of Drug Abuse funded in New York and we have worked closely with NIDA and the Food and Drug Administration and the New York State Office of Alcoholism and Substance Abuse Services to help develop models of opiod treatment based on community pharmacies so that we can expand opiod assisted treatment to people in need, particularly in rural communities.

We anticipate, with the work of others in the field, including NIDA, the release of a new product called Buprenorphine sometime this year which will assist us in allowing primary care docs in communities to use another medication in addition to methadone.

SAMHSA has been working with State medical boards and their Federation of State Medical Boards, as well as the American Society of Addiction Medicine, the American Osteopathic Academy of Addiction Medicine, the American Academy of Addiction Psychiatry and the American Psychiatric Association and other medical organizations to create a standardized medical curriculum, a treatment improvement protocol with guidelines, best practices, and a number of continuing education courses. We had, in fact, a course in March of 2000; we sponsored a Buprenorphine training course in Newport, RI so that we could get physicians trained. We have trained about 1,500 physicians.

We have also consulted with States. In July of 2000 we were in Bangor, ME at the invitation of the mayor, city council and the citizens and we were talking about medication-assisted therapies, specifically methadone, as a result of their OxyContin and heroin problem.

So we realize that this is going to be an on-going process. We will continue to work with local communities, States, the FDA, the Department of Justice, Drug Enforcement Administration, and others so that we can make sure that the issue of treatment and prevention and the mental health component because I would like to point out that many people who become dependent on opiods also have concomitant psychiatric problems that need to be addressed, so we are working aggressively with the community and continue to take instructions from members of this committee and the Congress on this issue.

We would like to point out that most people who have pain and take OxyContin for the pain do not become addicts and that is an important thing. In fact, the data seem to suggest that the people who have problems with OxyContin have problems with addiction and not with pain. Now that does not mean that there is no overlap but I think it is an important thing to keep in mind because members of this committee have raised that issue and we would like to echo that.

And pain patients, pain does not necessarily protect the patient who may otherwise be at risk for addictive disorders. Pain patients with addictive histories require additional safeguards when opiods are required for management of the pain. Withholding opiod analgesics from these patients, however, is not necessarily the safest course of treatment. They often know all too well where they can obtain what they need for pain relief but from a much more dangerous source. Patients with both chronic pain and opiod addiction require careful management but they can be and should be managed for both disorders concurrently.

Medical experience in this area is growing. We are participating with—we have contributions from people on your panels and from people who are interested in the appropriate management of pain patients and we will continue to work with them.

Mr. Chairman, thank you again for the opportunity to appear before this committee.

Senator REED. Thank you very much, Dr. Clark.

[The prepared statement of Dr. Clark follows:]

PREPARED STATEMENT OF H. WESTLEY CLARK, M.D., M.P.H., J.D.

Mr. Chairman, I am grateful for the opportunity to address this Committee regarding the treatment of OxyContin(A) addiction and the prevention of further drug abuse through effective medical interventions for addiction to OxyContin and other prescription and nonprescription opioids. Before delivering my remarks on this very important and timely topic, I would like to thank the Committee for its attention to this issue, and for your recognition of the importance of addiction treatment in the drug abuse equation, that you demonstrate by today's invitation to the Substance Abuse and Mental Health Services Administration (SAMHSA). As the Director of SAMHSA's Center for Substance Abuse Treatment (CSAT), I am responsible for leading SAMHSA's substance abuse treatment effort.

As you know, SAMHSA is the lead Federal agency for improving the quality and availability of substance abuse prevention, addiction treatment and mental health services in the United States. SAMHSA has both funding authority and certain key regulatory responsibilities that will play a central role in the national response to abuse of and addiction with OxyContin and the many other prescription analgesics which can be abused by Americans in the grip of opioid addiction. It must be recognized that the abuse of OxyContin is not primarily by those who are pain patients but by those who are opioid addicts. In diverting and abusing prescription opioids, these addicted Americans hurt not only themselves, their families and those around them, but they also hurt the pain patients, who have ongoing needs for these medi-

cations, and for whom these medications sustain life and improve function, rather than endangering life and destroying function, as they do in the untreated disease of opioid addiction. I have worked as a physician for many years in this area of practice, and have published on the use of opioids in the treatment of chronic pain and on the assessment of addiction in that setting.

Most people who take OxyContin and other prescription opioids, as prescribed, do not become addicted. With prolonged use of opioids, however, pain patients often do become tolerant, that is, require larger doses, although this does typically reach a plateau, which can vary markedly between different patients and different pain conditions. Chronic pain patients can also become physically dependent on their medications. However, most patients who receive opioids for pain, even those undergoing long-term therapy, do not become addicted to these drugs.

Addiction in the course of opioid treatment for pain should ideally be assessed after the pain has been brought under adequate control, though this is not always initially possible. Addiction is recognized by one or more of its characteristic features: impaired control, craving and compulsive use, and continued use despite negative physical, mental, and/or social consequences. Sometimes patient behaviors that might suggest addiction are simply a reflection of unrelieved pain. This has been called pseudo-addiction, and is an important misdiagnosis to be avoided in pain patients. Therefore, medical judgment must be used in determining whether a concerning pattern of behaviors in a pain patient signals the presence of addiction or whether it reflects a different medical problem.

In short, most individuals who take their prescribed OxyContin, or any other opioid such as 2 hydrocodone or morphine, under medical treatment for pain, will not become addicted, although some may become physically dependent on the drug and may need to be carefully withdrawn after their pain problem is otherwise resolved. Patients who are taking these drugs as prescribed should continue to do so, as long as they and their physician agree that taking the drug is a medically appropriate way for them to manage pain.

For patients who do run into addictive problems with their medication, or for persons who didn't start with a pain problem at all, but who obtained diverted prescription opioids to further an existing syndrome of drug, abuse and addiction, we have a range of very effective treatments, to be described in more detail below. However, the system that provides these treatments has historically been fragmented and underfunded. The Presidents' new budget addresses this important general problem by proposing an increase of $127 million for the next year of a five-year drug treatment initiative to help reduce this treatment gap in the United States, to reduce the difference between the number of Americans who need treatment for addictive disorders and the number that receive the treatment and services to manage their illness and rebuild their lives. The President's current proposal is for the second year of this five-year initiative. Secretary Thompson has confirmed that "There continues to be a great need to expand our nation's capacity to treat people who are addicted." and that "This administration is committed to supporting local programs that combat the personal despair and community disintegration brought by drug addiction." Our new fiscal year 2003 budget requests an increase of $60 million for the Substance Abuse Block Grants to the States and an additional $67 million for competitive drug treatment grants, which can be specifically targeted to urgent local needs such as those we are discussing today.

There is a particularly large treatment gap when it comes to treatment for opioid addiction, with estimates of over one million Americans addicted to licit or illicit opioids, and only about 200,000 patients enrolled in effective medical treatment programs. It is most difficult to find treatment for opioid addiction especially in the rural areas of our country. But that is exactly the location of the most urgent new reports of abuse and addiction with prescription opioids. 3 Many reports of abuse and addiction are occurring in rural areas that have labor-intensive industries, such as logging or coal mining. These industries are often located in economically depressed areas, as well. Therefore, people for whom the drug may have been legitimately prescribed may be tempted to sell their prescriptions for economic reasons. Substance abuse treatment providers tell us that OxyContin addiction is so strong that people will go to great lengths to get the drug, including robbing pharmacies and writing false prescriptions. A recently opened methadone treatment facility in southwest Virginia began receiving telephone calls from people seeking treatment for OxyContin addiction before it was even open. Eighty percent of patients entering this now fully- functional outpatient treatment program name OxyContin as their primary chug of abuse. The new millennium's continuing news reports of a rural OxyContin tragedy have brought this rural opioid treatment gap into even sharper contrast for those of us already familiar with the treatment gap as a whole.

Even before this tragic news began to break, SAMHSA was already planning to pilot new ways of working with the medical community to provide exemplary models of medical treatment for opioid addiction in rural areas. In September of 2000, we at CSAT initiated a small project with Dr. Seddon Savage, of the Dartmouth Medical School and the New Hampshire Medical Society. The New Hampshire Regional Medical Opioid Treatment and Education Project, (NH ReMOTE), was a groundbreaking treatment planning project. It's chief objectives were to assess addiction treatment needs and resources in various communities in New Hampshire, and to plan development of primary care office based management of addictive disease, including medical therapy of opioid addiction, at several sites around the State. NH ReMOTE was the first project in the United States to target development of a statewide office-based treatment system for opioid addiction.

Primary care physicians, interested in expanding their care of individuals with addictions, are being drawn from 8-10 sites geographically distributed through the state. Physicians will be linked with addiction counselors and social and vocational services in their region to form integrated care teams for patients with addictive disorders. Hospital or other established local pharmacies will dispense opioid medications to patients requiring opioid addiction treatment under direction of the treating physician. The NH ReMOTE Project will develop regulatory and documentation systems to support effective medical treatment practices.

A central resource group of professionals experienced in therapy of opioid addiction, will be available to provide consultation as needed to the regional care providers. This group will likely be drawn from existing free-standing specialty addiction treatment clinics. Patients requiring opioid therapy who cannot successfully be managed by the regional teams will receive care managed by this central group of experts.

All personnel involved in the regional care teams will receive training requisite to fulfilling their role on the care team. Physician training will include education in general addiction medicine and specific training in opioid therapies, including the use of methadone, LAAM, naltrexone and buprenorphine. I will return later to describe these specific medication assisted therapies for opioid addiction.

The initial response of the medical community to New Hampshire ReMOTE was very promising. So, while we were publishing our first CSAT Advisory on OxyContin: Prescription Drug Abuse, in April of 2001 (which I have brought for the Committee), we were already working on an additional $500,000 to be allocated to the CSAT Action Grant Program for similar purposes. The purpose of that special announcement, for which applications were received in September, 2001, was to provide leadership in developing consensus among key stakeholders in additional State and local communities toward the goal of developing opioid treatment services to meet the unique needs of rural communities, and to address new and emerging treatment needs related to the increased availability of heroin or prescription opioid medications, such as oxycodone or hydrocodone, and to support exemplary practice models for rural communities experiencing problems with opioid addiction. Proposed projects were intended to help treatment providers, including physicians, hospitals, community health centers and community mental health centers adopt exemplary practice models for opioid 5 treatment into their communities. These exemplary practices will be targeted at delivering medication assisted therapy to rural populations where previous access to opioid treatment services has been limited or nonexistent. We anticipate that grants will be awarded this Spring under this special funding opportunity. While I cannot comment on specific grant proposals currently under review, I will say that some excellent and important projects are anticipated to start this fiscal year.

We have also worked with the State of Connecticut, since 1997, to find pilot demonstrations of office-based opioid treatment (OBOT), which we believe may serve as one appropriate model of treatment that could be provided in the offices of rural physicians. Similar projects have been funded in New York by the National Institute on Drug Abuse (NIDA), and we have worked closely with NIDA, the Food and Drug Administration (FDA) and the New York State Office of Alcoholism and Substance Abuse Services to develop models of opioid treatment based on community pharmacies, such as may also be found in rural communities.

Now that I have spoken specifically to what we are doing about rural opioid addiction treatment, I would like to speak more generally about the medical therapy of opioid addiction, and CSAT's programs to increase the quantity and availability, as well as the quality and effectiveness, of treatment for this potentially devastating illness.

Abuse of prescription pain medications is not new. However, two primary factors, set apart OxyContin abuse from other prescription drug abuse:

• First, OxyContin contains a much larger amount of the active opioid ingredient (oxycodone) than most other prescription pain medications. By crushing the tablet and either swallowing or snorting it, or by injecting the dissolved tablet, abusers feel the effects of the opioid in a short time, rather than over a 12-hour span. It is this high rate at which drug gets to the brain, as well as the overall dose taken, that makes for a greater effect on the brain's reward centers and 6 the consequent chemical highjacking of those centers that we call addiction.

• Second, great profits can be made from the illegal sale of OxyContin. A 40-milligram pill costs approximately $4 by prescription, yet it may sell for $20 to $40 on the street, depending on the area of the country. OxyContin is comparatively inexpensive when purchased legitimately, especially if its cost is covered by insurance. However, because heroin is usually less expensive than OxyContin purchased illegally, the National Drug Intelligence Center reports that OxyContin abusers may often turn to heroin, if their insurance will no longer pay or they otherwise lose access to their OxyContin prescriptions.

Two types of treatment have been documented as effective for opioid addiction. One is a long-term, residential, therapeutic community type of treatment and the other is long-term, medication-assisted outpatient treatment. Medication-assisted opioid treatment can utilize medications that are agonists, antagonists, or partial agonists. An agonist medication is one that has the same basic effect at the brain cell membrane as the drug of abuse. However, there may be crucial differences in how fast it creates this effect and how long the effect lasts. An antagonist drug simply blocks the effect of agonist drugs, including the drug of abuse. A partial agonist drug has less effect at the brain cell membrane as the "Full" agonist, but it also serves to block the full agonist, so the partial agonist medication, such as buprenorphine, may combine certain treatment advantages of both other kinds of medication.

Some opioid-addicted patients with very good social supports may occasionally be able to benefit from antagonist maintenance with naltrexone. This treatment works best if the patient is highly motivated to participate in treatment, has strong social support, and has been adequately detoxified from the opioid of abuse. Most opioid-addicted patients in outpatient therapy, however, will do best with medication that is either an agonist or a partial agonist. Methadone and levo alpha acetyl-methadol (LAAM) are the two agonist medications currently approved for addiction treatment in this country. Prior to May of 2001, providers of this treatment were regulated by the Food and Drug Administration (FDA). In May, 2001, SAMHSA took over the regulation of opioid agonist treatment (OAT) providers under the new part 8 of 42CFR. We now have major initiatives underway to modernize, improve, mainstream and expand this 7 treatment modality. These include our use of an accreditation based system, similar to that used in most other kinds of medical facilities and along the lines that have previously been recommended by the 1995 Institute of Medicine (10M) Report on Federal Regulation of Methadone Treatment (available at: http://www.nap.edu/books/0309052408/html/) and the 1997 NIH Consensus Conference Report on Effective Medical Treatment of Opiate Addiction, (available at: http://odp.od.nih.gov/consensus/cons/108/108-intro.htm).

The guidelines for treating OxyContin addiction are basically no different than the medical guidelines for treating addiction to ANY opioid. There is one important thing to remember, however: because OxyContin contains higher dose levels of opioid than are typically found in other oxycodone-containing pain medications, higher dosages of methadone or other medications may be needed to adequately treat patients who are addicted to OxyContin.

Methadone or LAAM may be used for OxyContin addiction treatment or, for that matter, treatment for addiction to any other opioid, including the other prescription opioids. This is not a new treatment approach. Rural States have been seeing abuse and addiction with prescription opioids for some time. For instance, Alaska has reported there are about 15,000 prescription opioid abusers in the State and that most methadone patients are not heroin-addicted, but addicted to those prescription opioids. Even back when Arkansas opened its first methadone maintenance clinic in December of 1993, the vast majority of its new patients were not admitted for heroin addiction, but for addiction to prescription opioids. When seeking treatment previously, these patients had to travel to other States because methadone treatment had not been available in Arkansas. This continues to be the case, for example, in the State of Mississippi. Our colleagues at the American Association for the Treatment of Opioid Dependence (AATOD) report that they have documented at least 500 Mississippi residents needing opioid agonist treatment that must travel to one of the adjacent States who do allow for this life-saving medical therapy.

Some persons in the few States that still don't allow the fall spectrum of medical therapies for opioid addiction may believe their remaining problems will be solved

by the advent of buprenorphine, the new partial agonist opioid treatment. This kind of medication shares certain properties with the antagonist medication naltrexone as well as the opioid agonists, and is safer than, although not as therapeutically powerful as, Methadone or LAAM.

Partial agonist opioid medication will be an important new tool in the medical arsenal against addiction, but it certainly won't be able to replace the current medications. Presently there is no partial agonist approved by the Food and Drug Administration (FDA) for use in addiction treatment, although a form of Buprenorphine, researched by the National Institute on Drug Abuse (NIDA) and its partners in academia and industry, holds great promise and we are told that this medication is likely to be approved by the FDA in the next 3-6 months for the treatment of opioid addiction. This medication, in conjunction with new authority provided to DHHS and redelegated to SAMHSA under the Drug Addiction Treatment Act of 2000 (P.L. 106–310 (21 U.S.C. 823(g)(2)), is expected to make significant gains possible in expanding access to opioid addiction treatment in rural and other under-served areas of the country.

The Drug Addiction Treatment Act (DATA) amended the Controlled Substances Act to permit physicians to seek and obtain waivers to prescribe approved narcotic treatment drugs for the treatment of opiate addiction. The waivers will permit qualified physicians to prescribe Schedule III, IV, or V opioid medications, when approved by FDA for the treatment of opioid addiction. These physicians would be required to refer the patients for appropriate counseling and limit his or her practice of this treatment to 30 patients. However they would otherwise be exempted from the requirements of the Narcotic Addict Treatment Act (NATA) which otherwise governs the use of scheduled opioids for addiction treatment under 42CFR8, which as I mentioned before, is now also administered by SAMHSA. The NATA remains in place for Schedule II opioids approved for addiction treatment (Methadone and LAAM). Once there is a form of Buprenorphine approved by the FDA, and the new product is scheduled by the Drug Enforcement Administration (DEA) in Schedule III, IV, or V, then most of the provisions of the DATA will go into effect and SAMHSA will be accepting applications for waivers from qualified physicians.

The DATA contained a limited Federal preemption, to allow for rapid implementation of this new office-based treatment approach across all of the States. However, States can still opt out by passing new legislation. In states that do not opt out legislatively, use of Buprenorphine under the DATA will immediately become part of the medical practice of the physicians who obtain the waiver from SAMHSA and a corresponding number from DEA, related to their existing controlled drug registration number. SAMHSA staff have been working with the State Medical Boards and their Federation of State Medical Boards (FSMB) to develop guidelines to help the Boards fulfill their responsibilities for oversight of this new and unfamiliar area of medical practice.

SAMHSA has also been working with the American Society of Addiction Medicine (ASAM) the American Osteopathic Academy of Addiction Medicine (AOAAM), the American Academy of Addiction Psychiatry (AAAP), the American Psychiatric Association (APA) and other medical organizations to create a standardized medical curriculum, a Treatment Improvement Protocol (TIP) with guidelines for best medical practices, and a number of continuing medical education (CME) courses which have trained 1500 physicians from across the country, including many rural physicians who have been especially eager to prepare for this new opportunity to provide effective medical treatment for opioid addicted patients in their communities.

I This 1500 physicians SAMHSA and our partners have trained is in addition to those who may be already qualified by Virtue of having been previously certified as addiction treatment specialists by one or more of the organizations specified in the DATA. Although many physicians qualified by previous certification in addiction have also sought the additional eight hours mandated under the DATA for physicians who do not already have such recognized certification.

In addition to our partners in the States and in the medical organizations, we continue to work on these issues with our Federal partners, in a variety of ways. For instance, the Interagency Narcotics Treatment Policy Review Board (INTPRB), which I currently chair, has created a special working group on the problem of OxyContin and other prescription drug diversion. The organizations participating in the INTPRB and our work group are as follows:

1. Department of Justice (DOJ)
   1.1 Drug Enforcement Administration (DEA)
   1.2 National Drug Intelligence Center (NDIC)
   1.3 National Institute of Justice (NIJ)
2. Food and Drug Administration (FDA)
   2.1 Center for Drug Evaluation and Research (CDER)

3. Substance Abuse and Mental Health Services Administration (SAMHSA)
   3.1 Center for substance Abuse Treatment (CSAT)
   3.2 Office of Applied Studies (OAS)
4. National Institute on Drug Abuse (NIDA)
5. Office of National Drug Control Policy (ONDCP)
6. DHHS Office of the Secretary, Office of Public health and Science (OPHS)
7. Centers for Disease Control and Prevention (CDC)
8. Health Resources and Services Administration (HRSA)
9. Centers for Medicare & Medicaid Services (CMS), and
10. Veterans Health Administration (VHA).

I want to conclude by pointing out to the committee, that although physical dependence in a pain patient on opioids is differentiable from opioid addiction, pain does not necessarily protect the patient who may be otherwise at risk for addictive disorders. Pain patients with addictive histories may well require additional safeguards when opioids are required for management of their pain. Withholding opioid analgesics from these patients is not necessarily a safe course at all, as they may know all too well where they can obtain what they need for pain relief, but from a much more dangerous source that would significantly increase their risk of relapse. Patients with both chronic pain and opioid addiction may require very careful management, but they can and should be managed for both disorders concurrently. Medical experience in this area grows slowly and is not yet well defined. However, a notable case series reported in the Journal of Pain and Symptom Management (1996) by Dunbar and Katz, described 20 patients with both chronic pain and substance abuse problems, on chronic opioid therapy for intractable pain. Nine out of 20 did have at least some abuse of their medications, but the MAJORITY DID NOT. Of the eleven who did NOT abuse their medications, ALL were active in drug abuse recovery programs with good family support. This small but important study illustrates not only that some pain patients with histories of drug problems can benefit from, may require and can handle opioid pain management, but it also demonstrates the central importance of an active recovery program and good family support in the long-term management of opioid addiction, and for that matter, in the successful management of most addictions.

Mr. Chairman, I thank you again for this opportunity to appear before the Committee today. I would be happy to answer any questions that you or any other members of the Committee may have at the appropriate time.

Senator REED. Dr. Jenkins, you indicated in your testimony that the FDA was surprised that this very useful drug was being abused. Did that cause you and your agency to go back and look at the system of approval and retrospectively make any judgment about what you might have done differently?

Dr. JENKINS. Mr. Chairman, we did not predict when OxyContin was approved in 1995 that we would see this level of abuse and misuse of the product. Part of our thinking at that time was based on the fact that there is a similar product called MSContin that contains morphine that had been approved for approximately 8 years by the time OxyContin was approved in 1995 and we had not seen a significant problem of abuse and misuse of that product as we have with OxyContin. Of course, all opiates are subject to abuse and misuse.

In answer to your question, we have evaluated our structure and our procedures for approving sustained release as well as other opiates and we certainly will take into account the potential risk of serious abuse and misuse in any future approvals, particularly for sustained release products like OxyContin.

Senator REED. Doctor, your answer raises another question—what is the difference between OxyContin and MSContin? I mean both time release drugs.

Dr. JENKINS. They are both time release.

Senator REED. Both have an opiate base, I presume.

Dr. JENKINS. MSContin contains morphine. OxyContin contains oxycodone. They are both Schedule II narcotics with very similar abuse potential.

Senator REED. But is there any theory at this point from your perspective at the FDA why one was reasonably well tolerated by the public and the other one became so abused?

Dr. JENKINS. We really do not know the reason for the widespread abuse of OxyContin and the lack of such abuse of MSContin. The only suggestion of an explanation I have heard that I think has some credence is that most people in the community recognize the word morphine as being a narcotic and might be adverse to receiving a product that contains morphine, whereas OxyContin does not carry that same recognition and/or stigma in the community, so maybe patients and/or physicians were more comfortable prescribing something that was not called morphine.

Senator REED. Let me ask another question related to the approval process. Was OxyContin a priority, new drug application?

Dr. JENKINS. I do not believe it was, sir. I could check to be sure but I do not believe it was.

Senator REED. Before I turn to Dr. Clark, there are several elements within the chain of distribution of controlled substances—doctors and pharmacists, etc. Can you just briefly comment on the role in this OxyContin situation of physicians and pharmacists? Have you noticed any overprescriptions, any lack of education on the part of either the physician or the pharmacist?

Dr. JENKINS. As you know, Mr. Chairman, this is a Schedule II narcotic so there are restrictions in place under the Controlled Substances Act about recordkeeping and prescribing narcotics of this type.

Prescribing and dispensing a prescription is primarily a State-based activity, so we do not have specific data that we have collected on that, although we have heard reports in the media about physicians misprescribing or overprescribing and, of course, as has been mentioned here, we have heard of the reports of thefts from pharmacies, as well as from patients.

Senator REED. But that would go to a board of licensure in each State to follow through and investigate?

Dr. JENKINS. Right. The licensing of physicians and pharmacists is a State-based responsibility.

Senator REED. One final point, Doctor. You mentioned that you have been working with the manufacturer and you are not aware of any direct promotion of OxyContin to the larger public; that is being handled through just physicians.

I would note that I am not suggesting this is the manufacturer but we went on the Web and discovered that you can find access to OxyContin at the click of your mouse and I would hope that as you go back to the FDA and law enforcement authorities would look also into this situation. I do not know and I do not suspect that this is the company in any way doing it but somebody is out there marketing directly to the general public.

Dr. JENKINS. Mr. Chairman, we have no knowledge that Purdue Pharma has anything to do with these types of Internet sales.

Senator REED. I am not suggesting they are.

Dr. JENKINS. We are aware of these Internet sites. As you can imagine, it is very difficult in many cases to regulate what appears on the Internet because a lot of these tend to be foreign sites. We generally have deferred in this area to the Drug Enforcement Administration to take legal action in these cases but we are concerned about the types of sites that you are displaying.

Senator REED. Thank you very much, Doctor.

Dr. Clark, let me ask a question of you. From your perspective, are these cases of OxyContin abuse concentrated in rural areas? Is it spreading into other areas? What can you tell us about the distribution of the abuse, if you will?

Dr. CLARK. Well, as Senator Collins pointed out, it came to our attention about OxyContin when we went to Bangor, ME and, as she pointed out very correctly, it was completely absent in the mass media. And when I, as part of my job, I would go to places across the country and I would ask about OxyContin based on my experience in Maine and California had not heard of it in terms of treatment programs, etc.

But with the ensuing focus and attention, addicts are very sophisticated. They read the newspaper; they are on line and there has been a lot of information. I think unfortunately we have a case of the dog chasing his tail in terms of more information and with more information, people start trying it. The newspapers in Bangor, that is where I found out about crushing the pill and scraping it away; there was a whole description of that.

So I think addicts pay close attention to the media and as a result of that, we have got, for economic reasons perhaps in rural America, the exchange of OxyContin, and I have heard that argument put forth a lot. But now we are seeing in other jurisdictions, as Senator Clinton pointed out, the OxyContin abuse surfacing, so it is no longer restricted to rural America. It is seen as an effective way of getting high. So it is diffusing into the rest of America, if you will.

Senator REED. Thank you very much.

Senator Collins?

Senator COLLINS. Thank you very much, Mr. Chairman.

Dr. Clark, I first want to start by acknowledging and thanking you for the attention and assistance that you have given my State as it is attempting to deal with this unexpected epidemic.

You mentioned in your statement the treatment gap that makes it very difficult for people living in more isolated areas and rural areas to access substance abuse services and that is certainly a problem in Washington County and other rural areas of my State. So therefore I would be remiss if I did not let you know that the State of Maine has at least two grant proposals pending in your office that would deal with this treatment shortage and I certainly hope that you will take a close look at those because in all seriousness, this is a real problem, just getting these addicted individuals the services and the help that they need.

Dr. Jenkins, I want to follow up on the issue of the marketing of OxyContin. Asa Hutchinson, who is the administrator of the Drug Enforcement Administration, recently testified over on the House side on issues relating to the abuse of OxyContin and in his testimony he first noted, "a dramatic increase in the elicit avail-

ability and abuse of OxyContin" and went on to conclude that there has been "a disproportionate abuse of the drug due in part to the aggressive marketing and promotion of OxyContin by Purdue Pharma, who represented the product as having a lower abuse potential than other opiate pain relievers. Purdue Pharma accentuated the problem by suggesting that physicians prescribe OxyContin as a substitute for a variety of less addictive existing medications."

As the agency responsible for oversight of drug marketing, I would like to ask your assessment of the DEA administrator's testimony, whether you agree with that, whether you think FDA needs to take further actions on the marketing of this drug.

Dr. JENKINS. Thank you, Senator. FDA does regulate the promotion and marketing of drugs approved by our agency and we have reviewed the materials that have been submitted by Purdue Pharma as part of their promotion and marketing campaign and with the single exception I cited in my testimony, all those have been found to be within the FDA regulations for being not false and misleading, to be fair and balanced, and to accurately represent the product as it was labeled at the time the advertisements were being disseminated.

We do not regulate the extent to which a company may choose to promote or market their product. By that I mean the number of advertisements or the frequency of advertisements.

So overall, we are not aware of promotional or marketing activities that have been in violation of our act or our regulations, except for that one case where we had an objection and the company very quickly withdrew that advertisement.

Senator COLLINS. So you would not agree with Administrator Hutchinson's analysis of the marketing of this drug?

Dr. JENKINS. Well, I would not say that I am agreeing or disagreeing with Administrator Hutchinson. I will let him draw his own conclusions about whether there is a link between the marketing and the current problem. From our perspective we have not seen anything that has been in violation of our regulations.

Senator COLLINS. Was there not an FDA warning letter issued to Purdue Pharma with regard to the marketing of MSContin? Are you familiar with that?

Dr. JENKINS. Senator, off the top of my head I do not know the details of that particular warning letter. I would be happy to get back to you, if there was such a letter, with the details.

Senator COLLINS. I believe there was and I would ask you to get back to us on that.

Dr. Clark, do you have any insights on the question that has been raised about the marketing of this drug and whether or not it has been appropriate and whether physicians, particularly family practitioners who may not have as much expertise in pain treatment as a pain specialist, are receiving adequate information?

Dr. CLARK. Actually, Senator Collins, I do not. I recognize that physicians—as a physician, much of our education comes from formal courses but also from detailing from the pharmaceutical industry and I always found that, as a busy practitioner in the field, to be very helpful.

So as long as it is clear that the marketing is directed to physicians, the fact of the matter is we have had a problem, an epidemic of undertreatment of pain and I have been very much interested in that for years. I have a paper from 1993 that is on the table over there that addressed this question and this preceded OxyContin, that physicians were reluctant to adequately treat pain.

So I think what people in the field were trying to do is to educate practitioners about this, so I do not think it is a simple matter of marketing. I think what we have is a complex social phenomenon and we need, as you have pointed out, multiple solutions for it that include law enforcement, education, prevention, treatment, and putting our heads together and figuring out how to keep a good drug on the market, pain patients, with medications that they need.

Senator COLLINS. I certainly agree with your premise that we too often have undertreated pain in this country and I have been working with Senator Jay Rockefeller for some time now on end-of-life care and having greater access to pain medications and to hospice care but I think we need to strike the right balance in our educating physicians both ways on this issue, and that is something we look forward to working with you on.

Just one quick question because I know my time is running out. That is it has been suggested, and I would like both of you to comment briefly on this, that reformulating OxyContin might be the answer to the dilemma of making sure that this valuable drug is available for those suffering from chronic pain and yet could not be so easily abused, as it is now, by being crushed and dissolved or snorted. Dr. Jenkins, are you optimistic about that?

Dr. JENKINS. Senator, we are aware that the company is undertaking efforts to try to reformulate the product to add an opiate blocker, another ingredient that would block the effect of the oxycodone if the product were crushed and injected intravenously and possibly also block the effects of oxycodone if the product were crushed and then snorted. So we are hopeful that that will come to fruition.

One important point that we all need to be aware of, or actually two important points, one is much of the abuse of this product has been by the oral route, so the addition of the blocking agents that are currently available will not be effective by that route, since those agents are not absorbed from the stomach. So it will help potentially in some of the abuse by the intravenous and the internasal route but it may not help with the oral abuse of the product.

The second thing that we always have to remember when we start adding a second active ingredient to a product is that the legitimate patients who are taking the product do not need that second active ingredient, so you have to be careful that that second active ingredient is not compromising the effectiveness of the oxycodone and also is not exposing them to an undue risk of adverse reaction.

So we are eagerly working with Purdue Pharma on those efforts at reformation. I think they can be useful but they will not solve the entire problem.

Senator COLLINS. Thank you.

Dr. Clark, in 30 seconds?

Dr. CLARK. Well, reformulation will help educate physicians about the importance of addiction as a possible risk associated with the use of the drug and I think that is the most important point. If people want to defeat the reformulation, they will be able to figure out ways to defeat it. That is something that you need to be aware of. As they say in the 12-step programs, addiction is cunning, baffling and powerful, so you are dealing with people who figure these things out because they do not have to go through the NIH human subjects committees to experiment with ways of dealing with these issues. Nor do they have to get their techniques approved by the FDA.

Senator COLLINS. Thank you very much.

Senator REED. Senator Dodd?

Senator DODD. Thank you very much, Mr. Chairman, and thank you both for the excellent testimony, I think this is helpful to us here.

As I said at the outset in my prepared statement, I represent Purdue Pharma, they are constituents of mine, and I know them well and the people who work there. I have been down there on numerous occasions during my service in the Senate. I have a very, very high regard for them and their employees who work very, very hard producing quality products.

I think you have identified here that the problem goes far beyond a company. It is easier to identify a company when you are trying to address this but I think the problem is far more pernicious than the product produced by a single company. I think that is what your testimony sort of indicates and I want to just run through a couple of steps, if I can.

One, Dr. Jenkins, Purdue Pharma chose not to engage in direct-to-consumer advertising of OxyContin. Is that not correct?

Dr. JENKINS. To our knowledge, they have not done any direct-to-consumer advertising.

