IN THE DISTRICT COURT OF CLEVELAND COUNTY
STATE OF OKLAHOMA

STATE OF OKLAHOMA, ex rel., MIKE HUNTER, ATTORNEY GENERAL OF OKLAHOMA,	
Plaintiff,	Part 1A
vs.	**Case No. CJ-2017-816** **Judge Thad Balkman**
(1) PURDUE PHARMA L.P.; **(2) PURDUE PHARMA, INC.;** **(3) THE PURDUE FREDERICK COMPANY;** **(4) TEVA PHARMACEUTICALS USA, INC.;** **(5) CEPHALON, INC.;** **(6) JOHNSON & JOHNSON;** **(7) JANSSEN PHARMACEUTICALS, INC;** **(8) ORTHO-MCNEIL-JANSSEN PHARMACEUTICALS, INC., n/k/a JANSSEN PHARMACEUTICALS;** **(9) JANSSEN PHARMACEUTICA, INC., n/k/a JANSSEN PHARMACEUTICALS, INC.;** **(10) ALLERGAN, PLC, f/k/a ACTAVIS PLC, f/k/a ACTAVIS, INC., f/k/a WATSON PHARMACEUTICALS, INC.;** **(11) WATSON LABORATORIES, INC.;** **(12) ACTAVIS LLC; and** **(13) ACTAVIS PHARMA, INC., f/k/a WATSON PHARMA, INC.,**	**Special Master:** **William Hetherington**
Defendants.	

PLAINTIFF'S MOTION TO SHOW CAUSE FOR PURDUE'S NON-COMPLIANCE WITH COURT ORDER

A Court is powerless if it does not enforce its own orders. That is especially true when, as here, a litigant refuses to participate fully and fairly in the discovery process. And it is even more true when, as here, the Court appointed a discovery master—at this specific litigant's request ostensibly for the purpose of facilitating efficient discovery so that the case can get to trial—yet

the litigant that requested the discovery master defies his orders. Yet, that is exactly what is happening here.

The Court compelled Purdue to produce documents from other opioid cases and to produce sales training and education materials **four months ago**. ***Purdue has not complied with this Order***. Purdue has defied this Order. In fact, Purdue has not produced a single document since the case was remanded on August 3.

The State requested documents Purdue had produced in other litigations and criminal proceedings because they are highly relevant. The documents were previously produced in other matters. On March 9, 2018, the State first brought these requests to the Court's attention, and the Court stated: "That's easy to produce. I think we ought to do it." Hearing Transcript, Mar. 9, 2018 at 65:01-14. The Court gave Defendants an opportunity to specifically identify any documents they would not produce. *Id.* at 66:5-10. Purdue refused to identify any such documents beyond certain documents to which the parties agreed.

The State then filed a Motion to Compel, and the Court officially ordered Purdue to produce all such documents following Plaintiff's Motion to Compel on April 4:

> RFP No. 1 – State's motion to compel is sustained to the extent production shall include any information about public, nonpublic or confidential governmental investigations or regulatory actions pertaining to any Defendants that have been produced previously in any other case;
> RFP No. 2 – State's motion to compel is sustained with objections thereto overruled;

Order of Special Discovery Master on State's First Motion to Compel at 2. Following a motion for reconsideration, the Court then reiterated its Order to produce these documents on April 25:

> RFP No. 1 – Defendants' various motions to strike or modify are overruled subject to the previous ruling that Defendants must specifically identify any category of documents from other cases they intend to withhold as non-public or confidential governmental investigations or regulatory actions;

> RFP No. 2 - Defendants' various motions to strike or modify are overruled subject to the previous ruling that Defendants must specifically identify any category of documents from other cases they intend to withhold as non-public or confidential governmental investigations or regulatory actions.

Orders of Special Discovery Master on April 19th 2018 Motion Requests at 6.

The Court made it clear: Purdue must produce these documents. Four months have passed since the Court first compelled this production. Four months. That is almost one-third of the time the Court gave the parties to complete discovery. Purdue has defied the Court. Purdue has produced none of these documents. They are not producing them on a "rolling basis." They simply refuse to produce them.

This conduct is contempt of a Court order. There is no other word for it.

Regarding sales training and education materials, this information is highly probative to this case. Indeed, Purdue pled guilty to a federal felony related to how it trained and utilized its sales force to lie about the addictive nature and efficacy of Oxycontin. The Court compelled that these documents be produced in April. *See id.* at 6-7. Purdue has produced some of these documents but not all of them. Further, since Purdue fraudulently removed this case, it stopped any effort to conduct a "rolling" production of these documents. Purdue has not produced any such documents in nearly three months. For example, Purdue has never produced its budget plans from the early years of its OxyContin marketing strategies. The State had to find those independently. The documents directly relate to Purdue's sales and marketing tactics and training. *See* Exhibit A. The 2001 plan states Purdue will continue to "aggressively promote[] [OxyContin] for use in the non-malignant pain market." *Id.* at PP00265. Purdue's objective was to "Convince MDs to prescribe" OxyContin and to "[c]onvince health care professionals... to aggressively assess and treat both non-cancer pain and cancer pain." *Id.* at PP00266. Purdue acknowledges in the document that it supported the JCAHO initiatives and pain standards that the White House

Opioid Commission finds is partially at fault for the opioid epidemic. *See id.* at PP00260; Exhibit B at 9, 21. Thus, the documents are responsive and should already have been produced as part of Purdue's sales training and marketing materials.

Additionally, the budget plans appear to have previously been produced in other cases; they have what looks like a Bates number. *See, e.g.*, Exhibit A. And, one website on which they remain publicly available identifies them as having come from an investigation by the Florida Attorney General.[1] Based on the time period, they were likely also produced as part of the Kentucky litigation. Purdue still has not produced the Kentucky documents even though they contain a deposition transcript of the infamous Richard Sackler. In short, these budget plans are responsive to several requests the Court compelled but Purdue has never produced them. Nor has Purdue produced all of the documents related to how it trained its sales representatives to "aggressively promote" these drugs and convince doctors to prescribe them.

Instead, Purdue has complained during depositions about the State's use of the publicly available versions of the documents, claiming they are incomplete or misleading and they would object to their use. Indeed, during a recent deposition, Purdue's counsel stated that he did not know what the document was, complained about pages missing (many of which were apparently redacted by Purdue originally) and stated he would have to "raise a lot of objections." While the State opposes such objections, they potentially impact the significance of any testimony the State elicits on this highly important document. The State needs these documents to effectively cross-examine witnesses on their contents. Had Purdue produced them as ordered by the Court, no such objections would have been raised based on the source of the documents during the deposition. Moreover, Purdue has been ordered to produce such documents in this case. If Purdue wants the

[1] https://khn.org/news/purdue-and-the-oxycontin-files/.

State to use complete and unredacted versions, instead of what is available publicly, then it should produce them.

As the State has previously informed the Court, the State is in the process of deposing Purdue sales representatives. By the end of this week, the State will have completed three depositions of Purdue sales representatives. The State has subpoenaed nine additional Purdue sales representatives to testify between now and the end of September. The State has no choice but to proceed with depositions due to the rapidly approaching discovery deadline. But the State has had to take these depositions (and prepare for those to come) without these documents. Purdue is delaying production so that these witnesses cannot testify under oath regarding their contents. Purdue must produce these documents now and comply with the Court's Order.

Purdue will likely respond that they have already produced millions of pages. And, they will complain that the State has not produced enough. But, the State requested document production as soon as it filed this case a year ago. Purdue sought to delay discovery by six months—succeeded in doing so—and waited to serve the State with any requests during that entire time. And, while Purdue had a six month head start in this case but chose to do nothing, it had more than a 15-year head start with respect to gathering the documents at issue because it has had to respond to document requests from federal and state prosecutors and agencies regarding these very matters. Further, Purdue overstates the significance of the documents it has produced. The vast majority of documents Purdue has produced to date are documents it provided to the FDA.

More importantly, Purdue has blatantly ignored Court Orders regarding documents the Court already ordered Purdue to produce to attempt to obtain a strategic advantage. Purdue should be ordered to show cause as to why it should not be held in contempt and, failing to show cause, be ordered to immediately produce the documents. Otherwise, this Court's orders ring hollow.

And the Court runs the very real risk that no litigants, here or otherwise, will do what they are told.

Indeed, that is already happening here.

Dated: September 11, 2018

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2001

BUDGET PLAN

PP 00252

EXHIBIT

A

OxyContin® Tablets

Pages 4-28 through 4-37 redacted

II. ASSUMPTIONS

A. Market Overview

To date the market for OxyContin® Tablets consists of patients with both cancer pain and non-cancer pain. The non-cancer pain market is the significantly larger market. In 1999 sales of opioids were $1.7 billion for non-cancer pain compared to $261 million for cancer pain. The primary promotional focus will continue to be for OxyContin Tablets in non-cancer pain. However, due to the delay of the launch of HHER Capsules, as well as the potential for new competitive threats in the treatment of cancer pain, a renewed focus on cancer pain will be essential for protection of the oncology/cancer pain franchise. In addition, we expect that new single agent and combination analgesics will expand their promotion to nonmalignant pain as well.

The classic model utilized in the treatment of cancer pain is the World Health Organization (WHO) Three Step Analgesic Ladder. While treatment of non-cancer pain often varies by the specific pain state, and the use of opioids is much more controversial compared to cancer pain, some physicians use the WHO ladder as a guide for treatment of non-cancer pain. The recommendations of the WHO are:

Step 1: Use NSAIDs to treat mild pain, e.g., aspirin (ASA), acetaminophen (APAP), and non-steroidal anti-inflammatory agents (NSAIDs).

Step 2: Use weak opioids to treat moderate pain, e.g., codeine, oxycodone, and hydrocodone combinations.

Step 3: Use strong opioids to treat severe pain, e.g., morphine, hydromorphone, fentanyl, etc.

OxyContin Tablets are recommended and promoted for Steps 2 and 3 of the W.H.O. analgesic ladder. In addition, OxyContin Tablets should be initiated after NSAIDs, Tramadol or Cox 2 fail in patients with persistent around-the-clock pain of a moderate to severe nature who require opioid therapy. Physicians' understanding of the utility and appropriateness of OxyContin Tablets therapy for persistent pain lasting more than a few days will be essential to our efforts to compete with the Step 2 opioid combination products.

B. Fixed Combination Opioids

Prior to the introduction of OxyContin and MS Contin Tablets, oral opioid choices for treating moderate-to-moderately severe pain in Step 2 had been limited to combination products containing oxycodone, hydrocodone, codeine, and either ASA (example: Percodan®) or APAP (example: Percocet®). The short duration of action of these oral products causes peaks and valleys in blood levels, which can contribute to increased side effects and poor, inconsistent pain control. The short duration of

action is also problematic for patients who need around-the-clock dosing of their pain medication. Dosing every four-to-six hours does not allow a patient to sleep through the night, or participate easily in many normal activities. Even dosing every eight hours may interrupt activities or sleep. The combination of an opioid with APAP or ASA limits the number of tablets that can be prescribed because of potential liver or gastrointestinal toxicity. The APAP or ASA component also has the potential to mask fever in cancer patients and other patients with infections. All of these factors, associated with the choice of opioid analgesics in Step 2, as well as the large dollar and prescription volume of this class of drugs, provide a continuing opportunity for a single-entity, long-acting oxycodone product, OxyContin Tablets.

- Percocet®

  Endo Pharmaceuticals launched three new product line extensions between November 1, 1999 and February 1, 2000. Percocet 2.5/325 mg, 7.5/500 mg and 10/600 mg oxycodone/APAP opioid combination products were launched to capitalize on the growing success of oxycodone made possible by OxyContin Tablets.

C. Single Entity Opioids

Long-acting morphine and transdermal fentanyl provide physicians with two long-acting products to meet the needs of patients with moderately severe to severe pain as described in Step 3. However, these products possess disadvantages such as the stigma that surrounds morphine and the reluctance of physicians, nurses, and pharmacists to use them. They are also considered "potent" opioids, which physicians may be reluctant to prescribe until the pain is severe. Hydromorphone is considered a potent opioid analgesic, but has been limited in its use for chronic pain due to the need to dose it at least every six hours for consistent around-the-clock pain relief. OxyContin Tablets is now being utilized for severe pain, as evidenced by an increase in the sales volume of the 40 mg, 80 mg, and 160 mg OxyContin Tablet strengths during 2000.

The availability of the 160 mg dosage strength represents a significant opportunity for OxyContin Tablets to compete in the severe pain Step 3 analgesic ladder. The 160 mg tablet provides a competitive advantage relative to long-acting morphine and Duragesic, as well as being a barrier to entry for other long-acting opioids which may enter the market.

