STONE MOUNTAIN HEALTH SERVICES

St. Charles Community Health Clinic

Serving St. Charles and Surrounding Communities

P O Drawer S ◆ St. Charles, VA. 24282
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Jan. 1, 2002

Dear Ms. Topper,

It is my understanding that the Anesthetic and Life Support Drugs Advisory Committee will be meeting 1/30-1/31/02 to review issues concerning opioids. I have had a major interest in all these issues over the last few years, having been witness to the enormous problems in our region stemming from an epidemic of OxyContin abuse. I was scheduled to testify to the US Senate Committee on Health, Education, Labor, and Pensions in their hearings on OxyContin which were scheduled earlier this fall, and had to be cancelled. Thus far, this hearing has not been re-scheduled but I wanted to share this information with you and your committee. This information has bearing on many of the difficult issues that your committee will be addressing.

Thank you for your time and attention in these matters!

Sincerely,

Art Van Zee MD

Art Van Zee,MD

Testimony to the US Senate
Committee on Health, Education, Labor and Pensions

October 23, 2001

by Art Van Zee,MD

--Testimony

--Attachment A: Supporting Details and Information

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Testimony to the US Senate
Committee on Health, Education, Labor, and Pensions
October 23, 2001
by Art Van Zee,MD

The OxyContin Abuse Problem

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.

In the 25 years I have practiced as a general internist in St. Charles, Virginia, 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 possible way by their opioid addiction. Opioids--as derivatives of opium--are the most powerful pain medications--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: (1) the increasing prevalence of prescription drug abuse in this country; (2) the mis-prescribing and over-prescribing by at least some physicians; (3) and lastly, and I think a major factor, the promotion and marketing practices of the maker of this drug. I have included in the attachments a detailed look at this promotion and marketing as I see it.

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.

(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 available opioids[1] 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 US 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. Even though I feel strongly that a good part of the responsibility for the Oxycontin problem was related to how the drug was promoted and marketed, to my knowledge, that promotion was not out-side the FDA guidelines. It is my contention that the public health would be best served by a re-examination of the ways pharmaceutical companies would be allowed to promote and market controlled--i.e., potentially abusable drugs.

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

Art Van Zee, MD

Art Van Zee,MD
St. Charles Clinic
St. Charles, Va. 24282

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

Attachment A

Testimony to the US Senate
Committee on Health, Education, Labor, and Pensions
October 23, 2001
by Art Van Zee,MD

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 kids were good kids with bright, promising futures that had 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 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 similar 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

problems 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 non-malignant pain , there has been a new willingness to review previous aversion to the use of opioids in chronic nonmalignant 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 pnonouncements 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 from controlled clinical trials. Controlled clinical trials of long-term opioid therapy are needed, but the 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 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)

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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

Symptom Management

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 testmony 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 cosumption 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. 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.

(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 US in the last 25 years, all other measures taken to stem the diversion and abuse will fall far short of what is needed.

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3 statistics, DEA, Office of Diversion Control

4 The Medical Letter Sept 17, 2001

5 statistics, DEA, Office of Diversion Control

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 (eg, 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.

Art Van Zee,MD
St. Charles Clinic
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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 barage 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]

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[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(1):270-3

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.

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 role 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 morphine--MS Contin--in 1985 for the treatment of cancer pain, began to promote MS Contin for noncancer pain as well.

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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

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 pruduct 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

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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

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 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 form 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.

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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

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 re-inforces 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.

Art Van Zee, MD 8/22/2001

Stone Mountain Health Services St. Charles Clinic St. Charles, Va. 24282

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10 US 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.

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"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.

(cont.)--Patient/Caregiver

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.

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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 substantial 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."

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(cont.) "Professional Education"

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.

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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 hve 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 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

(continued)

(2) Perry S. "Management of Pain during Debridement: a Survey of US Burn Units" Pain 13 (1982) 267-280
--a questionairre survey of 151 US 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 (eg, "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 meaningful 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 websiste has for physicians and patients over-sold 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.