Senator DODD. So these web sites, these are not Purdue Pharma web sites.

Dr. JENKINS. Not to my knowledge.

Senator DODD. But there are currently no prohibitions against it. With the Schedule II drugs, Purdue Pharma would have been completely within its rights on a Schedule II product to market that product directly to consumers. Is that not correct?

Dr. JENKINS. That is correct.

Senator DODD. So they made that decision not to do that.

Now the question arises do you believe that there should be some restriction on Schedule II drugs in terms of should they all be following the Purdue Pharma example of just marketing to physicians and health-related agencies or the like?

Dr. JENKINS. Senator, I think we can commend Purdue Pharma for the decision that they have made not to engage in that activity. Whether there is need for change in the act would require legislation and I do not think it is appropriate for me to comment without the administration having a chance to take a position on any proposed legislation.

Senator DODD. I know, but you are not just talking to the two of us. If I cannot get it from you, who am I going to get it from? You are the FDA. Who am I supposed to call? Dick Cheney?

We are going to have testimony on the next panel. Dr. Van Zee on panel two is suggesting in his testimony that OxyContin does not offer any major advantages over similar medications and I wonder from a regulatory perspective can you comment on this and why we need a number of similar opiod medications to treat pain? That is not an illegitimate question and what is the answer to it?

Dr. JENKINS. Senator, in our regulations in order for a company to have a superiority claim, for example, in their labeling saying we are superior to another product they have to have substantial data from adequate, well controlled trials. OxyContin currently does not have those types of claims in its labeling.

I think the reason OxyContin was developed in the first place as a controlled release mechanism was to allow patients who have chronic pain to have a regimen that does not force them to be constantly redosing every few hours because they are having breakthrough pain because those products only last a short period of time.

So the sustained release nature of the product I think is a very valuable addition to the armamentarium. There are other sustained release opiates that are approved and marketed in the United States. We mentioned MSContin earlier. There are other sustained release morphine products and there is actually a sustained release transdermal patch of a narcotic called Fentanyl and I think they are very valuable additions but there is not evidence to my knowledge to suggest that a controlled release product is more effective in treating pain than an immediate release product.

Senator DODD. Is there also something in the notion of physiology? There are letters and other people who have testified. This one woman here, I am quoting here now: "I take OxyContin every day for my pain. I am finding it more and more difficult to get the medicine because of media coverage and I panic every day I go to get my medicine, praying I will be able to on that day get it filled," and so forth.

Are there people who would react more positively to, say, OxyContin than another similar type of product so that the idea of saying well, let us just take this one off the shelf and leave similar products out there, are there people like Donna Isaacs, who sent this—I presume I can use her name—that she would not respond as well to a similar product?

Dr. JENKINS. Senator, in medicine it is often true that drugs in the same class you will find a patient will respond to one better than they will to another or alternatively, a patient may have adverse reactions to one member of a class and may have fewer or no adverse reactions to a similar member of the class. We also have the issue of allergies.

So we generally believe that it is beneficial to have choices for patients and physicians to go to when they are trying to find the right treatment for the individual patient.

Senator DODD. So the fact that there are serious addiction problems here with this product obviously in places like my friend from Virginia and my colleague from Maine and other places around the

country, it would not be your recommendation that this product ought to be taken off the shelf.

Dr. JENKINS. We have not initiated any actions that would result in OxyContin being removed from the market. As I said in my testimony, we consider it to be a safe and effective product when used according to its labeling to treat moderate to severe pain.

Senator DODD. You had some problem with the company. This has been raised before. There was a letter that the FDA sent to the company in May of 2000 regarding an advertisement they sponsored that the agency felt was being promoted in a false and misleading manner.

How often does the agency, FDA, send out these letters?

Dr. JENKINS. My understanding is that the agency sends approximately 100 of those types of letters per year to sponsors of marketed products.

Senator DODD. And you told us here earlier the response was a positive one from the company. Whatever the problem was, they changed it immediately?

Dr. JENKINS. The company responded by withdrawing that advertisement and we considered the issue to be closed.

Senator DODD. Is that normally what happens with letters like this?

Dr. JENKINS. The type of letter that was sent to the company usually asks the company to withdraw the advertisement and does not ask for any further action and that is what happened in this case.

Senator DODD. Is that normally what happens when letters go out like that?

Dr. JENKINS. It often is what happens. Sometimes companies will disagree with the FDA's judgment and will try to make their case that the advertisement is not false or misleading and will try to continue using that advertisement.

Senator DODD. Last, Dr. Clark, I did not mean to avoid you in all of this but I was trying to pull out the numbers on the budgets because it really comes down to obviously this is a serious issue to look at this particular product but I am struck by the percentages. There are 1 million addicts of opiods; is that correct?

Dr. CLARK. That is the estimated number, yes, sir.

Senator DODD. And we are treating about 20 percent of them; is that not correct?

Dr. CLARK. Yes, sir. Opiod-dependent addicts.

Senator DODD. What is that?

Dr. CLARK. Opiod-dependent.

Senator DODD. That is what I said, opiod-dependent. About 20 percent of those.

Two questions. One, how large a role does the stigma surrounding opiate addiction play in this particular low percentile of people getting any kind of treatment? And second, what sort of budget numbers are we talking about? I know that there has been—and the president, to his credit, has talked about trying to close the gap and so forth in this area but I think our budget, $127 million for next year of a five-year drug treatment initiative to replace the gap—is that the number?

Dr. CLARK. Yes, sir.

Senator DODD. Overall, is that number adequate for treatment of the addiction problems we face in this country, particularly in this area?

Dr. CLARK. Obviously the addiction problem is a multifaceted and complex phenomenon. We are trying to—that $127 million focuses on principally SAMHSA's budget but there are other resources to address the issue of addiction within the budgets of other agencies and one of the themes that Secretary Tommy Thompson and Mr. Curry, who is the administrator of the Substance Abuse Administration, wants to make clear is that we partner with other agencies in the department so that we can leverage the resources that we have.

Senator DODD. My point is we spend billions of dollars in going after interdiction and so forth, a lot of money is spent. How much of that budget do we spend on treatment and is it adequate in your view?

Dr. CLARK. Well, clearly the whole budget process is a very complex process.

Senator DODD. I think I got my answer here.

Thank you, Mr. Chairman.

Senator REED. Senator Warner?

Senator WARNER. Thank you very much for participating in this hearing. Your responses have been very well informed and I commend you both for your service to mankind in your respective positions.

Let us return to this reformulation issue raised by my colleagues. Purdue Pharma, as my colleague Senator Dodd said, is of good reputation and they certainly do not want to be associated with the criminal element of this thing and I am confident they are conscientiously doing everything they can in this area of reformulation.

So my question to you, Dr. Jenkins, is it within the State of the art to—you repeatedly used the word hope. Do you think it is achievable?

Dr. JENKINS. Senator, there are other products on the market that have the blocking agent added to try to avert the abuse of the product. A classic example is a drug called Talwin that was widely abused many years ago and the blocking agent was added and the abuse of that product fell off remarkably. The abuse of that product was primarily by intravenous injection where the addition of the blocking agent could be very effective.

The technology almost certainly exists to reformulate a sustained release product to add the blocking agent and maintain the effectiveness of the product in legitimate patients. The concern I expressed is that it will not address all of the problem.

Senator WARNER. I understand but do you think that there is a hope?

Dr. JENKINS. Yes.

Senator WARNER. Is there any other prescription drug that is being sold or has been sold in the past that was so heavily abused soon after FDA approval?

Dr. JENKINS. Senator, first of all, the abuse of OxyContin really started almost 5 years after the approval of the product. It was approved in 1995 and the first reports started coming in in about the

year 2000 and the reports that we have been receiving at the FDA really started increasing in the year 2001. So it took several years after that product was approved before we started seeing widespread reports.

Whether we have seen more rapid abuse for other products, I really cannot say at this time but it did take some time for OxyContin to be widely abused.

Senator WARNER. Last, Dr. Clark talked about the rural identification with this problem and my colleague Senator Collins and I both have these beautiful, pristine rural areas of our State which are so heavily concentrated with this problem, problems which we normally associate, I guess, with the inner city and poverty and all the other unfortunate things related to inner cities and here they are out in two of the most beautiful parts of our respective States. Yet I can go a bare 100 miles in one direction from this particular rural area where we have a problem, which has been devastating economically because of frankly the textile industry just being driven out of our State and out of the United States, offshore, yet there is not that problem.

Can anybody throw any light on why this happens? Can you add anything? Then I will go back to Dr. Clark.

Dr. JENKINS. I really do not have an explanation for that phenomenon, Senator. I think Dr. Clark may be more learned in this area than I am on substance abuse.

Senator WARNER. Dr. Clark, we will let you wrap up for this panel.

Dr. CLARK. Well, we are also dealing with a phenomenon associated with pain. Initial access to OxyContin comes through what we call the four P's—the pharmaceutical company, the physician, the patients, as well as the pharmacies. All of them play a role. Unlike drugs that you can make in your bathtub or drugs you can grow in the field, this is a drug that comes from very tightly controlled channels. What we clearly need is not only the actions of the pharmaceutical company, which we have heard about, physician education, but patient education, both those who are addicts and those who are not addicts but have shared their prescriptions for economic reasons, and that is one of the things that we have heard, that there are people who are forced for economic reasons that you described in terms of the economic changes in the community, to share their prescriptions with others and, in fact, receive compensation for sharing those prescriptions, and then making sure that we have adequate pharmacy safeguards.

Those are the things that will help those of us in addiction treatment, help law enforcement to address those four P's so that we can address this issue.

Senator WARNER. Thank you very much.

Thank you, Mr. Chairman.

Senator REED. Thank you.

Senator Dodd?

Senator DODD. John, in response, there was a first-rate story in yesterday's New York Times, the front page, that I am sure many of you may have seen—"As drug use drops in big cities, small towns confront upsurge." Just to quote in here, it is a very good story, I thought, and it cites different places. "In Dawson County

in Western Nebraska the problem is methamphetamines. The percentage of meth-related crimes is going through the roof. You are either stealing or dealing and if you are not using, you are a cop." That is the quote of the sheriff in that area.

"In the State as a whole, officials discovered 38 methamphetamine laboratories in 1999. Last year they discovered 179."

John, they say one reason for the growth in rural drug problems, Federal officials say, is that "Aggressive prosecution in cities has led dealers to seek safety in the farms, forests of rural counties, which have far fewer law enforcement officers. We have seen drugs and crime migrate to rural areas in the past several years to get away from law enforcement," and it goes on.

I do not know if that is the only reason but statistically in rural areas we are seeing a significant increase and actually a decline in some urban areas, but I thought maybe having this article, Mr. Chairman, as part of the record might be——

Senator REED. Without objection, we will include that.

[The article follows:]

(The article was not available at press time, however, a copy is maintained in the Committee files.)

Senator REED. Thank you, gentlemen, very much. I would like to call the next panel forward.

I welcome and thank this second panel. First, Dr. Richard Payne. Dr. Payne heads the Sloan-Kettering Pain and Palliative Care Service. He is a graduate of Yale University and the Harvard Medical School. He has served on the faculty of the University of Cincinnati Medical School. He has been Chief of the Pain and Symptom Management Section and professor of neurology at the University of Texas. He is currently the President-elect of the American Pain Society, as well as an editorial board member of the Journal of Pain. Thank you very much, Dr. Payne, for joining us today.

Dr. Art Van Zee is a 1973 graduate of Case Western Reserve University School of Medicine and is a board-certified internal medicine physician with a specialization in geriatrics. In 1976 he served as the first full-time physician to the St. Charles Clinic, a community-initiated clinic which has grown into a federally funded health clinic serving five counties in Southwest Virginia. He is a co-founder of the Lee Coalition for Health and is an adjunct faculty member at East Tennessee State University. Welcome, Dr. Van Zee.

I would now like to yield to my colleague, Senator Collins, to introduce Ms. Nancy Green.

Senator COLLINS. Thank you, Mr. Chairman.

It is indeed a pleasure for me to introduce Nancy Green, a certified nurse-midwife in private practice in Calais, ME. Ms. Green is not only a health care provider; she is the president of Neighbors Against Drug Abuse, a community organization created in response to the OxyContin epidemic in Washington County, Maine. She is also a registered alcohol and drug counselor so she brings a number of valuable perspectives to this debate and it is a great pleasure to welcome her to the committee today.

Senator REED. Thank you, Senator Collins.

Our next panelist is Lieutenant William R. Bess. Lieutenant Bess has served in the Virginia Department of State Police since

October 1987. He is currently special agent in charge at the Wytheville Field Office Drug Enforcement Division and prior to that served in the Pharmaceutical Diversion Unit for 10 years. Lieutenant Bess has practiced law in Roanoke, VA for 10 years, served in the Chesterfield County Police Department and is a veteran of the United States Marine Corps. Thank you very much, Lieutenant, for joining us.

Dr. Paul Goldenheim joins us from Purdue Pharma, where he currently serves as Executive Vice President of Worldwide Research and Development and is currently responsible for the research and development centers of Purdue Pharma and all its associated companies in the United States, Canada, the United Kingdom and Germany. Dr. Goldenheim received both his bachelors and medical degrees from Harvard University and has served as Clinical Director of the Pulmonary Unit at Massachusetts General Hospital. Thank you for joining us today, Dr. Goldenheim.

Again all of your statements will be fully included in the record. You are urged to summarize. We have five panelists and we have an eager and attentive group of senators who would like to ask questions.

Dr. Payne?

STATEMENTS OF RICHARD PAYNE, M.D., CHIEF, PAIN AND PALLIATIVE CARE SERVICE, DEPARTMENT OF NEUROLOGY, MEMORIAL SLOAN-KETTERING CANCER CENTER, NEW YORK, NY; ART VAN ZEE, M.D., LEE COALITION FOR HEALTH, ST. CHARLES, VA; NANCY GREEN, C.N.M., PRESIDENT, NEIGHBORS AGAINST DRUG ABUSE, CALAIS, ME; LIEUTENANT WILLIAM R. BESS, J.D., DRUG ENFORCEMENT DIVISION, VIRGINIA STATE POLICE, WYTHEVILLE, VA; AND PAUL D. GOLDENHEIM, M.D., VICE PRESIDENT FOR RESEARCH, PURDUE PHARMA, L.P., STAMFORD, CT

Dr. PAYNE. Thank you, Senator Reed. With that I would actually like to go right into my statement.

I wish to emphasize in the strongest possible terms the need to maintain balance in our drug regulatory policy so as to improve the availability of essential opiod medications for the treatment of pain while meeting our responsibility to control drug diversion and elicit drug use. This point was emphasized in a recent press conference back in October at which time a position statement "Promoting Pain Relief and Preventing Abuse of Pain Medications: A Critical Balancing Act," was released from 21 health care organizations and the Drug Enforcement Administration. Mr. Hutchinson, the administrator of the DEA, spoke at that press conference and acknowledged that the achievement of a balanced approach to drug regulations was an important objective of DEA policy. I have the statement here and would like to introduce——

Senator REED. Without objection, we will include it in the record, Dr. Payne.

[The statement follows:]

(The statement was not available at press time, however, a copy is maintained in the Committee files.)

Dr. PAYNE. I appeal for balance in drug policy because I am keenly aware of the negative consequences for the care of patients

suffering from pain if the consequences of controlled substance regulation further restricts access to essential pain medications. I take this position for several reasons, which are based on my own research work and experiences from 25 years in clinical practice.

I wish to make several brief points. One, for many patients opiod analgesics—morphine, oxycodone, Fentanyl patches, even methadone, which can be administered for pain—are the most effective way to treat pain of moderate to severe intensity and often the only treatment that provides significant relief. My clinical experience is quite consistent with the evidence-based clinical practice guidelines widely published for the management of pain, which emphasize the need for the availability of multiple pain medications for clinicians so as to enhance our ability to select the right drug for the right patients, to speak to Senator Dodd's question earlier.

It is now very clear that with respect to the use of opiods to manage pain, one drug does not fit all. In my cancer center, for example, up to 15 to 20 percent of our patients require an opiod drug other than morphine to provide the best pain relief with the minimum number and intensity of side effects. In fact, a study from our center reported that 80 percent of our patients required at least one switch of opiod medications, 44 percent required two or more switches, and 20 percent required three or more switches of opiod medications to get to the right medication to manage their pain in the most optimal manner.

Even though opiods derived from the same general chemical family, there are important clinical differences in the ways in which patients respond to specific drugs. Patient A may not tolerate morphine but will tolerate oxycodone while Patient B may be just the opposite. Therefore, it is essential to have many opiod medications available to clinicians.

Point two, OxyContin, a controlled release formulation of oxycodone, is as effective as any other opiod for the treatment of pain and has a similar profile of adverse effects, including abuse liability. The well publicized cases of OxyContin abuse are, in my opinion, related to the fact that it is so much more widely prescribed and therefore more available to those with criminal intent than other opiods. There is little data that oxycodone per se has any inherently increased abuse liability compared to morphine or other opiods.

The reason that OxyContin is so widely prescribed relates in part to the fact that it is an effective alternative medicine for patients who do not tolerate oral morphine and for whom the other long-acting alternatives—Fentanyl patches or methadone—are not good choices because of particular clinical circumstances. Generally it's much easier to adjust the dose of OxyContin to respond to the clinical needs of the patient in comparison to the other available long-acting pain medications.

In my clinical practice these factors—the advantages, the clinical advantages of high oral bioavailability, short half-life, long duration of effect, predictable pharmacokinetics—all of these factors have as much to do with the relative popularity of OxyContin for the treatment of pain and much more so than any marketing details by the pharmaceutical industry.

The third and final point, undertreatment of pain is a serious problem for all Americans. Like other aspects of medical care, patients from minority and poor communities suffer from disparities in health care outcomes and are at greater risk for undertreatment of pain than the general population, at least 10 recent studies of documented disparities in pain management for patients in minority communities. For example, as reported in the New England Journal of Medicine several years ago, 46 percent of patients suffering from cancer were undertreated. Members of minority groups had at least a threefold increased risk of undertreatment within this group.

Similar racial and ethnically-based disparities in pain treatment have been observed in emergency room treatments for pain and in postsurgical pain management. Poor pain assessment skills and, contrary actually to current opinions noted in the media, an exaggerated fear of addiction by health care providers are important reasons documented to drive this undertreatment by physicians, particularly as it relates to poor and minority patients.

A recent study published in the New England Journal of Medicine reported that 72 percent of pharmacies in affluent and nonminority areas of New York City stocked opiod drugs whereas only 25 percent of pharmacies in poor and nonwhite communities stock these drugs in New York City. So a major disparity in terms of the pharmacies even carrying the drugs.

We have documented that this relative unavailability of opiods in poor neighborhoods produces serious hardships and increased suffering, especially for patients, families and doctors managing terminal illnesses outside of the hospital. Any drug regulations that further limit access to opiods, OxyContin included, will particularly impact on these very vulnerable patients.

So in summary, I wish to restate that we must pursue policies that make pain management services and essential pain medications equally available to all Americans. I join many of my colleagues in pledging to work on strategies that ensure the availability of essential opiod medications for pain while incorporating ways to prevent their illicit diversion and abuse. I thank the committee for hearing me.

Senator REED. Thank you, Dr. Payne.

[The prepared statement of Dr. Payne follows:]

PREPARED STATEMENT OF RICHARD PAYNE, M.D.

I thank you for the opportunity to speak with the Committee. My name is Richard Payne. I am a physician with expertise in pain management and palliative care, practicing at Memorial Sloan-Kettering Cancer Center in New York City. In my capacity as Chief, Pain and Palliative Care Service I see patients, teach medical students and post-graduate physicians-in-training, and direct a program of pain and palliative care research. I have also had the privilege to serve on The Agency for Health Care Policy and Research (AHCPR) committees charged with writing clinical practice guidelines for acute pain and I co-chaired the cancer pain management panel. I have been a consultant to the Institute of Medicine and the National Cancer Policy Board to advise these agencies on the deficiencies of care provided to Americans at the end of life, particularly on the disparities in pain management and palliative care at the end of life care experienced by minority patients. Although I am president-elect of the American Pain Society, my appearance here today reflects my own personal views and not necessarily the views of the American Pain Society.

I wish to emphasize, in the strongest possible terms, the need to maintain balance in our drug regulatory policy so as to improve the availability of essential opioid

medications for the treatment of pain while meeting our responsibility to control drug diversion and illicit use of opioids. This point was emphasized in a recent press conference (October 23, 2001) at which time, a position statement, *"Promoting Pain Relief and Preventing Abuse of Pain Medications: A Critical Balancing Act"* was released from 21 health care organizations and the Drug Enforcement Administration. Mr. Asa Hutchinson, Administrator, Drug Enforcement Administration (DEA) spoke at the press conference and acknowledged that the achievement in of a balanced approach to drug regulations was an important objective of DEA policy.

I appeal for balance in drug policy because I am keenly aware of the negative consequences for the care of patients suffering from pain if the consequences of controlled substance regulation further restricts access to essential pain medications. I take this position for several reasons, which are based on my own research work and experiences from 25 years in clinical practice. I wish to make several points:

• Undertreatment of pain is a serious problem for all Americans, and, like other aspects of medical care, patients from minority and poor communities suffer from disparities in health care outcomes and are at greater risk for undertreatment than the general population. At least ten recent studies have documented disparities in pain management for minority patients. For example, although as reported in the New England Journal of Medicine several years ago, although 46% of patients suffering with cancer-related pain were undertreated, members of minority groups have at least a three fold increased risk of undertreatment. Similar racial and ethnically-based disparities in pain treatment have been observed in emergency room treatments for trauma and in post-surgical pain management.

Poor pain assessment skills and—contrary to the current opinions noted in the media—an exaggerated fear of addiction by health care providers, are important reasons documented to drive this undertreatment, particularly in minority patients. Another important factor driving racial and ethnically-based disparities in pain management is caused by a substantial problem with lack of availability of essential opioid medications in poor and minority neighborhoods. For example, a recent study published in the New England Journal of Medicine (April 6, 2000) reported that 72% of pharmacies in white neighborhoods of New York City stocked opioid drugs, whereas only 25% of pharmacies in poor and non-white neighborhoods stocked opioids for the treatment of pain. We have documented that this relative unavailability of opioids in poor and minority neighborhoods produces serious hardships and increased suffering, especially for patients, families and doctors managing terminal illnesses outside of the hospital. Drug regulations that further limit access to opioids will particularly impact on these very vulnerable patients.

• For many patients, opioid analgesics (e.g., morphine, oxycodone, fentanyl patches, methadone) are the most effective way to treat pain, and often the only treatment option that provides significant pain relief.

My clinical experience is quite consistent with the evidence-based clinical practice guidelines for the management of pain, which emphasize the need for the availability multiple pain medications to clinicians so as to enhance our ability to select the right drug for the right patients. It is now very clear that with respect to the use of opioids to manage pain, one drug does not fit all. In my cancer center, up to 15–20% of our patients require a opioid drug other than morphine to provide the best pain relief with the minimum number and intensity of side effects. A study from Sloan-Kettering reported that 80% of patients required one switch of opioid medications; 44% of patients required two or more switches and 20% of patients required three or more switches of medication to manage their pain in the most optimal manner. Even though opioids derive for the same general chemical family, there are important clinical differences in the ways in which patients respond to specific drugs—patient A may not tolerate morphine, but will tolerate oxycodone, while patient B may be just the opposite. Therefore, it is essential to have many opioid medications available for clinicians—morphine, oxycodone, fentanyi, and methadone—to provide the appropriate clinical flexibility that allows optimization of therapy and individualization of the treatment of patients.

• OxyContin®, a controlled-release formulation of oxycodone, is as effective as any other opioid for the treatment of pain, and has a similar profile of adverse effects, including abuse liability, as other opioids. The well publicized cases of OxyContin® abuse are, in my opinion, related to the fact that it is so much more widely prescribed-and therefore more available to those with criminal intent—than other opioids. There is little data that oxycodone per se has any inherently increased abuse liability compared to morphine or other opioids. The reason that OxyContin® is so widely prescribed relates, in part, to the fact that it is an effective alternative medication for patients that do not tolerate oral morphine, and for whom fentanyl patches or methadone are not good choices because of particular clinical circumstances. Generally, it is much easier to adjust the dose of OxyContin® to re-

spond to the clinical needs of the patient, in comparison to the other available long-acting pain medications, such as methadone or transdermal fentanyl (patches). In my clinical practice, these clinical factors have as much to do with the relative popularity of OxyContin@ for the treatment of pain, as did any marketing details by the pharmaceutical industry. In summary, I wish to restate that we must pursue policies that make pain management services and essential pain medications equally available to all Americans. I join many of my colleagues in pledging to work on strategies that ensure the availability of essential opioid medications for pain while incorporating ways to prevent their illicit diversion and abuse. I thank the committee for hearing my statement.

Senator REED. Dr. Van Zee?

Dr. VAN ZEE. Thank you very much for the opportunity to be here today and present our viewpoint. I come to you as a representative of a group called the Lee Coalition for Health, a nonprofit group of professionals and community persons who have for the last 10 years worked in Lee County, Virginia to promote health and wellness issues. The last 2 years of our efforts have been consumed by trying to help deal with the OxyContin problems in our region.

In the 25 years I have practiced as a general internist in St. Charles, which is a small Appalachian coal mining town, there has never been anything to compare to the epidemic of drug abuse and addiction that we have seen the last 3 years with OxyContin. Contrary to what is sometimes portrayed in the media as long-term addicts switching to the drug du jour, what we have seen for the most part is numerous young people recreationally using OxyContin and then becoming very rapidly addicted. Many of these kids are good kids, good families with bright, promising futures that are being destroyed in every way by their opiod addiction.

Opiods, as derivatives of opium, are the most powerful pain medication, with morphine being most familiar to you. OxyContin addiction is opiod addiction, the same as morphine or heroin addiction, and wrecks the same havoc on individuals, families and communities. It is hard to find a family in Lee County that has not been touched directly or indirectly by the problem of OxyContin abuse. This is a sadly repetitive story for the numerous areas of the country now affected by this, from Washington County, Maine to Southern Florida.

My own personal view of the complicated OxyContin abuse problem is that there are at least three major elements involved. First, there has been an obvious problem with physician misprescribing and overprescribing of this drug. Second, this epidemic has been a vicious indicator of the alarming degree of prescription drug abuse in our society. Third and perhaps the one closest to this committee and the FDA is that the promotion and marketing of OxyContin by Purdue Pharma has played a major role in this problem.

Purdue Pharma, in the most extensive opiod promotion in the history of the industry, has used sophisticated marketing data to determine which physicians in the country prescribe opiods most liberally and, in some cases, least discriminately and coupled that data with lucrative financial incentives to their sales representatives. One sales rep in Florida made $50,000 in 1999, $100,000 in 2000 over and above her $50,000 salary because of the high OxyContin sales in her territory.

Purdue has used thousands of company-sponsored talks and seminars, which are well shown in the medical literature to influence

and increase physician prescribing of a particular product. Purdue heavily lobbied primary care physicians for the use of OxyContin and primary care physicians traditionally have had meager training in pain management and addiction issues.

The company used promotional free OxyContin pills for patients and beach hats and music CDs for physicians. In addition, Purdue engaged in an extensive and sophisticated nonbranded promotion of opiods in general in which the benefits of opiods for chronic, nonmalignant pain were much overstated and the risk trivialized.

A testimony to the success of the promotional marketing campaign is reflected in the fact that from 1996 to 2000 the use of other commonly used opiods grew 23 percent while OxyContin prescription dispensed during the same period increased by over 1,800 percent. The fact that OxyContin does not offer any major advantages over appropriate doses of other opiods again is testimony to the success of Purdue's campaign.

The current regulations governing the way the pharmaceutical industry can market and promote opiods or any controlled drug has not served well the public health in this situation. Not to drastically change these types of regulations at this point would give sanction and safe harbor to the drug companies for the continuation of such business practices, which do not serve any of us well.

The Lee Coalition for Health nearly a year ago now initiated a national petition to recall OxyContin until it can be reformulated to a less abusable drug. The rationale for this is as follows. We do have equally effective opiods for treatment of severe pain. All Purdue-funded studies to date have shown this; that is, that OxyContin is a good drug but not a superior drug to what we have available. The medical letter in September 2001 made similar conclusions and for nonmedical people, the medial letter is kind of a gold standard for prescribing physicians around the country in terms of assessing drugs, their proper use, indications, benefits, and so on.

Some of the alternatives for OxyContin are much more cost effective and some have less abuse potential than OxyContin. Particularly in the light that we have equally effective opiods to treat severe pain, it is clear that the pain and suffering brought by the abuse of the drug far surpasses its benefits. With the fastest growing epidemic of prescription drug abuse in the United States in the last 25 years, all other measures taken to stem the diversion and abuse will fall far short of what is needed.

The recall of OxyContin is not a recall of opiods. OxyContin is unique and its abuse unprecedented. The economics of OxyContin diversion and abuse will now perpetuate this disaster, regardless of the full array of measures taken to stem the tide.

It is time Purdue Pharma did what Sterling Laboratories did in 1983 when its narcotic was the source of increasing abuse, addiction, medical complications and overdose deaths in the country. It voluntarily recalled Talwin until it could be reformulated to a preparation with much less abuse potential.

This is the end of my prepared comments. If there is any time at the end, I would like to respond to why it has appeared in some parts of the country and also about is this an isolated problem or is this a national problem.

Senator REED. Thank you, Doctor. You will have such an opportunity.

[The prepared statement of Dr. Van Zee follows:]

PREPARED STATEMENT OF ART VAN ZEE, M.D.

I come to you as a representative of a group called the Lee Coalition for Health, a non-profit group of professionals and community persons who have for the last ten years worked in Lee County, Virginia to promote health and wellness issues. The last two years of our efforts have been consumed by trying to help deal with the OxyContin problem in our region.

In the 25 years I have practiced as a general internist in St. Charles, a small Appalachian coal mining town, there has never been anything to compare to the epidemic of drug abuse and addiction that we have seen the last 3 years with OxyContin. Contrary to what is sometimes portrayed in the media as long term drug addicts switching to the drug du jour, what we have seen for the most part is numerous young people recreationally using OxyContin and then becoming very rapidly addicted. Many of these kids are good kids, good families, with bright, promising futures that are being destroyed in every way by their opioid addiction. Opioids—as derivatives of opium—are the most powerful pain medication—with morphine being most familiar to you. OxyContin addiction is opioid addiction, the same as morphine or heroin addiction and wreaks the same havoc on individuals, families, and communities. It is hard to find a family in Lee County that has not been touched directly or indirectly by this problem of OxyContin abuse. This is a sadly repetitive story for the numerous areas of the country now affected by this from Washington County, Maine to southern Florida.

My own personal view of the complicated OxyContin abuse problem is that there are at least three major elements involved. First, there has been an obvious problem with physician mis-prescribing and over-prescribing of this drug. Secondly, this epidemic has been a vicious indicator of the alarming degree of prescription drug abuse in this society. Thirdly, and perhaps the one closest to this committee and the FDA, is that the promotion and marketing of OxyContin by Purdue Pharma has played a major role in this problem.

Purdue Pharma, in the most extensive opioid promotion in the history of the industry, has used sophisticated marketing data to determine which physicians in the country prescribe opioids most liberally (and, in some cases, least discriminately) and coupled that data with lucrative financial incentives to their sales representatives. One sales rep in Florida made $50,000 in 1999 and $100,000 in 2000 in bonus incentives—over and above her $50,000 salary because of the high OxyContin sales in her territory. Purdue used thousands of company sponsored talks and seminars—well shown in the medical literature to influence and increase physician prescribing of a particular product. Purdue heavily lobbied primary care physicians for the use of OxyContin—and primary care physicians traditionally have had meager training in pain management and addiction issues. The company used promotional free OxyContin pills for patients and beach hats and music CDs for physicians. In addition, Purdue engaged in an extensive and sophisticated non-branded promotion of opioids in general—in which the benefits of opioids for chronic non-malignant pain were much over-stated and the risks trivialized. A testimony to the success of the promotional and marketing campaign is reflected in the fact that from 1996 to 2000, the use of other commonly used opioids grew 23% while OxyContin prescriptions dispensed during the same period increased by over 1800%. The fact that OxyContin does not offer any major advantages over appropriate doses of other opioids again is testimony to the success of Purdue's campaign.

The current regulations governing the way the pharmaceutical industry can market and promote opioids, or any controlled drug—has not served well the public health in this situation. Not to drastically change those types of regulations at this point would give sanction and safe harbor to the drug companies for the continuation of such business practices which do not serve any of us well.

The Lee Coalition for Health nearly a year ago now, initiated a national petition to recall OxyContin until it can be re-formulated to a less abusable drug. The rationale for this is as follows:

(1) we have available equally effective opioids for treatment of severe pain. All Purdue funded studies to date have shown this—that is, OxyContin is a good drug but not a superior drug to what we have available. The Medical Letter (9/17/01) made similar conclusions. Some of our alternatives are much more cost effective, and some have less abuse potential than OxyContin;

(2) particularly in the light that we have equally effective opioids to treat severe pain, it is clear that the pain and suffering brought by the abuse of the drug far surpasses its benefits;

(3) that with this fastest growing epidemic of prescription drug abuse in the U.S. in the last 25 years, all other measures taken to stem the diversion and abuse will fall far short of what is needed;

(4) the recall of OxyContin is NOT a recall of opioids. OxyContin is unique and its abuse unprecedented. The economics of OxyContin diversion and abuse will now perpetuate this disaster regardless of the full array of measures taken to stem the tide. It's time Purdue Pharma did what Sterling-Winthrop Laboratories did in 1983 when its narcotic was the source of increasing abuse, medical complications, and over-dose deaths in the country. It voluntarily recalled Talwin until it could be reformulated to a preparation with much less abuse potential.