- MS Contin Tablets/Generic Sustained Release Morphine

  - MS Contin Tablets remains the gold standard for treating moderately severe to severe cancer pain (WHO Step 3). In fact, some physicians, particularly oncologists, continue to switch patients with more severe pain from OxyContin Tablets to MS Contin Tablets®. Many health care providers who can treat cancer pain continue to believe that MS Contin Tablets is more potent than OxyContin Tablets. This may be due in part to the transfer to OxyContin Tablets of the perception of Percocet as a weaker Step 2 drug. Faced with stiff competition from Duragesic®, Oramorph SR™, OxyContin Tablets and generic sustained-release morphine (Endo's AB rated generic), MS Contin Tablets prescriptions have decreased 15.6% (71,123) in 2000 year-to-date (January through June 2000) compared to the same time period in 1999.

  - MS Contin prescriptions, plus our generic prescriptions, have decreased 12.7% (60,681) 2000 year-to-date June compared to the same period in 1999.

  - Generic sustained release morphine continues to be an alternative that decreases the cost of opioid therapy with q12h dosing. An AB-rated generic to MS Contin is produced by ENDO. When distribution is adequate, it is likely that a "maximum allowable charge" (MAC) will be developed for MS Contin Tablets, increasing significantly the rate of substitution. To date the MAC has not occurred; however, it was proposed and delayed in 2000. In addition, generic MSER has now captured approximately 23.4% of the prescription volume of the long-acting morphine category.

  - All morphine sulfate distributed by ABG Labs was discontinued effective August 1, 2000.

- Duragesic

  Duragesic is another competitor to OxyContin Tablets. Janssen has been targeting the moderate-to-moderately severe pain market for the past two to three years. Their progress has been slow but steady in obtaining patients coming directly from fixed combination opioids, as they stress convenience, less side effects (particularly constipation), and increased quality of life. In 2000 Janssen is seeking to replace Percocet, OxyContin Tablets and MS Contin Tablets prescriptions. Janssen is expected to gain FDA approval for a 12.5 mcg patch, in 2000/early 2001. It is expected to be targeted to the early treatment of non-cancer pain and pain in the frailer elderly patient.

  Field reports have revealed at least one direct head-to-head study of Duragesic and OxyContin Tablets in nonmalignant pain. In addition, Janssen was asked by the

FDA in 2000 to remove Propulsid®, a G.I. motility drug with sales in excess of $1 billion U.S., from the market. This has produced a renewed focus on Duragesic by Janssen, and the weekly prescription volume for Duragesic continues to reach new records.

Janssen has a dedicated sales force targeted specifically to the long-term care (LTC) market. In addition to marketing Duragesic, they are promoting Ultram® for Ortho-McNeil in this market. Ultram is provided as a Step 1 to Step 2 analgesic, while Duragesic is promoted as a Step 2 to Step 3 analgesic.

Janssen has been stressing decreased side effects, especially constipation, as well as patient quality of life, as supported by patient ratings compared to sustained release morphine. We do not have such data to support the OxyContin promotion. They have expanded their patient preference claims to oral opioids. In addition, Janssen has been using the "start with...stay with" message in promotion of Duragesic for noncancer pain.

Due to the above initiatives, it is probable that Janssen will continue to target primary care physicians (internists and selected family practice physicians), as well as oncologists. We estimate that their 2000 journal spend will be approximately $680,000 based on $170,000 in journal spend January-March 2000. This compares to $2,210,000 spent in 1999.

Market Research

Market research from recent focus groups continues to show that Duragesic is perceived to be less effective than MS Contin Tablets and, in most cases, OxyContin Tablets. It is also perceived by physicians to have a slow onset of action, lacking the ability to be titrated quickly, and not considered cost effective. We will be taking advantage of these Duragesic weaknesses in our 2001 OxyContin Tablets promotions.

- Kadian®

In 2000 Faulding continued active promotion of Kadian. The promotion of Kadian centers on its 24-hour dosing, its sprinkle formulation, and cost effectiveness. In addition, Kadian added the indication for use in NG tubes and began promotion in 2000. Due to these features Kadian is being positioned as a better alternative to MS Contin Tablets.

Faulding's main program to support Kadian has been the continuation of their "sample" program with a free supply of Kadian at the retail pharmacy through use of a special coupon and the patient's prescription.

Kadian prescriptions have increased 53% (+6,616) year-to-date 2000 through June compared to the same period in 1999. On average, Kadian prescriptions remain at 2,715 per month for the time period July 1999 through June 2000. Recent weekly data indicate a sharp increase in Kadian prescriptions. This is due mainly to the introduction of color-coded capsules.

- Oramorph SR

Roxane is expected to continue promotion of Oramorph SR by positioning it as a cost-effective alternative to MS Contin and OxyContin Tablets. Individual Roxane representatives are also promoting Oramorph SR as a cost effective alternative to OxyContin Tablets, utilizing a 1:1 conversion of morphine to oxycodone.

During 2000 Roxane continues an Oramorph SR promotion that combines promotion of their pain products with other palliative care products under a Roxane Palliative Care Products umbrella.

As a result of the continued promotion of Oramorph SR versus MS Contin, Oramorph SR prescriptions increased 22.4% (+24,008) YTD through June 2000, compared to the same period last year. It is important to note that the absolute numbers for the category are growing in 2000.

- PCA Pumps

During 1999 sales of injectable morphine were $73,119,000. The 2000 year sales of injectable morphine are forecasted for $78,441,000, an increase of approximately 7.3%. Market research lists PCA pumps as a form of cancer pain management used (along with MS Contin Tablets and Duragesic) when OxyContin Tablets is perceived to be ineffective, or no longer tolerated. While a percentage of the patients changed to PCA pumps may not be able to swallow, it is likely that a number of patients were switched to a PCA pump strictly due to lack of perceived OxyContin Tablets efficacy, or reimbursement issues.

Medtronics has been aggressively promoting their implantable pump (Synchoromed) in the hospice market, as well as for other chronic pain patients. For non-hospice patients reimbursement issues can play a role. Medicare will pay for pump implantation as well as the medication refills. Medicare does not reimburse for oral analgesics like OxyContin Tablets; however the debate regarding a Medicare drug benefit in Congress has heated up in 2000.

In the post-operative patient OxyContin Tablets are positioned for post-PCA pain management. A clinical study (Ginsberg) has supported OxyContin Tablets use in the post-operative patient. However, the planned program to capitalize on the addition of postoperative use to the P.I. has not been launched because of a

delay in the project. Abbott Pharmaceutical has the main responsibility for promotion in this market. Recently, Abbott signed an agreement with Knoll Laboratories to promote Vicoprofen® for acute postoperative pain.

D. OxyContin Future Opportunities

- OxyContin 160 mg Tablet

  FDA approval of OxyContin 160 mg Tablets was received in March of 2000. Currently, almost 46% of OxyContin 80 mg Tablet prescriptions are for the management of non-cancer pain. Although the targeted promotion of the 160 mg OxyContin Tablet will be in non-cancer pain, this new strength provides an opportunity to protect the cancer pain market for OxyContin. The 160 mg tablet also provides an entry barrier for impending competition in the cancer market, as well as the severe non-cancer pain market based on the ability to "stay with" OxyContin Tablets for escalating pain.

- JCAHO Pain Management Initiative

  In June 2000 JCAHO (Joint Commission for the Accreditation of Health Organizations) approved the final phase of the proposed pain standards. Scoring related to the pain standards will begin in January 2001. Purdue supported the educational efforts of the JCAHO in an exclusive agreement throughout 2000 by supporting two pain summits and three educational efforts, including a video on the "Continuum of Care," a pain education book, and a media education campaign for the JCAHO pain standards with unrestricted educational grants. Another significant opportunity presents itself in 2001 for Purdue to support the efforts of JCAHO. This initiative represents an opportunity to provide true value-added education on pain management and, at the same time, continue Purdue's leadership in pain management. As a whole, the JCAHO initiative has provided the field force with many door-opening opportunities to conduct in-service presentations and to position OxyContin appropriately for pain.

E. Expected Entries

- MorphiDex™

  Algos Pharmaceuticals expected to launch MorphiDex in August of 1999. The FDA issued a nonapproval letter August 2, 1999. This product was expected to claim equally effective analgesia at a lower number of milligrams of morphine, due to the potentiating effects of the dextromethorphan. It appears unlikely that a claim of less development of tolerance to the analgesic effects, compared to morphine alone, will be given based on the clinical data we have seen to date. However, it is expected that Algos will discuss the research supporting NMDA

inhibitor's impact on the development of tolerance to analgesia and allow the health care practitioner to make the transition to MorphiDex. It is likely that MorphiDex will be promoted for malignant and nonmalignant pain.

Algos merged with Endo Pharmaceuticals. Pending new clinical data in support of MorphiDex, it is anticipated that Algos/Endo will refile the NDA for Morphidex in 2001.

An additional promotional message will be geared to physicians' desire for a pain medication with the effectiveness of an opioid with less side effects. A claim of less opioid side effects, due to lower morphine milligram quantities, may be expected. Physicians reported in market research that a decrease of 25% or more in opioid related side effects would be significant enough for them to change their opioid prescribing habits. However, even a smaller percent difference is likely to have some impact on prescribing habits.

The dosing interval for MorphiDex is likely to be q6h or q8h. This is not a sustained release product, but rather the expansion of duration of effect of the immediate release morphine by the dextromethorphan. It is likely that Algos/Endo will also promote MorphiDex for nonmalignant pain.

- Roxicodone SR™

The launch of Roxicodone SR by Roxane Labs has been delayed due to successful litigation based on patent infringement of OxyContin Tablets.

- Dilaudid SR

Knoll Pharmaceuticals received an approvable letter for controlled-release hydromorphone in early 2000. It is anticipated that this Oros® formulation of a once daily hydromorphone will be launched in the first or second quarter of 2001. Dilaudid SR poses the biggest threat to OxyContin to date. In 2001 the following challenges are anticipated:

- It is anticipated that Dilaudid SR will be available in 8 mg, 16 mg, 32 mg, and 64 mg once-daily tablet strengths.

- The promotion of a 5:1 morphine to hydromorphone conversion will match each of the OxyContin dosage strengths including the 160 mg tablet.

- It is likely that initial promotions will target cancer pain due to lower market entry barriers and acceptability of hydromorphone in the treatment of cancer pain.

- Knoll may employ the use of a co-promotion sales force which has a presence in both oncology and primary care.

- Subsequent promotion will target high prescribers of hydromorphone and OxyContin in the treatment of non-cancer pain.

- The q24h dosing of a single entity hydromorphone from the Palladone research indicates that Dilaudid SR will have great market acceptance if it delivers the q24h pain control.

The promotional objective for OxyContin Tablets will be to minimize the market penetration of Dialudid SR in both cancer and non-cancer pain, protect OxyContin Tablets from potential market erosion, and enable continued growth of OxyContin Tablets in both the cancer and noncancer pain markets. The delay in availability of Palladone XL may allow Knoll to obtain a first mover advantage, undermining our own expectations in this category.

- Ziconitide

  An NDA on a fast track status for Ziconitide (SNX-111) was submitted, and approval of this entity was received in July 2000. Ziconitide is marketed by Elan. Initially, this product will only be available for epidural use. It is expected that Ziconitide will be indicated for intractable neuropathic pain. Ziconitide will present a challenge to OxyContin by competing for neuropathic pain patients, who are currently on high doses of opioid to treat their pain. Ziconitide will be prescribed by anesthesiologists who are aggressive pain treaters employing the use of the implantable pump.

F. Managed Care

MCOs have adopted three-tiered formularies to encourage the use of generics and less expensive, preferred brands. As drug costs continue to rise, MCOs are finding ways to share costs. Three-tiered copayments require consumers to pay out of pocket for a drug of choice. In a typical formulary structure generic drugs are in the lowest tier, formulary brands are in the middle tier, and nonformulary brand products are in the highest tier. Drugs in tier 1 cost the consumer an average of $5 to $10; drugs in tier 2 cost $15-$20, and drugs in tier 3 cost $35-$40.

OxyContin must maintain its brand name formulary status to eliminate the threat of a $35-$40 per prescription cost to the consumer, who in turn may request a generic alternative. Three-tiered financial incentives encourage physicians to write less expensive products, even when a more expensive product is clinically superior. Clinical presentations must be supported with an economic message such as reducing long-term costs.

G. Abuse/Diversion

In 2000 OxyContin Tablets experienced significant challenges regarding its abuse and diversion in the states of Maine, Ohio, Virginia, Louisiana, and Florida. These challenges will continue to be a threat to the continued success of OxyContin Tablets. Educational and public relations efforts will continue in 2001 with a focus on provider education to recognize patients in need of substance abuse counseling and on actions they can take to prevent abuse and diversion.