Art Van Zee MD

Art Van Zee,MD
8/18/2001

Attachment C

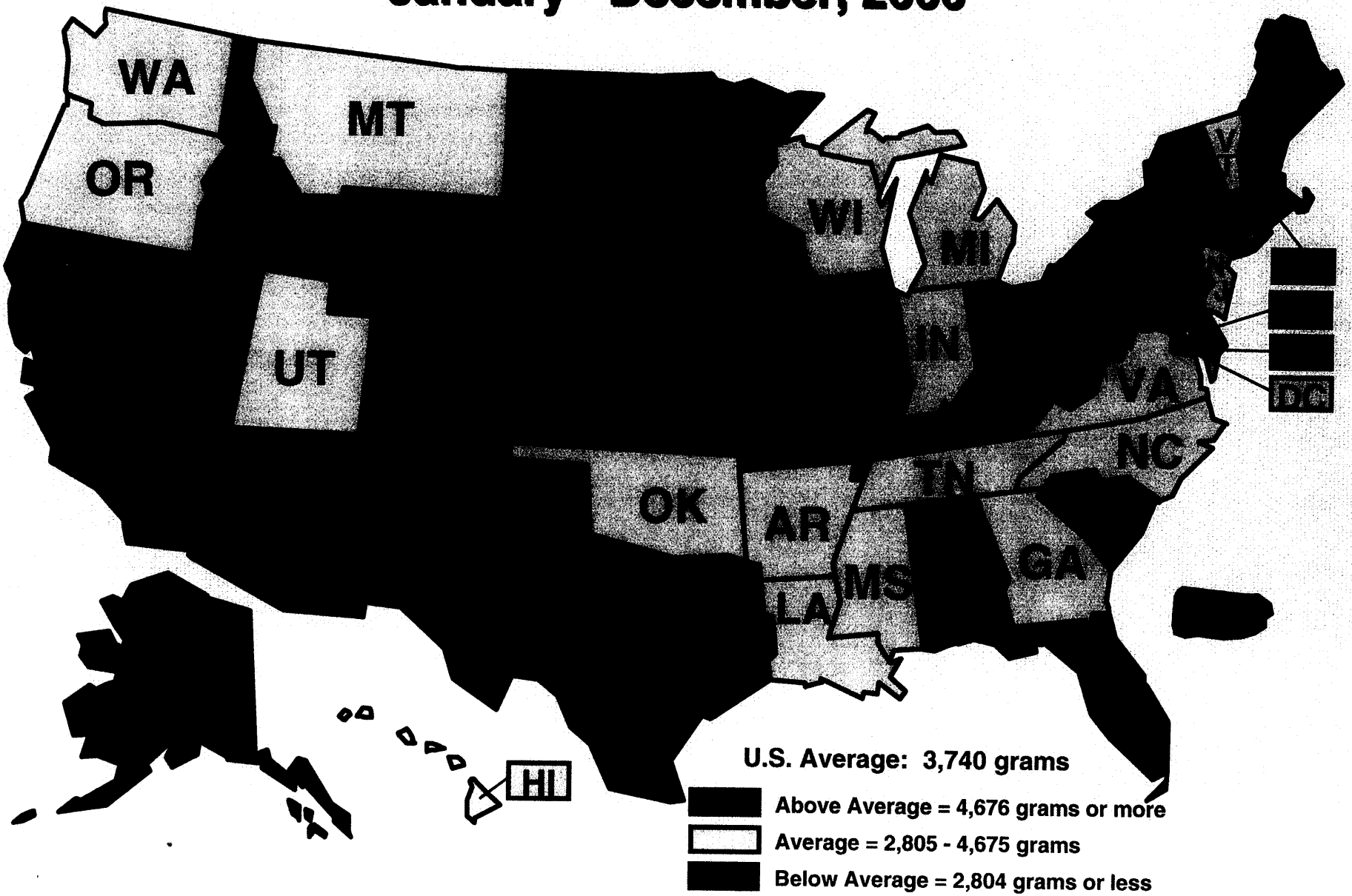
OxyContin Consumption per 100,000 Population
January-December, 2000