Thank you for the opportunity to speak to you today, and thank you for your attention.

ATTACHMENT A

After the tragic national events of a few weeks ago, I know that other problems facing the nation seem less consequential than they did on September 10th. But I know that we do need to continue on in facing that and other challenges for this country, and I do want to thank the committee for the opportunity to present our views today on the OxyContin abuse problem. I come to you as a representative of a group called the Lee Coalition for Health, a non-profit group of professionals and community persons who have for the last 10 years worked in Lee County, Virginia to promote health and wellness issues. The last two years of our efforts have been consumed by trying to help deal with the OxyContin problem in our region.

For the last 25 years, I have practiced as a primary care general internist in St. Charles, Virginia, a small coal mining town in southwest Virginia. There has always been a certain back-ground level of prescription drug abuse in the region, and a very limited amount of opioid dependence. Opioids, as derivatives of opium—like morphine—are our strongest pain medication available for patients with severe pain. Unfortunately, opioids can for some people be the most addictive drug, with heroin and morphine being the most well known in this context. About two years ago we began to see rapidly increasing abuse and addiction to OxyContin in southwest Virginia. OxyContin was being snorted or injected IV, males and females, mid-teens to early forties. We were seeing frequent overdoses, infections, occasional cases of heart valve infections, and escalating Hepatitis C—a serious and sometimes fatal liver infection transmitted by IV drug use. It is anticipated that more HIV cases will follow. Many of these kids were ones that I had held in my arms when they were babies, and had taken care of their parents and their grandparents. Many of these recreationally used OxyContin and had become rapidly addicted. The addiction to OxyContin—as with any opioid—is similar to the more familiar heroin addiction. Numerous young people were stealing from their families and neighbors, and losing their jobs, vehicles, houses, and sometimes their own children to this addiction. County sheriffs throughout the region have estimated that 70–90% of all serious crimes in the last two years have been drug related crimes, and most of that OxyContin related. The number of children placed in foster care in Lee County has increased 300% in the last three years, primarily related to OxyContin abuse. In a school survey in May, 2000—in the Lee County school system—9% of our 7th graders and 20% of our 12th graders had used OxyContin. At our closest detox facility in Lebanon, Virginia, they reported a 330% increase in the number of admissions that were opioid dependent from 1996 to early this year. The Life Center of Galax—about 3 hours drive from us—opened an out-patient methadone maintenance treatment program in March, 2000—expecting about 12 patients in a year's time based on the prevalence of heroin addiction in the region. They had 30 patients within 2 weeks of opening, and 254 patients within 8 months, and roughly 90% of these patients were OxyContin dependent. A simple medical-social-legal picture has unfortunately been seen in multiple areas throughout the country related to OxyContin abuse. Methadone maintenance clinics in multiple states have been filling up with OxyContin dependent patients.

The long term history of opioid addiction—whether it's heroin or OxyContin addiction—is quite grim with long term statistics showing high rates of illness, associated criminal activity, family dissolutions, death rates and even with the best of treatments, a significant life long relapse rate.

My own personal view of the complicated OxyContin abuse problem is that there are at least three major elements involved: (1) the increasing prevalence of prescription drug abuse in this country, both by patients and by recreational users; (2) the

mis-prescribing and over-prescribing by a segment of the physician community; (3) and lastly, and I think a major factor, the promotion and marketing practices of Purdue Pharma, in regards to OxyContin and the use of opioids in the treatment of chronic nonmalignant pain. I have included in the attachments a detailed look at Purdue's promotion and marketing as I see it. To focus in more clearly on the use of opioids in the treatment of pain, I would submit that there is nothing at all controversial in the medical community-at-large about the role or use of opioids in acute severe pain (trauma, post-operative pain, kidney stones, etc.) nor in the use of opioids—our strongest pain medication—in the treatment of patients with cancer pain or other terminal conditions. In those situations, the dose of opioids is whatever it takes to provide comfort and compassionate care. The particular issue of contention in the medical community-at-large revolves around the precise role of opioids in the treatment of chronic nonmalignant pain (not cancer related) and more specifically, the surrounding issues of the therapeutic efficacy of opioids in this situation, the adverse problem including side effects of opioids in this situation, and probably most importantly, the risk of opioid addiction and abuse. In the last decade, based on a few studies showing some effectiveness for opioids in chronic nonmalignant pain, there has been a new willingness to review previous aversion to the use of opioids in chronic non-malignant pain. There has been a wide spectrum of opinion in the medical community up to the present about these issues. One of the foremost leaders in this field, Dr. Russell Portenoy at Memorial Sloan-Kettering Cancer Center in New York, concluded in his 1996 review of the topic—

> "The available data do not support doctrinaire pronouncements about the role of opioid therapy for nonmalignant pain. If misconceptions about tolerance physical dependence, side effects, and addiction can be eliminated, the clinician will still be left with the challenging process of judging the appropriateness of the approach in individual cases without the benefit of a scientific foundation derived controlled clinical trials. Controlled clinical trials of long-term opioid therapy are needed, but lack of these trials should not exclude empirical treatment when medical judgment supports it and therapy is undertaken with appropriate monitoring." [1]

In another comprehensive look at the issues, Dr. Dennis Turk concluded in 1996—

> "At this particular point in time, decisions about the chronic use of opioids appear to rely more on opinion appear to rely more on opinion and clinical experience. The available data has numerous flaws and is easily subject to interpretation both for and against the use of opioids . . ." in chronic nonmalignant pain. [2]

What Purdue Pharma has done in their promotion and marketing of OxyContin—and the use of opioids for chronic non-malignant pain in general—is to enthusiastically over-state the benefits of opioids and to trivialize the risks. A testimony to the success of the promotional campaign is reflected in the fact that from 1996 to 2000, the use of other commonly used opioids (codeine, hydrocodone, morphine, and hydromorphone) grew 23% while OxyContin prescriptions dispensed during the same period increased by over 1800%.[3] The fact that OxyContin does not offer any major advantages over appropriate doses of other opioids[4] again is testimony to the success of Purdue's campaign.

Conventional wisdom in medicine is that if a drug is abusable, it will be abused. By extension, if an abusable drug is widely available, it will be widely abused. That has certainly been the experience with OxyContin. The attached DEA map of OxyContin consumption in the United States does show as expected that, by and large, those states with the largest amount of OxyContin prescription purchases are the states reporting the most extensive abuse. The map of Virginia clearly reflects one of the major reasons why southwest Virginia has been so hard hit with this problem. (The maps are maintained in the Committee files) In some of our counties in the southwest, the OxyContin consumption has been 500–700% higher than the national average![5]

The Lee Coalition for Health in March of this year initiated a national petition to recall OxyContin until it can be re-formulated to a less abusable drug. The rationale for this has been as follows:

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[1] Portenoy RK Opioid Therapy for Chronic Non-malignant Pain: A Review of the Critical Issues J Pain Symptom Management 1996 Apr; 11(4):203–217.

[2] Turk DC Clinicians' Attitudes about Prolonged Use of Opioids. J Pain Symptom Management 1996 Apr; 11(4):218–230.

[3] Statistics, DEA, Office of Diversion Control.

[4] The Medical Letter Sept. 17, 2001.

[5] Statistics DEA Office of Diversion Control.

(1) that the pain and suffering brought to countless individuals and communities by the abuse of this drug far exceeds the benefits of the drug;

(2) that physicians can continue responsible treatment of acute and chronic pain without the presence of OxyContin on the market. There are no studies that show that this is a clearly superior drug. There are equally effective opioids[6] that can be used to treat patients for their severe pain needs if OxyContin was recalled; and some of these have less abuse potential than OxyContin;

(3) that with this fastest growing epidemic of prescription drug abuse in the U.S. in the last 25 years, all other measures taken to stem the diversion and abuse will fall far short of what is needed.

A large overlying issue in this whole thing, and one that falls particularly under the realm of this committee, is that of the kind of regulations that govern the pharmaceutical industry's marketing and promotional practices. From my perspective, just as there is a very real difference between non-controlled drugs and controlled drugs, there needs to be much more stringent regulations about how the industry can promote controlled drugs. I would submit that the use of promotional items (e.g. beach hats and CDs); company sponsored meetings and symposia; aggressive detailing by pharmaceutical reps; the use of elaborate marketing data to influence physician prescribing of opioids; web sites that promote opioid use—misrepresenting the benefits and trivializing the risks—and the general non-branded promotion of opioids in a variety of different ways—have not served well the public health.

I would also propose to this committee to consider the possibility of funding well designed, well controlled scientific studies—independent of financial ties or obligations to the pharmaceutical industry—that could bring much more light than heat to the controversy about the real benefits and attendant risks in using opioids for chronic nonmalignant pain.

I want to thank all of the committee for your attention and interest in these matters of increasing national importance.

ATTACHMENT B

The OxyContin Abuse Problem: Spotlight on Purdue Pharma's Marketing

There appear to be at least three major factors which have played a major role in the epidemic of OxyContin abuse which has affected so many regions of the country. First, there has been an obvious problem with physician mis-prescribing and over-prescribing of this drug. Secondly, this epidemic has been a vicious indicator of the alarming degree of prescription drug abuse in this society. Thirdly, the promotion and marketing of OxyContin by Purdue Pharma has played a major role in this problem. Below is a more detailed look at some of these promotion and marketing practices.

1. Beach Hats and CDs

Long past the time last year when Purdue Pharma was aware of rapidly increasing abuse, addiction, over-doses, and accelerating drug related crime in certain regions of the country—the company was giving out to physicians beach hats sporting the "OXYCONTIN" logo in bold letters, CDs of swing music ("Swing in the Right Direction") and pedometers—OxyContin—"A step in the right direction". While Purdue has since stopped this kind of promotion amidst a barrage of criticism, it is reflective of their attitude, marketing, and promotion.

2. Pain Management Talks and Seminars

In recent years, Purdue brought in 2,000 to 3,000 doctors to three day retreats in Arizona, California, and Florida for company sponsored work-shops on pain management. Some of these physicians were then recruited by Purdue to serve as paid speakers at Purdue sponsored medical meetings.[1] It is well documented that this type of pharmaceutical company sponsored symposia very significantly influence physician prescribing even though the physicians who attend such symposia believe that such enticements do not alter their prescribing patterns.[2]

Additionally, Purdue sponsored an estimated 7,000 "pain management" seminars around the country—stressing the importance of aggressive treatment of pain with an enthusiastic emphasis on opioids for chronic non-malignant pain.

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[6] The Medical Letter Sept. 17, 2001

[1] New York Times, March 5, 2001 "Use of Painkiller Grows Quickly, Along with Widespread Abuse".

[2] Orlowski JP The Effects of Pharmaceutical Firm Enticements on Physician Prescribing Patterns. Chest 1992; 102(1l):270—3.

3. Other Targeted Marketing and Promotion to Physicians

It is well documented that drug companies compile "prescriber profiles" on individual physicians—detailing the prescribing patterns of physicians nation-wide—in an effort to influence or sway doctors' prescribing habits. Through the profiles, a particular drug company can identify the highest and lowest prescribers of a particular medicine in a single zip code, county, state or the entire country.[3] Purdue acquired from I.M.S. Health, a leading pharmaceutical market research company, the information of which physicians prescribed the largest numbers of opioids.[4] This information would apparently prove quite useful in the company's attempt to influence physicians' prescribing habits nation-wide.

4. Purdue and the Marketplace—Creating the Demand

Over the last 15 years, there has been a substantial change in the medical community in regards to many issues concerning pain and pain management. There was increasing attention paid to improving the treatment of pain not only with acute pain and cancer related pain, but with chronic non-malignant pain. There was increased attention by pain management specialists on the role of opioids in all three of these clinical situations. There were small and limited studies that suggested that there might be a rate for opioids, in chronic non-malignant pain in selective patients. Purdue Pharma not only recognized the changing clinical land-scape, but saw this as a business opportunity. Purdue, which had introduced a sustained-release morpbine—MS Contin—in 1985 for the treatment of cancer pain, began to promote MS Contin for noncancer pain as well.

Purdue's promotion and marketing of MS Contin did result in a strong "Warning Letter" from the FDA in 1996—". . . we have concluded that Purdue is disseminating promotional materials for MS Contin that contain statements, suggestions, or implications that are false or misleading in violation of the Federal Food, Drug, and Cosmetic Act. . . . This violation is occurring despite repeated notification to Purdue by DDMAC that claims of product superiority were unsupported and were false and/or misleading and in violation of the Act."[5]

Purdue actively promoted to patients and doctors that unmet pain needs were of epidemic proportion; that it was much more treatable than had been previously thought; and that in many cases, it could, and should, be treated with opioids. Purdue contributed generously to patient-advocacy organizations, including the American Pain Foundation, the National Foundation for the Treatment of Pain and the American Chronic Pain Association.[6] In Canada, Purdue has co-sponsored the "Patient Pain Manifesto"—recently announced by the Canadian Pain Society—which calls for a "Bill of Rights" for patients and their families regarding pain treatment.[7] Through its web-site "Partners Against Pain" Purdue consistently over-stated the benefits of opioids, in chronic non-malignant pain while trivializing the risks, particularly the risks of addiction. (see attached documentation—"Partners Against Pain" by this author)—All of the above mentioned direct and indirect marketing and promotion for the liberalization of the use of opioids in chronic non-malignant pain raises a multitude of serious questions for the medical community in general, the pain management community in particular, for the FDA which is charged in part with regulation of the pharmaceutical industry for the protection of the public health, and for the DEA which is left with having to deal with so much of the difficulties of a catastrophe like this—whether it is the amphetamine disaster of a few decades ago, or the tragic OxyContin disaster now.

While no experienced practitioner of medicine or any student of the issues involved would suggest that there is never a place for opioids in chronic non-malignant pain, the issues in contention revolve around how selective one needs to be in initiating treatment with opioids for chronic non-malignant pain, and what the risks are of addiction. Dr. Russell Portenoy, an expert of international eminence in these issues and an advocate for opioid therapy in very selected patients with chronic non-malignant pain, wrote in his review of the subject in 1996—"The limited number of controlled trials, combined with disparities and inherent biases of the survey literature, preclude definitive conclusions about the risks and benefits of long-term opioid therapy. Nonetheless, it is reasonable to infer from these conflicting results

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[3] New York Times Nov 16, 2000 "High-Tech Stealth Being Used to Sway Doctor Prescriptions".

[4] Personal meeting—Lee Coalition for Health with Purdue Pharma, March 26, 2001 information by Michael Friedman, Exec VP, Purdue.

[5] FDA letter to Dr. Richard Sackler, President, Purdue—available for review on the FDA web site.

[6] New York Times Magazine July 29, 2001 "The Alchemy of OxyContin: From Pain Relief to Drug Addiction".

[7] Greg Woods reports, Wednesday, June 6, 2001.

that there is a spectrum of patient responses. On one end of this spectrum is a "successful" subpopulation that achieves sustained partial analgesia, without the development of treatment-limiting toxicity, functional deterioration, or aberrant drug-related behaviors. Some of these patients achieve functional gains as pain declines. On the other end is a subpopulation that deteriorates during opioid therapy. This deterioration can be characterized by worsening pain and disability, the development of aberrant drug-related behaviors, or both."

"Most pain specialists, endorse this view of opioid therapy and, consequently, no longer debate the role of opioid therapy in absolute terms. For pain specialists, the issue is not whether opioid drugs should ever be used in the treatment of chronic pain, but when and how. Although this shift in consensus may not be shared by all specialists, and has certainly not disseminated widely to other professional disciplines, it is noteworthy, and suggests that the use of opioid therapy for chronic non-malignant pain must now be evaluated as a potentially salutary therapeutic option for carefully selected patients. From this vantage, all those who might become involved in this therapy—clinicians, pharmacists, regulators, and patients—could benefit from a clear understanding of the evidence that defines its risks and benefits."[8]

Unfortunately, since Dr. Portenoy's published article in 1996—citing the scientific literature's inability to make definitive conclusions about the risks and benefits of long-term opioid therapy, and advocating opioid therapy for carefully selected patients—there is not any further articles in the literature which would provide for the medical community more recent data that would define more clearly what the risks and benefits are of long-term opioid therapy in this population. That lack of good data has not hindered the enthusiasm of Purdue's marketing and promotion. Never has long term opioid therapy received such promotion—direct and indirect-by the pharmaceutical industry, as mentioned above. And never have the primary care physicians—whose back-ground in pain and addiction issues have admittedly been sub-optimal—been so targeted in the promotion of an opioid as they have by Purdue Pharma and OxyContin. The success of the promotional campaign was reflected in the fact that from 1996 to 2000, the use of other commonly used opioids (codeine, hydrocodone, morphine, and hydromorphone) grew 23% while OxyContin prescriptions dispensed during the same period increased by over 1800%.[9] The fact that there are no studies in the medical literature demonstrating clear-cut superiority over older preparations such as sustained release morphine makes the promotion and marketing an even greater commercial success for Purdue Pharma.

Personal Conclusions

1. I would re-iterate that I feel there are at least three major factors involved in the OxyContin abuse epidemic—physician mis-prescribing and over-prescribing; the alarming prevalence of prescription drug abuse in this country; and the promotion and marketing practices of the maker of the drug, Purdue Pharma.

2. Clearly most of the regions of the country that are most affected by the OxyContin abuse epidemic have been the areas of the country where it was simply most available, i.e., where it was prescribed in unusually large amounts.[10] This reinforces the old observation that if a drug can be abused, it will be abused. And simply, by extension, if an abusable drug is widely available, it will be widely abused.

3. I would hope that several concrete changes can come out of what has been learned from the OxyContin abuse epidemic.

(A) It would be my hope that there is a change in the regulations that govern the pharmaceutical industry's marketing and promotional practices. Just as there is a very real difference between non-controlled drugs and controlled drugs, there needs to be a very real difference in regulations for how pharmaceutical companies can promote and market controlled drugs versus non-controlled drugs. The existing regulations have not served the public health well.

(B) Hopefully, with available technology, it would be a standard in the pharmaceutical industry that any marketed opioid would need to be formulated so as to minimize the abuse potential—as in the Talwin/NX story or with Purdue's current efforts to re-formulate sustained release oxycodone with naltrexone. It can be done with available technology, it will be done, and hopefully this will become an expectation and standard for the marketing of any opioid in the future.

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[8] Portenoy RK "Opioid Therapy for Chronic Nonmalignant Pain: Clinicians' Perspective" J Law Med Ethics 1996 Winter; 24(4):296–309.

[9] Statistics, DEA, Office of Diversion Control.

[10] U.S. map of OxyContin consumption by state, DEA, Office of Diversion Control.

"PARTNERS AGAINST PAIN"

On the "Partners Against Pain" web-site sponsored by Purdue Pharma, there is frequent mis-representation of facts that—when taken as a whole—tend to falsely over-sell the benefits and trivialize the risks in the use of opioids for chronic non-malignant pain. Examples follow.

From—"Patient/Caregiver" menu

"There are 75 million Americans living with pain, although pain management experts say they don't have to. And the statistics on the cost of pain in America are alarming." . . . 3 paragraphs later . . . "With the treatments available today, experts say we do not have to live in pain. An array of effective therapies, ranging from relaxation and physical therapies, to prescription pain medications, such as opioid analgesics, can help meet the needs of patients who suffer from various degrees of pain."

Reality: Opioids are the strongest pain medication available and can alleviate severe pain effectively for many patients. Opioids do not eliminate pain. For medication treatment of pain, it would be customary of good medical practice to use a step approach, beginning with non-controlled drugs and, in quite select circumstances, advance to opioids if needed for severe pain.

"In addition, education programs such as Partners Against Pain, play a central role in offering the latest information on pain treatment at the grassroots level.

"Neil Irick, M.D., a noted pain expert in Indianapolis, added—

> "Educational efforts such as Partners Against Pain, which inform patients and physicians about the latest developments in pain management, coupled with the new JCAHO standards, form the cornerstone of providing all patients with the very best pain care available, regardless of where they are being treated."

Reality: The above gives false reassurance to the patient and caregiver that this is a reliable, non-biased, non-commercial educational site. Dr. Irick has been a paid speaker for Purdue including being featured in promotional videos for Purdue.

Under 'Pain Killers'

"Recently, however, pain has begun to emerge as a treatable entity in its own right with doctors who specialize in pain management. There are also several methods for enhanced medication delivery including the now ubiquitous patient controlled analgesia (PCA), transdermal opioid patches, and time-release opioids that can be taken as few as two times a day. Another avenue pain specialists pursue is to try 'adjuvant' medications which are approved for uses other than pain but are effective in treating pain (e.g., epilepsy drugs, clonidine). Despite these advances, pain is often left untreated or undertreated for long periods of time before patients find an appropriate doctor and adequate treatment. Unfortunately, pain that is chronically untreated or undertreated may lead to further complications such as poor healing, depression, and immunosuppression. . . ."

Reality: A stepped approach for pain medication has been the standard in medicine, beginning with drugs with the least potential side effects and progressing if needed in certain patients to controlled drugs, opioids. The patient or caregiver reading the above would not get an accurate view of the customary approach to medication treatment of chronic pain.

From the "Professional Education" Menu

"Opioids for Chronic Nonmalignant Pain"

"Recent studies (mostly case studies) have shown that chronic pain patients can take opioids on a long-term basis with favorable results. These studies show that pain reduction was better in patients who used morphine while their functional and cognitive status remained the same. Additionally, with acceptable compliance, patients showed an improvement in pain control which led to an increased amount of activity without excessive tolerance to the selected opioid. It is important for the health care practitioner to keep in mind that some patients may not experience complete relief. It is imperative that physicians inform their patients about their responsibilities when they are prescribed opioids for pain management. The author suggests the use of an agreement form which makes the patient's responsibilities unambiguous." (Belgrade MJ. Postgraduate Medicine 1999:; 106(6): 115–124)

Reality: Going directly to the original article, on finds that Belgrade indicates that it is a "new myth" that 'Addiction almost never occurs when opioids are used for pain control.' He goes on to say that "Although opioids themselves may not cause addiction, the high prevalence of addiction in the general population and the even higher comorbidity of addictive disorders with psychiatric illness mean that a sub-

stantial minority of patients with chronic pain treated with opioids display problem behavior that make opioid management arduous, if not impossible. The proportion of problem cases appears to be 10–15% of patients with chronic pain selected for opioid maintenance analgesia."

From "Opioid Analgesia" an Essential Tool in Chronic Pain"

"Opioid therapy in chronic malignant and non-malignant pain is beneficial and safe for most people. This article suggests that by following a few basic guidelines, physicians can help patients in pain realize that pain is avoidable."

Reality: These statements over-state the benefits and falsely under-estimate the risks of opioids for chronic non-malignant pain.

From "Opioids and Back Pain: The Last Taboo"

"When will we recognize the role of opioids in chronic back pain? That's a question that more and more medical professionals are asking, as the media focuses new attention on the sad fact that back pain remains poorly controlled."

"Responsibly used, opioids can improve care for selected patients with back pain. But many people still have the out-dated attitude that opioids are taboo in back pain because they 'create' addicts. While opioids can be abused and may be habit forming, clinical experience shows that 'addiction' to opioids legitimately used in the management of pain is very rare . . . in trials in almost 25,000 patients with no history of drug dependence, there were only 7 cases of iatrogenic drug dependence, there were only 7 cases of iatrogenic drug addiction."

Reality: Tracing back to original literature, the above figure comes from 3 separate studies summarized below.

(1) not a study, but a letter to the editor NEJM by J. Porter and H. Jick, 1980, Jan 10; 302(2): 123—reported that of 11,882 patients who received at least one narcotic preparation while hospitalized, there were only four cases of reasonably well documented addiction.

(2) Perry S. "Management of Pain during Debridement: a Survey of U.S. Burn Units" Pain 13 (1982) 267–280.
—a questionnaire survey of 151 U.S. burn units, regarding analgesic practices for debridement.
—10,000 patients—"not one case of actual iatrogenic addiction could be documented. The 22 patients reported to abuse drugs after discharge all had a prior history of drug abuse".

(3) Medina J. "Drug Dependency in Patients with Chronic Headaches" Headache, March, 1977, 12–14.
—review of 2,369 patients seen in their clinic with headaches 1975–1976—only 62 patients were actually included in the study; of these only 23 were taking narcotics (propoxyphene or codeine) and of the 23, three were felt to be abusers of their medication.

Reality: These studies are quoted on the web site, in literature given to physicians (e.g. "Dispelling the Myths about Opioids"), and in literature given to patients who take OxyContin. The reality is that these citations are all in patients who have been exposed to opioids in the acute care pain situation, most hospitalized. They do not give a meaningfull assessment of the risks of addiction for patients taking opioids for chronic non-malignant pain.

Dr. Russell Portenoy, an expert of international eminence and an advocate for opioid therapy in very selected patients with chronic non-malignant pain, in reviewing these studies stated "It must be emphasized, however, that neither this observation nor any of the data described previously directly assesses the risk of addiction among chronic nonmalignant pain patients administered opioids for prolonged periods." Portenoy RK "Chronic opioid therapy in nonmalignant pain" J Pain Symptom Manage 1990 Feb; 5(1 suppl): S46–62.

Personal Conclusions

The above review of Purdue Pharma's "Partners Against Pain" website does not purport to be a comprehensive review. However, what is reviewed, I would conclude, does reflect that Purdue through this website has for physicians and patients oversold the benefits of opioid therapy for chronic non-malignant pain, while providing false reassurance about what the real risks are of addiction for patients taking opioids for chronic non-malignant pain.

ATTACHMENT C—OXYCONTIN CONSUMPTION PER 100,000 POPULATION—JANUARY–DECEMBER, 2000—USA & VIRGINIA

DEPARTMENT OF JUSTICE—DRUG ENFORCEMENT ADMINISTRATION—ARCOS 2—REPORT 4—CUMULATIVE CONSUMPTION IN GRAMS PER 100,000 POPULATION

Reporting Period: 01/01/2000 to 12/31/2000

Drug name: OxyContin

Rank	State	Population	Grams to date	Grams/100K Pop. to date
1	ALASKA	637,786	52,956.66	8,303.20
2	WEST VIRGINIA	1,834,977	149,287.45	8,135.66
3	FLORIDA	15,123,712	1,135,140.96	7,505.70
4	MAINE	1,254,228	87,938.59	7,011.37
5	MISSOURI	5,519,767	378,785.99	6,862.35
6	CONNECTICUT	3,284,638	219,394.44	6,679.41
7	NEW HAMPSHIRE	1,215,820	80,748.41	6,641.48
8	PENNSYLVANIA	12,196,657	741,776.32	6,081.80
9	DELAWARE	762,928	45,679.15	5,987.35
10	KENTUCKY	3,983,524	227,718.40	5,716.51
11	SOUTH CAROLINA	3,842,027	212,139.37	5,521.55
12	MARYLAND	5,256,181	289,561.06	5,508.96
13	OHIO	11,308,118	610,639.43	5,400.01
14	ALABAMA	4,434,285	235,440.62	5,309.55
15	RHODE ISLAND	997,867	52,238.45	5,235.01
16	MASSACHUSETTS	6,191,180	319,220.82	5,156.06
17	NEVADA	1,837,560	92,588.43	5,038.66
18	ARIZONA	4,732,567	235,103.17	4,967.77
19	WASHINGTON	5,817,823	257,019.97	4,417.80
20	OREGON	3,369,788	148,379.53	4,403.23
21	NORTH CAROLINA	7,723,277	339,758.19	4,399.15
22	VERMONT	613,933	25,920.94	4,222.11
23	VIRGINIA	6,960,521	292,844.70	4,207.22
24	MICHIGAN	9,670,334	375,023.55	3,878.08
25	GEORGIA	7,811,632	302,894.25	3,877.48
26	NEW JERSEY	8,158,375	312,519.06	3,830.65
27	INDIANA	6,023,368	225,414.48	3,742.33
28	LOUISIANA	4,419,367	161,829.82	3,661.83
29	MISSISSIPPI	2,806,081	102,563.29	3,655.04
30	TENNESSEE	5,598,896	197,738.81	3,531.75
31	WISCONSIN	5,309,409	185,332.92	3,490.65
32	MONTANA	942,485	31,910.26	3,385.76
33	UTAH	2,172,245	72,257.59	3,326.40
34	DISTRICT OF COLUMBIA	527,376	16,640.36	3,155.31
35	HAWAII	1,250,999	38,878.69	3,107.81
36	ARKANSAS	2,618,315	76,300.57	2,914.11
37	OKLAHOMA	3,365,270	96,736.33	2,874.55
38	IDAHO	1,325,236	34,888.00	2,632.59
39	COLORADO	4,126,972	106,250.36	2,574.54
40	NEW MEXICO	1,839,278	41,398.41	2,250.80
41	KANSAS	2,659,522	58,835.21	2,212.25
42	MINNESOTA	4,806,626	102,590.70	2,134.36
43	NEBRASKA	1,698,165	35,247.47	2,075.62
44	TEXAS	19,989,625	413,683.05	2,069.49
45	CALIFORNIA	32,432,678	637,119.27	1,964.44
46	NORTH DAKOTA	659,786	12,725.82	1,928.78
47	SOUTH DAKOTA	772,409	14,177.88	1,835.54
48	WYOMING	520,976	8,982.15	1,724.10
49	IOWA	2,895,100	47,791.65	1,650.78
50	NEW YORK	18,154,793	282,320.23	1,555.07
51	ILLINOIS	12,030,766	156,076.10	1,297.31
52	PUERTO RICO	3,915,798	9,653.60	246.53
53	VIRGIN ISLANDS	119,827	155.22	129.54
54	TRUST TERRITORIES	228,400	8.95	3.92

DEPARTMENT OF JUSTICE—DRUG ENFORCEMENT ADMINISTRATION—ARCOS 2—REPORT 4—CUMULATIVE CONSUMPTION IN GRAMS PER 100,000 POPULATION—Continued

Reporting Period: 01/01/2000 to 12/31/2000

Drug name: OxyContin

Rank	State	Population	Grams to date	Grams/100K Pop. to date
	U.S. TOTAL	277,749,273	10,388,225.10	3,740.14

THE RELEASE OF INFORMATION SUBJECT TO DEA APPROVAL.