III. PRODUCT INITIATIVES

A. Objectives

- To achieve $1.4 billion in factory sales.
- To protect our market share from new competitors.
- To continue to expand OxyContin Tablets use in the non-malignant pain market by positioning it as the opioid to "Start With and Stay With."
- To establish OxyContin Tablets as the opioid of choice in Step 2 of the WHO analgesic ladder by positioning it as the opioid to "Start With" for cancer and non-cancer pain management.
- Continue to establish OxyFAST® and OxyIR® as the ideal medications for breakthrough and/or incidental pain for patients on OxyContin Tablets.
- Effectively position OxyContin Tablets 160 mg for high dose cancer and non-cancer pain patients.
- Enhance the acceptance of opioids for non-cancer pain through educational efforts.
- Continue to educate physicians on actions they can take to limit abuse and diversion.
- Increase the use of OxyContin Tablets in the mature patient, with new clinical data on osteoarthritis.
- Increase the use of OxyContin Tablets in acute and sub-acute conditions (e.g., post-op pain, trauma, and fractures) where pain lasts more than a few days.

B. Product Attributes/Core Messages

- The analgesic efficacy of immediate-release oxycodone. The familiarity of physicians with oxycodone is an important part of the message and has led to rapid acceptance. This familiarity is a principal factor that should lead to continued growth of OxyContin Tablets.
- Onset within one hour, comparable to immediate-release oxycodone. Recent market research focus groups, discussing product attributes, indicated OxyContin Tablets is perceived as being very effective, with a lower side effect profile than its competitors and with a favorable dosing schedule. The onset of action message is very important in the post-operative pain market.
- When an opioid naïve patient needs an opioid analgesic, physicians should prescribe OxyContin Tablets. The many benefits of OxyContin Tablets make it logical as the opioid to start with (for patients who would otherwise be started on Percocet, Lortab®, Vicodin®, Tylenol® #3 or Darvocet®, WHO Step 2), and the opioid to stay with through proper titration as the disease progresses.
- One to stay with. In 2000 OxyContin Tablets has been marketed for moderate to severe non-cancer pain. The primary strategy in the non-cancer pain market will be to establish OxyContin Tablets for a broader range of use than is available to combination opioids. OxyContin Tablets will be positioned as an opioid

physicians can initiate and patients can stay with through the entire course of therapy.

- Effective in non-malignant pain states. In 2001 OxyContin Tablets will continue to be aggressively promoted for use in the non-malignant pain market. The most common diagnoses for non-malignant pain are back pain, osteoarthritis, injury, and trauma pain. The major competitors for these diagnoses will be oxycodone and hydrocodone combination products. OxyContin Tablets will be positioned as providing the equivalent efficacy and safety of combination opioids, with early onset of pain relief and the benefit of a q12h dosing schedule. The promotional efforts will focus on specific disease syndromes such as back pain, osteoarthritis, reflex sympathetic dystrophy, trauma/injury, neuropathic type pains, etc.
- A single agent with no acetaminophen, aspirin, or ibuprofen. OxyContin Tablets is a single entity opioid agent without the dosing limitations present in products that are fixed combinations of an opioid and a second agent such as acetaminophen, aspirin, ibuprofen, or dextromethorphan. There is added dosing flexibility with a single agent, since a variety of co-analgesics and adjuvant medications can be used to enhance the individual patient's pain relief, while having the freedom to dose OxyContin Tablets as high as is clinically necessary. There is also a decreased risk of side effects, or organ toxicity, compared to products containing acetaminophen, aspirin, or ibuprofen.

C. Competition

- Combination opioids, (oxycodone, hydrocodone, codeine, and propoxephine with APAP, ibuprofen, or ASA): moderate-to-moderately severe pain (Step 2 of the WHO ladder), including the Percocet 2.5 mg, 7.5 mg, and 10 mg.
- Ultram SR: non-cancer pain.
- Duragesic: cancer and non-cancer pain. Duragesic 12.5 mcg. patch in non-cancer pain.
- Actiq: Fentanyl oralette used for breakthrough cancer pain.
- Methadone: Market research, as well as reports from the sales force, indicate that methadone use is increasing in both the management of cancer pain and non-malignant pain due to its low cost. Clinical studies have also been published over the last year regarding the effective use of methadone for cancer pain management. While not yet a serious competitor, this trend needs to be monitored.
- MorphiDex: As noted earlier, this product may become a competitor in the future, although its future is quite uncertain at this time.
- Generic morphine sulfate extended release

D. Communication Objectives

- Recently completed clinical trials in osteoarthritis have produced significant data for OxyContin Tablets. Future promotional objectives will be to communicate this data to health care professionals.
- Convince MDs to prescribe, (as well as RNs and appropriate pharmacists to recommend), OxyContin Tablets, instead of combination opioids for opioid-naïve or opioid-exposed patients with moderate-to-severe pain lasting more than a few days. Through proper dosing and titration, eliminate or delay the need for other long-acting opioids.
- Broader OxyContin Tablets usage among various pain syndromes (e.g., back pain, osteoarthritis, neuropathic pain, post-operative pain, etc.) will be stressed.
- Convince health care professionals (physicians, nurses, pharmacists, and managed health care professionals) to aggressively assess and treat both non-cancer pain and cancer pain. The positive use of opioids will be stressed, with particular emphasis on OxyContin Tablets.
- Convince patients and their families to actively pursue effective pain relief. The importance of patients assessing their own pain and communicating the status to the health care giver will be stressed.
- Educate physicians regarding abuse and diversion issues.

E. Evolution of OxyContin Tablets

OxyContin Tablets is expected to achieve $942 million in factory sales in 2000. Given the new millennium and the significant achievement of the OxyContin Tablets brand, it is important to examine the history of OxyContin Tablets in order to understand the future of the brand.

Campaign Evolution

The initial launch of OxyContin Tablets in 1996 was successful with a promotional campaign focusing on "The Old Way, the New Way" along with a core message of "The Opioid to Start With and Stay With." In 1997 the OxyContin Tablets promotional campaign focused on "The Hard Way, The Easy Way." Both of these promotional campaigns targeted the "Start With" message, which was vital to the success of OxyContin Tablets. In 1998 OxyContin Tablets continued a rapid growth phase and market expansion with the "Patient Profiles" campaign, which utilized patient types from the clinical study data in a profile format to support the expanded utility of OxyContin Tablets. This campaign focused mainly on non-cancer pain. In 1999, facing the eminent launch of MorphiDex, the OxyContin Tablets promotion campaign shifted to "Keep It Simple." The message of the Keep It Simple campaign was to specifically address the issue of the irrational combination of a fixed amount of morphine and dextromethorphan in MorphiDex. This targeted "Keep It Simple" message was directed to anesthesiology and oncology in an effort to block acceptance of MorphiDex in these specialties. The "Keep It Simple" OxyContin

Tablets promotional campaign continued in 2000 and capitalized on the growing acceptance of aggressive pain treatment and widespread acceptance of the benefits of OxyContin Tablets over fixed combination analgesics. In light of future competition, 2001 will prove to be a challenging year. There is a growing need to keep the promotional campaign focused by building on the proven effectiveness of the ability of OxyContin Tablets to "meet the challenge" of moderate to severe pain patients.

Promotional Initiative Evolution

OxyContin Tablets began a market penetration campaign in cancer pain. This was imperative based on acceptability of oxycodone in cancer pain. In addition, this initiative was imperative to penetrate the barriers by managed care organizations.

After the initial penetration phase and widespread formulary acceptance of OxyContin Tablets by Managed Care, the promotional initiative focused on market expansion in noncancer pain through aggressive promotion and education on proper pain management. In addition, the American Pain Society and AAPM introduced a position paper on the aggressive and appropriate treatment of nonmalignant pain, employing the use of opioids. Purdue continued the growth of OxyContin Tablets by educating physicians on the benefits of OxyContin Tablets in non-cancer pain through patient profiles and case studies. Patients who had suffered for long periods of time were soon telling their physicians that OxyContin Tablets "gave me my life back."

In 1998 and 1999 the aggressive promotional initiatives for OxyContin Tablets continued. Facing a potential threat from MorphiDex and Roxicodone SR, the promotional efforts also employed an initiative to create market entry barriers to these new competitors. **Near the end of 1999 and through the year 2000, additional corporate initiatives and partnering efforts were very successful with the Veterans Administration, American Pain Society, and JCAHO in an effort to make Pain: The 5th Vital Sign. This "call to action" was an important promotional initiative for Purdue. In addition to building sales for OxyContin Tablets, it also positioned Purdue as the leader in pain management education.**

Competitive Evolution

The competitive marketplace continues to evolve for OxyContin Tablets. Initial competitive threats to OxyContin Tablets include MS Contin Tablets, Oramorph SR, Kadian, and Duragesic in the cancer market. As OxyContin Tablets continued to grow in non-cancer pain, competitive threats included short-acting combination hydrocodone and oxycodone preparations. New combination and single entity products (MorphiDex and Roxicodone SR) continue to threaten OxyContin Tablets.

Going forward in 2001 and 2002 many new competitors will enter the OxyContin Tablets market. The most serious competitive threats to date for OxyContin Tablets will be Dilaudid SR. The single entity 24-hour dosing of hydromorphone in Dilaudid SR may have some advantages over OxyContin Tablets. The market research data from Palladone XL shows a high level of market acceptability of this potential new competitor. In addition, new long-acting single entity opioids and other nonopioid entities, such as Ziconitide, will be a future threat to OxyContin Tablets.

Future Evolution of OxyContin Tablets Brand

In spite of impending competitive threats, the future for OxyContin Tablets is very bright. Future growth of OxyContin Tablets will be achieved through targeted efforts to penetrate:

- Rheumatology
- OB/GYN
- Dentistry
- Physician Assistants and Nurse Practitioners
- Surgical
- Oncology
- Dentistry
- Sports/Physical Medicine/Rehabilitation

The promotional campaign utilized to achieve further market penetration in the above-mentioned categories will be a pronouncement of the widespread success of the OxyContin Tablets brand to treat various pain states. A focus on the wide clinical use and acceptance (documented by NDTI) will be the bridge used to raise awareness and interest in OxyContin Tablets. In addition, a focus on intermittent versus persistent pain will be a key positioning tactic used to gain physician starts with OxyContin Tablets. A continued focus on the benefits of around-the-clock pain control with the flexibility of q12h dosing will be critical to differentiate OxyContin Tablets from current and future competitors. The flexibility of q12h in terms of patient titration along with the analgesic onset and quality of life claims will be expanded and reinforced.

Market research data (NDC Health Information Services data) indicates that among OxyContin Tablet patients, 42% were opioid naïve when initiated therapy on OxyContin Tablets. In addition, 58% of OxyContin Tablet patients were on a prior opioid or opioid-like analgesic when initiated therapy with OxyContin Tablets. Among those OxyContin Tablet patients who were on a prior therapy, 72% of patients were on combination opioids containing hydrocodone or oxycodone.

It will be imperative for the promotional focus of OxyContin Tablets to emphasize the "Start With" message. Market research (NDC) data also indicates that physicians are less likely to switch opioid therapy in patients who have been

initiated on opioids to control their pain. This is further evidence of the importance of the OxyContin Tablets "Start With and Stay With" promotional theme.

The "Start With" message in non-cancer pain will focus on patients whose pain is currently not controlled on NSAID/Cox-2 medications or combination opioids taken on a p.r.n. basis. OxyContin Tablets provides the logical next step in these patients based on their persistent or around-the-clock pain. The "Start With" message in cancer pain will focus on patients who are uncontrolled on p.r.n. combination opioids or maximum doses of Ultram SR.

The "Stay With" message in non-cancer pain will focus on the value of OxyContin Tablets in improving quality of life, mood, and sleep. In addition, the clinical data with OxyContin Tablets supports our claims of no significant tolerance development. Tolerance is a great barrier for most physicians who have concerns relative to the use of opioids in chronic non-cancer pain. The "Stay With" message in cancer pain will be focused on the availability of the 80 and 160 mg dosage strengths. The flexibility and convenience of these dosage strengths allows OxyContin Tablets to be titrated to "meet the challenge in cancer pain."

F. Target Audiences

1. Primary Audiences

Audiences	Site	Targets	Frequency	Comments	Total Calls Required
A. Physicians (Primary) • IMs • FP/GPs • DOs • ANS • Oncologists • Surgeons • Physical Medicine • Neurologists • Rheumatologists • OB/GYN • Other	• Office and Hospital	80,000 77,358	10 6	Target List Contains 100% of decile 10 and 50% of decile 9 combo and single entity unique prescribers Target List Contains 50% of decile 9, and 100% of decile 8 combo and single entity unique prescribers.	800K 464K
B. Nurses (Secondary) • ONC RNs • Nurse Practitioners • Physician Assistants	• Hospice • Home Care • Office • Hospital	27,000			
C. Managed Care Organizations • Directors of Pharmacy • Clinical Pharmacists • Case Managers • Quality Assurance Managers • Other	• Managed Care Facilities	TBD		• PBMs • IPAs • Staff Models • IHN	
D. Long-Term Care • Consultant Pharmacists • Nursing Home MDs and RNs	• Long-Term Care Facilities	6,000 10,000		Influential decision-makers at LTC facilities and corporate level nursing home chains	

2. Secondary Audiences

Secondary Audiences	Site	Targets	Comments
A. Patients and Caregivers			
B. Residents/Fellows	Teaching Hospitals	TBD	Provides the ability to influence physicians still in training. Chief residents can be especially influential in teaching facilities.
C. Wholesalers		150	
D. Pharmacies	• Hospital • Retail	6,000 60,000	To assure appropriate stocking of the five dosage strengths.

