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ON BEHALF OF PURDUE PHARMA L.P.

BEFORE THE

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

FEBRUARY 12, 2002

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. <u>What is the nature of the problem?</u>

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 US 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 US 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 others 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 pharmaceutical 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 physicians 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." (page 1)
- "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." (page 1)
- "All such prescribing [of controlled substances] must be based on clear documentation of unrelieved pain and in compliance with applicable state or federal law." (page 2)
- "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…" (page 2)

- "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." (page 3)

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 US 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 Hutchison 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.