STATE OF VIRGINIA BY COUNTY

2000 OxyContin Consumption Per 100K Population

Sorted by: Grams Per 100K

County	Population	Total Grams	Grams Per 100K
Dickenson	16,061	4,143.85	25,800.70
Lee	21,931	5,131.10	23,396.56
Buchanan	29,262	5,599.82	19,136.83
Scott	22,761	4,170.85	18,324.55
Roanoke City	80,893	14,344.04	17,732.12
Tazewell	45,273	7,757.23	17,134.34
Winchester City	23,458	3,575.65	15,242.77
Manassas City	40,081	5,905.64	14,734.26
Fauquier	57,972	8,344.94	14,394.78
Wythe	26,770	3,810.82	14,235.41
Wise	45,938	6,265.65	13,639.36
Roanoke	110,067	14,830.34	13,473.92
Pulaski	50,924	6,094.35	11,967.54
Russell	29,423	3,471.04	11,797.03
Falls Church City	15,115	1,619.46	10,714.26
Giles	16,883	1,706.81	10,109.64
Fredericksburg City	22,284	2,103.65	9,440.18
Bland	7,032	519.63	7,389.51
Orange	21,617	1,574.83	7,285.15
Richmond City	128,156	9,043.45	7,056.60
Loudoun	162,766	10,127.12	6,221.89
Washington	50,142	3,074.81	6,132.20
Montgomery	76,323	4,654.45	6,098.36
Smyth	31,875	1,904.88	5,976.09
Botetourt	22,188	1,151.96	5,191.82
Portsmouth City	98,311	4,971.43	5,056.84
Prince William	274,516	12,965.87	4,723.17
Bristol City	16,066	751.25	4,676.02
Fairfax	969,354	45,285.94	4,671.76
Isle of Wight	28,778	1,228.86	4,270.14
Gloucester	35,057	1,448.94	4,133.10
Poquoson City	11,590	462.08	3,986.89
Bedford	96,262	3,825.81	3,974.37
Warren	27,268	1,077.91	3,953.02
Franklin	44,303	1,732.96	3,911.61
Lancaster	11,502	433.79	3,771.43
Page	22,838	846.28	3,705.58
Alleghany	22,670	801.38	3,534.98
Louisa	29,877	1,010.48	3,382.13
Augusta	107,884	3,637.04	3,371.25
James City	66,773	2,190.57	3,280.62
Newport News City	184,149	5,888.73	3,197.81
Henry	69,158	2,175.01	3,144.99
Henrico	307,243	9,620.00	3,131.07
Hanover	84,301	2,617.52	3,104.97
Patrick	16,719	480.38	2,873.26
Williamsburg City	1,162	32.82	2,824.44
Hampton City	142,549	3,861.27	2,708.73
Grayson	30,508	821.58	2,693.00

STATE OF VIRGINIA BY COUNTY—Continued

2000 OxyContin Consumption Per 100K Population

Sorted by: Grams Per 100K

County	Population	Total Grams	Grams Per 100K
Southampton	27,392	722.17	2,636.43
Spotsylvania	88,917	2,308.38	2,596.11
Chesterfield	315,728	8,148.37	2,580.82
King William	16,957	433.47	2,556.29
Richmond	9,028	230.14	2,549.18
Lynchburg City	58,240	1,467.29	2,519.39
Rockbridge	33,263	820.39	2,466.37
York	44,035	1,025.41	2,328.62
Pittsylvania	108,653	2,527.73	2,326.42
Accomack	32,471	728.30	2,242.92
Alexandria City	120,636	2,634.43	2,183.78
Suffolk City	65,617	1,428.21	2,176.59
Nottoway	16,149	349.26	2,162.73
Amherst	29,579	597.22	2,019.07
Mecklenburg	31,390	632.65	2,015.45
Cumberland	18,025	357.27	1,982.08
Arlington	180,826	3,523.79	1,948.72
Chesapeake City	211,847	4,019.92	1,897.56
Stafford	94,093	1,774.74	1,886.16
Prince George	65,072	1,197.89	1,840.87
Culpeper	36,983	676.60	1,829.49
Appomattox	10,714	194.32	1,813.70
Rockingham	93,552	1,676.05	1,791.57
Greensville	16,826	289.25	1,719.07
Essex	9,533	162.92	1,709.01
Westmoreland	16,457	274.90	1,670.41
Shenandoah	35,438	578.37	1,632.06
Albemarle	115,999	1,849.51	1,594.42
Carroll	23,503	374.20	1,592.14
Mathews	9,852	150.45	1,527.10
Clarke	13,648	202.40	1,483.00
Frederick	57,113	826.67	1,447.43
Norfolk City	209,101	2,939.91	1,405.98
Middlesex	10,539	138.61	1,315.21
Virginia Beach City	441,859	5,795.74	1,311.67
Buckingham	19,318	253.22	1,310.80
Lunenburg	12,489	153.93	1,232.52
Sussex	13,281	157.55	1,186.28
Halifax	36,475	395.66	1,084.74
Floyd	12,120	121.63	1,003.55
Bath	5,467	54.60	998.72
Caroline	22,379	203.29	908.40
Radford City	1,437	11.35	789.84
Rappahannock	8,069	63.58	787.95
Goochland	15,387	119.98	779.75
Madison	10,552	76.06	720.81
Northampton	12,733	87.67	688.53
New Kent	15,871	103.79	653.96
Northumberland	11,771	76.04	645.99
Powhatan	22,289	140.48	630.27
King George	18,275	111.86	612.09
Charlotte	10,203	58.13	569.73
Amelia	10,035	51.02	508.42
Fluvanna	18,224	89.45	490.84
Dinwiddie	17,189	70.73	411.48
Campbell	44,705	181.67	406.38
Brunswick	16,983	55.46	326.56
Nelson	17,300	47.39	273.93
Greene	15,249	8.96	58.76
Charles City	6,709	0.00	0.00
Craig	6,180	0.00	0.00

STATE OF VIRGINIA BY COUNTY—Continued

2000 OxyContin Consumption Per 100K Population

Sorted by: Grams Per 100K

County	Population	Total Grams	Grams Per 100K
Fairfax City	859	0.00	0.00
Harrisonburg City	3,369	0.00	0.00
Highland	2,487	0.00	0.00
King and Queen	6,407	0.00	0.00
Manassas Park City	1,730	0.00	0.00
Martinsville City	2,653	0.00	0.00
Petersburg City	1,460	0.00	0.00
Prince Edward	11,872	0.00	0.00
Surry	5,926	0.00	0.00
VA Total	6,960,521	292,844.70	4,207.22
VA Average − 25%	3,155		
VA Average	4,207		
VA Average + 25%	5,259		

ATTACHMENT D

ALTERNATIVES TO OXYCONTIN

There are several strong pain medications (opioids) which are just as effective as treating severe pain as is OxyContin. There are no studies in the medical literature which demonstrate OxyContin has clear cut superiority over immediate release oxycodone, controlled release morphine, transdermal fentanyl patches, or methadone when used in the treatment of severe pain. Some of these have less abuse potential, and some of these offer significant cost savings over OxyContin. In reviewing oxycodone and OxyContin in the September 17, 2001 issue, The Medical Letter concluded:

"OxyContin is a q12hour controlled-release formulation of oxycodone that can be used effectively in the treatment of pain due to cancer and, occasionally, other types of chronic pain. There is no evidence that oxycodone offers any advantage over appropriate doses of other opioids, and it appears to have the same potential for addiction as morphine."

Some of the studies are summarized briefly below—

Comparison: Immediate Release Oxycodone Versus OxyContin

Hale ME, et al. Efficacy and Safety of Controlled-Release Versus Immediate-Release; Oxycodone: Randomized, Double-Blind Evaluation in Patients with Chronic Back Pain; Clin J Pain 1999 Sep:15(3): 179–83 **

Conclusions: 47 patients randomized—"controlled-release oxycodone given every 12 hours was comparable with immediate-release oxycodone given four times daily in efficacy and safety . . .

Kaplan R, et al.; Comparison of Controlled-Release and Immediate-Release Oxycodone Tablets in Cancer Pain; J Clin Oncol 1998 Oct;16(10):320–7 **

Conclusions: 160 patients, double blind study—"CR and IR oxycodone were equally effective in the management of cancer-related pain"; —". . . the adverse event profiles of CR and IR oxycodone were similar. Overall, however, significantly fewer adverse events were reported for CR oxycodone compared with IR oxycodone . . ." (somewhat less)

Stambaugh JE, et al.; Double-Blind, Randomized Comparison of the Analgesic and Pharmacokinetic Profiles of Controlled- and Immediate-Release Oral Oxycodone in Cancer Pain Patients; J Clin Pharmacol 2001 May; 41(5):500–6 **

Conclusions: 32 patients—"CR provides equivalent analgesia as IR oxycodone with the same patient acceptance profile"; ". . . similar incidences and numbers of reports of individual adverse events considered related to the IR and CR drug"

Comparison: Controlled-Release Morphine Versus Controlled-Release Oxycodone (OxyContin)

Heiskanen T and Kalso E.; Controlled-release oxycodone and morphine in cancer related pain. Pain 1997 Oct; 73(1):37–45 **

Conclusions: 45 patients in a double-blind, randomized, cross-over; "the two opioids provided comparable analgesia"; "the total incidence of adverse experiences reported by the patients was similar, but significantly more; vomiting occurred with morphine, whereas constipation was more common with oxycodone."

Mucci-LoRusso P, et al.; Controlled-release oxycodone compared with controlled-release morphine in the treatment of cancer pain: a randomized, double-blind, parallel-group study. European Journal of Pain (1998) 2:239–249 **

Conclusions: 100 patients—"controlled-release oxycodone was as effective as controlled-release morphine in relieving chronic cancer-related pain. . ."; "the side-effect profiles of CR oxycodone and CR morphine were similar overall in this trial."

Bruera E, et al.; Randomized, Double-blind, cross-over trial comparing safety and efficacy of oral controlled-release oxycodone with controlled-release morphine in patients with cancer pain. J. Clin Oncol. 1998 Oct; 16(10):3222–9

Conclusions: 23 patients—"There were no significant differences detected between the two treatments in . . . adverse events, or clinical effectiveness . . ."; There are no studies that we are aware of comparing controlled-release oxycodone (OxyContin) with transdermal fentanyl or oral methadone for treatment of severe chronic pain. There are a few studies comparing transdermal fentanyl with oral morphine.

Transdermal Fentanyl Versus Oral Morphine

Payne RJ; Quality of life and cancer pain: satisfaction and side effects with transdermal fentanyl versus oral morphine. Clin Oncol 1998 April 16(4):1588–93

Conclusions: 504 patients—"these data suggest that patients are more satisfied with transdermal fentanyl compared with sustained-release morphine".

Ahmedzai S.J.; Transdermal fentanyl versus sustained-release oral morphine in cancer pain: preference, efficacy, and quality of life. J. Pain Symptom Management 1997 May: 13(5):254–61

Conclusions: both were equally effective in terms of pain control; there was less constipation and sedation with fentanyl.

**Purdue Pharma funded studies

ATTACHMENT E—THE MEDICAL LETTER—VOL. 43 (ISSUE 1113)—SEPTEMBER 17, 2001

The Medical Letter has for decades been a gold standard of thoughtful integrity for the evaluation of pharmaceutical drugs. For the practicing physician, it has served as the most respected reference for the evaluation of the proven safety and efficacy of medications, as well as the appropriate role of a particular medication in the pharmaceutical armamentarium.

The September 17, 2001 issue of the Medical Letter reviewed oxycodone and OxyContin. Enclosed is the review.

Oxycodone and OxyContin

Recent reports of inappropriate use and diversion of *OxyContin* tablets have prompted Purdue Pharma to include a "Black Box Warning" in the product labeling to call attention to the potential for abuse and to reinforce the FDA-approved indication ". . . for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time . . ."

HISTORY—Oxycodone is a semisynthetic opioid analgesic structurally related to morphine and codeine. It has been used in Europe by injection and orally since 1917. Oral oxycodone 5-mg has been available in the U.S. since the 1950's in combination with aspirin *(Percodan)* and acetaminophen (*Percocet, Tylox, Roxicet,* and others). Subsequently single-entity oxycodone became available in the U.S. as 5-mg immediate-release tablets *(Roxicodone, Percolone)* and in liquid formulations. Since 1996, Purdue Pharma has marketed controlled release oxycodone *(OxyContin)* 10-, 20-, 40-, and 80-mg tablets intended for use every 12 hours. A 160-mg tablet was approved in March 2000 and withdrawn from the market earlier this year. In street abuse, *OxyContin* tablets are being crushed to make the entire dose immediately available, and then snorted or dissolved in water and injected intravenously (IV). When taken in this way by people with no tolerance to the drug, a single 80-mg dose of *OxyContin* can be fatal.

ANALGESIC EFFICACY—In controlled clinical trials, the relative analgesic potency of parenteral oxycodone to morphine has ranged from 0.7 to 1.5. Parenteral

oxycodone is 10 to 12 times as potent as codeine. Oral oxycodone is about 7 to 9.5 times as potent as oral codeine. For treatment of cancer pain, *OxyContin* q12h has been equal in analgesic effect to the same total daily dose of immediate-release oxycodone q6h, 1.5 to 2 times as potent as controlled-release morphine *(MS Contin)* q12h, and about 25% as potent as controlled-release hydromorphone q12h (*Hydromorph Contin*—available in Canada) (P Mussi-LoRusso et al., Eur J Pain 1998; 2:239; JE Stambaugh et. al., J Clin Pharmacol 2001; 41:500; NA Hagen and N Babul, Cancer 1997; 79:1428). No studies are available comparing oxycodone with other opioids used for treatment of chronic cancer pain such as methadone or fentanyl (*Drugs of Choice from the Medical Letter* 2001, page 138). In general, some patients who do not respond to or cannot tolerate one opioid may respond to or tolerate another.

OxyContin has also been used for treatment of moderate to severe chronic non-malignant pain including back pain, osteoarthritis-related pain, and during rehabilitation following total knee arthroplasty. No studies are available comparing *OxyContin* with other opioids or any other analgesics, such as nonsteroidal anti-inflammatory drugs, for treatment of chronic non-malignant pain.

ADVERSE EFFECTS—The adverse effects of oxycodone are dose-related and the same as those of other opioids. Common effects include confusion, somnolence, dizziness, nausea, vomiting, constipation, pruritus, dry mouth and sweating. Overdose may result in hypotension, respiratory depression, cardiac arrest and death.

DRUG DEPENDENCE AND ABUSE—Oxycodone is a Schedule II controlled substance with a dependence or addiction liability comparable to that of morphine. Psychological dependence, physical dependence and tolerance can develop with repeated administration. Withdrawal of the drug in a physically dependent person results in an abstinence syndrome like that of morphine and other strong opioids.

CONCLUSION—*OxyContin* is a q12h controlled-release formulation of oxycodone that can be used effectively in the treatment of pain due to cancer and, occasionally, other types of chronic pain. There is no evidence that oxycodone offers any advantage over appropriate . . . to have the same potential for addiction as morphine.

Senator REED. Ms. Green?

Ms. GREEN. Thank you. First of all, I am very privileged to be here.

I am representing Neighbors Against Drug Abuse. We are not a professional group. We are four women in Down East, Maine—a nurse-midwife, a nurse practitioner, a prevention health specialist who works in the school system, and the secretary of the medical staff at Calais Hospital. I am bringing their voice, I am bringing the voice of my pregnant patients, their unborn babies, and I am bringing you the voice of all the addicts in Washington County. So I really am privileged to be sitting so close to all these wonderful people and I have a lot of messages for you.

OxyContin, a prescription pain medication introduced in 1995 by Purdue Pharma, has become a major drug of abuse in Maine over the past 5 years. We realize this problem is not unique to our State. Over the past 2 years Maine and, in particular, Washington County's growing problem with OxyContin has received international attention. The ready availability of prescription narcotics, as well as the enormous profits to be made by its illegal sale are too great to ignore.

Recreational use of the drug grew rapidly after its introduction on the market and Maine became one of the first States to report widespread abuse of OxyContin. Treatment for narcotic abuse has increased by 500 percent since 1995. The number of people admitted to treatment due to drugs such as OxyContin rose from 232 in 1995 to 1,299 as of July 2001.

I am a certified nurse-midwife by profession but the circumstances in our community have obliged me to become a drug and alcohol counselor and also to spend many, many, many hours with Neighbors Against Drug Abuse, which is our volunteer work.

I have had the opportunity through this to really get an inside look at the lives of some of our addicts and their families and I will give you some examples.

A young man describes how during the height of his addiction, while snorting an Oxy, he had a massive nose bleed. He tried to catch the blood with his hands and put it back in his nose. He could see that he was losing some of his crushed pills in his blood and was therefore losing his maximum high. He was more concerned with getting his Oxy back into him than catching his blood.

An elderly woman diagnosed with cancer came into my office questioning whether the pharmacy had made a mistake in the number of pills they had given her. Yesterday her bottle contained 30 OxyContin pills but today she only counted 10. One of her grandchildren, unknown to her, had been stealing her medication for his own use and for sale to fund his addiction.

One of my clients during a counseling session even asked me for money for drugs, she was so desperate.

Parents in my town call the police in order to have their addicted children arrested. At least then they know that they are temporarily safe and off the streets. I am a parent. I would never want to make that choice.

A mother of four was given OxyContin for legitimate pain relief but after some time was told by a friend that if she snorted it it would be more effective. She became an addict, lost her home, lost her children, and recently completed a two-and-a-half-year prison sentence.

Local high school addicts now in recovery tell me that eight out of 10 kids in their class are abusing some form of substance and of this 80 percent, OxyContin was their substance of choice.

A teenage client that knows I am here today has asked me to give you the following message. "Take OxyContin off the market," and I am quoting her directly. "But if you cannot or you will not, then please make a rule where there is much more supervision, regulation and control over it and change it so that it is not so addictive and do not make it so easy for us to get."

Ten of my 40 mothers delivered just last year were opiate abusers. They chose a prescription drug because they thought it was safe. How could something legally available from doctors possibly harm them or their babies? Needless to say, no newborn baby should have to endure narcotic withdrawal as its introduction into the world.

This drug problem is contributing to the break-up of our families. An estimated 50 percent of child protective and custody cases in the court systems in our State involve family abuse of prescription drugs.

Opiates used to be the end of the line for drug addicts. Now it appears that prescription opiates may be one of the first drugs abused. In correlation with this finding, the incidence of hepatitis C and HIV have escalated into major public health risks.

I could keep you here for hours and hours and hours telling you story after story after story and the desperation in our town. Believe me when I tell you that since the legal introduction and illegal diversion of OxyContin, a dark cloud hangs over Down East, Maine and I do not see it clearing for a long time.

Even if OxyContin, Dilaudid, heroin and others by some form of miracle or magic disappeared, we would still be left with a community that is scarred forever. The consequences of these addictions are life-long.

Unlike other affected communities, we have an addicted population which is isolated geographically with no access to treatment facilities. We have nothing. We have no transportation. We have minimal counseling and we need more support and education.

In order to address the dramatic problem of the abuse of OxyContin and other prescription drugs, we are making the following recommendations. Increase access and funding for treatment. We are in desperate need of local detox and rehab. Increase funding for public education and prevention. Increase funding for law enforcement to address diversion of legal drugs to illegal use, targeting areas with the greatest need and fewest resources.

Develop State-wide Federal and international electronic prescription monitoring programs so that there is dialogue between the physician, the pharmacy, and a central databank. We are encouraging the FDA—and thank you for being here—we really would like Buprenorphine. We have been waiting for almost 2 years.

And finally, Purdue Pharma, please stop sending OxyContin in the mail to clients on their patient assistant program. These shipments are easily intercepted. It would be irresponsible for you to continue.

We also know that you are very, very busy helping everyone else in our country. I am only asking you to please do not forget us. Thank you.

Senator REED. Thank you, Ms. Green.

[The prepared statement of Ms. Green follows:]

PREPARED STATEMENT OF NANCY GREEN, C.N.M.

"Never doubt that a small group of thoughtful, committed citizens can change the world. Indeed, it is the only thing that ever has."—Margaret Mead.

Mr. Chairman, and Members of the Committee, I am Nancy Green, a certified nurse midwife in Calais, Maine. I have a Bachelor of Science in Nursing from Duquesne University and a Master of Science in Nursing from Case Western Reserve University, and I am certified as a nurse midwife from Frontier School of Midwifery and Family Nursing. I am board certified through the American College of Nurse Midwives. I am also one of the founders and now president of Neighbors Against Drug Abuse (N.A.D.A.), a "grass roots" group of citizens who have come together because of our concern with our current and still evolving substance abuse epidemic and crisis in Washington County, Maine.

The Problem

Washington County, population 35,352, is entirely rural, with a natural resource and service based economy. Its 47 towns, ranging in population from 10 to 4000, are widely dispersed in a heavily wooded region encompassing 2569 square miles, which corresponds to 14 persons per square mile in an area roughly twice the size of Rhode Island. Severe winters, poor road conditions and lack of public transportation contribute to the geographic isolation of the county.

The extreme poverty, poor economic environment, and low education achievement in the rural and isolated Washington County contribute to a social climate characterized by high stress, broken families, and poor preventative health care. These conditions contribute as risk factors to high rates of substance abuse starting with school age children and eventually leading to the high rates of prescription opiate abuse, which are poorly addressed by the limited resources for treatment and preventative interventions.

The geographic isolation, combined with a lack of transportation, contribute to a substantial barrier for substance abuse patients to access medical and mental health care or social services. In addition to difficulties for patients to travel, these

factors pose a major challenge for health programs to deliver services and coordinate patient care in a timely and cost effective manner. Moreover, the stigma of drug abuse and the lack of anonymity in small towns are well known barriers for clients seeking services in a rural area.

Emergence of the Current Epidemic

In 1999, the Office of the U.S. Attorney for the District of Maine noticed that law enforcement seizures and arrests for illegal possession of OxyContin and other abused synthetic narcotic prescription drugs had jumped nine fold. Arrests for illegal possession have quadrupled in four years. In Washington County, adult arrests for possession of synthetic narcotics were 2.5 times that for the state. The rate of possession of opiates or cocaine was twice the state average, and reports of arrests for breaking and entering were elevated 67 percent over the state (source: Maine Department of Public Safety).

In October 1999, U.S. Attorney Jay McCloskey traveled to Washington County to meet with concerned citizens. "The prescription pain medication abuse is the most serious criminal problem facing Maine and may be the most pressing social problem," he said at the meeting. I attended the meeting because a phone call from Carrie MacDonald, a friend and patient of mine, who works for the Calais school system as the prevention coordinator under the Safe Schools and Healthy Students Initiative. She felt that this would be an important meeting for me, as a health care provider, in particular caring for women and newborns, to attend. And, she was right.

I still remember how I felt that October day last year. What a coincidence that this same day, I was approached by one of my patients, a 19 year old expecting her second baby, who was in her second trimester of pregnancy, asking for help. "Please get help for me," she said, "I was arrested for selling opiates outside the Calais Junior High School. I have been addicted to opiates for four–five years. I need to get 'clean'."

I made several phone calls to the emergency room at the Calais hospital and to Calais mental health counselors. They told me that there was NO help for her in this part of the state. I made phone calls to Mercy Hospital in Portland, Maine, a four hour drive away. They accepted her as a patient, but only because of her advanced stage of pregnancy. Otherwise, waiting lists for patients to get into "detox" were and still are four to six months long.

One week later, I received a phone call from this patient from Portland, in tears, asking me to take her back as a patient. "I miss home. I know you and trust you. I want you to deliver my baby." I explained to her that she could NOT come home, since there was nothing for her here in the way of substance abuse treatment, support or counseling. Also, she could not come back to the same environment she left from, same "circle of friends," "same life." I told her, "it's not safe for you to come home." What a coincidence that this took place about one hour before our meeting with U.S. Attorney McCloskey. I was able to share my very recent encounter with him and the group in attendance.

By January 2001, I was caring for six pregnant women, at all stages of pregnancy, with addiction to "legal" prescription medications. By now, I was becoming an "expert in addiction." One of my patients who had transferred her care from another provider in January, delivered her baby four weeks prematurely. I could not understand why she was having such an unusual labor pattern, and why so early. She finally admitted to me in the birthing room, while laboring, that she was an opiate addict. Things became very clear to me—she had "snorted" four days before, but not since then. What I was seeing was actual withdrawal, not just hers but that of her soon to be born baby. She told me she "snorted oxys." I told her she was now going to have an addicted baby, and she said to me:

> "My friends told me it was safer for me to snort OxyContin because it was a legal prescription, written by doctors, and that nothing would happen to the baby."

She ended up having the baby who went through withdrawal in the nursery (e.g., high pitched crying, difficult to console, exaggerated movements, tremors). Our pediatricians provided excellent care to this baby. The baby's grandmother adopted the baby in order to avoid the Department of Human Services "placing the baby with a stranger." My patient, I'm glad to say, has done extremely well with detox and rehab, through my support and the support of the few substance abuse counselors we have in the community.

"The drug problem is contributing to the break-up of families," according to Circuit Court Judge John Romei, who estimates that half of the child custody cases he handles involve family abuse of prescription drugs. "If there is a bigger problem in regard to the criminal justice system in this county, I don't know what it is . . ..

I've taken children away from numerous young moms because of prescriptive narcotic abuse."

An attorney in the area stated that she has served as court appointed attorney for approximately 40 young women in child protective cases involving prescription drugs. "I had my first child protective case involving opiates three or four years ago. Now it's just routine," she said.

Two more of my patients delivered this past week. With again, support from me, the one substance abuse counselor in town, education and determination, these women have been drug free for the past four to five months. Their babies were born weighing approximately five pounds at term. Luckily, and so far, this was the only consequence of their mothers' addiction earlier in their pregnancies. Several of my other addicted patients have suffered pregnancy losses, again at differing stages of their pregnancies.

A very dangerous consequence of substance abuse, and a serious public health issue, is the recent rise of Hepatitis C. According to Maine Center for Disease Control reports, a 47 percent elevation over state levels of Hepatitis C was identified within the county in 2000. This correlates with the epicenter of the recent epidemic of synthetic narcotics. Only 10 percent of opiate addicts have been tested for Hepatitis C and, of those tested at least 30 to 40 percent have tested positive. That percentage may actually be higher since there is at least a six month time lag from exposure to Hepatitis C and any resulting infection to testing positive. If we assume a similar rate of infection among untested addicts. It means that 90 percent of Hepatitis C cases among the addict population have yet to be identified.

When speaking to our addicted patients who are still in recovery, they explain to us how they "crush the tablets" and then snort them with straws or use the bottom parts of pens, and/or they dissolve the tablets with water and inject them. Crushing or dissolving the tablet disarms the timed-release action of the medication causing a quick, powerful high similar to that of heroin. Hepatitis C is transmitted through blood to blood contact. When snorting, the mucous membranes in the nose become weakened and bleed. Addicts share their "snorting utensils" and, therefore, share Hepatitis C. HIV takes much longer to "show-up" in a person. Hepatitis C sbows up within a short period of time.

Listening to people affected with addiction is the most heart wrenching experience. One young man described how he moved along the progression of addiction from marijuana and alcohol to Percocets and Dilaudid (i.e. other forms of opiates). But when introduced to OxyContin, "bam what an experience!" "Nothing else compares to it." "An immediate sense of euphoria and that can't be described." The feeling with OxyContin is so magnificent that all other drugs of abuse pale by comparison. "I didn't want anything else." "I knew I was 'hooked' within two days of trying 'oxys'." "I needed and wanted more." "I couldn't wait to get up in the morning to snort another one." "It is cheaper for me to buy oxys in Canada because it is much cheaper than in Maine. I can buy a 40 (40 mg. Tablet) for $20.00 U.S. instead of $40.00 here at home."

Parents and grandparents describe how their families have been afflicted by this crisis. One family had their bible, which had been in the family for over 100 years, stolen by their child in order to get money to sustain her habit. Her own family called the police and had her arrested "because we just couldn't deal anymore with this problem."

Some quotes from the extensive press coverage of the OxyContin epidemic in Washington County highlight the large impact. For example, from a March 23, 2001, *Boston Globe* article, "Painkiller Tears Through Maine":

> "OxyContin, a remarkably effective painkiller, is shredding the social fabric of parts of Maine, creating a Wild West-like anarchy in many communities. Pharmacies are being held up, the gunmen demanding only pills. Neighbors are robbing, even assaulting, one another. One couple tried to smuggle the drug from Canada, where it is cheaper, in the underpants of their handicapped child."

Why rural Maine has been subject to this rapid growth in prescription narcotic abuse appears attributable to several factors, including the following:

- The ready availability of the drug from the diversion of prescriptions or fraudulent prescriptions allowed abuse to develop among a larger population of users than typically have ready access to heroin.
- A Maine legislative rule in 1999 contributed to the problem by requesting doctors to treat pain more aggressively.
- The great profits to be made by its illegal sale are an additional reason why OxyContin abuse has grown so quickly. A 40 milligram pill costs approximately four dollars by prescription, yet it may sell for $35 to $40 on the street. Thus, a 100 tablet bottle purchased for $400 or subsidized through Medicaid, can sell for as much

as $4,000 on the black market. In areas already beset by high unemployment and poverty rates, such high profits can tempt even "average" citizens to sell some or all of their family member's legitimate prescription. From this level of diversion, progressively more criminal steps predictably follow for addicts who need to sustain their habit and/or dealers seeking profits. These include "doctor shopping" with fake back injuries, forging or altering prescriptions, theft from incapacitated relatives with chronic disease, robberies of homes and pharmacies and, ultimately, armed robberies with assaults on those with legitimate prescriptions.

Neighbors Against Drug Abuse (N.A.D.A.)

N.A.D.A. was formed after hearing reports from the Maine U.S. Attorney and the Maine Office of Substance Abuse, and professional contact with substance abuse in our practices. It has five members: a prevention specialist with the Calais school system, a nurse practitioner, parents of an addicted son, and a certified nurse midwife.

N.A.D.A. is a group of citizens who have come together because of our concern over the very high and increasing problem of substance abuse in Washington County, in particular the abuse of opiates. We act as a fact finding and steering committee. Our group is further subdivided, focusing on prevention/education, treatment, law enforcement and funding (i.e., local, state, federal, private). We organized in December 2000. We work out of our kitchens, cars, anywhere we find space, and we have functioned without a budget! However, we have been able to bring awareness to the community, having launched an enormous public campaign through public meetings and media interviews. We applied for a $100,000.00 per year for five years grant from the federal Office of Juvenile Justice and Delinquency Prevention (OJJDP) to fund prevention efforts in northeastern Washington County. We have had no response. As a result of a workshop we organized in March 2001, the Washington County Planning Commission on Opiate Addiction Treatment was formed.

The Plan

I. The Planning Commission has determined there are a number of treatment services that are considered critical to effectively treat opiate addicts in the county. These are:

a) Intensive outpatient program
b) Replacement therapies
c) Outpatient counseling
d) Medical care
e) Nutrition counseling
f) Support services (intensive supports for recovering person including case management, help to reconstitute the family, employment, housing, financial assistance, recreation, transportation, drug testing and others)
g) Family counseling
h) Education

Unlike other affected communities, we have an addicted population that is isolated geographically, with no access to treatment facilities, transportation, counseling, support or education.

II. A federal Substance Abuse and Mental Health Administration Center for Substance Abuse Treatment (SAMHSA/CSAT) Grant for treatment services of $500,000 per year for three years was submitted on September 7, 2001. If awarded, this grant would not become available until the summer of 2002.

III. A smaller proposal for support to continue the work of the Commission over the next year, on detailed implementation and planning for the treatment services, has been submitted.

IV. $100,000.00 per year for five years to fund prevention efforts (Office of Juvenile Justice and Delinquency Prevention) for N.A.D.A.

V. Continued support from the Main Office of Substance Abuse (OSA). We hope to obtain direct funding next year from OSA for partial support.

VI. Help from the county delegation to build support in the state legislature for replacing this $500,000.00 per year federal grant within three years, assuming we get the grant.

VII. The Washington County Sheriff's Office has reported that there are now over 1000 known opiate addicts in the county. The plan is to be able to offer intensive outpatient services to 30 percent of this population within the second year of operation.

Recommendations

1. Make awards of grants now. Money is needed now, not in July 2002. This crisis is present and worsening. Addiction experts have calculated that for every one dol-

lar spent on rehabilitation of addicts approximately seven dollars are saved in the criminal justice system.

2. Nine months to "read and decide" over a grant application is too long. Particularly since it takes time to recruit professionals and set up licensed treatment facilities.

3. $500,000 per year is a beginning but barely scratches the surface of what we need in order to provide comprehensive care. One cannot deal with a problem of this magnitude with $500,000 per year.

4. We recommended that awards of S500,000 per year be given to help addicted adults and an additional $500,000 per year to help addicted adolescents initially over a period of three years. Ongoing assistance will definitely be needed.

5. We are asking that Purdue-Pharma establish foundations and make donations to help affected communities deal with opiate addiction. We feel that this is the moral thing to do especially because the fabric of our community is being destroyed mainly by addiction to OxyContin, a Purdue-Pharma product that the company heavily promoted.

Concluding Thoughts

While we don't know where the story of opiate addiction begins for the addicts of Washington County, we can predict that their current prospects, and the prospects of the towns in which they live, are bleak unless access to a comprehensive treatment program becomes available immediately. The energy behind this planning effort comes from the stark realization that the future of this isolated rural county is hanging in the balance.

Senator REED. Lieutenant Bess?

Lt. BESS. Mr. Chairman and Members of the Committee, I would like to mention that I have with me today senior special agency Al Cameron from our Fairfax field office and senior special agent Tim Price from our Wytheville field office. Although diverse areas, both have seen OxyContin problems.

The Virginia State Police Pharmaceutical Diversion Investigative Unit, now the Drug Diversion Unit or DDU, was implemented in the fall of 1987. The mission of the unit since its inception has been the statewide investigation of criminal diversion of illegal drugs to the illegal market, the establishment of a database to assist in the identification of the scope of the diversion activities in the Commonwealth, and the education of health care professionals, law enforcement and general public concerning the problems of diverted drugs.

The demand for OxyContin as a street drug is quite high in certain areas of Virginia. In southwestern portions of the State, local law enforcement agencies indicate that the demand for OxyContin is exceeding the demand for illicit drugs such as heroin. Also, in some areas of Northern Virginia such as Fairfax and Prince William Counties, the demand for OxyContin is increasing. The number of diversion complaints reported to DDU involving OxyContin has increased from 13 in 1997 to over 300 in 2000, the last year we have the statistics for.

OxyContin is being diverted primarily through doctor-shopping and to some extent illegal prescribing by a relatively few physicians and when individuals obtain more than is medically necessary, the drug is often sold on the street. DDU is investigating cases in which patients travel from West Virginia and Kentucky into Northern Virginia and Tidewater to obtain OxyContin. We recently had a case in which a lady drove from North Carolina into Southwest Virginia to sell OxyContin.

The Department of State Police have several recommendations to help reduce the diversion and abuse of these, as well as other prescription drugs. First, we strongly support the creation of a pre-

scription monitoring program in our State or nationwide. This system would essentially capture data on the type and amount of substances dispensed, the prescribing physician, the dispensing pharmacist and the patient receiving the medication. The data is submitted electronically by the dispensing pharmacy on a periodic basis. The program allows for medical privacy and gives no one access to pharmacy records that does not currently have access to those records.

The second recommendation to be made to the Virginia General Assembly is to increase the penalty for the distribution of Schedule III and IV controlled substances from a misdemeanor to a felony. I believe Virginia and Maine are a few of the last States that have misdemeanor distribution of those schedules.

A third recommendation is to require a customer to produce photographic identification when obtaining a Schedule II drug.