VI. TACTICS

A. Sales Force Allocation

The deployment of our most valuable and substantial promotional resource, the sales force, is critical to the continued success of OxyContin Tablets. Heavy promotional support will continue in order to ensure appropriate awareness of OxyContin Tablets in the opioid market.

Due to the launch of Ultram SR, 50% of the calls to oncologists and surgeons will be allocated to OxyContin Tablets. OxyContin Tablets will remain the primary product accounting for 100% of calls on all other specialties, with the exception of anesthesiology, where OxyContin Tablets will account for 70% of primary calls.

The share of voice for OxyContin Tablets among anesthesiology will be critical to the continued success. The physicians in this important specialty are the innovators and early adopters of new products and technology. An effort to remain the dominant voice with anesthesiologists will prevent market penetration by future competition.

B. Representative Delivered Promotional Materials

Wholesalers/Chain Headquarters (National Account Managers)
Contacts will be made with wholesalers to ensure that there are appropriate inventory levels for the 10 mg, 20 mg, 40 mg, 80 mg, and the 160 mg strength tablets. Adequate inventory levels of OxyIR and OxyFAST will also be ensured.

Pharmacies
Representatives will call on chain and independent retail stores to make sure there is adequate stocking of the OxyContin Tablets strengths, with particular emphasis on increasing distribution of the 40 mg, 80 mg, and the 160 mg strength. Representatives will also continue to increase the distribution of OxyIR and OxyFAST at the retail level.

Hospitals
In an effort to continue gaining hospital formulary acceptance of OxyContin Tablets, representatives will work with their Abbott counterparts to make calls on all Pharmacy and Therapeutic (P&T) committees.

The hospital formulary kit and product data brochure will be utilized by the sales force to provide the appropriate clinical data necessary to continue to add OxyContin Tablets to hospital formularies. In addition, representatives will continue to use the OxyContin Tablets tabletop hospital display panels. Speakers' Bureau lectures will be conducted during grand rounds, tumor boards, etc. The focus of these presentations will be the addition of OxyContin Tablets to the analgesic treatment armamentarium.

JCAHO (Joint Commission Agency that accredits hospitals) will continue to be a major initiative focusing on pain assessment and treatment. Purdue has taken a major leadership role in helping hospitals meet the JCAHO requirements in this area through the development of pain assessment and pain management materials geared to the hospital setting.

Managed Care Organizations

Managed Care Account Executives will target all major PBMs and IPA plans where OxyContin Tablets are not on formulary. They will also promote the formulary inclusion of OxyIR and OxyFAST, as well as adding the 160 mg strength of OxyContin Tablets. P&T committee members will be provided with formulary kits and product data brochures.

The Partners Against Pain® program will continue to be expanded for the managed care market, providing customized materials to meet their needs. Educational materials will be offered to managed care organizations with their plan "indicia" printed on them. Consultations with pain management specialists, etc. are being explored as a possible value-added service offered through the Partners Against Pain program.

C. Direct Mail/E-Detailing

Mailings

A number of mailings are planned to support OxyContin Tablets in 2001. Mailings will be done to support key OxyContin Tablets messages following the launch of Dilaudid SR as well as to support the use of OxyContin Tablets in treating non-cancer pain, with a focus on quality of life. In addition, Internet detailing initiatives will be directed to targeted physicians to support representatives' efforts.

Representative Follow-up Mailings

Representatives will be able to send follow-up mailings to MDs and RNs after making a call. This will be accomplished through the Quest® system.

D. Journal Advertising

The journal ad for OxyContin Tablets will focus on "meeting the challenge" as well as the patient profile campaign for non-cancer pain management. This humane, quality of life look, with pictures of patients with their pain under control with OxyContin Tablets, will discuss specific pain states. This will be a component of our Patients' Profiles campaign that highlights specific pain states, such as osteoarthritis and low back pain. The journal schedule and publications used will be chosen based on important specialties for treating cancer and non-cancer pain.

E. Conventions

The OxyContin Tablets exhibit structure will feature graphic panels of the OxyContin Tablets core creative concept as seen in our journal ads and visual aids. Panels highlighting specific pain states from our Patients' Profiles campaigns will be utilized at appropriate conventions. For example, a panel highlighting the use of OxyContin Tablets for osteoarthritis will be utilized at primary care conventions, as well as the rheumatology and consultant pharmacist conventions. Various promotional activities will be conducted at the booth to draw attendees into a discussion with our representatives about OxyContin Tablets.

F. 2001 Consumer Initiatives

NEW

The 2001 consumer non-branded initiative program is designed to increase the number of chronic pain patients who speak with their physician about their pain and seek effective treatment. This will be accomplished through tactics that raise the level of discussion between health care professionals and consumers about the right to adequate pain relief and the availability of effective pain relief options.

The program will continue to build and strengthen ongoing relationships with consumer and medical trade and third-party affiliates in 2001. The primary focus, however, is consumer-based for the following reasons:

- Consumers want information that empowers them to make informed choices about the issues affecting their lives. They want to feel informed and in control when reviewing alternatives. They want to understand what their health care options are and participate in the decision making process. By educating consumers about their right to adequate pain management, available pain management therapies, myths and misconceptions about addiction and tolerance and the types of questions they should be asking their physician, the program provides them with the information they need to have a voice in their treatment options.
- More than half of chronic pain patients currently initiate dialogue with their physician about their pain management. However, there is still a large percentage that relies on their health care professional to begin the conversation. If the health care professional is uncomfortable discussing pain management or doesn't recognize its value, the patient will remain under-treated. This reinforces the need for the consumer initiatives program to provide patients with the information they need to feel comfortable when talking with their health care professional.
- JCAHO has issued new evidence-based pain management standards to ensure that health care providers respond appropriately to patients' pain, an initiative that educates a segment of the physician population currently prescribing Purdue Pharma product. These standards require that every patient has the right to seek and receive appropriate pain assessment and management. Adherence to the

Joint Commission (JCAHO) standards will provide a framework for patients to receive appropriate pain management. Effective pain management is expected as part of the optimal achievable care represented by JCAHO accreditation. Health care professionals working at a JCAHO accredited facility must adhere to JCAHO's guidelines for effective pain management.

- Purdue Pharma's corporate goal is to be one of the Top 10 pharmaceutical companies by 2010. This goal can be measured both in terms of sales and image or professional standing within the industry and community. High visibility consumer initiatives that focus a positive spotlight on the company will enhance its image and reputation, as well as build its sales. Porter Novelli believes that the consumer-directed tactics recommended in this plan will help Purdue Pharma recognize its goal.
- The sales force is an excellent vehicle for one-on-one communication and combined with Purdue's attendance at medical meetings, will reinforce messages communicated in medical journals.

OXYCONTIN Tablets Promotional Plan

Program	Total Cost 2001	First Quarter Jan	Feb	Mar	Second Quarter Apr	May	Jun	Third Quarter July	Aug	Sept	Fourth Quarter Oct	Nov	Dec
Promotional Materials/ Reorders	$5,000,000	X	X	X	X	X	X	X	X	X	X	X	X
Pain Education													
New Reprints	$500,000	X	X	X	X	X	X	X	X	X	X	X	X
"Complete Pain Management" Selling Brochure	$60,000	X	X	X									
"Complete Pain Management" Self-Assessment Quiz Pads	$200,000	X	X	X									
New Market Opportunities													
Surgical													
Surgical Setting Flashcard	$120,000				X	X	X						
Quick Reference Dosing Card	$60,000				X	X	X						
OB/GYN													
OB/GYN Case Study Flashcard	$160,000				X	X	X						
OB/GYN Consensus Panel Symposium on Pain	$250,000							X	X	X			
PA/NP													
AANP Leadership Summit on Pain Management	$200,000							X	X	X			
Hospital CME Program	$250,000	X	X	X									

OXYCONTIN Tablets Promotional Plan

Program	Total Cost 2001	First Quarter Jan	Feb	Mar	Second Quarter Apr	May	Jun	Third Quarter July	Aug	Sept	Fourth Quarter Oct	Nov	Dec
Core Market													
Oncology													
"OxyContin Meets the Challenge" Visual Aid	$100,000	X	X	X	X	X	X	X	X	X	X	X	X
Cancer Control Journal Supplement	$80,000	X	X	X									
Anesthesia/Pain Management													
American Academy of Pain Medicine Symposium Highlights	$100,000				X	X	X						
CME "Critical Pathways in Pain Management" CD ROM	$200,000				X	X	X						
Oncology and Pain Management Nurses													
"Hospice Care in the Long-Term Care Facility" Video	$200,000				X	X	X						
Primary Care													
Primary Care Visual Aid	$89,000	X	X	X									
CME "Communicating with your Patients About Pain"	$250,000							X	X	X			
American Pain Society (APS) Arthritis Treatment Guidelines	$400,000				X	X	X						

OXYCONTIN Tablets Promotional Plan

Program	Total Cost 2001	First Quarter Jan	Feb	Mar	Second Quarter Apr	May	Jun	Third Quarter July	Aug	Sept	Fourth Quarter Oct	Nov	Dec
Pharmacy/Clinical Pharmacy													
Community Pharmacy Residency Program in Pain Management	$96,000	X	X	X									
School of Pharmacy Curricular Review	$90,000	X	X	X									
The Pharmacist's Role in Pain Management Compendium	$100,000	X	X	X									
Competition													
National Experts on Pain CD ROM	$155,000	X	X	X									
JCAHO													
Regional Program Sponsorship/Highlights	$500,000	X	X	X	X	X	X	X	X	X	X	X	X
Partners Against Pain Clipboards	$750,000	X	X	X	X	X	X	X	X	X	X	X	X
Special Populations Video	$100,000										X	X	X
Abbott/Northwestern CD ROM	$120,000	X	X	X	X	X	X	X	X	X	X	X	X
Internet													
Web/MD Resource Guide	$200,000							X	X	X			
Internet Branding	$500,000	X	X	X	X	X	X	X	X	X	X	X	X
E-Detailing	$1,500,000	X	X	X	X	X	X	X	X	X	X	X	X

OXYCONTIN Tablets Promotional Plan

Program	Total Cost 2001	First Quarter Jan	Feb	Mar	Second Quarter Apr	May	Jun	Third Quarter July	Aug	Sept	Fourth Quarter Oct	Nov	Dec
Special Programs													
Strategic Alliance Building	$500,000	X	X	X	X	X	X	X	X	X	X	X	X
Patient Starter Program	$4,000,000	X	X	X	X	X	X	X	X	X	X	X	X
Veterans Administration Pain Team Grant	$200,000	X	X	X	X	X	X	X	X	X	X	X	X
Partners Against Pain Programs	$2,000,000	X	X	X	X	X	X	X	X	X	X	X	X
Direct Mail													
JCAHO Direct Mail	$150,000	X	X	X	X	X	X	X	X	X	X	X	X
Case Study Direct Mail	$450,000				X	X	X						
PA/NP Mailer Cards	$100,000				X	X	X						
OB/GYN Mailer	$100,000				X	X	X						
"Meet the Challenge" Mailers	$288,000	X	X	X	X	X	X	X	X	X	X	X	X
Journal Ad Production – Osteo – Post-op – OB/GYN – Cancer	$100,000	X	X	X	X	X	X						
Journal Advertising	$4,000,000	X	X	X	X	X	X	X	X	X	X	X	X
Managed Care													
CME Programs													
Cancer Pain CME	$150,000	X	X	X									
Patient Profile Series CME	$125,000							X	X	X			