USA

Virginia

OxyContin Consumption Per 100,000 Population

January - December, 2000



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

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DRUG NAME: OXYCONTIN

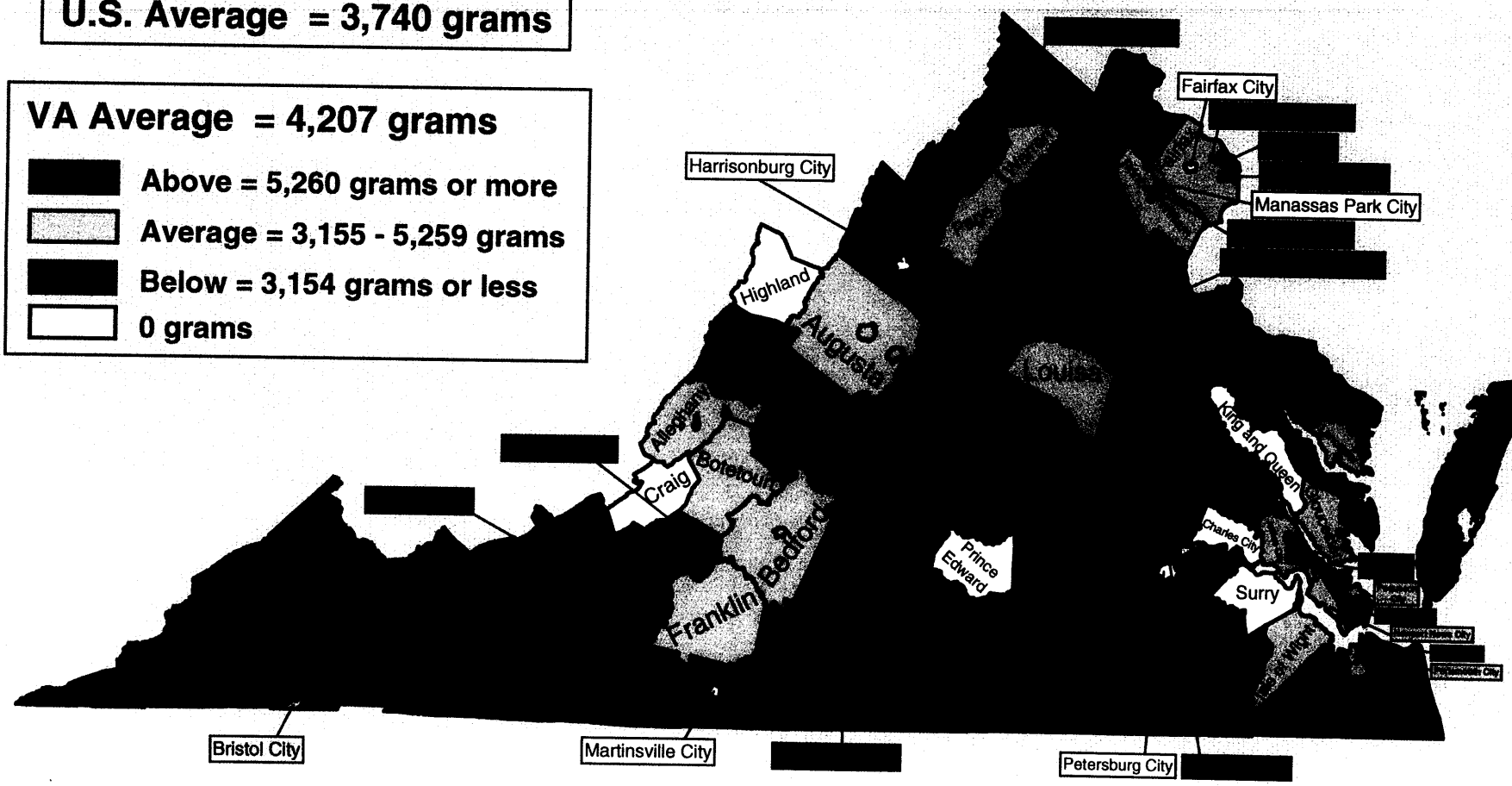
RANK	STATE	POPULATION	GRAMS TO DATE	GRAMS/100K POP. TO DATE
42	MINNESOTA	4,806,626	102,590.70	2,134.36
43	NEBRASKA	1,698,165	35,247.47	2,075.62
44	TEXAS	19,989,625	413,683.05	2,069.49
45	CALIFORNIA	32,432,678	637,119.27	1,964.44
46	NORTH DAKOTA	659,786	12,725.82	1,928.78
47	SOUTH DAKOTA	772,409	14,177.88	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
	U.S. TOTAL	277,749,273	10,388,225.10	3,740.14

State of Virginia
by County
2000 OxyContin Consumption
Per 100K Population

U.S. Average = 3,740 grams

VA Average = 4,207 grams

- Above = 5,260 grams or more
- Average = 3,155 - 5,259 grams
- Below = 3,154 grams or less
- 0 grams



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

Date Prepared: 07/24/2001

State of Virginia by County
2000 OxyContin Consumption Per 100K Population

Sorted by:	Grams Per	100K	
County	**Population**	**Total Grams**	**Grams Per 100K**
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
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

Date Prepared: 07/24/2001

State of Virginia by County
2000 OxyContin Consumption Per 100K Population

Sorted by:	Grams Per	100K	
County	**Population**	**Total Grams**	**Grams Per 100K**
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

Date Prepared: 07/24/2001

State of Virginia by County
2000 OxyContin Consumption Per 100K Population

Sorted by:	Grams Per	100K	
County	**Population**	**Total Grams**	**Grams Per 100K**
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
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		

Date Prepared: 07/24/2001

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 rondomized, 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.

Art Van Zee,MD
Lee Coalition for Health
10/1//2001

** Duragesic Pharmacokinetic studies

Attachment E

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.