The Department of State Police also feel that any legislation enacted should not hinder access to medication by persons who have a true, legitimate medical need for the drug. Those people in pain should have pain relief.

That concludes my statement.

Senator REED. Thank you very much, Lieutenant.

[The prepared statement of Lt. Bess follows:]

PREPARED STATEMENT OF LIEUTENANT WILLIAM R. BESS

Mr. Chairman, and Members of the Committee: I am pleased to be here today to discuss with you what we feel is a very important public safety issue, the abuse of OxyContin.

The Virginia State Police Pharmaceutical Diversion Investigative Unit, now the Drug Diversion Unit (DDU), was implemented in the fall of 1987 with the receipt of federal and state grants. The mission of the unit, since its inception, has been the statewide investigation of criminal diversion of legal drugs to the illegal market; the establishment of a data base to assist in the identification of the scope of the diversion activities in the Commonwealth, and the education of health care professionals, law enforcement and the general public concerning the problem of diverted drugs. Currently, the Unit is funded solely by the Department of State Police.

The Virginia Department of Health Professions deal with excessive prescribing, a regulatory matter. The Virginia State Police deal with illegal prescribing, a criminal matter. In investigating the diversion of prescription drugs since it's creation, DDU has seen the drug of choice and the popularity of different drugs change. Until recently it was felt that RITALIN was in line to become one of the most popularly diverted drugs. Ritalin has now been surpassed by OXYCONTIN as one of the leading diverted drugs. Hydrocodone has and continues to be a leader in diverted drugs as well. Hydrocodone is one of the most popular drugs diverted for personal use by health care professionals. Many other drugs of all Schedules II–VI are often diverted.

The diversion and abuse of Ritalin (Methylphenidate) and OxyContin (Oxycodone) continues to be a problem in Virginia. The demand for OxyContin far exceeds the demand for Ritalin. Across the Commonwealth, State Police Drug Diversion Agents report that investigations involving the diversion of Ritalin are relatively small in comparison with the diversion of Hydrocodone and Oxycodone products.

The Drug Enforcement Administration reports that the number of prescriptions for Ritalin has increased 600% over the last five years, nationwide. The State Police Drug Diversion Unit received 3 complaints of Ritalin diversion in 1998, 9 in 1999 and 7 in 2000. To date this year, the Unit has received 8 complaints of Ritalin diversion.

The demand for OxyContin as a street drug is quite high in certain areas of Virginia. In southwestern portions of the state, local law enforcement agencies indicate that the demand for OxyContin is exceeding the demand for illicit drugs such as heroin. Also in some areas of northern Virginia, such as Fairfax and Prince William Counties, the demand for OxyContin is increasing. The number of diversion complaints involving OxyContin has increased from 13 in 1997 to over 300 in 2000. The

increase can in part be attributed to the fact that OxyContin is a new drug, marketed since 1996. The demand on the street has steadily increased since the drug became available. Improperly used OxyContin has the same effect as heroin.

OxyContin is being diverted primarily through "Doctor Shopping" and to some extent illegal prescribing by a relatively few physicians. When individuals obtain more than is medically necessary, the drug is often sold on the street. In addition, it is reported that some OxyContin, and other drugs, are being imported from Mexico and Canada by individuals who travel to those countries to obtain drugs, also we hear antidotal reports of individuals using the internet to obtain controlled substances. There are some instances in which prescriptions are forged or altered in an attempt to obtain the drug. OxyContin is abused by crushing the tablet and then snorting the powder or mixing it with water and injecting the solution. Oxycodone is the single active ingredient in OxyContin and is similar to Morphine in dependence liability.

In some areas of the Commonwealth, "patients" are travelling to North Carolina in an attempt to obtain prescriptions for OxyContin. North Carolina State Bureau of Investigation Agents relate that North Carolina is the largest source of OxyContin in the country. A portion of that will appear on the street in Virginia. OxyContin sells for about one dollar per milligram on the streets in Virginia (about 10 times its retail price). DDU is investigating cases in which "patients" travel from West Virginia and Kentucky to Northern Virginia and Tidewater for OxyContin.

The use of Ritalin and OxyContin for non-medical purposes is a problem among school-aged children and college students in the Commonwealth. However, the number of instances these drugs are abused by this age group is relatively small in comparison with those that are not students. Local law enforcement agencies have made arrests of students involved in the unlawful possession and/or distribution of these drugs. Other drugs, such as Ecstasy, Ketamine and GHB appear to be the choice for younger people.

Campus police agencies at Virginia Commonwealth University, Virginia Tech and Radford University report no arrests involving Ritalin or OxyContin on campus. Arrest statistics compiled by the Virginia State Police reveal that the largest age group of persons arrested for all prescription drug violations is between 31 and 40 years old.

In an effort to assist other agencies in diversion investigation, the Department of State Police conducted its first Drug Diversion School, September 17–21, 2001. This training was provided free of charge to law enforcement officers from across Virginia and across the nation. Over 70 State, Federal, and local police officers involved in drug diversion investigations signed up to attend this training. In addition to basic drug investigations, the school covered such topics as the legitimate use of narcotic analgesics by the medical community, club drugs, steroids, insurance fraud and other matters.

The Department of State Police has several recommendations to help reduce the diversion and abuse of these, as well as other, prescription drugs. First, we strongly support the creation of a Virginia Prescription Monitoring Program. This program, already in place in 17 states, allows a state agency to monitor the dispensing of controlled substances. It essentially captures data on the type and amount of substance dispensed, the prescribing physician, the dispensing pharmacist and the patient receiving the medication. The data is submitted electronically by the dispensing pharmacy on a periodic basis to the agency managing the program. The program allows for medical privacy and gives no one access to pharmacy records that does not currently have access to those records. It simply makes the access readily available to doctors, pharmacists and selected law enforcement officers.

Currently, if a physician has reason to believe that a patient may be "doctor shopping" in an effort to obtain controlled substance, the physician has no mechanism to determine that, short of calling all other physicians in the state. Under the proposed Virginia monitoring program, the physician can fax in a request to the program manager and request that data. A pharmacists who suspects a patient is abusing drugs could also request data to determine if the medications being dispensed could react badly to other drugs being received by a patient, The ability of Virginia health care professionals to receive this critical information is not the norm for existing prescription monitoring programs. In addition, State Police Special Agents who are designated by the Superintendent to conduct drug diversion investigations (currently only 14 agents and two supervisors) could access the data on a specific criminal investigation. Those agents currently have the authority to obtain pharmacy records, but they must travel to each pharmacy and interrupt the pharmacist to get the information.

A prescription-monitoring program allows health care professionals with specific patient concerns and law enforcement officers investigating a specific diversion case

access to data with the least intrusion on pharmacists, physicians and patients. This program will help prevent drug abuse by those persons seeking narcotics for non-medical purposes and help ensure that those patients who do need medication have access to it.

A second recommendation, to be made to the Virginia General Assembly is to increase the penalty for the distribution of a Schedule III and IV controlled substance from a misdemeanor to a felony. The illegal distribution of drugs such as hydrocodone products (Vicodin, Lortab, Anexsia and others), Ketamine, Valium, Xanax, Talwin and others are far more common than other drugs. Current law makes it a felony to obtain these drugs by fraud, but only misdemeanor if they are sold on the streets. Savvy drug users know that increased amounts of Schedule III drugs will give the same effect as smaller amounts of Schedule II drugs. The reduced scrutiny and penalties for violations involving Schedule III drugs often result in drug seekers obtaining those drugs instead of Schedule II drugs.

A third recommendation is to require a customer to produce photo identification when obtaining any Schedule II drug. The name on the identification would have to match the name used on the "sign out log" maintained by the pharmacy. This procedure would allow accurate identification and create a record of who is picking up a Schedule II drug and eliminate most situations involving identity fraud. By state law, pharmacists may currently ask for identification, but are not required to do so.

Agents assigned to this unit have a higher caseload than in any other area of the Bureau of Criminal Investigation. Because there is a need to increase resources available to the State Police Drug Diversion Unit additional agents are being requested across the state. In addition to conducting investigations, these agents are heavily involved in training police officers and health care professionals in the investigation and prevention of this type of crime.

The Department of State Police also feel that any legislation enacted should not hinder access to medication by persons who have a true legitimate medical need for the drug. In addition, the Department feels that any legislation should not be "product specific" but rather relate to a drug Schedule or class of drug. Simply changing the name of the drug could easily circumvent any legislation directed toward a brand name.

Senator REED. Dr. Goldenheim?

Dr. GOLDENHEIM. Thank you very much. Mr. Chairman, on behalf of Purdue Pharma, the distributor of OxyContin tablets, thank you for taking the time to hold this hearing, which bears on a significant question of health policy—how to address the problems of abuse and diversion which accompany the sale of a controlled drug like OxyContin without, as we have heard, restricting its availability to meet the needs of patients for the effective management of pain. I would like to take a few moments this afternoon to describe some of our efforts and idea for addressing the abuse and diversion of prescription drugs.

Once Purdue became aware of the problems of abuse and diversion of OxyContin, addressing this issue became a corporate priority. Purdue's number one research priority is to develop medicines that would reduce drug abuse while, at the same time, function as intended for patients in pain.

Contrary to what some seem to think and as noted by Dr. Jenkins, this is a formidable undertaking as there is no existing proven technology to achieve this goal. Purdue will have spent more than $100 million by the end of this year to research and develop new forms of abuse-resistant pain relievers.

Perhaps the single most important tool to prevent abuse is education. According to a survey released in December by the National Association of State Control Substance Authorities, its members believe that diversion education and pain management education for prescribers are more effective than any other means of combating drug abuse.

Purdue's objective in communicating with doctors through our trained sales representatives, literature and educational programs, is to inform them about the proper use of OxyContin. Increasingly this role has focussed on avoiding abuse and diversion. Responsible physicians will only prescribe OxyContin if it is the right product for their patients with pain.

Let me please call your attention to examples of some of the materials our field force uses when it calls on physicians. Dr. Jenkins referred to the "Dear Health Care Professional" letter that Purdue distributed to help educate health care professionals about the risk. We have also distributed hundreds of thousands of these documents from the American Pain Society and the American Academy of Pain Medicine since 1997 entitled "The use of opiods for the treatment of chronic pain."

Additionally, we have furnished for the record the following material. Purdue has worked from the FDA to develop the special patient information leaflet, and Dr. Jenkins referred to it, intended to be given by the physician or pharmacist to every patient receiving a prescription for OxyContin. Purdue has also developed and distributed these brochures on prevention of abuse and diversion to virtually all the physicians who prescribe and pharmacists who dispense opiod analgesics in the United States. Our representatives have distributed these opiod therapy documentation kits, again since about 1997, and over 250,000 copies of the model guidelines for the use of controlled substances for the treatment of pain.

These materials supplement Purdue's extensive training and educational efforts that are described in my written testimony, including our sponsorship of significant programs for doctors that are geared specifically toward preventing abuse and diversion.

Educating teenagers about the risks and dangers of prescription drug abuse is critical and we have initiated an important program that we are calling Painfully Obvious. Please take a look at this packet of information about the program that we have furnished for the record. All of this material is designed to help capture the attention of teenagers and convey the message that abusing drugs is not cool. This program will be rolled out by midyear in Florida, Pennsylvania, Ohio, West Virginia, Kentucky, South Carolina, Maine, Massachusetts and Virginia.

Other Purdue initiatives described in my written statement including supplying tamper-resistant prescription pads to physicians, supplying placebo OxyContin tablets to law enforcement for reverse buy-and-bust sting operations, and developing a better system for gathering more reliable and timely information about abuse and diversion. To assist law enforcement in determining the country of origin in drug seizures Purdue changed the tablet markings on OxyContin exported to Mexico and Canada.

Purdue feels strongly that prescription monitoring programs, PMPs, would help. Purdue supports the adoption by all States of prescription monitoring programs meeting appropriate standards and we have submitted for the record our policy on PMPs. We encourage this committee to develop legislation to provide States with incentives to provide such prescription monitoring programs. They can reduce doctor-shopping and diversion from good medical prac-

tices by giving physicians a way to identify patients who are receiving controlled substances from other doctors.

According to official positions taken by the American Medical Association, the Food and Drug Administration, the Drug Enforcement Administration, the Department of Veterans Affairs and even the Congress of the United States, which has declared this the decade of pain control and research, the management of pain is a critical priority of health care in this country. OxyContin has proven itself an effective weapon in the fight against pain, returning many patients to their lives, to their families, to their work and to their enjoyment of life.

We cannot turn back to an era when physicians did not treat significant chronic pain. The answers to the problems of abuse and diversion require the cooperation of many elements in our community in providing increased education, information, and enforcement, not restrictions that will deny patients effective treatment of their pain. Purdue is taking a leadership role in these efforts. Thank you very much.

Senator REED. Thank you very much, Dr. Goldenheim, and thank you all very much for your testimony this afternoon.

[The prepared statement of Dr. Goldenheim follows:]

PREPARED STATEMENT OF PAUL D. GOLDENHEIM, M.D.

Mr. Chairman: On behalf of Purdue Pharma L.P., the distributor of OxyContin tablets, thank you for taking the time to hold this hearing which bears on a significant question of health policy: how to address the problems of abuse and diversion which accompany the sale of a controlled drug like OxyContin® without restricting its availability to meet the needs of doctors and patients for the effective management of pain. This question is neither new nor unique to OxyContin®. It has existed as long as opioid analgesics have been available. It is a critical question, and we are confident that Purdue has devoted more resources and efforts than has any pharmaceutical company in seeking the answers. Purdue has taken a leadership role and has provided, and continues to provide, extensive assistance to the medical and law enforcement communities in working to prevent the abuse of OxyContin®.

1. WHAT IS THE NATURE OF THE PROBLEM?

OxyContin® is an opioid analgesic used to treat pain. Each tablet of OxyContin® delivers controlled-release oxycodone to the patient over a period of twelve hours. Like morphine, OxyContin® is a Schedule II drug with recognized abuse potential. Purdue and the Food and Drug Administration assessed and acknowledged the potential for abuse at the time of its initial approval. From inception, the package insert and promotional material for OxyContin® has cautioned:

> "TABLETS ARE TO BE SWALLOWED WHOLE, AND ARE NOT TO BE BROKEN, CHEWED OR CRUSHED. TAKING BROKEN, CHEWED OR CRUSHED OxyContin® TABLETS COULD LEAD TO THE RAPID RELEASE AND ABSORPTION OF A POTENTIALLY TOXIC DOSE OF OXYCODONE."

Additionally, the following language has always appeared on the package insert:

- "Patients should be advised that OxyContin® is a potential drug of abuse. They should protect it from theft, and it should never be given to anyone other than the individual for whom it was prescribed."
- "Oxycodone may be expected to have additive effects when used in conjunction with alcohol, other opioids or illicit drugs which cause central nervous system depression."
- "As with all such drugs, care should be taken to prevent diversion or abuse by proper handling."

Since early in the year 2000, there have been a significant number of reports of OxyContin® tablets being diverted and abused by drug abusers, and we at Purdue deeply regret the tragic consequences that have resulted from the misuse of this medicine. The patterns of abuse involve crushing the tablets to obtain immediately the full dose of oxycodone and then ingesting, snorting or injecting the drug. In a

number of cases, there have been deaths associated with overdose. We believe that virtually all of these reports involve people who are abusing the medication, not patients with legitimate medical needs under the treatment of a healthcare professional. Further, the vast majority of those deaths involve the abuse of multiple medications including other opioids (illicit and legal) and frequently alcohol and sedatives such as benzodiazepines—not oxycodone alone.

2. WHAT IS PURDUE DOING TO REDUCE THE ABUSE AND DIVERSION OF OXYCONTIN®?

Purdue was deeply distressed when it became aware of the occurrences of abuse and diversion of OxyContin® and immediately formed a response team of top Company executives and physicians who immersed themselves in the problems of abuse and diversion and made its solution a corporate priority. To help understand and address the problems, Purdue's Chief Operating Officer, General Counsel, and senior medical officers have attended numerous meetings with State Attorneys General and U.S. Attorneys, and many additional meetings have been held with FDA, Drug Enforcement Administration, medical opinion leaders and others. Virtually all of these meetings were initiated by Purdue, including the very first such meeting in September of 2000 with then United States Attorney for Maine, Jay McCloskey. Mr. McCloskey, who is now serving as a consultant to Purdue, is here today and available to answer questions you may have about the abuse of OxyContin® and other drugs in Maine. We believe that his 23 years of experience as a Federal prosecutor, dealing with the very issues which are the subject of this hearing, can provide invaluable insight to this Committee.

Additionally, Purdue has established an internal Health Policy Group devoted to guiding the company in its policies and programs to address the issues of abuse and diversion, including the education of law enforcement. The Health Policy Group includes three full time physicians who are well known experts in the fields of addiction and pain management and a former career law enforcement officer who managed the largest pharmaceutical diversion unit in the nation.

Purdue's efforts to address the problem include the following specific actions:

• A long-term solution to the problem of prescription drug abuse includes the development of medicines that are inherently resistant to such abuse. This was and is a formidable undertaking as, contrary to comments that have been made by some who have not studied the matter, there was no existing proven technology to achieve this goal. By the end of 2002, Purdue will have spent over $100 million to research and develop new forms of strong pain relievers that would be resistant to abuse while at the same time provide safe and effective pain relief to legitimate patients. In December 2001, we announced the beginning of clinical studies of a new pharmaceutical product combining the opioid analgesic oxycodone in a controlled-release formulation with an opioid antagonist, naloxone. We expect that this product will be resistant to abuse by injection and perhaps, also by intranasal snorting. We are working with the FDA to accelerate the availability of this drug and are planning to begin filing a New Drug Application this year. As our research continues we expect to submit for approval to FDA drugs utilizing other technologies which will make them resistant to oral abuse as well.

• Purdue is especially concerned that school children do not understand the potentially tragic consequences of abusing prescription drugs. Purdue has consulted with experts in problems of drug abuse in teenagers, and hired an agency that specializes in communication to teenagers to develop a specific program targeted towards educating them about the dangers of prescription drug abuse and diversion. These materials have been reviewed with police officials and educators in various states, and several thousand demonstration kits have been distributed to those involved in teen drug awareness education. We call the program "Painfully Obvious" and have established a website at painfullyobvious.com. These materials have been piloted in test markets in Florida, Pennsylvania, Ohio, and West Virginia. We are now incorporating feedback and will start roll-out plans expanding the program in those four states later this month, and in five new states, including Maine, Massachusetts, and Virginia, by midyear. We want kids to know that prescription drugs when abused can be every bit as dangerous as street drugs. Materials from the Painfully Obvious program are being furnished for the Record.

• Purdue has worked with the FDA to strengthen warnings on the OxyContin® package insert and to communicate those warnings to physicians throughout the country. Upon hearing of the abuse and diversion of OxyContin®, Purdue asked for a meeting with the FDA to discuss the problem. The result of a series of meetings with the FDA, involving Purdue's Chief Medical and Scientific Officer, Chief Operating Officer, and General Counsel, in collaboration with the FDA, was the development of a new package insert that could become the standard for opioid analgesics.

FDA has called upon other makers of such drugs to reexamine their own package inserts and make similar changes where appropriate. So far, we are aware of no company other than Purdue that has made these changes. Purdue mailed a letter and new prescribing information to 550,000 medical professionals throughout the country. Our field force also reviewed the new labeling during their calls on physicians. Dr. John Jenkins, who is also a witness at this hearing, led FDA in a cooperative effort to work with us to develop better labeling for drugs like OxyContin®. We commend Dr. Jenkins for this effort and call upon other pharmaceutical companies to follow our lead and make similar changes to their product labeling.

• In addition to the revised package insert, Purdue has worked with the FDA to develop a special information leaflet intended to be given by the physician or pharmacist to every patient receiving a prescription for OxyContin®. This leaflet has recently been approved by the FDA and will alert patients to the risks of misuse and abuse, and to the diversion issues. A copy of the text of that Patient Information leaflet is being furnished for the Record. We are aware of no other company that has produced such an informed and informative patient information leaflet for a controlled substance.

• Upon learning of the abuse and diversion problems in 2000, Purdue immediately began efforts to understand the pattern of abuse. Purdue developed a mathematical model that attempted to identify areas where abuse potential was expected to be highest. Purdue used this model as the basis for its "100 County" program. As part of the program, company sales representatives were brought to Purdue's home office specifically for the purpose of training them to actively participate in stopping the abuse and diversion of OxyContin®. These training sessions were conducted with the assistance of the Drug Enforcement Administration. The sales representatives attending the training were told that, in the 100 counties where abuse potential was highest, their goal was not to sell OxyContin®. The sales representatives were instructed to give the physicians additional training regarding abuse and diversion and to provide additional tools for proper pain assessment. If physicians were not willing to use these tools, the sales representatives were instructed to ask them to stop prescribing OxyContin® for their patients.

• During visits with several U.S. Attorneys and State Attorneys General, Purdue learned that a significant source of diversion was "doctor shopping"—abusers and criminal diverters fraudulently misleading doctors. Law enforcement officials believe that those physicians require education and information to enable them to avoid being misled. To deal with the problem, Purdue is sponsoring significant educational programs specifically geared towards preventing abuse and diversion, and is sponsoring abuse and diversion training programs for thousands of additional doctors.

As part of its ongoing educational effort, Purdue has developed and distributed brochures on prevention of abuse and diversion to virtually all the physicians who prescribe, and pharmacists who dispense, opioid analgesics in the United States. These brochures have been distributed to over 500,000 doctors and 50,000 pharmacists, and copies are being furnished for the Record.

• Even before the current experience with OxyContin® abuse, Purdue had been providing physicians with important information about the proper prescribing of opioid analgesics. Our representatives have distributed opioid therapy documentation kits since 1997 and over 250,000 copies of "Model Guidelines for the Use of Controlled Substances for the Treatment of Pain" (the "Model Guidelines") since early 1999. These materials emphasize the need to properly evaluate patients and help teach physicians about proper documentation and alert them to the possibilities of abuse and diversion at the same time that proper pain management is emphasized. The Model Guidelines were approved by the Federation of State Medical Boards of the United States in May of 1998 after development by a blue ribbon panel and with the support of the American Academy of Pain Medicine, the American Pain Society, the American Society of Law, Medicine and Ethics, and the University of Wisconsin Pain and Policy Studies Group. Copies of these important documents are being furnished for the Record As the Model Guidelines state: "The Federation believes adoption [by State Medical Licensing Boards] of guidelines based on this model will protect legitimate medical uses of controlled substances while preventing drug diversion and eliminating inappropriate prescribing practices."

• Purdue has developed a program to provide tamper resistant prescription pads to physicians in 16 states that were deemed to have the highest potential for abuse and diversion of OxyContin®. To date, we have funded over 7,500 orders from doctors requesting these pads. Purdue is expanding this program to additional states. In addition, to encourage use of these pads on a broad scale, Purdue is conducting multiple mailings in selected states to encourage physicians to order these pads.

• Purdue has taken significant and escalating steps to thwart diversion of its product from Mexico and Canada to the United States. As initial steps, Purdue

stopped shipping 40-milligram tablets to Mexico, and changed the tablet markings on OxyContin® exported to Mexico and Canada to assist law enforcement in determining country of origin in drug seizures. Following the theft of a significant number of OxyContin® tablets in Mexico City in December 2001, Purdue halted all shipments of OxyContin® to Mexico.

• Purdue has supported the efforts of law enforcement by supplying placebo OxyContin® tablets for "reverse buy and bust sting operations." In several areas, law enforcement has praised these efforts as critical in their efforts to stop diversion. In one hard hit area, the County Sheriff noted that our efforts were instrumental in helping to reverse the course of OxyContin® abuse.

• Purdue has initiated the development of a system to monitor abuse and diversion of prescription drugs throughout the United States. Currently, there is no monitoring system that adequately measures abuse and diversion, especially in rural areas of the country, where the abuse of prescription drugs is prevalent. Purdue has already had several meetings of an advisory board comprised of distinguished experts from law enforcement, addiction treatment, pain treatment, and health policy fields. Several studies have been initiated as part of this program to gain further information about abuse and diversion. In addition, Purdue has met with NIDA and hopes to involve NIDA in the development and operation of this system.

3. WHAT IS THE SOLUTION?

Perhaps the single most important tool to prevent abuse is education. A survey released in December 2001 by the National Association of State Controlled Substances Authorities (NASCA) reveals that NASCA members believe that diversion education and pain management education for prescribers are more effective than any other means of combating prescription drug abuse. To that we would add—as our own commitment to educational initiatives demonstrates—education of youngsters, community leaders, non-prescriber health care professionals and law enforcement personnel.

Education of healthcare professionals about the issues of prescription drug abuse is critical. Education of responsible doctors and pharmacists can arm them with the tools they need to stop diversion from their practices. Purdue has assumed a leadership role. Educating teenagers about the risks and dangers of prescription drug abuse is critical, and we have taken an important step with our Painfully Obvious program.

Better information is critical, and we have initiated efforts to develop more reliable and timely information. A better information system can allow us to know where abuse and diversion is cropping up and allow timely medical education and law enforcement to act earlier to nip these problems in the bud. It is critical that we all evaluate the problem of OxyContin® abuse in the context of the broader problem of abuse of prescription drugs. The level of frustration over the absence of good information defining the problem was notable at the meeting of the Food and Drug Administration Anesthetic and Life Support Drugs Advisory Committee held on January 30 and 31 to consider the medical use of opioid analgesics (the "FDA Advisory Committee meeting"). The transcript of that hearing is not yet available, but it is of such direct relevance to the subject of today's hearing that we request the opportunity to submit it along with some additional comments from Purdue for the Record when it becomes available.

Prescription Monitoring Programs ("PMPs") would help. The PMPs in Kentucky and Nevada can serve as useful models. PMPs can reduce doctor shopping and diversion from good medical practices by giving physicians a way to identify patients who are receiving controlled substances from other doctors. Purdue supports the adoption by all states of Prescription Monitoring Programs meeting appropriate standards. Purdue encourages Congress to develop legislation to provide states with incentives to adopt such PMPs. Purdue is eager to work with Congress to develop and support such legislation. In addition, Purdue is prepared to utilize its resources to explain the benefits of such a system to physicians and to gain support for such legislation from the medical community. We are submitting for the Record a copy of Purdue's policy paper on PMPs that sets forth what we believe to be the attributes of a successful program. Purdue is willing to devote promotional resources to introduce such programs to physicians.

Tamper resistant prescriptions can reduce copying or alteration. Development of abuse resistant products can reduce the incidence of abuse.

Ultimately, solving the problem of prescription drug abuse requires the cooperation of many elements in our community: law enforcement, the schools, religious institutions, parents and family, the courts, the medical community, the press, federal and state legislators, government agencies, social services providers, and the phar-

maceutical industry. This is a long-standing societal problem that requires a reasoned solution. Purdue is trying to help through our specific programs and our cooperation with the other elements in the community, but we can't emphasize enough that what is needed is cooperation and common purpose. We would welcome the opportunity to work more directly toward a solution with this Committee and with all others who are involved, especially the DEA.

4. THE BENEFITS OF OXYCONTIN®

The availability of OxyContin® is critical for countless patients who are suffering from moderate to severe pain where a continuous around-the-clock analgesic is needed for an extended period of time. Unfortunately for those patients, concern generated by the abuse of OxyContin® has mushroomed to the point of hysteria in some locations, with the result that some patients are asking their doctors to switch them to less effective drugs, some doctors are refusing to renew patients' prescriptions for OxyContin® and some pharmacies are no longer willing to carry OxyContin® for their patients. This situation was described over and over by witnesses appearing at the FDA Advisory Committee meeting.

While all of the voices in this debate are important, we must be especially careful to listen to the patients who, without medicines like OxyContin®, would be left in pain. Purdue frequently hears stories of how OxyContin® has enabled people to return to their families and to productive lives after suffering disabling pain. We urge you to talk directly to some of those patients. They are not addicts. They are not criminals. They are people who, because of cancer, sickle cell anemia, severe back injuries, or some other physical insult or disease have had their lives taken away from them by unrelenting pain. There were many powerful examples presented at the FDA Advisory Committee meeting that we will reference for the Committee when the transcript becomes available.

Amidst all the publicity and controversy, a few facts stand out.

• First, the problem of chronic pain in this country is enormous and expensive. According to organizations like the American Pain Foundation, an estimated 50 million Americans suffer from chronic pain, with a cost approximating $100 billion a year attributable to lost workdays, excessive or unnecessary hospitalizations, unnecessary surgical procedures, inappropriate medication and patient-incurred expenses from self-treatment. But even those staggering numbers fall far short of capturing the essence of chronic pain in America. Pain cannot be expressed in numbers. It is individual and it is personal. It is intense. It is debilitating. It destroys the capacity to perform life's simplest functions and can even destroy the will to live. Anyone who has cared for a loved one in pain knows more about the impact of pain than I can ever describe. For those fortunate enough not to have experienced pain themselves or to have cared for a sufferer, let me ask you to imagine a life in which you can't go to work, take a walk, pick up your child, hug your spouse or even kneel in prayer. That can be the life of a chronic pain sufferer.

• Second, chronic pain has been historically under treated. Only in this past decade has public and medical opinion swung decisively in the other direction, based on the proven effectiveness of individualized therapy, including opioids, in treating pain, and the startling improvement in quality of life such therapy offers to patients.

—In 1994, the Department of Health and Human Services issued new guidelines encouraging the use of opioids in the treatment of cancer pain.

—In February of 1999, the Veterans Administration added pain as a fifth vital sign (along with pulse, temperature, respiration, and blood pressure) that should be checked regularly as a major indicator of health.

> "VA officials said the change in routine is designed to call physicians' attention to what is widely considered one of the most unrecognized and untreated symptoms in American health care. In a study of 10,000 dying patients published in 1995 in the Journal of the American Medical Association, for instance, researchers found that almost half died in severe pain; other studies report that as many as three-quarters of advanced cancer patients are in pain." Washington Post, February 1, 1999.

Many other healthcare professionals and organizations have adopted this practice of checking pain as a fifth vital sign.

—On October 28, 2000, Public Law 106-386 was enacted declaring the decade commencing on January 1, 2001 to be the "Decade of Pain Control and Research." Bills currently pending in both the House and Senate (The Conquering Pain Act of 2001, S. 1024 and H.R. 2156) recognize that "chronic pain is a public health problem affecting at least 50,000,000 Americans," and seek long-lasting changes that would

enable all Americans to effectively manage medical conditions associated with chronic pain.

• Third, OxyContin® is widely recognized as a highly effective treatment for pain. When properly used under the supervision of a physician, it is also an extremely safe medication. Its twelve-hour controlled-release mechanism affords an extended dose of pain medication, allowing patients to sleep through the night and to avoid sharp spikes in blood levels of medicines that can cause side effects. Many patients have told their doctors and Purdue that OxyContin® has given them back their lives. Purdue is furnishing for the Record representative communications that it has received from patients and their families describing the importance of OxyContin® in managing their pain, along with a paper prepared by Pinney Associates, Inc. that describes OxyContin's® importance to public health.

5. WHAT IS OXYCONTIN®?

No legal drug in the United States is more rigorously regulated than OxyContin®. It is a Schedule II drug under the Federal Controlled Substances Act. OxyContin® is monitored by state and federal health and law enforcement officials in its production, marketing, distribution, and prescription. Both the FDA and DEA oversee OxyContin®.

The sole active ingredient in OxyContin® is oxycodone, a semi-synthetic opioid first developed in 1916. Oxycodone has been sold in various forms in the United States for over 60 years. Percodan, Percocet, and Tylox are examples of oxycodone products. Typically, but not always, these forms of oxycodone have been combined with a co-analgesic agent such as aspirin or acetaminophen (Tylenol), in which case they are referred to as "combination analgesic products". In large doses those non-opioid analgesics may be toxic to the liver, stomach and kidneys. Therefore, drugs containing either aspirin or acetaminophen are limited in their usefulness because a patient can only take up to a set amount per day to avoid aspirin or acetaminophen toxicity. Even if a patient needs more pain relief, the non-opioid component limits the maximum dose of the combination analgesic. The medical profession made it clear to us that it wanted oxycodone in a controlled-release form without any other active ingredients that could impose limits on the dose a patient could take in a day. Purdue responded by introducing OxyContin® tablets in December 1995.

Because of the efficacy of this single entity, controlled-release product, doctors have found OxyContin® extremely effective in properly managed programs of pain treatment.

6. WHO IS PURDUE PHARMA?

Purdue Pharma is a privately held pharmaceutical company founded by physicians. Purdue's headquarters are in Stamford, Connecticut. OxyContin® is manufactured at facilities in Totowa, New Jersey and Wilson, North Carolina.

Family ownership of Purdue and its associated companies began with the purchase of The Purdue Frederick Company in 1952. In those early days, Purdue's main products were Betadine antiseptics and Senokot laxatives. Since the early 1980s, Purdue has focused its research and development efforts primarily on medications for pain management. One of the most significant advances introduced by Purdue is the use of controlled-release opioid analgesics for the treatment of moderate to severe pain. Controlled-release opioid analgesics, pain medicines which last for 12 hours or more, enable patients to sleep through the night and provide better control of pain than drugs that require dosing every 4 to 6 hours. Purdue introduced MS-Contin tablets, a controlled-release form of morphine, in 1984, and a controlled-release oxycodone product, OxyContin® tablets, in December 1995.