OXYCONTIN Tablets Promotional Plan

Program	Total Cost 2001	First Quarter			Second Quarter			Third Quarter			Fourth Quarter		
		Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sept	Oct	Nov	Dec
Case Managers													
Cancer Program In-Service	$5,000				X	X	X						
Managing Pain in Managed Care In-Service Program	$5,000							X	X	X			
Patient Profile In-Service	$5,000										X	X	X
Case Management Society of America (CMSA) Grant	$35,000	X	X	X									
Case Manager Premium Item	$75,000				X	X	X						
Publication Plan													
Chevelle Study Data	$50,000				X	X	X						
0C96-1003 Osteoarthritis Study Data	$50,000				X	X	X						
Protocare Sciences Patient Survey and Algorithm	$150,000							X	X	X			
Reprint/References Fund	$60,000	X	X	X	X	X	X	X	X	X	X	X	X
Reorders	$269,000	X	X	X	X	X	X	X	X	X	X	X	X
Business Plan Template/Toolbox	$800,000	X	X	X	X	X	X	X	X	X	X	X	X
Formkit.com	$200,000	X	X	X									
NCQA/HEDIS Report	$50,000							X	X	X			
Strategic Alliances													
Corporate Branding	$100,000	X	X	X	X	X	X	X	X	X	X	X	X
American Hospital Association Grant	$100,000	X	X	X	X	X	X	X	X	X	X	X	X

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Program	Total Cost 2001	First Quarter Jan	Feb	Mar	Second Quarter Apr	May	Jun	Third Quarter July	Aug	Sept	Fourth Quarter Oct	Nov	Dec
Long-Term Care													
Nursing Programs													
Relaunch of Seminars in Pain Management Educational Program	$500,000	X	X	X									
New Nurse Packet	$75,000				X	X	X						
Pain Map Assessment Tool	$50,000				X	X	X						
Consultant Pharmacist													
AGS Quick Reference Guide	$150,000	X	X	X									
Pain in the Elderly LTC Resident CME/CE	$150,000							X	X	X			
The Consultant Pharmacist Review Article	$120,000				X	X	X						
Medical Directors													
Managing Pain in the PPS Environment Series - A collaboration with American Medical Directors Association (AMDA)	$100,000				X	X	X	X	X	X	X	X	X
Third Party Reference Compendium	$75,000							X	X	X			
Philadelphia College of Pharmacy LTC Treatment Guidelines Publication	$50,000	X	X	X									
Pain in the Elderly Visual Aid	$90,000	X	X	X									

OXYCONTIN Tablets Promotional Plan

Program	Total Cost 2001	First Quarter Jan	Feb	Mar	Second Quarter Apr	May	Jun	Third Quarter July	Aug	Sept	Fourth Quarter Oct	Nov	Dec
Managed Care													
Journal Advertising	$500,000	X	X	X	X	X	X	X	X	X	X	X	X
Agency Fee	$1,690,000	X	X	X	X	X	X	X	X	X	X	X	X

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Promotional Materials/ Reorders	To provide reprints of successful promotional materials based on 2000 utilization and field force expansion. Includes outsert purchases used for promotional items. Includes giveaways such as pens/pads/etc.	Repeat	N/A	N/A	N/A	N/A	N/A	1,250,000	1,250,000	1,250,000	1,250,000	$5,000,000
Pain Education												
New Reprints	Purchase of new reprints for OxyContin.	New	125,000	125,000	125,000	125,000	500,000	$125,000	$125,000	$125,000	$125,000	$500,000
"Complete Pain Management" Selling Brochure	A brochure which features the eight slide kit series on pain management for promotion by representatives.	New	100,000				100,000	$60,000				$60,000
"Complete Pain Management" Self-Assessment Quiz Pads	A self-assessment tool designed to quiz healthcare professionals on the content of the "Complete Pain Management" Series	New	400,000				400,000	$200,000				$200,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
New Market Opportunities												
Surgical												
Surgical Setting Flashcard	A flashcard which graphically depicts the operating room with the message "control the pain, control the recovery." This will be targeted to multiple types of surgeon subspecialties.	New		80,000			80,000		$120,000			$120,000
Quick Reference Dosing Card	A small pocket-sized quick reference dosing card for OxyContin. Targeted to all surgical subspecialties.	New		80,000			80,000		$60,000			$60,000
OB/GYN												
OB/GYN Case Study Flashcard	A case study series which focuses on the most prevalent pain conditions in gynecology.	New		80,000			80,000		$160,000			$160,000

OXYCONTIN Tablets Promotional Plan

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Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
OB/GYN Consensus Panel Symposium on Pain	A roundtable consensus panel of thought leaders on the topic of pain in the female patient. Includes production for enduring educational materials.	New			60,000		60,000			$250,000		$250,000
PA/NP												
AANP Leadership Summit on Pain Management	A cancer/non-cancer pain management summit with nurse practitioners designed to develop a position paper by the AANP on the treatments of pain, including new information addressing abuse and diversion.	New			50,000		50,000			$200,000		$200,000
Hospital CME Program	An educational grant to Cogent Healthcare for the development of a CME program specifically for the practicing hospitalists on pain management.	New	5,000				5,000	$250,000				$250,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Core Market												
Oncology												
"OxyContin Meets the Challenge" Visual Aid	A visual aid designed to relaunch OxyContin in cancer pain with targeted promotion to oncologists.	New	40,000				40,000	$100,000				$100,000
Cancer Control Journal Supplement	A journal supplement for distribution by representatives which focuses on cancer pain management and favorably represents OxyContin.	New	80,000				80,000	$80,000				$80,000
Anesthesia/Pain Management												
American Academy of Pain Medicine Symposium Highlights	An educational program developed out of the symposium at AAPM entitled "Benefits of Drug Screening" at the 2001 AAPM annual meeting.	New		50,000			50,000		$100,000			$100,000

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OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
CME "Critical Pathways in Pain Management" CD ROM	A case study format designed to challenge the pain treating physician.	New		20,000			20,000		$200,000			$200,000
Oncology and Pain Management Nurses												
"Hospice Care in the Long-Term Care Facility" Video	A video designed to help hospice nurses educate the LPN in the long-term care facilities regarding cancer pain management.	New		20,000			20,000		$200,000			$200,000
Primary Care												
Primary Care Visual Aid	A visual aid which addresses the issues faced by primary care physicians in the treatment of pain, including new information addressing abuse and diversion.	New	40,000				40,000	$80,000				$80,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
CME "Communicating with your Patients About Pain"	An educational program designed to educate PCP on the value of using pain as a diagnostic tool. This will be developed in conjunction with APS. Includes recognition of the addict, pseudoaddict, etc.	New			100,000		100,000			$250,000		$250,000
American Pain Society (APS) Arthritis Treatment Guidelines	To purchase and distribute the APS treatment guidelines for arthritis.	New		200,000			200,000		$400,000			$400,000
Pharmacy/Clinical Pharmacy												
Community Pharmacy Residency Program in Pain Management	Purdue will support, through APhA, a residency program in the community setting designed to focus on pain management and palliative care.	New	N/A				N/A	$96,000				$96,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
School of Pharmacy Curricular Review	This program will commission the AphA to do a review of pharmacy school curricula to determine how pain management and palliative care are integrated into Doctor of Pharmacy programs through the nation. In addition, it will uncover the resources which would be most helpful to support their teaching efforts in pain management.	New	N/A				N/A	$90,000				$90,000
The Pharmacist's Role in Pain Management Compendium	A compendium of six articles focusing on the role of the pharmacist in the treatment of patients in pain, including new information addressing abuse and diversion.	New	50,000				50,000	$100,000				$100,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Competition												
National Experts on Pain CD ROM	A branded promotional CD ROM which features national experts on pain. Experts on the topic of neuropathy, sickle cell, post-operative pain, cancer pain, and arthritis pain give their opinions of the effectiveness of OxyContin Tablets in these pain states.	New	3,000				3,000	$155,000				$155,000
JCAHO												
Regional Program Sponsorship/Highlights	A series of regional educational programs will be conducted focusing on pain standards implementation. Purdue will underwrite the costs as well as publish the results to attendees.	New	N/A	N/A	N/A	N/A	1,200	$125,000	$125,000	$125,000	$125,000	$500,000
Partners Against Pain Clipboards	A pain assessment educational resource provided as a service of Purdue and Partners Against Pain.	Repeat	75,000	75,000	75,000	75,000	300,000	$187,500	$187,500	$187,500	$187,500	$750,000

OXYCONTIN Tablets Promotional Plan

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Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Special Populations Video	A video developed by the Joint Commission to educate providers on pain management in special populations.	New				5,000	5,000				$100,000	$100,000
Abbott/Northwestern CD ROM	A multi-hour accredited educational program promoted by the Medical Liaison group to key targeted institutions in the country. Developed by Abbott/Northwestern Hospital.	New	100	100	100	100	400	$30,000	$30,000	$30,000	$30,000	$120,000
Internet												
Web/MD Resource Guide	Sponsorship of a reference guide to medical information on the Internet targeted to physician Internet users.	New			100,000		100,000			$200,000		$200,000
Internet Branding	A series of tactical programs designed to effectively position OxyContin on web browsers.	New	N/A	N/A	N/A	N/A	N/A	$125,000	$125,000	$125,000	$125,000	$500,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
E-Detailing	An Internet detailing program targeted to high prescribers of combination opioids with a branded OxyContin message. This program is a follow up to the pilot program which ran in 2000.	New	TBD	TBD	TBD	TBD	TBD	$375,000	$375,000	$375,000	$375,000	$1,500,000
Special Programs												
Strategic Alliance Building	A series of programs targeted at major institutions, organizations, and thought leaders in pain management including AAPM, APS, American Academy of Pain Management, and Veterans Administration as well as major teaching institutions in the country, including new information addressing abuse and diversion.	New	TBD	TBD	TBD	TBD	TBD	$125,000	$125,000	$125,000	$125,000	$500,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Patient Starter Program	A PCS program targeted to key "early adapters" of new products or technology. This program will be used as part of a pre-emptive competitive strategy. In addition, it will be used to capture the early patient who is a candidate for opioids.	Repeat	N/A	N/A	N/A	N/A	N/A	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$4,000,000
Veterans Administration Pain Team Grant	A grant program which focuses on quarterly roundtable meetings among Veterans Administration National Pain team members at the VISN level.	New	TBD	TBD	TBD	TBD	TBD	$50,000	$50,000	$50,000	$50,000	$200,000
Partners Against Pain Programs	To expand the influence of Partners Against Pain through public relations and build brand influence with consumer initiatives.	New	TBD	TBD	TBD	TBD	TBD	$500,000	$500,000	$500,000	$500,000	$2,000,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Direct Mail												
JCAHO Direct Mail	Targeted to hospital administration and JCAHO liaisons in the institutional setting. Designed to build a database of leads for the sales force.	New	2,000	2,000	2,000	2,000	8,000	$37,500	$37,500	$37,500	$37,500	$150,000
Case Study Direct Mail	Combines existing profiles with reminder points to PCPs.	New		150,000			150,000		$450,000			$450,000
PA/NP Mailer Cards	Cards with quick reminders of OxyContin features and benefits.	New		200,000			200,000		$100,000			$100,000
OB/GYN Mailer	A direct mail campaign focusing on quality of pain management after operative gynecological procedures.	New		10,000			10,000		$100,000			$100,000
"Meet the Challenge" Mailers	A direct mail campaign focusing on "early adapters" of new technology or medications in light of future competition.	New	50,000	50,000	50,000	50,000	200,000	$72,000	$72,000	$72,000	$72,000	$288,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Journal Ad Production – Osteo – Post-op – OB/GYN – Cancer	Creation of new ads which incorporate the message of "meets the challenge."	New	TBD	TBD			TBD	$50,000	$50,000			$100,000
Journal Advertising	Expanded focus for 2001 to include oncology, primary care, orthopedics, OB/GYN, surgery, anesthesia, rheumatology, emergency medicine, and dental.	Repeat	TBD	TBD	TBD	TBD	TBD	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$4,000,000
Managed Care												
CME Programs												
Cancer Pain CME	A CME program by Eric Chevlen focusing on the treatment of cancer pain. This will be targeted to providers through MCOs.	New	100,000				100,000	$150,000				$150,000
Patient Profile Series CME	A CME program focusing on patient profiles in chronic pain management.	New			100,000		100,000			$125,000		$125,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Case Managers												
Cancer Program In-Service	An in-service program built off the cancer CME targeted to case managers at MCOs.	New		20			20		$5,000			$5,000
Managing Pain in Managed Care In-Service Program	An in-service program built from the Cole CME program.	New			20		20			$5,000		$5,000
Patient Profile In-Service	An in-service program built from the Patient Profile CME series.	New				20	20				$5,000	$5,000
Case Management Society of America (CMSA) Grant	A grant to produce a supplement to the Purdue sponsored symposia at CMSA in 2001.	New	20,000				20,000	$35,000				$35,000
Case Manager Premium Item	A premium item to remind the case manager of OxyContin and Partners Against Pain.	New		10,000			10,000		$75,000			$75,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Publication Plan												
Chevelle Study Data	A strategy to capitalize on the most effective use of the results from the study by Andrea Chevelle, MD in *Journal of Bone and Joint Surgery*.	New		TBD			TBD		$50,000			$50,000
0C96-1003 Osteoarthritis Study Data	A strategy to capitalize on the publication of this study data showing improved function in patients with osteoarthritis taking OxyContin.	New		TBD			TBD		$50,000			$50,000
Protocare Sciences Patient Survey and Algorithm	A patient survey with algorithm development designed to help identify patients in need of pain intervention. Phase II of the program will be implemented during 2001.	New			TBD		TBD			$150,000		$150,000
Reprint/References Fund	To allow for the purchase of reprints for account executive distribution.	Repeat	TBD	TBD	TBD	TBD	TBD	$15,000	$15,000	$15,000	$15,000	$60,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Reorders	Designated to cover the cost of reprinting promotional materials for use by account executives.	Repeat	TBD	TBD	TBD	TBD	TBD	$67,250	$67,250	$67,250	$67,250	$269,000
Business Plan Template/Toolbox		Repeat	N/A	N/A	N/A	N/A	N/A	$200,000	$200,000	$200,000	$200,000	$800,000
Formkit.com	A reworking of the OxyContin product data in the formulary kit and subsequent availability on formkit.com a targeted Internet site which is password protected and used by key P&T Committee members.	New	10,000				10,000	$200,000				$200,000
NCQA/HEDIS Report	A report publishing the importance of pain management program in overall quality improvement.	New			50,000		50,000			$50,000		$50,000

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Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Strategic Alliances												
Corporate Branding	A publication which is designed to give a corporate overview of Purdue and discuss our initiatives to aid patients in pain, including new information addressing abuse and diversion. In addition, this would discuss present and future marketing focus by Purdue. Target of publication will be MCO executives/decision makers.	New	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	$100,000
American Hospital Association Grant	A grant to aid in pain management efforts on behalf of the American Hospital Association and Purdue.	New	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	$100,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Long-Term Care												
Nursing Programs												
Relaunch of Seminars in Pain Management Educational Program	A relaunch of this valuable program to the LTC pharmacy providers at the corporate level. In addition, modules 6-10 will be developed. Includes major publicity to LTC providers.	New	TBD				TBD	$500,000				$500,000
New Nurse Packet	A kit containing primary educational tools in pain management for distribution to new nurses in the long-term care setting.	New		10,000			10,000		$75,000			$75,000
Pain Map Assessment Tool	A tool designed from the Weiner, et al article in the journal *Pain*.	New		25,000			25,000		$50,000			$50,000
Consultant Pharmacist												
AGS Quick Reference Guide	A quick reference guide adapted from the AGS Guidelines for the treatment of chronic pain.	New	50,000				50,000	$150,000				$150,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Pain in the Elderly LTC Resident CME/CE	A CME/CE program discussing the challenges of pain management in the long-term care setting.	New			100,000		100,000			$150,000		$150,000
The Consultant Pharmacist Review Article	A review article to accompany the consultant pharmacist journal on pain management.	New		30,000			30,000		$120,000			$120,000
Medical Directors												
Managing Pain in the PPS Environment Series - A collaboration with American Medical Directors Association (AMDA)	A series of quick reference cards designed to educate medical directors of LTC facilities on the value of proper pain management in a PPS environment.	New		20,000			20,000		$50,000	$25,000	$25,000	$100,000

OXYCONTIN Tablets Promotional Plan

Program	Usage	New or Repeat	1st Qtr. No. Pieces	2nd Qtr. No. Pieces	3rd Qtr. No. Pieces	4th Qtr. No. Pieces	Total Pieces 2001	1st Qtr. Cost	2nd Qtr. Cost	3rd Qtr. Cost	4th Qtr. Cost	Total Cost 2001
Third Party Reference Compendium	A compendium of third party references which outline the issues of pain management in the long-term care setting. Includes information from HCFA, JCAHO, AGS, AMDA, and other journal articles on pain in the elderly. Also includes the Philadelphia College Guidelines.	New			20,000		20,000			$75,000		$75,000
Philadelphia College of Pharmacy LTC Treatment Guidelines Publication	To publish the guidelines developed by the Philadelphia College.	New	50,000				50,000	$50,000				$50,000
Pain in the Elderly Visual Aid	An updated visual which incorporates a renewed focus on pain in the elderly.	New	30,000				30,000	$90,000				$90,000
Managed Care												
Journal Advertising	Updated corporate ad and expanded circulation.	Repeat	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	$500,000
Agency Fee	LLNS							$422,500	$422,500	$422,500	$422,500	$1,690,000

V. Total S&P Overview
(000s)
OXYCONTIN*

	1999		2000		2001		% Change	
	Actual	% of Sales	Est.	% of Sales	Proj.	% of Sales	00/99	01/00
Sales	$621,640	100%	$1,100,000	100%	$1,440,000	100%	77.0%	30.9%
Marketing & Promotion								
Promotional Materials	$6,448	1.0%	$8,960	0.8%	$13,710	1.0%	39.0%	53.0%
Direct Mail	$572	0.1%	$1,711	0.2%	$1,088	0.1%	199.1%	-36.4%
Journal Advertising	$2,278	0.4%	$4,125	0.4%	$4,500	0.3%	81.1%	9.1%
Internet	$0	NA	$592	NA	$2,200	0.2%	NA	271.6%
Total Direct Mail/Journal Advertising	$2,850	0.5%	$5,836	0.5%	$5,588	0.4%	104.8%	-4.2%
Samples	$0	0.0%	$0	0.0%	$0	0.0%	0.0%	NA
Agency Fee	$952	0.2%	$1,387	0.1%	$1,690	0.1%	45.7%	21.8%
Special Promotions	$2,692	0.4%	$8,915	0.8%	$6,700	0.5%	231.2%	-24.8%
Co-op Advertising	$0	0.0%	$0	0.0%	$0	0.0%	NA	NA
Conventions	$1,096	0.2%	$1,551	0.1%	$1,555	0.1%	41.5%	0.3%
Abbott Commission	$40,310	6.5%	$71,664	6.5%	$98,241	6.8%	77.8%	37.1%
Total Marketing & Promotion	$54,348	8.7%	$98,313	8.9%	$129,684	9.0%	80.9%	31.9%
Total Allocation & Other	$87,290	14.0%	$154,336	14.0%	$173,688	12.1%	76.8%	12.5%
Total S&P	$141,638	22.8%	$252,649	23.0%	$303,372	21.1%	78.4%	20.1%

* Includes MHC and LTC

V. Total S&P Overview
(000s)
MS CONTIN / OXYCONTIN*

	MSC 2000		MSC 2001		OXY 2000		OXY 2001		Combined	
	Est.	% of Sales	Proj.	% of Sales	Est.	% of Sales	Proj.	% of Sales	MSC+ OXY 2001	% of Sales
Sales	$100,058	100%	$57,515	100%	$1,100,000	100%	$1,440,000	100%	$1,497,515	100.0%
Marketing & Promotion										
Promotional Materials	$1,308	1.3%	$650	1.1%	$8,960	0.8%	$13,710	1.0%	$14,360	1.0%
Direct Mail	$216	0.2%	$216	0.4%	$1,711	0.2%	$1,088	0.1%	$1,304	0.1%
Journal Advertising	$0	0.0%	$0	0.0%	$4,125	0.4%	$4,500	0.3%	$4,500	0.3%
Total Direct Mail/Journal Advertising	$216	0.2%	$216	0.4%	$5,836	0.5%	$5,588	0.4%	$5,804	0.4%
Samples	$0	0.0%	$0	0.0%	$0	0.0%	$0	0.0%	$0	0.0%
Agency Fee	$0	0.0%	$0	0.0%	$1,387	0.1%	$1,690	0.1%	$1,690	0.1%
Special Promotions	$200	0.2%	$0	0.0%	$8,915	0.8%	$6,700	0.5%	$6,700	0.4%
Co-op Advertising	$0	0.0%	$0	0.0%	$0	0.1%	$0	0.0%	$0	0.0%
Conventions	$0	0.0%	$0	0.0%	$1,551	6.5%	$1,555	0.1%	$1,555	0.1%
Sales Agent Commission	$0	0.0%	$0	0.0%	$71,664	6.5%	$98,241	6.8%	$98,241	6.6%
Total Marketing & Promotion	$1,724	1.7%	$866	1.5%	$98,313	8.9%	$127,484	8.9%	$128,350	8.6%
Total Allocation	$6,368	6.4%	$4,679	8.1%	$154,336	14.0%	$175,888	12.2%	$180,567	12.1%
Total S&P	$8,092	8.1%	$5,545	9.6%	$252,649	23.0%	$303,372	21.1%	$308,917	20.6%

* Includes MHC and LTC

MS Contin® Tablets

THE PRESIDENT'S COMMISSION ON COMBATING DRUG ADDICTION AND THE OPIOID CRISIS

Roster of Commissioners

Governor Chris Christie, Chairman
Governor Charlie Baker
Governor Roy Cooper
Congressman Patrick J. Kennedy
Professor Bertha Madras, Ph.D.
Florida Attorney General Pam Bondi

EXHIBIT

B

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November 1, 2017

The Honorable Donald J. Trump
President of the United States
The White House
1600 Pennsylvania Avenue NW
Washington, DC 20500

Dear President Trump,

On behalf of the President's Commission on Combating Drug Addiction and the Opioid Crisis, we thank you for entrusting us with the responsibility of developing recommendations to combat the addiction crisis that is rampantly impacting our country.

Your speech in the East Room of the White House, along with the remarks of the First Lady, made it clear to the country that fighting this epidemic is a top priority of your Administration. On behalf of the Commission, we thank you for your leadership on this issue and on the clarity of your call to action.

When you declared the opioid crisis a national public health emergency under federal law on October 26, 2017, you acknowledged this crisis as one of epic proportion, impacting nearly every community across all 50 states. You signaled to the country that the force of the federal government should and will mobilize to reverse the rising tide of overdose deaths. You gave the millions of Americans fighting addiction hope that we can overcome this crisis, and we are prepared to win the fight.

Mr. President, as you acknowledged when you addressed the nation last week, the reason behind the urgent recommendations presented to you today by this Commission is that the leading cause of unintentional death in the United States is now drug overdose deaths.

Our people are dying. More than 175 lives lost every day. If a terrorist organization was killing 175 Americans a day on American soil, what would we do to stop them? We would do anything and everything. We must do the same to stop the dying caused from within. I know you will.

Without comprehensive action, including your national public health emergency, the death count will continue to rise. I know that is unacceptable to you. I know you will win this fight for the people who elected you.

You've met hundreds of parents who have buried their children, so these numbers are no longer simply statistics. Instead, they represent the injured student-athlete who becomes addicted after first prescription, ending her academic and athletic career, the newborn infant who is red and screaming from withdrawal pain, the grandparents using their retirement savings to raise young kids when the parents can't, the mom who just buried her only son, and the addict who cycles in and out of jail, simply because without access to treatment he is unable to stay sober and meet the terms of his parole.

It is time we all say what we know is true: addiction is a disease. However, we do not treat addiction in this country like we treat other diseases. Neither government nor the private sector has committed the support necessary for research, prevention, and treatment like we do for other diseases.

The recommendations herein, and the interim recommendations submitted by the Commission in July, are designed to address this national priority. These recommendations will help doctors, addiction treatment providers, parents, schools, patients, faith-based leaders, law enforcement, insurers, the medical industry, and researchers fight opioid abuse and misuse by reducing federal barriers and increasing support to effective programs and innovation.

Obviously, many of the recommendations that follow will require appropriations from Congress into the Public Health Emergency Fund, for block grants to states and to DOJ for enforcement and judicial improvements. It is not the Commission's charge to quantify the amount of these resources, so we do not do so in this report.

You have made fighting the opioid epidemic a national priority, Mr. President. And, the country is ready to follow your lead. Now, we urge Congress to do their constitutionally delegated duty and appropriate sufficient funds (as soon as possible) to implement the Commission's recommendations. 175 Americans are dying a day. Congress must act.

Here is what your Administration has already done:

- You acted to remove one of the biggest federal barriers to treatment by announcing the launch of a new policy to overcome the restrictive, decades-old federal rule that prevents states from providing more access to care at treatment facilities with more than 16 beds. This action will take people in crisis off waiting lists where they are at risk of losing their battle to their disease and put them into a treatment bed and on the path to recovery. We urge all Governors to apply to CMS for a waiver. This policy will – without any doubt – save lives. Governors across this nation thank you for listening to our call for help.
- In the interim report, the Commission also called for prescriber education and enhanced access to medication-assisted treatment for those already suffering from addiction. You acknowledged the need for these recommendations and directed all federally employed prescribers to receive special training to fight this epidemic. This is a bold step by you to deal with this issue.
- We recommended that the Department of Justice, which has already acted forcefully to stop the flow of illicit synthetic drugs into this country through the U.S. Postal Service,

continue its efforts. The aggressive enforcement action being taken by your Administration is critical in our efforts to reduce the rise of overdose deaths in this country.