Since 1984, Purdue has worked diligently to inform doctors and other healthcare professionals about appropriate use of opioid-based medicines. This has required a significant investment, as medical schools have traditionally spent little time teaching doctors how to assess and treat pain or how to use our best medicines for moderate to severe pain. For example, when Purdue started selling opioid analgesics in 1984, many doctors were not aware that morphine could be given orally as a treatment for pain. Today, administration of oral controlled-release morphine is considered standard practice for the treatment of cancer pain.

Purdue has extensively studied the use of these medicines in the treatment of moderate to severe pain associated with both malignant and various non-malignant diseases. Such pain requires a careful assessment of the patient and an individualized treatment plan. There are many important therapeutic modalities including opioid analgesics. Without opioid therapy, many patients suffer and are disabled. Purdue's clinical research has provided valuable experience and data to guide physi-

cians in properly using these medicines; for example, on determining the proper dose and dealing with side effects.

7. PURDUE'S PROMOTION AND MARKETING OF OXYCONTIN® TABLETS

Purdue's marketing of OxyContin® tablets has been criticized for being overly aggressive thereby possibly contributing to excessive abuse. The criticisms have ranged from charges that Purdue gave doctors ballpoint pens containing conversion charts to allegations that Purdue marketed OxyContin® as a more effective replacement for less addictive drugs. Conversion charts with information similar to that contained in the pen are distributed by most pharmaceutical companies and many prestigious medical institutions. The pen/conversion chart is an essential informational tool to be used only after the physician has determined that OxyContin® is appropriate therapy for the patient.

The notion that these conversion charts are an attempt to encourage physicians to switch patients to OxyContin® from less abusable drugs is unfounded. These charts are intended, and understood by physicians, to be used when those lower scheduled drugs are not working. Physicians understand that with all classes of medicines, if patients are doing well on their current regimen, then that regimen is not to be changed. If, however, the patient still has significant pain despite the use of other medicines and the physician has made a determination that OxyContin® is worth trying for that patient, then this chart merely helps the physician choose the proper dose.

Purdue is scrupulous in training its field sales force to promote OxyContin® only for its approved indications. Under any circumstance, recognize for a moment that even if marketing prompts a legitimate but misinformed doctor to inappropriately prescribe OxyContin® to a legitimate patient (which should never happen), that surely is an insignificant part of the problem of OxyContin® abuse. Reports of patients becoming addicted to OxyContin® are rare. That would not excuse aggressive marketing, but blaming the drug abuse problem on aggressive marketing is unjustified. Purdue's marketing practices have not played a role in the criminal activities of doctors who illegally prescribe OxyContin® in exchange for cash, and have not encouraged robberies from pharmacies or from patients.

OxyContin® tablets are not promoted to consumers. The few advertisements that appear are solely in medical journals. Rather than promoting aggressive marketing, Purdue's marketing practices focus on teaching doctors to only prescribe OxyContin® in appropriate circumstances. Purdue managers monitor its field force for compliance with that policy. Sales representatives are told that in the event of a violation of our marketing policies, the offender will be subject to discipline, up to and including termination.

(a) Marketing for appropriate use.

Purdue's sales and marketing practices focus exclusively on the management of pain and the proper use of OxyContin® in patients for whom such a pain medication is appropriate. Our marketing program amounts to an extensive educational effort that teaches physicians how to make the best decisions for their patients with pain. Responsible physicians will only prescribe OxyContin® if it is the right product for their patients with pain. From time to time, after a physician has decided that OxyContin® is the right prescription for his or her patient, we have underwritten the cost of the patient's prescription for the first week of therapy. In this way, the physician and patient could decide if OxyContin® was working for that particular patient. We have never provided samples to patients or physicians.

In fact, Purdue's marketing has encouraged physicians to take actions that would reduce the abuse and diversion of OxyContin®. Purdue has asked physicians to carefully:

—Prescribe only the quantity of product that the physician deems necessary based upon a complete history and physical examination and careful assessment of the patient's pain;

—Determine that the nature and severity of the patient's pain requires an opioid analgesic for an extended duration;

—Prescribe a quantity of medicine based upon the dosage that the patient requires; and

—Follow up carefully with each and every patient on a regular basis.

An example of Purdue's efforts to promote only appropriate use of the drug in appropriate patients is the use of various medical guidelines that were incorporated in the original package insert and distributed by our field force, including those from the World Health Organization, the Agency for Healthcare Policy and Research, and the American Pain Society. As these guidelines evolved, Purdue distributed revised versions to keep physicians up to date. The original package insert is

quite clear regarding the appropriate use of OxyContin®, and we were quite clear in promoting the use of OxyContin® in a manner consistent with this package insert. In the Precautions section it states:

> Selection of patients for OxyContin® should be governed by the same principles that apply to the use of similar controlled-release opioid analgesics . . . Physicians should individualize treatment in every case, using non-opioid analgesics, prn [on an as needed basis] opioids and/or combination products, and chronic opioid therapy with drugs such as OxyContin® in a progressive plan of pain management such as outlined by the World Health Organization, the Agency for Healthcare Policy and Research, and the American Pain Society.

As noted in Section 2, other examples of Purdue's efforts to promote only appropriate use of the drug in appropriate patients and to caution physicians against indiscriminate use include Purdue's distribution to physicians of opioid therapy documentation kits, brochures on prevention of abuse and diversion, and the Model Guidelines. A reading of the Model Guidelines makes clear that rather than encouraging indiscriminate use of OxyContin®, Purdue's educational efforts were directed at teaching physicians how to use these drugs responsibly and appropriately for appropriate patients. For example, the Model Guidelines provide:

- "All physicians should become knowledgeable about effective methods of pain treatment as well as statutory requirements for prescribing controlled substances."
- "The Board recognizes that inappropriate prescribing of controlled substances, including opioid analgesics, may lead to drug diversion and abuse by individuals who seek them for other than legitimate medical use. Physicians should be diligent in preventing the diversion of drugs for illegitimate purposes."
- "All such prescribing [of controlled substances] must be based on clear documentation of unrelieved pain and in compliance with applicable state or federal law."
- "The physician should discuss the risks and benefits of the use of controlled substances with the patient. The patient should receive prescriptions from one physician and one pharmacy where possible. If the patient is determined to be at high risk for medication abuse or have a history of substance abuse, the physician may employ the use of a written agreement outlining patient responsibilities."
- "Special attention should be given to those patients who are at risk for misusing their medications and those whose living arrangements pose a risk for medication abuse or diversion. The management of pain in patients with a history of substance abuse or with a comorbid psychiatric disorder may require extra care, monitoring, documentation, and consultation with or referral to an expert in the management of such patients."

In distributing the Model Guidelines, Purdue was fulfilling an important responsibility to educate physicians in the appropriate use of OxyContin® and other opioid analgesics. Such guidelines were just being developed by the medical community as the pain movement grew and the need to treat patients in pain was recognized. As these and other guidelines were developed we added them to our educational efforts. While some may characterize these activities as "aggressive marketing," we believe that our efforts to alert the medical community to the vast under treatment of pain in the United States and to the fact that opioid analgesics such as OxyContin® had a role to play in appropriate patients, was in fact in the interest of the public health.

(b) Healthcare professional education.

Purdue sponsors extensive training for the medical community. There is widespread consensus that medical practitioners, in the course of their medical education, receive limited and often inadequate training in the management of pain. Physician education has always been a principal feature of Purdue's marketing and medical education efforts. As early as 1984 we saw that physicians wanted and needed more information about how to assess pain in their patients, how to determine the right dose of pain medicine, how to treat side effects, and more recently, how to deal with the risks of abuse and diversion. At the outset we realized that this task required us to create a highly professional and highly trained field force supported by an extensive medical education effort.

(c) Purdue's training of its sales representatives.

Virtually all of Purdue's field force is recruited from within the pharmaceutical industry. New sales representatives, despite their prior experience, are enrolled in

a 26-week training program, which includes three weeks of classroom training at the home office. Sales representatives are given extensive training in the principles of proper promotion of pharmaceutical products. They are directed to promote only those uses of our products which are approved by the FDA and to use only those promotional materials which are approved for use after rigorous medical, regulatory and legal review. During this training, representatives are told that our standard of conduct is that during every sales call they should act as if they were accompanied by an FDA inspector. Upon returning from their home office training, new representatives are closely monitored by their managers who will spend time in the field, visiting doctors with them. In addition, field trainers from the local area and the home office will often accompany new representatives.

Moreover, in July 2001, Purdue established a telephone "hot line" to receive comments from any physician who believes a Purdue sales representative has in any way promoted our products in an inappropriate manner. Purdue knows of no other pharmaceutical company that has gone to such lengths to insure that on a day-to-day basis its sales representatives comply with the high standards that are established during their training. The results have been reassuring; rather than being critical, the vast majority of calls to the hot line have complimented the professionalism of our sales representatives.

(d) Limit on sales commissions.

In response to requests from law enforcement officials, Purdue has changed its variable compensation plan. When Purdue visited with U.S. Attorney Crouch of Virginia, a concern was expressed that Purdue's incentive plan for its sales personnel enabled a representative to earn large commissions as a result of the prescribing practices of any single doctor. Purdue was asked to consider changing this aspect of its variable compensation plan. Purdue investigated how this could be done while dealing with the technical complexity of carrying out such computations for thousands of doctors and keeping faith with its relationship with its sales employees. These problems were resolved and such a cap on commissions from prescriptions of any one physician is now in place.

8. WHAT IS THE SOURCE OF DIVERTED OXYCONTIN®?

According to law enforcement experts, OxyContin® and other legitimate prescription drugs find their way into illicit channels by means of prescription fraud, "doctor shopping", physicians criminally selling prescriptions, theft from patients or pharmacies, diversion from Mexico, Canada, and Internet pharmacies. Unfortunately, several months ago Purdue had an incident that we are aggressively addressing. OxyContin® tablets are manufactured in two locations. Despite a 17 year history of manufacturing controlled substances without an incident of theft, earlier this year Purdue discovered that two company employees had stolen OxyContin® tablets from the production line at the Totowa, New Jersey plant. Manufacturing officials immediately notified local police and the DEA and terminated the employment of these individuals, who were taken into custody by the police. The company as well as the local police, DEA, and FDA are conducting further investigations and Purdue is fully cooperating with these law enforcement agencies. All internal security procedures have been analyzed and any weaknesses are being addressed.

9. COULD PURDUE HAVE FORESEEN THE PROBLEM?

In the past two decades, a variety of opioid analgesics containing sufficient amounts of morphine-like drugs to be subject to abuse and addiction have been marketed as Schedule II controlled substances and have been associated with a limited amount of abuse and diversion. Examples of such drugs include Demerol (meperidine hydrochloride), Duragesic (transdermal fentanyl), Dilaudid (hydromorphone) immediate release morphine preparations, and immediate release oxycodone preparations. In addition, for some 17 years Purdue has marketed MS-Contin (morphine sulfate controlled-release), a drug with abuse potential similar to OxyContin® that is available in a single tablet at doses as high as 200mg. It is significant that there have been no unusual signals throughout the marketing of MS-Contin that would suggest that this controlled-release dosage form would be particularly attractive to abusers. Purdue had no reason to expect otherwise with OxyContin®. Neither Purdue, nor the FDA, nor the DEA, nor the medical community anticipated the extent of this problem, which surfaced in February 2000 with reports of abuse or diversion in rural parts of Maine.

10. HOW WIDESPREAD IS THE PROBLEM OF OXYCONTIN® ABUSE?

Both Purdue and law enforcement are trying to understand the extent of this problem. Initially, the abuse of OxyContin® tablets was concentrated in a few parts of a few states, generally along the spine of Appalachia, where abuse of other prescription drugs has long been a problem due to many factors, including poverty and lack of opportunity. In those areas the problem of the abuse of OxyContin® is serious. Today, the geographic scope is broader. Regrettably, widespread media attention may have contributed to this wider geographic scope by calling to the attention of potential abusers in all parts of the country that OxyContin® is a desirable drug of abuse.

The real issue here is prescription drug abuse. To emphasize that point, DEA Administrator Hutchinson was quoted in the February 6, 2002 New York Times as making the following statement about methamphetamine: "I would call it the No.1 drug problem in rural America." OxyContin® is a part of this larger problem. The table which follows is the most recently available annual data published by the U.S. Government's Drug Abuse Warning Network (DAWN) for several of the drugs mentioned most frequently in all drug-related Emergency Room visits in which abuse was suspected in 2000.

Drug	Number of Mentions	Percent of Total Episodes
Cocaine	174,896	29.06
Marijuana/Hashish	96,446	16.03
Acetaminophen	33,613	5.59
Hydrocodone	19,221	3.19
Diazepam	12,090	2.01
Oxycodone	10,825	1.80

Furthermore, not only were hydrocodone incidents considerably higher than oxycodone in 2000, earlier DAWN data shows virtually parallel rising trend lines since the introduction of OxyContin® through 2000 in the growth of both hydrocodone and oxycodone.

Additional data were collected in 2000 for various drug categories by the National Household Survey of Drug Abuse (NHSDA) that helps to provide some indication of the scope of the problem. Among the pain relievers, there were specific data included for a number of drugs, including OxyContin®. The NHSDA concluded that the non-medical use of OxyContin® was rare in 2000, but acknowledged that the data showed evidence of an emerging problem. The relative numbers of non-medical use of common pain relievers acknowledged to have been used by persons 12 years of age and older during their lifetimes were striking. Hydrocodone non-medical use was more than four times greater than OxyContin®; Demerol® was more than five times greater; non-medical use of Vicodin®, Lortab® or Lorcet® was more than 16 times greater than OxyContin®; Percocet®, Percodan®, or Tylox® was 16 times greater; and non-medical use of Darvocet®, Darvon®, or Tylenol® with codeine was 34 times greater than OxyContin®.

It remains difficult to obtain hard evidence on the extent of OxyContin® abuse. As a result of a recent survey of Medical Examiners, the DEA categorized a tragic number of deaths associated with oxycodone in 2000 and 2001 as either "OxyContin® verified," 117, or "OxyContin® likely," 179. OxyContin® is the drug of the hour, and the DEA acknowledged that the media has attributed hundreds of deaths to OxyContin® that cannot be verified. Even in those deaths that were "OxyContin® verified," the DEA acknowledged that in the majority of them toxicological screens reflected polydrug use, in other words, an ingestion of a "cocktail" of legal and illegal drugs, and frequently alcohol as well, in the blood of the decedent. In these cases, death is usually attributed to the abuse of multiple drugs.

Unquestionably OxyContin® is being abused, and Purdue accepts its responsibility to help address the problem. But just because OxyContin® may be the drug of the hour, focusing on OxyContin® without attempting to address the broader problem of prescription drug abuse would be unfortunate. Statistics should not be used to minimize the tragedy of even a single loss of life, but they help demonstrate the complexity of this problem. In recent months we have seen several reports suggesting that the problem of OxyContin® abuse may have crested in some areas and that it continues to be regional and is not spreading. We do not offer this information as definitive, but it provides encouragement that the concerted efforts of law enforcement, the medical community and Purdue might be bearing fruit. We would welcome the opportunity to share this data with the Committee.

11. IS RESTRICTING THE USE OF OXYCONTIN® THE SOLUTION?

Some have suggested that restricting availability of OxyContin® will help alleviate the problem. We are convinced this is not so. Those intimately involved with the problem agree. Local law enforcement officers have told us that in most of the reported cases of overdose and death, OxyContin® was neither the first nor the sole drug abused. Knowledgeable law enforcement officers have said that if OxyContin® were not available, those abusing and diverting drugs would not stop their behavior, but would simply transfer to other legal and illegal drugs. We have been advised by law enforcement officials that when effective measures have reduced the availability of OxyContin® to abusers and diverters, they return to their prior drugs of abuse. For this reason, the only real impact of restricting the availability of OxyContin® tablets would be to make it more difficult for the legitimate patients who benefit from this drug to obtain it.

At the FDA Advisory Committee meeting, the point was made repeatedly that if the prescribing of drugs like OxyContin® was limited to pain specialists, countless patients in pain, and certainly a high percentage of the rural, under-served, and low economic status population, would have no adequate treatment available to them. We will reference that information for the Committee when the transcript of the FDA Advisory Committee meeting is available. Perhaps the overriding message to emerge from the FDA Advisory Committee meeting was that there is no easy solution, no "silver bullet" that will solve the problem being addressed by this hearing today, balancing the risks and benefits of OxyContin®.

12. CONCLUSION

Purdue is committed to fighting abuse and diversion of controlled medicines. Abuse and diversion harm the abusers. They harm patients with pain. They harm the cause of pain management, and they harm Purdue and its products. Importantly, abuse and diversion threaten sound health policy, whose course should be driven by the health needs of millions of patients, not the actions of diverters.

The dilemma of addressing the problems of abuse and diversion without restricting the sale of a controlled drug like OxyContin® to meet the needs of doctors and patients for the effective management of pain was the subject of an important event in Washington, D.C. this past fall. On October 23, 2001, the DEA joined with 21 health organizations and issued a joint statement, a copy of which is being furnished for the Record, addressing the complex issue of combating prescription drug abuse while protecting the medical needs of patients. The Joint Statement expressly recognized:

> Undertreatment of pain is a serious problem in the United States, including pain among patients with chronic conditions and those who are critically ill or near death. Effective pain management is an integral and important aspect of quality medical care, and pain should be treated aggressively.

and also acknowledged what we at Purdue know all too well:

> Drug abuse is a serious problem. Those who legally manufacture, distribute, prescribe and dispense controlled substances must be mindful of and have respect for their inherent abuse potential. Focusing only on the abuse potential of a drug, however, could erroneously lead to the conclusion that these medications should be avoided when medically indicated generating a sense of fear rather than respect for their legitimate properties.

Today's hearing is an important step to paraphrase the Joint Statement in the direction of preventing drug abuse while not hindering patients' ability to receive the care they need and deserve.

The management of pain is a critical priority of healthcare in this country. Chronic pain affects as many as 50 million Americans and costs the country $100 billion annually. OxyContin® has proven itself an effective weapon in the fight against pain, returning many patients to their families, to their work, and to their enjoyment of life. That advance should not be stunted or reversed because of the illegal activities of those who divert and abuse the drug. We cannot turn back the clock. The answer to these problems is increased education, information and enforcement, not restrictions that will deny patients effective treatment of their pain.

RESPONSE FROM DR. GOLDENHEIM TO A QUESTION ASKED BY SENATOR REED

PURDUE PHARMA L.P.,
STAMFORD, CT 06901–3431,
February 26, 2002.

Hon. EDWARD M. KENNEDY,
U.S. Senate,
Washington, D.C. 20510.

DEAR CHAIRMAN KENNEDY: At the February 12, 2002 hearing of your Committee on the subject of OxyContin®, Senator Reed asked me about Purdue Pharma's marketing of MS-Contin®. I was not able to fully answer his question at the time, but agreed to furnish that information for the Record.

Purdue continues to sell MS-Contin®, but our patent protection has expired and as is customary in the pharmaceutical industry for drugs facing generic competition, we are no longer actively promoting it. While we were still actively promoting MS-Contin®, our marketing activities were similar to that for OxyContin®. Except for the initial launch period for OxyContin® and the fact that MS-Contin® has never been subject to a cap on commissions available to sales representatives, the compensation plan for our sales representatives has been virtually the same for the two medicines. The literature, mailings, and advertising for MS-Contin® were comparable to those for OxyContin®, but since the overall sales of OxyContin® are larger, we spend more on the promotion of OxyContin® when measured in absolute dollars and less as a percentage of sales.

If you have any additional questions, please let me know.

Sincerely,

PAUL D. GOLDENHEIM, M.D.,
Executive Vice President,
Worldwide Research & Development.

Senator REED. I would like to first turn to the practitioners, Dr. Payne and Dr. Van Zee and Ms. Green. It seems to me that one of the critical elements in this situation is the physician knowing their patient and prescribing appropriately what is a very serious narcotic. This is not something I would assume you would prescribe lightly. As a physician, you would have to believe that the person was in a great deal of pain, that other treatments would not work, etc.

However, it strikes me from listening to the dialogue here and especially some of the points Lieutenant Bess made about people targeting physicians who prescribe liberally that the solution might be better controls on physicians and greater responsibility by physicians prescribing OxyContin, Dr. Payne and Dr. Van Zee and Ms. Green?

Dr. PAYNE. I think you are absolutely correct that the issue is physicians making adequate and appropriate assessments of pain and then crafting an appropriate treatment plan. And the issue here with drugs being abused is not so much with the drug per se but with the people prescribing it and the people using it because, as I said, there is very little evidence actually that any one opiod is more inherently abusable than any other opiod.

So all of the clinical practice guidelines, and in my written testimony I have stated that there have been Federal panels now which have looked at evidence and created clinical practice guidelines for physicians, all emphasize this fact, that appropriate pain assessment should precede appropriate treatment and a critical aspect of pain assessment is knowing the patient and in crafting a plan that not only helps relieve pain but improves the patient's ability to function. So yes, it is critical to know the patient.

Senator REED. And Dr. Van Zee, I have to assume you know every physician in Lee County. Is that a fair assumption?

Dr. VAN ZEE. There is a small number, yes, sir.

Senator REED. So, where are all these young kids who—I agree with you, whose lives are being ruined, getting access to this OxyContin if your colleagues are as attentive as you are?

Dr. VAN ZEE. Well, that is a complicated problem and one does not know the answer. Now the black market and diversion market is so sophisticated now that it can hire nine commanders to stage a major robbery in Mexico City, which happened in the last 2 months in which there was a huge amount of OxyContin taken that way.

I certainly share some of Dr. Payne's feeling about the extreme importance of physicians being most careful about knowing their patients very well and then being most careful about their assessment, diagnosis and treatment. I think in addition to a prescription drug monitoring program, which most people are advocates of, I think as part of that component you need to have some kind of physician profiling, as well. Prescription drug monitoring will tell you if patients are visiting multiple doctors. Most of those may not have a way to recognize if one physician is extraordinarily overprescribing this drug.

I would foresee that as some kind of computerized database going into the State board of medicine, not law enforcement, and there would be some kind of template that could be used to look at on-going data so if we find physicians like has been in this kind of tragedy, enormously overprescribing, misprescribing this drug, that we do not find out about it two and 3 years later after ultimate problems have developed.

Obviously if somebody is way off the curve in terms of their opiod prescribing, that does not in any way necessarily mean that they are misprescribing. It may mean that they are a pain management specialist that has taken on multiple difficult patients which many other physicians do not want to do. But it means that if you are a far-out blip on the curve and that is the scope of your practice, you are going to accept the fact that you are going to be reviewed and that you would be reviewed by the State board of medicine.

And a good practitioner has absolutely nothing to hide. I mean there is a very important role for opiods in chronic nonmalignant, which has been testified today. What is just not known about is what subpopulation of people needs to get it, what are the risks of receiving opiods, what are the benefits, and those kinds of things we have very little data about.

Senator REED. Thank you, Dr. Van Zee.

Ms. Green, do you have a comment from your perspective as a nurse-midwife?

Ms. GREEN. As a nurse-midwife I do not prescribe OxyContin.

Senator REED. No, but you have patients who apparently have access to it.

Ms. GREEN. My patients have access to it through illegal diversion. It is not prescribed to them. As far as I know, no one in our county has prescribed OxyContin to a pregnant woman.

Senator REED. So they would buy from someone else.

Ms. GREEN. They obtain it illegally through the diversion. But I concur with comments being made as far as physicians in rural communities, in particular. You know, we have to drive two hours to a tertiary care center through very difficult road conditions for a specialty. So we have family physicians and internal medicine providers in our community that I think are very vigilant now of their prescription habits in particular with OxyContin. Several years ago we did have a physician who is no longer practicing in Washington County that was writing prescriptions for OxyContin, as they say, like candy.

The other issue that I think really needs to be looked at is family physicians know their patients in the office—no question about that. But family physicians cover the emergency room; they do not know these patients. So I think having the monitoring system in an emergency room so that a physician can gather that information, of has this patient been going to Drs. A, B, and C and likewise the emergency rooms and obtaining the same prescription would be very, very valuable.

Senator REED. Thank you.

Lieutenant Bess, as a police officer in rural Virginia, you are investigating this abuse constantly. Your perception about how most people are getting hold of their OxyContin, is it from a physician, a misprescription, or are they obtaining it through other means?

Lt. BESS. It is a combination of both the doctor-shopping, which puts a significant amount out, and those few doctors who do overprescribe, in effect, become pill mills and put a large quantity of drugs on the market.

Mr. Price is working with the State and Federal task force in Southwest Virginia called Operation Octagon. He has been investigating continuous doctors since 1997 and as they close out a case on one or two doctors, others have already been added into that.

Special Agent Cameron is working in Northern Virginia with a Federal task force called Operation Cotton Mouth, which is finding the same thing. They are about to form a State and local task force to work in the Northern Virginia area.

With regard to the database being in the board of medicine, we feel that it would be better served to be in a law enforcement agency because it is going to reveal criminal activity, not regulatory misconduct. And while they could have access to it, the main thing we would be looking at is the criminal conduct that it would reveal by those doctors who are outside the curve, as Dr. Van Zee speaks of.

The thing that doctors and health care professionals need to be aware of is that the volume that they prescribe is never the basis of why a physician is targeted by our group. That is the last thing we look at. We look at what type of practice they are involved in and what types of drugs they are prescribing. For instance, we know that some people require valium before they will go to a dentist's office and sit in that chair and two valium every 6 months is not going to be a problem. When we start seeing 300 every 2 weeks, that is a serious dental problem and we might take a look.

We understand that veterinarians prescribe human medicine to dogs. We know that oxycodone is not an appropriate thing; it is not taught by the veterinarian schools. So when we see Rex or Tabby

getting prescriptions for Percoset or OxyContin, we are probably going to take a look at that individual.

Poor judgment on behalf of the physician by overpresribing is not going to draw our attention. It may get him lunch with his board but it will not get him investigated by us.

Senator REED. Thank you.

Let me change the subject just a bit and direct a question to Dr. Goldenheim before I yield to my colleague, Senator Collins.

There has been a suggestion, Doctor, that your marketing techniques have been very aggressive with respect to OxyContin, that you have identified and targeted physicians that heavily prescribe opiods. The suggestion is that there is a connection between selling OxyContin and compensation of your sales force. I want to give you an opportunity to respond to those specific issues, or anything else you think is appropriate in terms of your marketing techniques.

Dr. GOLDENHEIM. Thank you, Senator. I assume by aggressive you mean improper marketing and——

Senator REED. No, I just think it is that your company believes you have a great product and you want to get it out and are spending a lot of money to get it out. It might be proper or improper.

Dr. GOLDENHEIM. We have focussed on patients who already have significant experience prescribing narcotic analgesics and the reason for that is, as has been mentioned here, some physicians are comfortable treating pain patients and have experience and knowledge and others do not.

Our promotion has consisted of providing information for physicians and pharmacists—that has been the case since 1984 when we launched MSContin, which was talked a little bit about earlier today—because we recognize that the health care profession needed more information about proper pain management. That is why we focussed, for example, on handing out guidelines that have been produced by prestigious medical societies. That is why we have underwritten so many seminars and symposia at which many preeminent pain experts have spoken, including people like Dr. Payne and Dr. Portenoy, who have submitted written testimony.

So our focus has been on teaching people about how to properly use these medicines and increasingly, of course, we have focussed on teaching physicians and pharmacists how to avoid abuse and diversion.

Just to clarify one thing that came up earlier, no, we have never done any direct-to-consumer advertising. And every time we have seen anything pop up on the Internet, a site that is offering free OxyContin or whatever, we have immediately phoned the DEA to let them know.

The last thing I would just point out, and I think it has been made clear today, is that this is part of a larger problem. It is part of a prescription drug abuse problem. And if you look at all of the diversion in Virginia, for example, that has been collected by the DDU, the Drug Diversion Unit, as we have heard, oxycodone preparations are, in fact, not number one on that list for the last year.

In certain parts of Virginia obviously it has had devastating consequences and in Maine, even in Washington County, which has clearly been devastated by this problem and we have heard these very poignant stories. It is my understanding that hydromorphone

or Dilaudid was and remains one of the most important drugs of abuse and I think we heard that from SAMHSA. This is a very big, very broad, very deep-rooted problem.

Senator REED. Well, no one can disagree with the fact that it is a broad problem that goes beyond your product. It is about abusing prescription drugs.

I am going to ask one more question, if I may, and turn it over to my colleagues and then if we need a second round, we will do a second round.

Are you still marketing MSContin?

Dr. GOLDENHEIM. Yes, sir.

Senator REED. Are you marketing it with the same kind of campaign you are using for OxyContin—the same compensation scales, the same literature, the same sort of advertising?

Dr. GOLDENHEIM. I am not sure I can fully answer those questions today. I believe that it is fairly similar but I would have to get more specific information for you.

Senator REED. Thank you, Doctor.

Senator Collins?

Senator COLLINS. Thank you, Mr. Chairman.

Ms. Green, I suspect that many of your addicted patients would never have considered trying heroin, for example. Is that correct?

Ms. GREEN. That is correct.

Senator COLLINS. So what is it about OxyContin that made it so attractive? You are treating a high-risk, vulnerable population because pregnant women obviously are a large part of your practice.

Ms. GREEN. Through all these months of work that I have done with addicts and mothers that are addicted, I have certainly learned a lot about addiction, although I am not an expert like everyone else. However, I think it is the purity and the dose of OxyContin. It is the safety. It is prescribed by the physician. It is legal, unlike heroin, when they do not know what purity levels they are getting.

What I am told from the community is that there is a food chain among addicts. At the top of the food chain is the person that snorts OxyContin. They are the top. They are the elite. The next level down is those that use IV OxyContin. The next level down is the women that use sexual favors in exchange for OxyContin and last it is the heroin addicts. There is a stigma with heroin and cocaine but there is not with an opiate.

Senator COLLINS. And that lack of stigma also translates into a lack of an alertness to the danger, does it not?

Ms. GREEN. Over and over and over again I am told by these women in particular and not just women that I care for but young men, as well, it was written by a doctor, it is legal, I know what is in it, so I'm going to use it and it is okay to use.

They did not realize—I had a woman in labor who had snorted 2 days before she went into labor and said to me she had no idea that OxyContin was addictive and that it was going to harm her baby.

Senator COLLINS. Are your patients generally first-time addicts or are they individuals who had problems with addictions who have now switched to OxyContin?

Ms. GREEN. It depends on the age group. I have, for example, just now she is 34 weeks pregnant and she is expecting her ninth baby. She is 30 and she has gone through the gamut of moving up from Tylox to Percoset, eventually ending up with OxyContin. OxyContin is the best thing that ever happened to her, as far as she is concerned.

Then I have younger women, 17, 18, 19, 20-year-olds, that know OxyContin is the first choice and best choice, so they are not even fooling around with anything else. They are going straight for OxyContin.

Senator COLLINS. Now Washington County borders Canada. In fact, I think your husband is a Canadian physician or at least practices in St. Steven, right across the border from Calais.

Ms. GREEN. Right.

Senator COLLINS. Is that a factor in the availability of OxyContin?

Ms. GREEN. I am so glad you brought that up. Unlike all the other rural communities in the United States, unlike the rest of the country, we are 50 yards away from Canada where prescriptions, all prescriptions, not just opiate prescriptions, are 50 percent cheaper than in the United States. So our addicts are going to St. Steven to buy OxyContin and Dilaudid and that is where your Dilaudid figures are coming in.

If they cannot get OxyContin in Washington County they are going to St. Steven and there is no question it is cheaper. They have to pay $40 in Maine for a 40 milligram tablet. They pay $20 Canadian, which is equivalent to $16 U.S. for the same tablet.

Senator COLLINS. So that suggests, when we are looking for solutions to this problem, that is one reason you mentioned in your testimony we need an international approach.

Ms. GREEN. Yes, yes.

Senator COLLINS. Because just solving the problem through, for example, if this were part of the solution, a prescription monitoring program in Maine, that is not going to stem that flow.

Ms. GREEN. It is not going to, absolutely not. And we are having a dialogue with New Brunswick now. In fact, we met with the governor of Maine just last week and we brought a representative from New Brunswick who is the administrator of the Charlotte County Hospital in New Brunswick who is trying to start a group just like we have and, in fact, they are going to join Neighbors Against Drug Abuse because New Brunswick at this point is still about a year and a half behind us in denial. "We do not have a problem. That is the one in the States. We do not have a problem." So it is widely available.

Senator COLLINS. Thank you.

Dr. Goldenheim, how much does Purdue Pharma spend in marketing and educational efforts on OxyContin since it was first introduced in 1995?

Dr. GOLDENHEIM. Senator, I do not have a total figure for you. I can tell you that last year about 19 percent of sales was spent on selling and promotional activities, which is a fairly typical figure for our industry.

Senator COLLINS. Could you translate that into dollars for me?

Dr. GOLDENHEIM. Sales last year were a little over $1 billion, so it is probably a little over $200 million. That would include the cost of the field force and other representatives and the various materials that they distribute.

Senator COLLINS. You showed us a number of excellent materials and I have been through them in your submitted packet to the committee that are designed to alert people to the dangers of abusing prescription drugs. They are excellent materials. I am curious whether they were provided to physicians by your field reps when you first began marketing OxyContin or whether these were only developed later, when it became evident that there was a serious problem with abuse of your product.

Dr. GOLDENHEIM. The answer is a little bit of both. Some of the materials, for example the opiod therapy documentation kit which talks about some of the issues that Dr. Payne raised about assessment and proper documentation and evaluating the patient and forming an individualized treatment plan, that and some of the guidelines were distributed as soon as they were available in 1997, some 3 years or so before I think any of us were aware that there was a problem.

I should say that previously we had distributed other guidelines from the AHCPR and the World Health Organization, which were actually incorporated into our original package insert. So we have disseminated these guidelines as they were developed by the medical community.

Some of the other materials, to fully respond to your question, for example the brochures on how to avoid abuse and diversion, tamper-resistant prescription pads, those were developed after we were alerted to the problem, typically in cooperation with law enforcement. We spent a great deal of time, the senior executives of Purdue, traveling up and down the Northeast corridor, starting in Maine, trying to learn what the problem was, what the sources were, and they have been described very nicely and we developed those materials in response to that.

Senator COLLINS. Doctor, I want to go back to the $200 million figure that you gave me earlier for the cost of your marketing efforts last year for this drug, and you said it was typical. Is it typical to spend that much for marketing on a drug where there is no direct-to-consumer advertising?

Dr. GOLDENHEIM. Yes, I think that is a fairly common figure in our industry because it is an all-in figure and, as I said, includes all the salaries of the field force, the representatives. There are 800 of them. It includes all the materials. It includes all the kinds of things that we are talking about here today.

Senator COLLINS. Dr. Van Zee, did any of Purdue Pharma's representatives market OxyContin to you?

Dr. VAN ZEE. It was late in the whole epidemic of things before I was seen by Purdue reps. I am not sure that was the case. It may have been our location, out of the way.

Senator COLLINS. Do you recall the nature of those marketing activities? Was there a caution given to you? Since you are an internist, you are not a pain specialist, I am assuming; is that correct?

Dr. VAN ZEE. That is correct. I treat general internal medicine patients. I treat cancer patients. I treat patients with chronic intractable pain.

Senator COLLINS. And perhaps you do not recall but when Purdue Pharma's representatives came to you did they come bringing the pamphlets that we have seen today warning about the potential for abuse of this product?

Dr. VAN ZEE. I honestly—it has been a long time and I cannot recall. I know I was reminded that there were doctors in California being sued for not treating patients appropriately with opiods but I was not struck personally by the inappropriateness of my individual Purdue sales rep, as I was by the way that the company has marketed and promoted this in general.

Senator COLLINS. I know my time has expired so let me just finish with one question to you. What led you then to conclude that the marketing of OxyContin was not appropriate?

Dr. VAN ZEE. Well, it is in the body of my statement but I was surprised to find out, when we found this out a year or so ago, that a pharmaceutical company would market a drug in such a way, particularly a highly abusable drug, where they develop physician profiles as to which physicians prescribe opiods most liberally. But, as I say, to me, that is very transparent in that it also tells you who prescribes least discriminately.

If you couple that with very lucrative financial—you give that kind of data to your sales reps with a very lucrative financial plan for them to increase their OxyContin sales in their territories, to me, that is a recipe for commercial success and public health problems.

Senator COLLINS. Thank you.

Thank you, Mr. Chairman.

Senator REED. Thank you, Senator Collins.

Senator Dodd?

Senator DODD. Thank you, Mr. Chairman.

It has been a great panel and I want to thank all of you. I have great admiration, Dr. Van Zee, for someone who has dedicated a good part of your career to work in an impoverished area of the country. I admire that immensely and Mrs. Green, as well, your work in—Washington County? I even like how you pronounce Calais. You know, we have a place in Connecticut called Versailles. We know how to pronounce those names in New England, do we not?

I am sorry I missed your testimony, Mr. Bess. I read it—Dr. Goldenheim, as well.

First of all, just as a matter of record, Mr. Chairman, it may have already been stated here and again let me state it for the record, one of my constituents is Purdue Pharma. I would not necessarily, because you are a constituent, be saying things in your favor for the sake of it. I know the company very well and know the employees there well and I think you have done a very good job testifying here about this and the steps you have taken.

I will ask unanimous consent that this be a part of the record but I want to just quote it. From day one, as I understand, as part of the insert with OxyContin going out, 1995 on—you correct me if I am wrong—has said the following, and I quote: "Patients

should be advised that OxyContin is a potential drug of abuse. They should protect it from theft. It should never be given to anyone other than the individual to whom it is prescribed. OxyContin may be expected to have addictive effects when used in conjunction with alcohol, other opiods or elicit drugs which cause central nervous system depression. As with all such drugs, care should be taken to prevent diversion or abuse by proper handling."

Has that been on the package? Am I correct that that has been part of the insert from the very beginning?

Dr. GOLDENHEIM. Yes, that is correct. In fact, when we launched the product the original package insert had at the time what I think was some of the most informed information wording, explanations about abuse and diversion and addiction.

I think it is also important to remember, and I think Dr. Jenkins alluded to this, that this has been sold as a Schedule II narcotic since the day it went on the market. There is no higher classification for a drug that can be legally prescribed.

So, for example, just the obvious signal that that sends to a physician is he or she knows that they cannot call a pharmacy the way I could call a pharmacy for any other medicine, as long as it is not a Schedule II. But for Schedule II I have to make a conscious decision to write out the prescription. So that is a very strong signal and, of course, that has always been known.

Senator DODD. Now let me ask you this. To what extent did you consider at the company about going directly to consumer marketing? I presume that was somewhat of a debate within the company, whether or not to go that route, which would have been legal, or to take the route that you took? And to what extent were the abusive drug addictive elements of this thing a part of that decision-making process, if any?

Dr. GOLDENHEIM. To be honest, it was not a debate. It has come up from time to time. Someone has said, gee, a lot of pharmaceutical companies are doing direct-to-consumer advertising; should we be doing it? And we have all immediately said no, we do not think that that is the right thing to do.

So it has not been a debate. These are complicated drugs to use. They do have abuse liability, which we have called out. And for that reason, among others, I do not think these medicines should be advertised directly to consumers.

Senator DODD. Senator Collins raised the issue of the different materials that you have sent out and you answered that there were some that went out initially and then some in response to the—what was it, approximately four or five years after the product was available that the awareness of the problems Ms. Green has seen with her patients and people she works with and Dr. Van Zee has seen.

How quickly did you, to close the loop on Senator Collins's question, you became aware of this as a problem with OxyContin when?

Dr. GOLDENHEIM. As Senator Collins has alluded to, around March of 2000. I think even before the report in the Bangor paper, which I think you said was April of 2000, we had a copy of a letter that the then-U.S. Attorney Jay McCloskey, who is now a consultant for Purdue—he is no longer the U.S. Attorney, and he is here today if you have any more detailed questions about our activities

in Maine—he wrote a letter to physicians because he became alerted to this problem, was concerned about this problem. I think the letter is dated February of 2000. I think we got it in March of 2000 and as soon as we got it we had one of our senior physicians call him and engage in a dialogue.

I think it took him a few months before he was comfortable talking to us. He was a little uncomfortable with talking to the manufacturer of the product that appeared to be associated with some problems. He actually sent some of his agents and a DEA agent to a medical education event that we were sponsoring and his people came back and were quite impressed with the detailed information about prescribing that was given and that it was generic, it was not branded, and that led to a meeting.

That was around September of 2000 and at that point we began to hear more and more reports and we traveled everywhere. We initiated meetings with Attorneys General, with U.S. Attorneys, FDA, DEA, to try to learn as much as we could about this and many, if not most of the ideas for these programs came as a result of that interaction with law enforcement, local community leaders, and health care professionals.

As one person said, one law enforcement official said, when we learned of the problem we jumped in with both feet.

Senator DODD. How quickly were these materials then produced?

Dr. GOLDENHEIM. Some within months of knowing about the problem. Another thing we did which goes back to March of last year was we developed a model based on the communities where we were hearing reports. We developed a model to try to predict where we might get other reports because we wanted to try to get ahead of the problem and the model, I think, was good and helpful and predicted about 100 counties. It included the counties, at that point six where we had heard of significant problems.

We called our field force in. I think it was about 180 representatives that cover those counties, gave them additional 3 days of intensive training. DEA participated in that training and we told them to go back out and call on physicians and emphasize only proper prescribing and how to avoid abuse and diversion and made it clear to those physicians that if they were not going to prescribe according to the proper guidelines of documentation and assessment and all of the important tools to avoid in abuse and diversion that we did not want them to write for our product.

Senator DODD. Let me just ask one more question if I can, Mr. Chairman. That is to Dr. Van Zee.

We had written testimony submitted to us by a Dr. Russell Portenoy. You are all familiar with him, I presume. Apparently he is a foremost expert, I am told, on pain management from Beth Israel Medical Center and he argues, and I am quoting now from his testimony, he says that "Any extreme response to OxyContin abuse, such as eliminating prescribing by nonspecialists or removing the drug from retail pharmacies, would do more than directly damage the large number of patients now benefiting from OxyContin," and we have heard testimony about that from the different responses.

He goes on to say, "It would have a chilling effect on prescribing overall. The overall result would be more undertreatment."

How do you respond to that? I mean you have heard this before and I hear what you are saying and what Ms. Green is saying, as well. Are you arguing, Ms. Green, by the way, that OxyContin ought to be taken off the market? Do you agree with Dr. Van Zee or you are somewhere less than that or take it off the shelves?

Ms. GREEN. If OxyContin remains the way it is now it should go off the market. If OxyContin is going to change its formula, add naltrexone to it, definitely it needs to stay. If they lower the dose, it needs to stay. If they lower the production of it, it should definitely stay. It definitely has a place in pain management and it should be available for hospice absolutely, oncology centers, cancer patients, and those that know how to treat chronic pain.

Senator DODD. Dr. Van Zee, how do you respond to Dr. Portenoy's point here? We all know about this. Everyone can cite a family member. I remember calling in the middle of the night with my closest boyhood friend all through school who died a few years ago of cancer and literally calling, sitting with him in the middle of the night calling his physician, waking him up because he was just in so much pain before he died. And just the battle I had to go through to get those—now he was dying. The only thing to do was to try to manage his pain so that his remaining hours would not be in agony and what a battle it was. And I am not alone. I have heard legions of these stories.

So I am not unmindful of the other side of the equation but boy, it is a serious, serious problem and this reluctance on the part of the medical community, this exaggerated fear of addiction. Is that a problem here?

Dr. VAN ZEE. If I could be a little circuitous in getting back to that, I would just say in response to some of these things, I think if we all left out of the room today we would be left with the impression that this is a problem in central Appalachia and in Maine and my contention is that it has become a national problem. I do not think the full picture has been mentioned today.

The president's Office of National Drug Control Policy in November 2000 pulled out their Pulse Check Report and they mentioned that OxyContin abuse has emerged as a significant problem in Baltimore, Boston, Denver, Detroit, New Orleans, Philadelphia, St. Louis, Washington, DC., Billings, Montana, Honolulu now.

So what we could see as a problem 15 months ago as Maine and Southwest Virginia is extended way beyond that in Pennsylvania, two methadone treatment centers in Southwest Virginia, 90 percent of all their admissions were involved. Louisiana, Arizona, South Carolina, Alabama all report high incidence of people entering methadone programs as being dependent on this.

Getting back to Dr. Portenoy, there are a couple of issues that need to be separated out. What is the role of opiods for people who have cancer and terminal diseases, like your friend that you lost? I think it is very clear that pain for those people has been poorly treated through the years and I think there has been a good and significant change about increasing awareness about how much better we have to be about that.

I think there is no issue about using opiods in cancer pain or any severe terminal illness. I mean you use whatever dose of opiods one can use in whatever combination to make things as comfortable

and merciful as it can. The real issue in the whole thing is what is the role of opiods in chronic, noncancer pain, chronic, nonmalignant pain? And the truth of that is that there are many things that we do not know about that.

I talked to Dr. Portenoy in a personal conversation a couple of weeks ago at the FDA meeting on opiods and he—as with any therapy, you have to evaluate what the risks are, what the benefits are of a certain type of therapy, what the risks are, and always carry with you the admonition that we, as physicians, should do no harm. So you need to have good information. What are the true benefits? What are the risks in treating this population of chronic nonmalignant pain?

Dr. Portenoy in his lecture said to the whole FDA meeting, we really do not know what the risks are of addiction developing from treating people with chronic nonmalignant pain and that is a fair summary of the state of our knowledge about that. We do not know.

Now if the rate of addiction disorders in general in the population can be 5 to 12 percent, a lot of people say 7, 8, 9 percent, you know, if the risk of opiod addiction in treating your patients and they take it exactly as you prescribe it is much less than 1 percent, that is one issue. If it is 5 percent and you have a million people on OxyContin, that means you have iatrogenically addicted 50,000 people and not only destroyed their lives but much of their family.

Now nobody knows what those figures are but to me, what I have seen as a tremendous push in the pain management community to use opiods very liberally in chronic nonmalignant pain has also been fueled by the industry with a lot of commercial enthusiasm and I think over the next decade we will find out that there has been a lot of unfortunate errors made about how much we have done with how little knowledge we have had to do it.

Senator DODD. Dr. Payne, do you want to comment on this?

Dr. PAYNE. I just want to say that chronic pain is a public health problem. It is a crisis. I mean the Congress declared this the decade of pain research. The American Pain Society, the American Pain Foundation have all declared this as a public health crisis.

I think just for the reasons that you mentioned, Senator Dodd, we have to strike a balance. I think the balance comes in prescription monitoring programs, in better education, and I personally react adversely to profiling issues, so I do not know if we want to go there but clearly there should be areas where the medical societies can review physician prescribing practices, as opposed to at least initial review being law enforcement. I think therein we can strike a balance to protect society on the one hand but to provide people with treatment that they need. Chronic pain is a public health crisis.

Senator DODD. Can I ask one more question?

Senator REED. Yes, Senator, you may.

Senator DODD. Dr. Van Zee, you raise the issue. I would like to know where is the evidence? I am not suggesting that there is not some but it just strikes me that the link between a manufacturer's marketing techniques and illicit use or inappropriate prescribing, you mentioned in your testimony and I quote here, "Conventional

wisdom says that if a drug is widely available, it will be widely abused." Is there more to this than that?

Dr. VAN ZEE. I think that is an old adage.

Senator DODD. Another one of those Appalachian things?

Dr. VAN ZEE. No, it goes way beyond. It is a national adage.

Senator DODD. I am only kidding.

Dr. VAN ZEE. That if you have a drug that can be abused, it will be abused. Then I would say by extension if you have an abusable drug that is widely available, it will be widely abused.

In Southwest Virginia the DEA has very nice figures compiled on OxyContin consumption in the United States and if by and large you look at that map of OxyContin consumption in the United States, the states that have the most consumption——

Senator DODD. But we are talking about illicit use here. How do you address illicit use by going after targeting and promotion of a product that is supposed to be used legally? I do not understand the connection between illegal use and marketing and promotion. I do not see the connection.

Dr. VAN ZEE. The connection is that in Southwest Virginia in the 14 counties affected by it, OxyContin was prescribed 600 to 800 percent higher than Virginia and the rest of the country in general. If you have that kind of availability of a drug, you do have a lot of recreational drug use. You have, like we had, 9 percent of our seventh graders having used OxyContin; 25 percent of our 11th graders having used OxyContin.

Senator DODD. That is a serious issue but we are kind of missing each other. We are passing in the night here. I am not sure we are talking to each other.

Dr. VAN ZEE. Let me try to make the connection. If you know that the area of your country that is having the problems with OxyContin abuse——

Senator DODD. They have a problem with drug addiction. You have a problem of kids who are—it is an OxyContin problem in the sense that they are using that product but there is something far more profound going on here than just the availability through legal channels of a painkiller.

Dr. VAN ZEE. Obviously we do not have all the information here but if you have an area of the country, and perhaps that is our area, that are high prescribers of controlled prescription drugs or opiods and you have a pharmaceutical company that finds out which physicians are most liberal prescribers of opiods and if you couple that with the sales representative force that has lucrative incentives to increase the OxyContin sales or whatever other drug is involved in their territory, I think it is a recipe for commercial success and public health problems.

Senator DODD. I thank you. You have been very patient. I apologize to both my colleagues.

Senator REED. Thank you, Senator Dodd.

Let me recognize Senator Collins for some brief comments and then I will close the hearing.

Senator COLLINS. Thank you very much, Mr. Chairman.

I first want to start by thanking you for calling this hearing and presiding over it. I think it was extremely informative and that all

of our witnesses helped us gain a better understanding of this problem.

To Dr. Payne, since I did not get a chance to question you, I want to thank you for the work that you are doing every day in helping people with chronic pain.

And to Mr. Bess, whom I also did not get a chance to question, thank you for your service on the law enforcement side of this problem.

But in particular I want to thank my constituent Nancy Green for coming down and sharing her first-hand perspective. She came all the way from Calais, ME and for those of you who do not know where that is, that is in far eastern Maine on the Canadian border. She had to drive two hours to even get to the airport in Bangor and you will probably not be surprised to hear that you cannot take a direct flight from Bangor to Washington.

Senator DODD. It is shocking to hear that.

Senator COLLINS. So it was a long journey but one well worthwhile because we learned——

Ms. GREEN. Just thank my mothers they did not go into labor while I am here.

Senator COLLINS. We very much benefited from your testimony and I think that you have given us a lot to think about and I very much admire your community activism, as well as your providing of health care to the people of a very rural part of Maine. So thank you very much and thank you, Mr. Chairman.

Senator REED. Thank you, Senator Collins.

I want to also thank the witnesses for their testimony. We have illuminated a very complex issue here, which involves medical practice, the sale of pharmaceuticals, the issues of pain, the issues of law enforcement, a whole host of complicated and interrelated issues that I suspect we will continue to think about and worry about going forward.

We have a situation where we have to ensure that there is access to palliatives because, as Dr. Payne pointed out, there is a public health crisis in the recognition and treatment of pain. However, we certainly have to stop and wonder what we can do if 9 percent of the seventh graders, as Dr. Van Zee pointed out, and 25 percent of high school students are experimenting with OxyContin. We really have a mutual responsibility, not just the Senate, not just the medical profession, not just the manufacturer and not just law enforcement, but all of us. We have to do better and I hope this hearing will allow us in some way to think harder and do better.

I would like to again thank the witnesses. The committee record will be open for 14 days to allow others who wish to submit written statements to do so and also allow colleagues on the committee to follow up with written questions to our witnesses. Senator Dodd made several requests to include documents. Those requests will be agreed to by unanimous consent.

[The prepared statement of Senator Jeffords follows:]

PREPARED STATEMENT OF SENATOR JEFFORDS

I am pleased that the full Committee is having this hearing today to discuss the issues surrounding the pain relief drug, Oxycontin. Reviewing news reports and the testimony to be offered

today, Oxycontin appears to either hold great promise for relief of those in pain, or great risk from its misuse. It is essential that Congress be aware of the issues surrounding this drug and this hearing is an important step in that process.

Oxycontin is a synthetic form of morphine used to treat severe pain—primarily in cancer patients. But a growing number of people in Vermont and the entire United States are abusing this prescription drug. For example, in my home state of Vermont heroin addicts have been grinding up Oxycontin and either snorting or injecting it to produce a high similar to that produced by heroin.

People have been obtaining Oxycontin through a variety of means, theft, false prescriptions, and even in some cases buying it from people that legitimately need the drug. Many users are willing to pay about a dollar a milligram which adds up to 80 dollars a pill.

The risks associated with this drug have lead some pharmacies in my state to refuse to carry Oxycontin or install expensive security systems to try and prevent its theft. In addition, concerns over the dangers of Oxycontin has led Governor Howard Dean to decide that Vermont's general assistance program will no longer cover the costs for these prescriptions.

While there are clearly risks associated with Oxycontin, its ability to provide relief to people suffering from severe pain is unquestioned. In a hearing on pain management I held in this committee in 1999, it became clear that far too many patients suffer needlessly and that more must be done to ensure that adequate pain relief is readily available to the tens-of-thousands of patients for whom severe and intractable pain is part of their daily lives.

This hearing will provide us with some important information on whether Oxycontin will fulfill its great promise for relief of those in pain, or continue to be known for its great risk of misuse. I look forward to the testimony of these witnesses, and once again thank the Chairman for holding this important informational hearing.

Senator REED. I now will thank you all and this hearing is adjourned.

[Additional material follows.]

ADDITIONAL MATERIALS

STATEMENT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

Mr. Chairman and Members of the Committee, the American Pharmaceutical Association (APhA) welcomes the opportunity to present the pharmacist's perspective on the use of OxyContin®. APhA and its members are committed to working with Congress, the Food and Drug Administration (FDA), the Drug Enforcement Administration (DEA), health care providers, and patients to find the appropriate balance between effective pain management and measures to curb the abuse and diversion of prescription drugs.

APhA, the national professional society of pharmacists, is the first established and largest professional association of pharmacists in the United States. APhA's more than 50,000 members include practicing pharmacists, pharmaceutical scientists, pharmacy students, pharmacy technicians, and others interested in advancing the profession. The Association is a leader in providing professional information and education for pharmacists and an advocate for improved health through the provision of comprehensive pharmaceutical care.

THE PHARMACIST'S ROLE IN PAIN MANAGEMENT

Opiate analgesics like OxyContin® are a valuable tool in the management of pain. Opiate analgesics have significant therapeutic value for the millions of patients who suffer from chronic pain due to disease, injury, or surgery—pain that other medications will not alleviate. However, pharmacists also recognize the potential for abuse with opiate analgesics, or any controlled substance, and are very concerned with the inappropriate use of any prescription drug product.

Prescription medications are safe and effective when used appropriately, but they can be deadly when used incorrectly. Pharmacists are the health care providers who work most closely with patients to make the best use of medications. Prescription drug abuse is one type of medication misuse. Pharmacists work collaboratively with prescribers and other health care providers to prevent the diversion of prescription medications and to identify incidents of abuse or addiction. As part of this process, pharmacists assess the appropriateness of every prescription order they review or dispense. Pharmacists watch for individuals who attempt to fill fraudulent prescriptions, visit multiple prescribers, or present prescriptions for unusually large quantities of medication. However, it is not always easy to determine if a prescription is legitimate—no simple algorithm determines appropriate use. And importantly, pharmacists cannot view every patient as a potential drug abuser without compromising their responsibilities as a health care provider.

EDUCATION—NOT RESTRICTED DISTRIBUTION—IS THE ANSWER

APhA strongly supports the FDA's and the DEA's efforts to ensure that legitimate users of opiate analgesics like OxyContin® maintain the ability to continue using these products, while reducing their diversion and abuse. Although APhA agrees that some action is necessary to address the diversion and abuse of opiate analgesics, we caution, however, against efforts to restrict the distribution of opiate analgesics or arbitrarily limit health care providers' ability to prescribe or dispense appropriate pain relief medications. With every barrier erected to limit diversion, the potential for those barriers to diminish appropriate prescribing increases exponentially. Restrictions in the drug distribution process can disrupt patient care by delaying access to medication therapy, disrupt existing patient-pharmacist-prescriber relationships, and potentially create an increase in the cost of medications. Also, any additional stigma attached to the drugs will have a significant chilling effect on health care providers' willingness to prescribe and dispense the appropriate pain medication and patients' interest in using the medications. Decreasing the number of patients using a medication may be seen as a "success" in managing risk. But this "success" is tempered by the accompanying "failure" of patients with legitimate need to access the same medication.

APhA believes that measures to curb abuse and addiction should be considered but discourages using any administrative barriers like triplicate prescriptions as a risk management solution.

In 1982, the state of Texas implemented a triplicate prescription law for controlled substances. A subsequent study of a 1200-bed teaching hospital found a 60% decrease in prescriptions for Schedule II controlled substances from 1981 to 1982.[1]

[1] Sigler K, Guernsey B, et al. Effect of a Triplicate Prescription Law on Prescribing of Schedule II Drugs. *American Journal of Hospital Pharmacy* 41 (1984), 108–111.

This shows that simply increasing recordkeeping requirements will discourage use of these medications. It is highly unlikely that 60% of these prescriptions were unnecessary. And in a survey conducted by New York State's Public Health Council, 71% of physicians surveyed reported that they do not prescribe the most effective pain medication for cancer patients if the prescriptions require a special state-monitored prescription form for controlled substances—even when the medication is legal and medically indicated for a patient.[2]

We do not believe that measures to curb abuse and addiction should be avoided, however, measures that simply increase providers' paperwork or restrict access to one troublesome product will not solve the problem. Those suffering from chemical dependency will find another way to obtain the product or find another product to achieve the same effect. These individuals need help to treat their substance abuse and addiction.

During a December 2001 U.S. House of Representatives Appropriations' Commerce, Justice, State, and Judiciary Subcommittee hearing on OxyContin®, both DEA Administrator Asa Hutchinson and Subcommittee Chairman Frank Wolf stated that they do not want or intend to restrict legitimate use of the drug. According to Hutchinson, the "DEA recognizes that the best means of preventing the diversion of controlled substances, including OxyContin® and all other drugs, is to increase awareness of the proper use and potential dangers of the products." The Association agrees, and notes that pharmacists can be an excellent communicator of that information.

APhA fully supports efforts to examine possible strategies to reduce the abuse and diversion of opiate analgesics without restricting access to drugs for patients with legitimate medical need. Last October, APhA in collaboration with 20 other health care organizations and the DEA, released a joint consensus statement on the need to prevent abuse of prescription medications while ensuring that they remain available for patients in need. The groups recognized that for many patients, opiate analgesics are the only treatment option to provide effective and significant pain relief. However, a narrow focus on the abuse potential of a drug could erroneously lead to the conclusion that these medications should be avoided when medically indicated—generating a sense of fear rather than respect for their legitimate purpose.[3]

APhA understands that one strategy to reduce the abuse and diversion of OxyContin® has already been initiated by the drug's manufacturer—Purdue Pharma. In August 2001, Purdue Pharma announced plans to reformulate OxyContin® to reduce the potential for abuse. The addition of naloxone to OxyContin® would prevent abusers who crush and inject the drug from obtaining the desired "high." APhA supports Purdue Pharma's efforts to reduce the potential for abuse of its product and we encourage Congress and the FDA to work with the manufacturer to accelerate the development and approval of the reformulated version. A reformulated version will continue to provide patients with effective pain management, while removing the stimulus for illegal abuse, and importantly for pharmacists, lessening the potential for pharmacy robberies related to OxyContin® abuse.

It is important that patients do not lose access to a valuable and effective pain medication because of a failure to prevent medication misuse. Restricted distribution is not the answer. The solution requires the education of health care professionals, law enforcement personnel, and the public on the use and abuse of pain medications.

Thank you for your consideration of the views of the nation's pharmacists.

PREPARED STATEMENT OF CHARLENE COWLEY

Mr. Chairman and Members of the Committee: The American Society of Pain Management Nurses (ASPMN) is an organization of professional nurses dedicated to promoting and providing optimal care of patients with pain, including the management of its sequelae. The organization feels strongly about advocating for appropriate care and against the many barriers that may affect care to patients with pain.

Currently, pain is "untreated, under treated or ineffectively treated for over 75 million Americans each year" (American Pain Foundation, 2000). A silent epidemic

[2] New York State Public Health Council, Report to the Commissioner of Health, *Breaking Down the Barriers to Effective Pain Management: Recommendations to Improve the Assessment and Treatment of Pain in New York State,* January 1984.

[3] A Joint Statement From 21 Health Organizations and the Drug Enforcement Administration. *"Promoting Pain Relief and Preventing Abuse of Pain Medications: A Critical Balancing Act."* Oct. 2001.

of pain and suffering is occurring in our nation. As nurses, we witness this tragedy every day and we are ethically bound to advocate for our patients. Opioids, including OxyContin® are one of many options that may be necessary for appropriate pain relief. Though there is a concern about misuse and diversion of these medications as a significant public health problem, there is another and even greater public health issue—the undertreatment of pain.

ASPMN would like to address the issue concerning the use of and access to opioids for patients who suffer with pain whether related to chronic conditions or life-threatening illness. Opioids are appropriate for chronic pain conditions and "an essential part of the pain management plan," as cited by the consensus statement from the American Academy of Pain Medicine and the American Pain Society (1997) as well as supported by the AHCPR Pain Guidelines (1992; 1994).

As one of the over 20 healthcare organizations, ASPMN supported the joint statement released in collaboration with the Drug Enforcement Administration in October 2001 (see attached). Overall, we support the call for balance and agree with the DEA Administrator Asa Hutchinson that there is no further need for legislative remedies to curb the illegal diversion of controlled substances. Yet there is a need to protect and improve access to all the treatment options to manage pain effectively.

ASPMN believes that people diagnosed with the disease of addiction should receive appropriate medical care. However, legitimate patients with pain should not be denied treatment because of the destructive behaviors surrounding addiction or, even worse, the activities of criminals. ASPMN would strongly oppose legislation that would increase barriers to legitimate patients obtaining needed appropriate medications. In 2000, Congress proclaimed this the Decade of Pain Control and Research. ASPMN supports legislation that:

- Provides for a National Report on the Problem of Pain
- Improves Pain Management Education for Healthcare Professional, Caregivers and the Public
- Reduces regulatory barriers that inhibit effective Pain Management
- Increases Federal Support for Pain Research
- Expands reimbursement for Pain Management Services
- Requires Pain Assessment and Treatment of Unrelieved Pain in all healthcare settings

Thank you for your thoughtful consideration of these issues. ASPMN offers its support and willingness to be available for collaboration to facilitate a balanced approach regarding OxyContin®.

STATEMENT OF THE NATIONAL ASSOCIATION OF CHAIN DRUG STORES

REDUCING THE INCIDENCE OF ARMED ROBBERIES INVOLVING OXYCONTIN IN COMMUNITY PHARMACIES

Mr. Chairman and Members of the Committee, NACDS appreciates the opportunity to submit this statement for the record regarding the abuse of OxyContin and measures to curb diversion and reduce the number of armed robberies in community pharmacies.

NACDS represents nearly 190 chain pharmacy companies that operate about 34,000 retail pharmacies all across the United States. Chain pharmacy is the single largest segment of pharmacy practice. We filled about 70 percent of the 3 billion prescriptions provided across the nation last year.

OXYCONTIN ROBBERIES ON THE RISE

Our members' pharmacies have been targeted by OxyContin abusers for armed robberies. We are concerned for the safety of our pharmacists, technicians, clerks, cashiers, and our customers. Some pharmacies have even contemplated not carrying the product. We support an all-out effort on the part of the manufacturer to reformulate the product to produce one that is equally effective for legitimate patients with chronic pain but, at the same time, resistant to potential diversion and abuse of the drug. Any pressure that can be exerted on the manufacturer, the Food and Drug Administration (FDA) and the Drug Enforcement Administration (DEA) to expedite the development of such a product will be instrumental in eliminating this public health crisis.

OXYCONTIN IS A SAFE AND EFFECTIVE DRUG WHEN USED AS PRESCRIBED

OxyContin is an opioid analgesic used to treat pain. Each tablet of OxyContin delivers to the patient, over a period of twelve hours, a controlled release dose of oxycodone. OxyContin is a Schedule II drug with recognized abuse potential. Intro-

duced by Purdue Pharma in 1995, OxyContin is used to treat chronic moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time. The benefit to patients who suffer with chronic pain is that medication is limited to two doses per day rather than four to six times per day.

OxyContin prescriptions have increased twenty fold since 1996 to approximately 6 million prescriptions in 2000. There is no doubt that OxyContin is safe when taken as prescribed and effective for treating chronic pain.

DIVERSION AND ABUSE OF OXYCONTIN

However, diversion and abuse of OxyContin is also on the rise. Diversion of OxyContin began in rural areas of Maine, Kentucky, and West Virginia and is now spreading into urban areas. To date, at least fourteen states have experienced increases in abuse and diversion of OxyContin. The controlled release formulation is easily compromised. Abusers crush the tablet and then swallow, snort or inject a solution to experience large amounts of oxycodone that give them a "high".

DEA's Office of Diversion Control reported 700 OxyContin thefts in the U.S. between January 2000 and June 2001. Florida reported 82 thefts compared to 90 in Pennsylvania, 69 in Kentucky, 74 in Ohio and 34 in California. Massachusetts has had over 60 robberies since January alone. Pharmacists are increasingly fearful of becoming the next target for an OxyContin robbery.

Deaths and overdoses have also been reported. Usually, these reports are the result of the abuse of opiates or a combination of drugs and alcohol. (Twenty U.S. metropolitan areas reported that oxycodone related deaths have increased 400% and emergency room visits have increased 100%.) Drug treatment programs in the most affected states (WV, PA, KY, and VA) report that 50–90% of newly admitted patients identified OxyContin as their primary drug of abuse.

DEA ACTION PLAN

DEA has implemented an action plan that NACDS fully supports. The plan includes investigation of unscrupulous and/or unethical medical professionals, forged and fraudulent prescriptions, pharmacy theft, and doctor shopping. DEA also has focused on gathering data to better define the scope of the problem. Information on prescriptions, deaths, emergency room visits, thefts, and drug treatment program admissions is targeted as well as investigations, arrests, and administrative actions.