- National Institutes of Health (NIH) Director Dr. Francis Collins has been partnering with pharmaceutical companies to develop non-addictive painkillers and new treatments for addiction and overdose. The Commission worked with Dr. Collins to convene a meeting with industry leadership to discuss innovative ways to combat the opioid crisis. The Commission also held a public meeting to highlight the progress and innovation occurring today resulting from the NIH's work. This type of scientific progress is a positive step to help free the next generation from the widespread suffering addiction is causing today.

Our interim recommendations called for more data sharing among state-based prescription drug monitoring programs and recognized the need to address patient privacy regulations that make it difficult for health providers to access information and make informed healthcare decisions for someone who has a substance use disorder. We recommended that all law enforcement officers across the country be equipped with life-saving naloxone.

Finally, we recommended full enforcement of the Mental Health Parity and Addiction Equity Act to ensure that health plans cannot provide less favorable benefits for mental health and substance use diagnoses than physical health ailments. You will see further recommendations in our final report regarding the Parity Act and calling for the Department of Labor to have enhanced penalty and enforcement powers directly against insurers failing those who depend on them for life-saving treatment.

All the interim recommendations remain extremely relevant today and are critical tools to reduce ever increasing overdose deaths plaguing our citizens. The Commission is grateful the Administration has begun the hard work of implementing these initiatives. We urge you to implement the others as soon as possible.

Today, the Commission, as one its most urgent recommendations among the more than 50 provided in the final report, is calling for an expansive national multi-media campaign to fight this national health emergency.

This campaign, including aggressive television and social media outreach, must focus on telling our children of the dangers of these drugs and addiction, and on removing stigma as a barrier to treatment by emphasizing that addiction is not a moral failing, but rather a chronic brain disease with evidence-based treatment options. People need to be aware of the health risks associated with opioid use, and they must stop being afraid or ashamed of seeking help when facing their addiction.

Today, only 10.6% of youth and adults who need treatment for a substance use disorder receive that treatment. This is unacceptable. Too many people who could be helped are falling through the cracks and losing their lives as a result.

Many states, including my State of New Jersey, have undertaken this media strategy with significant positive results. However, having a nation-wide campaign will serve to reinforce the message and ensure, for example, that youth and young adults no longer believe that experimenting with pills from a doctor is safer than experimenting with illegal substances from a drug dealer.

As part of its prevention recommendations, the Commission also calls for better educating

middle school, high school, and college students with the help of trained professionals such as nurses and counselors who can assess at-risk kids. Children have not escaped the consequences of addiction and our efforts to reduce overdose deaths must start early. Mrs. Trump's dedication and leadership in helping our nation's children will make this a top priority and help save innocent young lives.

One of the most important recommendations in this final report is getting federal funding support more quickly and effectively to state governments, who are on the front lines of fighting this addiction battle every day. Bureaucracy, departmental silos, and red tape must not be accepted as the norm when dealing with funding to combat this epidemic. Saving time and resources, in this instance, will literally save lives.

Accordingly, we are urging Congress and the Administration to **block grant federal funding for opioid-related and SUD-related activities to the states**. There are multiple federal agencies and multiple grants within those agencies that cause states a significant administrative burden from an application and reporting perspective. Money is being wasted and accountability for results is not as intense as it should be. Block granting them would allow more resources to be spent on administering life-saving programs. This was a request to the Commission by nearly every Governor, regardless of party, across the country. And as a Commission that has three governors as members, all of whom know the frustration of jumping through multiple hoops to receive the funding we need to help our constituents in this fight, we wholeheartedly agree.

Throughout the comprehensive recommendations of its final report, the Commission also identifies the need to focus on, deploy and assess evidence-based programs that can be funded through these proposed block grants. Many of the recommendations acknowledge a need for better data analysis and accountability to ensure that any critical dollars are spent on what works best to fight this disease.

From its review of the federal budget aimed at addressing the opioid epidemic, the Commission identified a disturbing trend in federal health care reimbursement policies that incentivizes the wide-spread prescribing of opioids and limits access to other non-addictive treatments for pain, as well as addiction treatment and medication-assisted treatment.

First, individuals with acute or chronic pain must have access to non-opioid pain management options. Everything from physical therapy, to non-opioid medications, should be easily accessible as an alternative to opioids. The Commission heard from many innovative life sciences firms with new and promising products to treat patients' pain in non-addictive, safer ways; but they have trouble competing with cheap, generic opioids that are so widely used. We should incentivize insurers and the government to pay for non-opioid treatments for pain beginning right in the operating room and at every treatment step along the way.

In some cases, non-addictive pain medications are bundled in federal reimbursement policies so that hospitals and doctors are essentially not covered to prescribe non-opioid pain management alternatives. These types of policies, which the federal government can fix, are a significant deterrent to turning the tide on the health crisis we are facing. We urge you to order HHS to fix it.

Second, as a condition of full reimbursement of hospitals, CMS requires that hospitals randomly survey discharged patients. HHS previously included pain question response information in calculations of incentive payment, but in 2017 thankfully abandoned this practice. However, all pain survey questions were not withdrawn from the surveys. The Commission recommends that CMS remove pain questions entirely when assessing consumers so that providers won't ever use opioids inappropriately to raise their survey scores. We urge you to order HHS to do this immediately.

The expectation of eliminating a patient's pain as an indication of successful treatment, and seeing pain as the fifth vital sign, which has been stated by some medical professionals as unique to the United States, was cited as a core cause of the culture of overprescribing in this country that led to the current health crisis. This must end immediately.

The Department of Labor must be given the real authority to regulate the health insurance industry. The health insurers are not following the federal law requiring parity in the reimbursement for mental health and addiction. They must be held responsible. The Secretary of Labor testified he needs the ability to fine violators and to individually investigate insurers not just employers. We agree with Secretary Acosta. If we do not get Congress to give him these tools, we will be failing our mission as badly as health insurance companies are failing their subscribers on this issue today leading to deaths.

Also contributing to this problem is the fact that HHS/CMS, the Indian Health Service, Tricare, and the VA still have reimbursement barriers to substance abuse treatment, including limiting access to certain FDA-approved medication-assisted treatment, counseling, and inpatient/residential treatment.

It's imperative that federal treatment providers lead the way to treating addiction as a disease and remove these barriers. Each of these primary care providers employed by the above-mentioned federal health systems should screen for SUDs and, directly or through referral, provide treatment within 24-to-48 hours. Each physician employee should be able to prescribe buprenorphine (if that is the most appropriate treatment for the patient) in primary care settings. As President, you can make this happen immediately. We urge you to do so.

A good example of this federal leadership occurred when Department of Veterans Affairs Secretary Shulkin, in response to the Commission's interim report release, immediately launched eight best practices for pain management in the VA health-care system. These guidelines included everything from alternatives and complimentary care, counseling and patient monitoring to peer education for front-line providers, informed consent of patients and naloxone distribution for Veterans on long-term opioid therapy. I had the opportunity to visit with doctors and patients at the Louis Stokes Northeast Ohio VA Healthcare System and witnessed first-hand the positive results of a hospital that has embraced a different continuum of care for pain management. The VA doctors, which included behavioral health specialists, acknowledge and treat those with addiction in the full complement of ways the medical community would tackle other chronic diseases. Let's use these VA practices as an example for our entire healthcare system.

As you will see in the Commission's recommendations, the Federal Government has a number of avenues through which it can ensure that individuals with addiction disorders get the

help they need; including changing CMS reimbursement policies, enforcing parity laws against non-compliant insurers, promoting access to rural communities through such tools as telemedicine, and incenting a larger treatment workforce to address the broad scope of the crisis.

For individuals with a substance use disorder, ensuring life-saving access to affordable health care benefits is an essential tool in fighting the opioid epidemic. Look at Indiana as an example. After Indiana used an insurance access program to rapidly respond to a rural, opioid-related health crisis, the Indiana Department of Health reported that such a program opened the door to life changing medical treatment.

We are recommending that a drug court be established in every one of the 93 federal district courts in America. It is working in our states and can work in our federal system to help treat those who need it and lower the federal prison population. For many people, being arrested and sent to a drug court is what saved their lives, allowed them to get treatment, and gave them a second chance.

Drug Courts are known to be significantly more effective than incarceration, but 44% of U.S. Counties do not have an adult drug court. DOJ should urge states to establish state drug courts in every county. When individuals violate the terms of probation or parole with substance use, they need to be diverted to drug court, rather than back to incarceration. Further, drug courts need to embrace the use of medication-assisted treatment for their populations, as it clearly improves outcomes. The criminal justice system should accept that medication, when clinically appropriate, can lead to lasting recovery; abstinence-only sobriety is not the only path to recovery.

Lastly, the Commission's recommendations identify multiple ways to reduce the supply of licit and illicit opioids and enhanced enforcement strategies. Recognizing the growing threat of synthetic opioids such as fentanyl, the Commission recommends enhanced penalties for trafficking of fentanyl and fentanyl analogues and calls for additional technologies and drug detection methods to expand efforts to intercept fentanyl before entering the country.

To help protect first responders, who are also on the front lines fighting this epidemic responding to overdoses sometimes multiple times a day, the Commission recommends the White House develop a national outreach strategy coordinating with Governors for the release and adoption of the Office of Homeland Security National Security Council's new Fentanyl Safety Recommendations for First Responders. The Commission thanks White House Homeland Security Advisor Tom Bossert for his support and hard work already on this initiative.

Many other thoughtful, vital recommendations are included herein. These recommendations were informed by expert testimony provided during the Commission's public meetings, which included treatment providers and experts, pharmaceutical innovators and insurers. They also were informed by thousands of written submissions accepted by the Commission as part of its public process.

The Commission acknowledges that there is an active movement to promote the use of marijuana as an alternative medication for chronic pain and as a treatment for opioid addiction. Recent research out of the NIH's National Institute on Drug Abuse found that marijuana use led to a 2 ½ times greater chance that the marijuana user would become an opioid user and abuser.

The Commission found this very disturbing. There is a lack of sophisticated outcome data on dose, potency, and abuse potential for marijuana. This mirrors the lack of data in the 1990's and early 2000's when opioid prescribing multiplied across health care settings and led to the current epidemic of abuse, misuse and addiction. The Commission urges that the same mistake is not made with the uninformed rush to put another drug legally on the market in the midst of an overdose epidemic.

The Commission extends our sincere gratitude to all of the individuals, organizations, families, companies, state officials, federal agency staff, and clinical professionals who provided personal stories, creative solutions, and thoughtful input to the Commission. The Commission members received thousands of letters, took hundreds of phone calls and meetings, and heard testimony from prominent organizations including non-profits, professional societies, pharmaceutical companies, health insurance providers, and most importantly, individuals and families that have been in the throes of addiction. These letters, conversations, and meetings were the impetus for the vast majority of recommendations made in this report.

The Commission is confident that, if enacted quickly, these recommendations will strengthen the federal government, state, and local response to this crisis. But it will take all invested parties to step up and play a role: the federal executive branch, Congress, states, the pharmaceutical industry, doctors, pharmacists, academia, and insurers. The responsibility is all of ours. We must come together for the collective good and acknowledge that this disease requires a coordinated and comprehensive attack from all of us.

The time to wait is over. The time for talk is passed. 175 deaths a day can no longer be tolerated. We know that you will not stand by; we believe you will force action.

Along with my fellow Commission members, and the thousands of people who contributed to this report by sharing their stories and ideas for solutions, I look forward to seeing these policy changes implemented. Thank you again for the opportunity to serve, and most of all thank you for your commitment to addressing this vital national public health emergency.

Sincerely,

Governor Chris Christie
Governor of New Jersey
Chairman, President's Commission on Combating
Drug Addiction and the Opioid Crisis

Summary of Recommendations

Federal Funding and Programs

1. The Commission urges Congress and the Administration to block grant federal funding for opioid-related and SUD-related activities to the states, where the battle is happening every day. There are multiple federal agencies and multiple grants within those agencies that cause states a significant administrative burden from an application and reporting perspective. Creating uniform block grants would allow more resources to be spent on administering life-saving programs. This was a request to the Commission by nearly every Governor, regardless of party, across the country.

2. The Commission believes that ONDCP must establish a coordinated system for tracking all federally-funded initiatives, through support from HHS and DOJ. If we are to invest in combating this epidemic, we must invest in only those programs that achieve quantifiable goals and metrics. We are operating blindly today; ONDCP must establish a system of tracking and accountability.

3. To achieve accountability in federal programs, the Commission recommends that ONDCP review is a component of every federal program and that necessary funding is provided for implementation. Cooperation by federal agencies and the states must be mandated.