POTENTIAL SOLUTIONS TO OXYCONTIN DIVERSION

NACDS has explored numerous potential solutions to OxyContin abuse and, in particular, as it impacts the increasing incidence of armed robberies in community pharmacies. We have commissioned a study to be conducted on the best practices for pharmacies. Recommendations will be given on practices that will reduce safety risks to employees and customers. Benchmarking current efforts by pharmacies, other retailers and banks as well as advice from law enforcement agencies will be used as the basis for the recommendations. The study will be presented at the NACDS Fall Conference scheduled for October 28–31, 2001 in San Antonio, Texas.

Reformulation of the product, in our estimation, is the number-one priority for stemming this serious public health problem. On August 8, 2001, the company announced the development of a reformulated version of OxyContin. The addition of naloxone, a narcotic antagonist, would deter intravenous abusers. (Naloxone was added to Talwin for the same reason several years ago and the product, Talwin NX, is no longer a commonly abused product.) Purdue Pharma has also mentioned the potential of developing a "smart pill" that would destroy oxycodone when crushed.

TIME IS OF ESSENCE

However, Purdue Pharma estimates this new formulation could take as many as three years to market. This timeframe is unacceptable. We urge the FDA and the manufacturer to expedite the approval, production and marketing of a reformulated version of OxyContin to make the new product available to the public as soon as possible. At the same time, all of the existing OxyContin should be phased out and recalled if necessary.

This reformulation would achieve the balance that we are all hoping to accomplish—keeping the product on the market for legitimate patients suffering with chronic pain and reducing the potential for abuse and diversion. Armed robberies that threaten our pharmacists, our customers and our stores would also decrease as a direct result. We thank you for the opportunity to comment on this serious public health issue.

STATEMENT OF THE NATIONAL INSTITUTE ON DRUG ABUSE

Mr. Chairman and Members of the Committee, I am pleased to submit the following statement for the record discussing what we have come to learn about psychoactive prescription drugs, their potential for abuse, and how we can both prevent and treat individuals who may abuse or become addicted to them. Because the specific topic of today's hearing is OxyContin, I will provide some information about this opiate and then broaden the discussion to give you an idea of how research on a specific drug like this fits into the National Institute on Drug Abuse's (NIDA's) overall research portfolio.

OxyContin as a prescribed medication is a very effective and efficient analgesic. When used for legitimate medical purposes, this controlled substance can improve the quality of life for millions of Americans with debilitating diseases and conditions. It is often prescribed for cancer patients or those with chronic, long-lasting pain. It is when a medication such as this is intentionally misused that it begins to pose a serious public health threat. This is what appears to be happening with this particular drug.

OxyContin is the brand name for an opioid analgesic that is prescribed by doctors for chronic moderate to severe pain. It was approved by the Food and Drug Administration in late 1995. Because it has the ability to slowly release its active ingredient oxycodone over about a twelve-hour period, it is an effective and efficient medication for the millions of people who suffer from chronic pain each year. OxyContin tablets are produced and manufactured by Purdue Pharma in various strengths ranging from 10mg to 160mg and are specifically developed to be taken orally. It is classified as a Schedule II drug, meaning it has a high potential for abuse and is only available by prescription by a licensed physician.

This Committee has recognized what we also perceive as an important emerging public health problem and why we launched last year a major initiative on prescription drug abuse and misuse. NIDA is encouraging more research in this area, particularly to understand the factors contributing to prescription drug abuse, and to develop more effective prevention and service delivery approaches as well as more behavioral and pharmacological treatments.

A variety of sources, including NIDA's own Community Epidemiology Work Group, a network of epidemiologists and researchers from 21 major U.S. metropolitan areas who monitor and report on community-level trends in drug abuse, are finding that people are "short circuiting" the time-release form of this medication by chewing, crushing, or dissolving the pills. Chewing or crushing the prescription drug corrupts or foils its time-release protection, enabling the users to experience a rapid and intense euphoria that does not occur when taken as designed and prescribed. Once having crushed the pills, the individuals are injecting, inhaling, or taking them orally, often with other pills, marijuana, or alcohol.

It is the active ingredient oxycodone, a synthetic opiate similar to morphine, that appears to be particularly attractive to the user and what is being used increasingly in urban, suburban, and rural areas. For example, according to the Substance Abuse and Mental Health Services Administration's (SAMHSA) Drug Abuse Warning Network, emergency room mentions of prescription drugs containing oxycodone (which may include drugs such as Percodan, Percocet, and OxyContin) increased 89 percent from 1993 to 1999 (from 3,395 to 6,429). Recently we have seen it increase by 68%, with 10,825 emergency room mentions in 2000.

It is this euphoric effect and the fact that many people perceive prescription pain killers as "safe" that are likely the reasons why this drug is being abused in such alarming numbers. The users want to receive the pleasurable effects, in the same way that people abuse and become addicted to drugs such as heroin or cocaine. In fact, there are some indicators suggesting that this drug may be used by some as a substitute for heroin.

Alternatively, some people may begin to use them appropriately as prescribed but over time may deviate from the prescribed regimen and may become addicted without intentionally setting out to abuse the drug in the first place. Reports of people becoming addicted to OxyContin, if used as prescribed, are rare.

Opioid drugs, such as oxycodone, work primarily through their interaction with the mu opioid receptors, especially in the brain and spinal cord. When activated, these receptors mediate the drugs' analgesic effects. However, they also mediate the ability to produce the euphoric state. Moreover, opioids like oxycodone have similarities to virtually every other drug of abuse, including nicotine, alcohol, marijuana, cocaine, heroin, and methamphetamine, in that they elevate levels of the neurotransmitter dopamine in the brain pathways that control the experience of pleasure.

Prolonged use of these drugs eventually changes the brain in fundamental and long-lasting ways, explaining why people cannot just quit on their own, and why treatment is essential. In effect, drugs of abuse take over the brain's normal pleasure and motivational systems, moving drug use to the highest priority in the individual's motivational hierarchy, thereby overriding all other motivations and drives. These brain changes, then, are responsible for the compulsion to seek and use drugs that we have come to define as addiction. This is likely the state people are in when they are reportedly "doctor shopping," feigning illnesses, and stealing from pharmacies to obtain the drug.

Fortunately, we have a number of effective options to treat addiction to prescription opioids and to help manage the sometime severe withdrawal syndrome that accompanies sudden cessation of drug use. These options are drawn from experience and clinical research regarding the treatment of heroin addiction. They include medications, such as methadone and LAAM (levo-alpha-acetyl-methadol), and behavioral counseling approaches.

Typically, the patient is medically detoxified before any treatment approach is begun. Although detoxification in itself is not a treatment for opioid addiction, it can help relieve withdrawal symptoms while the patient adjusts to being drug free. Once the patient completes detoxification, the treatment provider must then work with the patient to determine which course of treatment would best suit the needs of the patient.

Medications that were developed through NIDA-supported research, such as methadone and LAAM, can be used as effective treatments for addiction to opiates, if available to the patient. Methadone is a synthetic opioid that alters the effects of heroin and other opioids, eliminates withdrawal symptoms, and relieves drug craving. Treatment with methadone requires daily dosing. It has been used successfully for more than 30 years and has allowed many addicts to lead productive lives.

LAAM can alter the effects of opiates for up to three days. Research has demonstrated that, when methadone or LAAM are given appropriately, they have the ability to counter the euphoria caused by the opiate, if the individual does in fact try to take the drug. Researchers have also developed naltrexone, an opioid blocker that is often employed for highly motivated individuals in treatment programs that promote complete abstinence. Another medication, Naloxone counteracts the effects of opioids and is used mostly to treat overdoses.

As good as these treatments may be, there is no silver bullet for treating addiction to opiates. Research has shown, however that combining pharmacological approaches with behavioral therapies is the most successful approach to treating drug addiction. Behavioral therapies such as contingency management and cognitive-behavioral interventions, for example, have both been found to complement anti-addiction medications, such as methadone, successfully.

Unfortunately, many of the OxyContin abusers we are talking about today may be in locations where methadone clinics that can dispense medications are not easily accessible. This is one of the reasons we are trying to bring new, safe, and effective medications to the offices of physicians. NIDA is working with the Food and Drug Administration and the pharmaceutical industry on a new medication called buprenorphine. This medication has the potential for administration in less traditional drug-treatment environments, thus expanding treatment to populations who either do not have access to methadone programs or are unsuited to them, such as adolescents.

The point I would like to conclude with is that although the relatively sudden increase in drugs such as OxyContin and 3,4-methylenedioxymethamphetamine (MDMA) may be among our greatest concerns at this moment, they are just two of the many drugs out there that can harm the citizens of our Nation. The overall picture of drug abuse in the United States is constantly changing. As soon as we get a clear understanding of drug use patterns and gain some control over existing drug problems, new dangerous substances seem to emerge. Similar to the way a virus mutates, both regional and national drug abuse patterns are constantly reshaping and rarely remain static. By having our finger on the pulse of these constantly changing drug trends and by having a comprehensive research portfolio that covers all substances of abuse, NIDA is poised to use the power of scientific research and its application to avert emerging drug problems before they become national epidemics.

PREPARED STATEMENT OF CARLOS ORTIZ ON BEHALF OF CVS PHARMACY

The following is an offer of information for the Committee's consideration regarding Oxycontin on behalf of our pharmacists and pharmacy staff at CVS/pharmacy:

OXYCONTIN

Oxycontin, a controlled release oxycodone, entered the prescription drug market in 1995 as an opioid agonist and a Schedule II controlled substance indicated for the management of moderate-to-severe pain when a continuous around the clock analgesic is needed for an extended period of time. It was not intended for use on what the medical and pharmacy community would term a "prn" basis. PRN is an abbreviation of a Latin term (pro re nata) that means as needed.

Oxycontin is an extremely effective drug when prescribed for its intended use. The drug has a legitimate use of providing long-term pain relief especially to those who experience chronic pain and terminal cancer patients. These patients can maintain a better quality of life by ingesting fewer tablets and experiencing longer periods of time without pain.

ABUSE OF OXYCONTIN

Unfortunately, Oxycontin, like other opiates, has a high potential for abuse, whether legal or illicit. The media made the public aware that chewing, crushing, dissolving and injecting, snorting, or smoking the drug would provide a quick heroin-like euphoria.

Inappropriate prescribing, prescription fraud, prescription rings engaging in "Doctor Shopping", employee thefts, increased number of evening break-ins, and armed robberies, have been the direct result of the abuse of Oxycontin.

According to Jay P. McCloskey, a former U.S. Attorney in Maine from April 1993 to May 2001, Oxycontin was the prescription opiate most widely abused in Maine, with the exception of one county. He also noted that the speed with which prescription opiates and heroin became established among a growing population of high school age youth and kids in their late teens and early twenties was alarming and that these drugs were being used on a recreational basis.

ARMED ROBBERIES SPECIFICALLY FOR OXYCONTIN

Oxycontin losses in the form of employee pilferage and armed robberies were minimal until 2001.

For example, robbery loses in Massachusetts:

- 7 (1 armed robbery)
- 27 (5 armed robberies)
- 25 (2 armed robberies)
- 105 (87 armed robberies)
- From Jan to Feb 7, 2002 13 (13 armed robberies)

These figures were obtained from the Massachusetts Board of Pharmacy.

As you can see, Oxycontin targeted armed robberies are rising at an alarming rate. In addition to Massachusetts, Oxycontin armed robberies have occurred in Maine, Virginia, West Virginia, Kentucky, Alabama, New Hampshire, Vermont, Florida, Indiana and Rhode Island.

This is extremely frightening for all pharmacists, pharmacy staff, and their families. Some pharmacists have been robbed more than once. Some of the robberies have been violent. The incidences of armed robberies were rare prior to the onset of Oxycontin abuse.

We are very concerned about the safety of our colleagues as long as this drug is on the market in its current formulation.

ACTIONS REQUESTED FROM THE HELP COMMITTEE

- Increase penalties for individuals who commit armed robberies of healthcare providers.
- Encourage Purdue Pharma, L.P., manufacturer of Oxycontin, to reformulate the product to reduce the potential for abuse. It is our understanding that Purdue Pharma is working on this process. Please urge them to accelerate their activities.
- Encourage the FDA to "Fast Track" any reformulated product application.

We believe that these actions would significantly reduce the abuse of Oxycontin without significantly reducing its effectiveness as a pain relief medication or its availability. These actions would also help to protect health care workers, especially community pharmacists. At a time when pharmacists are in short supply and great demand, many community pharmacists are rethinking their decision to practice in the community. This, in many cases, is the direct result of the threat of violence attributable to the armed robberies associated with Oxycontin abuse.

Thank you for your consideration in this matter.

STATEMENT OF THE AMERICAN ACADEMY OF FAMILY PHYSICIANS

This statement is submitted to the Senate Health, Education, Labor, and Pensions Committee on behalf of the 93,100 members of the American Academy of Family Physicians (AAFP). The subcommittee will hear testimony today concerning OxyContin® diversion and abuse.

OxyContin® is a slow-release form of oxycodone hyrdochloride intended to treat moderate to severe chronic pain for up to 12 hours. When used appropriately, it is a safe, effective long-lasting opioid that has improved pain management and given new hope to thousands suffering from moderate to severe pain.

In recent months, news reports have noted the growing illicit use of OxyContin®, occasionally with deadly consequences. The medicine is a powerful narcotic with chemical compounds similar to morphine. The user experiences the full narcotic effect by tampering with the time-release coating and taking the drug intravenously or nasally. The pharmaceutical, when abused, is highly addictive. The resulting cases of addiction have led to a serious diversion problem in several states. Reports of OxyContin® diversion and abuse are disturbing both because of the speed with which this illicit use has occurred in rural, economically depressed communities and because of the deaths reportedly linked with the drug.

THE ROLE OF THE FAMILY PHYSICIAN IN TREATING PAIN

To address the growing problem of OxyContin® abuse without harming legitimate medical patients, it is essential to understand the role of the family physician in pain management. Family physicians see patients as the first point of contact for undiagnosed symptoms, the coordination of ongoing care plans and the management of multiple chronic medical conditions. We treat patients of all ages, often seeing patients through the end of their lives. Appropriate pain management is, therefore, an integral aspect of family medicine.

Family physicians take seriously the important responsibility of treating the entire person. According to "Facts About Family Practice" published by the AAFP based on data from the Department of Health and Human Services, family doctors receive one out of every four office visits made to all physicians. Family doctors are a vitally important source of medical care, including the managing of pain, for millions of Americans.

THE ROLE OF THE PAIN SPECIALIST

Family physicians often work in conjunction with pain specialists. Typically, family physicians either refer patients or request a consultation with a pain specialist in cases where the family physician is seeking an advisory opinion. Patients remain under the care of the family physician, who retains responsibility for coordinating their overall medical care, including the management of their pain. Given all that we do for patients in pain, even in consultation with pain specialists, it is not surprising that the American Academy of Hospice and Palliative Medicine reports 22 percent of its members serving as medical directors are family physicians.

FEDERAL RESPONSE TO PROBLEMS WITH OXYCONTIN®

The problems of diversion and abuse that have arisen with OxyContin® have demanded a response from federal law enforcement and regulatory agencies. Unfortunately, in several public statements and in testimony before Congress, several state and federal law enforcement officials have suggested that the right to prescribe OxyContin® should be limited to pain management specialists. Such proposals are troubling since they would create an immediate medical crisis for patients in legitimate need of pain management, especially in rural and underserved communities where family physicians are more likely to be practicing. The American Board of Pain Medicine lists only 1,179 certified pain specialists nationally who focus their medical practice on pain relief and treatment. Additionally, limiting the prescribing rights of certain physicians would create a dangerous new precedent of federal intervention into the practice of medicine. The American Academy of Family Physicians views such proposals as detrimental to the health of our patients and urges Congress to oppose such recommendations.

The AAFP recognizes the legitimate law enforcement authority of the federal Drug Enforcement Administration (DEA) and local law enforcement officials to prosecute physicians who are illegally prescribing OxyContin®. Physicians who abuse their prescribing privileges should not be allowed to hide behind their medical license to avoid strong and appropriate law enforcement penalties.

However, responses other than restricting prescription rights are more effective. For example, the Food and Drug Administration (FDA) recently suggested changes

to the labeling of OxyContin®. This new labeling includes a black box warning alerting physicians to the potential for abuse and addiction although OxyContin® continues to be approved for use in patients with moderate to severe pain who require continuous opioids for an extended period of time to adequately control their pain. The Academy commends the FDA for ordering these labeling changes and believes that the new labeling appropriately indicates the importance of careful physician supervision, as well as the potential for diversion that this drug poses.

The AAFP also recognizes that a federal response to diversion and abuse of OxyContin® is not enough. Physicians have a corresponding responsibility to provide thorough patient assessments and continued monitoring of patients for whom they have prescribed OxyContin®.

THE AAFP RESPONSE TO PROBLEMS WITH OXYCONTIN®

The Academy is responding to concerns about OxyContin® by educating physician members about the medicine's potential for diversion and abuse. In the August 2001 *FP Report,* the Academy published an article entitled, "Two Faces of OxyContin® in an effort to highlight concern over its abuse and the need to effectively screen patients for potential addiction. The article directed family physicians to the Center for Substance Abuse Treatment (CSAT) within the Substance Abuse and Mental Health Services Administration to obtain "Treatment Improvement Protocols" published by CSAT.

The article also highlighted a variety of methods for protecting the authenticity of physician prescriptions, as well as characteristics to beware of in strange or new patients who may be "doctor shopping." These included recommendations to protect prescriptions by keeping pads in secure locations and never signing an incomplete prescription. Family physicians were advised to write the quantity and strength of drugs on prescriptions in letters and numbers and to use tamper-proof prescription pads that could not be photocopied. The article also stated that prescriptions should include the name of the pharmacy that the patient intended to use or that they should be faxed directly to the pharmacy for authentication. Family physicians were advised in the article to never write their medical license on an empty prescription pad, but to include it as the prescription was written out.

Since "doctor shopping" is one of the methods that has been used to divert OxyContin®, the article goes on to advise family physicians to be wary of any stranger who:

- wants an appointment at the end of office hours or arrives after regular hours;
- demands immediate action;
- refuses a physical exam, permission to obtain medical records or undergo any diagnostic tests;
- is unable to give name of regular physician (may claim no health insurance);
- cannot recall hospital/clinic where past records are located or says it went out of business;
- has lost prescription, has forgotten to pack prescription, or says it was stolen;
- exaggerates or feigns medical symptoms;
- recites textbook symptoms with a vague medical history;
- has no interest in diagnosis or referral—wants a prescription now;
- shows unusual knowledge of controlled substances;
- requests a specific controlled substance and is unwilling to try another medication;
- states that specific nonopioid analgesics do not work or claims allergy to them.

In addition, the state chapters of the Academy have undertaken a variety of activities addressing long-term opioid prescribing. Such activities include continuing medical education seminars on appropriate pain management and screening abuse in Ohio, Texas, Mississippi, Alabama, and Tennessee. In addition, our chapters in Kentucky, Tennessee, Alabama, and Ohio have published articles outlining the importance of appropriate patient selection, screening for addictions, coordinating with pharmacists and other specialists to develop a care plan that also prevents diversion and assures long-term monitoring of the patient. All of these activities have stressed the importance of appropriate pain management including an assessment of the patient's pain, addressing nonopioid analgesics as a first resort, and appropriately monitoring patients who have been prescribed OxyContin® to preclude the possibility of diversion.

The Academy has addressed pain management in its publication, *American Family Physician*. Two recent articles were published in *American Family Physician,* "Twelve Pitfalls of Adequate Pain Control" (September 1997) and "Physician Attitudes a Barrier to Pain Management" (November 2000).

In addition, the Academy also has sent a letter to all state Attorneys General, expressing the Academy's interest in working collaboratively to prevent the diversion and abuse of OxyContin® and objecting to suggestions that the right to prescribe this effective pain management medicine be restricted to pain management specialists. The letter asks each Attorney General to contact the appropriate state chapter of the Academy to find out which education efforts have been undertaken at the state and local level.

Further, the Academy is educating physicians on strategies for identifying all forms of addiction and substance abuse. Earlier this spring, the Academy partnered with the National Institute on Drug Abuse (NIDA) and six other organizations to launch the National Initiative on Prescription Drug Misuse and Abuse. In AAFP publications sent to the entire membership, the Academy highlighted the NIDA online publication, *Research Report Series: Prescription Drug Abuse and Addiction.*

Finally, the Academy sponsors continuing medical education conferences that address addiction screening. At the AAFP's 23rd Annual Conference on Patient Education, which will be held in Seattle from November 15–18, 2001, the Academy will sponsor a lecture on recognizing the signs and symptoms of prescription medication addiction in specific populations. The Academy is currently exploring the possibility of producing continuing medical education materials, in both traditional and online formats, on appropriate pain management.

CONCLUSION

In closing, the AAFP is concerned that effective medicines, such as OxyContin®, remain accessible to primary care physicians and their patients who are in chronic pain. Likewise, the Academy is concerned about the illicit use of OxyContin® and has addressed the potential for its abuse in several ways. Through continuing medical education at the state and national level, the Academy has focused on drug abuse and OxyContin® in particular. Recent changes in the labeling of OxyContin® are important steps towards ensuring its appropriate use under the ongoing care of a physician.

The AAFP supports the response of the FDA in seeking OxyContin® labeling changes and of the DEA in prosecuting the illegal activity of physicians wherever it may occur. The Academy is committed to working with federal law enforcement officials and regulators to help family physicians care appropriately for their patients who are in pain.

The Academy appreciates the opportunity to submit this statement for the record to the Senate Health, Education, Labor, and Pensions Committee. We look forward to working with you to end the illicit use of OxyContin® without neglecting those patients who legitimately need relief from chronic or severe pain.

PREPARED STATEMENT OF RUSSELL K. PORTENOY, M.D.

I am grateful for this opportunity to contribute these comments to the Committee. I have extensive background in the area of pain management and opioid pharmacology. I am Chairman of the Department of Pain Medicine and Palliative Care at the Beth Israel Medical Center in New York City and Professor of Neurology at the Albert Einstein College of Medicine. I am a Past President of the American Pain Society, current Secretary of the International Association for the Study of Pain, a Director of the American Pain Foundation and the National Hospice Foundation, and Vice-Chairman of the American Board of Hospice and Palliative Medicine. For almost two decades, I have specialized in the treatment of patients with chronic pain and have been an educator and clinical investigator in the areas of pain and opioid pharmacology. I have had a particular interest in exploring the relationship between pain management and chemical dependency, and have helped organize four international conferences devoted to this topic.

My testimony is focused on the medical use and abuse of Oxycontin and is based on my experience as a clinician and my knowledge of pain medicine and opioid therapy. As disclosure, I will state that I have accepted honoraria for participating in educational symposia sponsored by several corporations that manufacture opioid drugs, including Purdue Pharma, and that my department has received grants from these companies for projects involving professional education and research.

Before September 11, media attention on Oxycontin abuse was intensifying. Frightening statistics concerning abuse, and the poignant stories of people whose lives have been damaged by addiction to Oxycontin, have justifiably raised concerns about the dangers associated with this drug. Some are now questioning the wisdom of continuing business as usual in providing access to Oxycontin, and perhaps to other potentially abusable drugs with legitimate medical purposes.

At the same time, however, the stories of abuse and addiction, and the potential for increased regulation of opioid drugs, have raised intense worries among pain specialists and patient advocates, who fear that over-regulation, ill-conceived enforcement policies, and worsening social stigma will lead to more undertreatment of pain, and hence more suffering for the millions of people with painful disorders.

The latter fear—that the unintended effects of regulation could hurt patients—was forcefully illustrated to me by two recent personal experiences. First I learned that a family member who requires long-term opioid therapy for a serious pain problem was told by her pharmacist that he would not dispense her medication any longer because he did not want to have patients who received such drugs on a regular basis. Soon thereafter, three of five patients I was seeing during one treatment session spontaneously expressed great fear that the government would "take away" their Oxycontin, causing them to return to states of unrelieved pain and severe disability. The government's response to Oxycontin abuse affects patients, and their interests must be considered.

STATUS OF OPIOID THERAPY IN THE UNITED STATES

To frame this issue, it is informative to review the history of opioid therapy during the past two decades. Since the 1980's, there has been a worldwide clinical consensus that opioid drugs should be the first-line treatment approach for severe acute pain and moderate to severe chronic cancer pain. Despite this consensus, numerous studies of cancer pain have demonstrated that opioid use often does not conform to published guidelines. The problem of undertreatment is complex, but it is certainly due, at least in part, to physician limitations, including inadequate knowledge of prescribing principles, an unrealistic fear of addiction and side effects, and concerns about regulatory scrutiny.

This last issue—fear of the government's reaction to the medical use of opioids—is very real and should be emphasized in this context. A 1998 survey of more than 1300 New York State physicians, for example, revealed that more than half were moderately to very concerned about regulatory oversight and that one-quarter to one-half admitted to changing their prescribing practices solely because of such concerns.

Despite persistent undertreatment, cancer patients did begin to benefit from pain treatment advances and clinician education in the 1980's. The release on the U.S. market of long-acting opioid drugs, the first of which was a morphine formulation developed by Purdue Pharma called MS Contin, was a significant advance in treatment. Purdue Pharma followed the launch of this drug with an extensive educational program, which was focused on the problem of cancer pain and sought to improve acceptance of opioid therapy by providing information and dispelling deeply held myths and misconceptions about these drugs. The later release on the market of other long-acting opioids was accompanied by similar marketing and educational strategies.

As opioid use for cancer pain was being encouraged, pain specialists began a major shift in thinking about the role of these drugs for noncancer pain. After more than a decade of debate, a 1997 consensus statement jointly issued by the American Pain Society and the American Academy of Pain Medicine rejected the traditional negative view of this therapy and acknowledged that long-term opioid administration was clearly beneficial for selected patients with chronic pain. A similar consensus statement followed from the American Society of Addiction Medicine. In response to this changing perspective, and the ongoing problem of undertreatment, the regulatory community and many state legislatures have tried to reassure clinicians that the legitimate use of opioids will not place them at risk of investigation or sanction.

Most pain specialists now recognize that opioids are no panacea for chronic noncancer pain, but are nonetheless probably greatly underused in the management of painful disease. Given the extraordinary prevalence of chronic pain, which is estimated to affect at least 50 million people in the U.S. alone, pain specialists generally also believe that primary care physicians must become skilled in the administration of opioids, and comfortable with the approach, if there is to be any hope that the benefits associated with these drugs can be brought to those who are appropriate to receive them.

Pain specialists and other physicians also recognize that the opioids are potentially abusable drugs. They may be diverted to illicit use, and patients who are predisposed to addiction may get into trouble when administered one of these drugs for a legitimate medical purpose. In this context, it is important to recognize that the word "addiction" refers to a disease characterized by loss of control over the drug, compulsive use, and use despite harm. This disease, which has a strong ge-

netic predisposition, can be activated by many types of medicine, including opioids. When prescribing any potentially abusable drug, the physician has an obligation to select patients carefully, monitor drug-related behaviors, and control the therapy. This is particularly important in patients with a history of chemical dependency, and in those who may be predisposed to develop addiction.

PERSPECTIVES ON OXYCONTIN ABUSE AND ADDICTION

The active ingredient in Oxycontin, the opioid oxycodone, has been commercially available for decades. Oxycontin provides a convenient long-acting delivery system for a drug that is commonly administered in many short-acting proprietary and generic formulations. There is no scientific evidence that oxycodone causes abuse or true addiction at any greater rate than any other opioid in its class. From the medical perspective, however, there is good evidence that individual patients vary greatly in their responses to different opioids, and that some patients have a much better outcome when given oxycodone than other opioid drugs. Experience with Oxycontin among pain specialists has confirmed that it is a convenient formulation that provides extraordinary benefit for some patients, and is less preferred by others.

When Purdue Pharma was developing Oxycontin, it opted to study the drug in populations with chronic noncancer pain, including those with arthritis pain and low back pain. The studies were positive. After the drug's launch, the company chose to market it to nonspecialists, and were permitted to do so based on the data from these studies. Their marketing, and the educational program they pursued in the primary care community, was very similar in style to the strategy that they and other companies pursued in trying to improve the management of cancer pain. It focused on benefits of pain control and the problem of undertreatment, taught the principles of opioid therapy, and tried to dispel the myths and misconceptions that stigmatize opioids and are barriers to appropriate opioid prescribing. This educational program did not strongly address the potential liabilities of abuse and addiction.

Presumably, the combination of marketing and education in the primary care community, combined with an enormous unmet need among patients, led to a rapid increase in Oxycontin prescribing. As sales increased, pockets of serious abuse began to occur, particularly in populations with known histories of abuse or addiction.

The reports indicate that most abuse and addiction occurred among those with known histories of chemical dependency. Undoubtedly, however, some abuse and addiction occurred among those who had not experimented much with opioid drugs before, but were predisposed to develop problems and were given Oxycontin for pain by a well-intentioned physician. For these individuals, Oxycontin was a "gateway" drug to serious abuse.

There is no evidence that the amount of abuse by known abusers, or the amount of "gateway" use, has been more than would be expected with any opioid that had a similarly rapid increase in medical use over a short time. It is also impossible to know whether the media attention on the drug is partly responsible for spread of abuse.

Having said this, however, it also is a reasonable presumption that the Oxycontin problem is greater than would have occurred if the marketing to clinicians had focused more on the potential liabilities of therapy, including the potential for abuse and addiction. The problem is presumably greater than would have occurred if the makers of Oxycontin, the makers of other opioids, and professional medical societies had been providing educational programs for physicians that had included more about the management of addictive disease.

A BALANCED APPROACH TO SOLUTIONS

The approach to opioid drugs with legitimate medical purposes must derive from three perspectives. First, we should all recognize that access to opioid therapy is essential for millions of patients with acute and chronic pain. In this regard, we should all acknowledge that the epidemic of undertreated pain is a huge public health problem, that opioid drugs can be safe and effective but are medically underused, and that the underuse of opioid drugs is partly determined by stigma associated with addiction and by physician fear of regulatory oversight.

Second, we should all agree that decisions concerning the regulation of opioid drugs should be based on the available scientific information and be informed by accumulated clinical experience. Policy should not be driven by anecdote or fear.

Third, we should all acknowledge that the potential for abuse and addiction is a liability associated with these drugs and that both clinicians and those in government have a common interest in minimizing these negative outcomes while ensuring

appropriate medical use. In this regard, the problem of Oxycontin abuse has been something of a "wake-up call" for those of us who believe that opioid therapy should be expanded and that the primary care community must take on this therapy to meet the needs of patients. It is now clear that physicians who wish to help patients by providing long-term opioid therapy must have the knowledge and skills to both optimize benefit and minimize risk.

These perspectives must be considered in discussing the government's response to the problem of Oxycontin abuse. What would a reasonable response be? We must first avoid extreme reactions that could have unintended negative consequences. Of course, actions that would limit access to Oxycontin also would probably lessen its abuse. The great concern, however, is that regulatory or law enforcement initiatives intended to reduce diversion and abuse may have the unintended effect of reducing the availability for patients who are truly in need. The clinical community already undertreats, in part, because of fear of the regulators. Any extreme response to Oxycontin abuse, such as eliminating prescribing by nonspecialists or removing the drug from retail pharmacies, would do more than directly damage the large number of patients now benefiting from Oxycontin. It would have a "chilling effect" on prescribing overall and increase the fear of these drugs among prospective patients and the public. The overall result would be more undertreatment.

The government must not interpret less prescribing as equal to less abuse. For example, eliminating Oxycontin from state medical programs for the indigent might lessen prescribing, but where is the evidence that this directly addresses the problem of abuse or addiction? This type of action is not justified without such evidence.

At the same time, we do need to be circumspect about the marketing of opioid drugs to the primary care community. Marketing must be done in tandem with education and support. We are not yet ready for direct marketing of opioids to the public.

We need to encourage an ongoing dialogue between clinicians and those in the regulatory and law enforcement communities. To their credit, the DEA and the FDA are already reaching out to the clinical community. The DEA should be particularly commended for joining with a large number of professional medical societies, including the American Medical Association and the American Pain Society, in signing on to a consensus statement supporting the concept of a balanced approach to opioid drugs. This type of collaboration should be duplicated by law enforcement and regulators in every state, particularly those affected by a high level of Oxycontin abuse. It will help ensure that no action is taken without a careful review of the potential impact on the problem of undertreated pain.

We need the government to encourage improved education for prescribers and pharmacists. Education should be pursued through partnerships among professional societies, industry, and government agencies.

We also need the government to support research related to many aspects of pain and chemical dependency. This is the Decade of Pain Control and Research, but research in pain is still woefully underfunded. We need studies to define the risk of abuse and addiction, determine the relative impact of many factors that could be contributing to these outcomes, and investigate various interventions to reduce abuse without adverse effects on pain management. If new laws or regulations are pursued, they should be accompanied by ongoing study of their effects on pain patients.

Finally, the treatment available for patients with addictive disease is inadequate. The current drug abuse treatment community needs support to develop models and novel therapies that can address the problem of opioid abuse in patients with acute and chronic pain.

[Whereupon, at 5:12 p.m., the committee was adjourned.]

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