Opioid Addiction Prevention

4. The Commission recommends that Department of Education (DOE) collaborate with states on student assessment programs such as Screening, Brief Intervention and Referral to Treatment (SBIRT). SBIRT is a program that uses a screening tool by trained staff to identify at-risk youth who may need treatment. This should be deployed for adolescents in middle school, high school and college levels. This is a significant prevention tool.

5. The Commission recommends the Administration fund and collaborate with private sector and non-profit partners to design and implement a wide-reaching, national multi-platform media campaign addressing the hazards of substance use, the danger of opioids, and stigma. A similar mass media/educational campaign was launched during the AIDs public health crisis.

Prescribing Guidelines, Regulations, Education

6. The Commission recommends HHS, the Department of Labor (DOL), VA/DOD, FDA, and ONDCP work with stakeholders to develop model statutes, regulations, and policies that ensure informed patient consent prior to an opioid prescription for chronic pain. Patients need to understand the risks, benefits and alternatives to taking opioids. This is not the standard today.

7. The Commission recommends that HHS coordinate the development of a national curriculum and standard of care for opioid prescribers. An updated set of guidelines for prescription pain medications should be established by an expert committee composed of various specialty

practices to supplement the CDC guideline that are specifically targeted to primary care physicians.

8. The Commission recommends that federal agencies work to collect participation data. Data on prescribing patterns should be matched with participation in continuing medical education data to determine program effectiveness and such analytics shared with clinicians and stakeholders such as state licensing boards.

9. The Commission recommends that the Administration develop a model training program to be disseminated to all levels of medical education (including all prescribers) on screening for substance use and mental health status to identify at risk patients.

10. The Commission recommends the Administration work with Congress to amend the Controlled Substances Act to allow the DEA to require that all prescribers desiring to be relicensed to prescribe opioids show participation in an approved continuing medical education program on opioid prescribing.

11. The Commission recommends that HHS, DOJ/DEA, ONDCP, and pharmacy associations train pharmacists on best practices to evaluate legitimacy of opioid prescriptions, and not penalize pharmacists for denying inappropriate prescriptions.

PDMP Enhancements

12. The Commission recommends the Administration's support of the Prescription Drug Monitoring (PDMP) Act to mandate states that receive grant funds to comply with PDMP requirements, including data sharing. This Act directs DOJ to fund the establishment and maintenance of a data-sharing hub.

13. The Commission recommends federal agencies mandate PDMP checks, and consider amending requirements under the Emergency Medical Treatment and Labor Act (EMTALA), which requires hospitals to screen and stabilize patients in an emergency department, regardless of insurance status or ability to pay.

14. The Commission recommends that PDMP data integration with electronic health records, overdose episodes, and SUD-related decision support tools for providers is necessary to increase effectiveness.

15. The Commission recommends ONDCP and DEA increase electronic prescribing to prevent diversion and forgery. The DEA should revise regulations regarding electronic prescribing for controlled substances.

16. The Commission recommends that the Federal Government work with states to remove legal barriers and ensure PDMPs incorporate available overdose/naloxone deployment data, including the Department of Transportation's (DOT) Emergency Medical Technician (EMT) overdose database. It is necessary to have overdose data/naloxone deployment data in the PDMP to allow users of the PDMP to assist patients.

Supply Reduction and Enforcement Strategies

17. The Commission recommends community-based stakeholders utilize Take Back Day to inform the public about drug screening and treatment services. The Commission encourages more hospitals/clinics and retail pharmacies to become year-round authorized collectors and explore the use of drug deactivation bags.

18. The Commission recommends that CMS remove pain survey questions entirely on patient satisfaction surveys, so that providers are never incentivized for offering opioids to raise their survey score. ONDCP and HHS should establish a policy to prevent hospital administrators from using patient ratings from CMS surveys improperly.

19. The Commission recommends CMS review and modify rate-setting policies that discourage the use of non-opioid treatments for pain, such as certain bundled payments that make alternative treatment options cost prohibitive for hospitals and doctors, particularly those options for treating immediate post-surgical pain.

20. The Commission recommends a federal effort to strengthen data collection activities enabling real-time surveillance of the opioid crisis at the national, state, local, and tribal levels.

21. The Commission recommends the Federal Government work with the states to develop and implement standardized rigorous drug testing procedures, forensic methods, and use of appropriate toxicology instrumentation in the investigation of drug-related deaths. We do not have sufficiently accurate and systematic data from medical examiners around the country to determine overdose deaths, both in their cause and the actual number of deaths.

22. The Commission recommends reinstituting the *Arrestee Drug Abuse Monitoring* (ADAM) program and the *Drug Abuse Warning Network* (DAWN) to improve data collection and provide resources for other promising surveillance systems.

23. The Commission recommends the enhancement of federal sentencing penalties for the trafficking of fentanyl and fentanyl analogues.

24. The Commission recommends that federal law enforcement agencies expressly target Drug Trafficking Organizations and other individuals who produce and sell counterfeit pills, including through the internet.

25. The Commission recommends that the Administration work with Congress to amend the law to give the DEA the authority to regulate the use of pill presses/tableting machines with requirements for the maintenance of records, inspections for verifying location and stated use, and security provisions.

26. The Commission recommends U.S. Customs and Border Protection (CBP) and the U.S. Postal Inspection Service (USPIS) use additional technologies and drug detection canines to expand efforts to intercept fentanyl (and other synthetic opioids) in envelopes and packages at international mail processing distribution centers.

27. The Commission recommends Congress and the Federal Government use advanced electronic data on international shipments from high-risk areas to identify international suppliers and their U.S.-based distributors.

28. The Commission recommends support of the Synthetics Trafficking and Overdose Prevention (STOP) Act and recommends the Federal Government work with the international community to implement the STOP Act in accordance with international laws and treaties.

29. The Commission recommends a coordinated federal/DEA effort to prevent, monitor and detect the diversion of prescription opioids, including licit fentanyl, for illicit distribution or use.

30. The Commission recommends the White House develop a national outreach plan for the *Fentanyl Safety Recommendations for First Responders*. Federal departments and agencies should partner with Governors and state fusion centers to develop and standardize data collection, analytics, and information-sharing related to first responder opioid-intoxication incidents.

Opioid Addiction Treatment, Overdose Reversal, and Recovery

31. The Commission recommends HHS, CMS, Substance Abuse and Mental Health Services Administration, the VA, and other federal agencies incorporate quality measures that address addiction screenings and treatment referrals. There is a great need to ensure that health care providers are screening for SUDs and know how to appropriately counsel, or refer a patient. HHS should review the scientific evidence on the latest OUD and SUD treatment options and collaborate with the U.S. Preventive Services Task Force (USPSTF) on provider recommendations.

32. The Commission recommends the adoption of process, outcome, and prognostic measures of treatment services as presented by the National Outcome Measurement and the American Society of Addiction Medicine (ASAM). Addiction is a chronic relapsing disease of the brain which affects multiple aspects of a person's life. Providers, practitioners, and funders often face challenges in helping individuals achieve positive long-term outcomes without relapse.

33. The Commission recommends HHS/CMS, the Indian Health Service (IHS), Tricare, the DEA, and the VA remove reimbursement and policy barriers to SUD treatment, including those, such as patient limits, that limit access to any forms of FDA-approved medication-assisted treatment (MAT), counseling, inpatient/residential treatment, and other treatment modalities, particularly fail-first protocols and frequent prior authorizations. All primary care providers employed by the above-mentioned health systems should screen for alcohol and drug use and, directly or through referral, provide treatment within 24 to 48 hours.

34. The Commission recommends HHS review and modify rate-setting (including policies that indirectly impact reimbursement) to better cover the true costs of providing SUD treatment, including inpatient psychiatric facility rates and outpatient provider rates.

35. Because the Department of Labor (DOL) regulates health care coverage provided by many large employers, the Commission recommends that Congress provide DOL increased authority to levy monetary penalties on insurers and funders, and permit DOL to launch investigations of health insurers independently for parity violations.

36. The Commission recommends that federal and state regulators should use a standardized tool that requires health plans to document and disclose their compliance strategies for non-quantitative treatment limitations (NQTL) parity. NQTLs include stringent prior authorization

and medical necessity requirements. HHS, in consultation with DOL and Treasury, should review clinical guidelines and standards to support NQTL parity requirements. Private sector insurers, including employers, should review rate-setting strategies and revise rates when necessary to increase their network of addiction treatment professionals.

37. The Commission recommends the National Institute on Corrections (NIC), the Bureau of Justice Assistance (BJA), the Substance Abuse and Mental Health Services Administration (SAMHSA), and other national, state, local, and tribal stakeholders use medication-assisted treatment (MAT) with pre-trial detainees and continuing treatment upon release.

38. The Commission recommends DOJ broadly establish federal drug courts within the federal district court system in all 93 federal judicial districts. States, local units of government, and Indian tribal governments should apply for drug court grants established by 34 U.S.C. § 10611. Individuals with an SUD who violate probation terms with substance use should be diverted into drug court, rather than prison.

39. The Commission recommends the Federal Government partner with appropriate hospital and recovery organizations to expand the use of recovery coaches, especially in hard-hit areas. Insurance companies, federal health systems, and state payers should expand programs for hospital and primary case-based SUD treatment and referral services. Recovery coach programs have been extraordinarily effective in states that have them to help direct patients in crisis to appropriate treatment. Addiction and recovery specialists can also work with patients through technology and telemedicine, to expand their reach to underserved areas.

40. The Commission recommends the Health Resources and Services Administration (HRSA) prioritize addiction treatment knowledge across all health disciplines. Adequate resources are needed to recruit and increase the number of addiction-trained psychiatrists and other physicians, nurses, psychologists, social workers, physician assistants, and community health workers and facilitate deployment in needed regions and facilities.

41. The Commission recommends that federal agencies revise regulations and reimbursement policies to allow for SUD treatment via telemedicine.

42. The Commission recommends further use of the National Health Service Corp to supply needed health care workers to states and localities with higher than average opioid use and abuse.

43. The Commission recommends the National Highway Traffic Safety Administration (NHTSA) review its National Emergency Medical Services (EMS) Scope of Practice Model with respect to naloxone, and disseminate best practices for states that may need statutory or regulatory changes to allow Emergency Medical Technicians (EMT) to administer naloxone, including higher doses to account for the rising number of fentanyl overdoses.

44. The Commission recommends HHS implement naloxone co-prescribing pilot programs to confirm initial research and identify best practices. ONDCP should, in coordination with HHS, disseminate a summary of existing research on co-prescribing to stakeholders.

45. The Commission recommends HHS develop new guidance for Emergency Medical Treatment and Labor Act (EMTALA) compliance with regard to treating and stabilizing SUD patients and provide resources to incentivize hospitals to hire appropriate staff for their emergency rooms.

46. The Commission recommends that HHS implement guidelines and reimbursement policies for Recovery Support Services, including peer-to-peer programs, jobs and life skills training, supportive housing, and recovery housing.

47. The Commission recommends that HHS, the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Administration on Children, Youth and Families (ACYF) should disseminate best practices for states regarding interventions and strategies to keep families together, when it can be done safely (e.g., using a relative for kinship care). These practices should include utilizing comprehensive family centered approaches and should ensure families have access to drug screening, substance use treatment, and parental support. Further, federal agencies should research promising models for pregnant and post-partum women with SUDs and their newborns, including screenings, treatment interventions, supportive housing, non-pharmacologic interventions for children born with neonatal abstinence syndrome, medication-assisted treatment (MAT) and other recovery supports.

48. The Commission recommends ONDCP, the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Department of Education (DOE) identify successful college recovery programs, including "sober housing" on college campuses, and provide support and technical assistance to increase the number and capacity of high-quality programs to help students in recovery.

49. The Commission recommends that ONDCP, federal partners, including DOL, large employers, employee assistance programs, and recovery support organizations develop best practices on SUDs and the workplace. Employers need information for addressing employee alcohol and drug use, ensure that employees are able to seek help for SUDs through employee assistance programs or other means, supporting health and wellness, including SUD recovery, for employees, and hiring those in recovery.

50. The Commission recommends that ONDCP work with the DOJ, DOL, the National Alliance for Model State Drug Laws, the National Conference of State Legislatures, and other stakeholders to develop model state legislation/regulation for states to decouple felony convictions and eligibility for business/occupational licenses, where appropriate.

51. The Commission recommends that ONDCP, federal agencies, the National Alliance for Recovery Residents (NARR), the National Association of State Alcohol and Drug Abuse Directors (NASADAD), and housing stakeholders should work collaboratively to develop quality standards and best practices for recovery residences, including model state and local policies. These partners should identify barriers (such as zoning restrictions and discrimination against MAT patients) and develop strategies to address these issues.

Research and Development

52. The Commission recommends federal agencies, including HHS (National Institutes of Health, CDC, CMS, FDA, and the Substance Abuse and Mental Health Services Administration), DOJ, the Department of Defense (DOD), the VA, and ONDCP, should engage in a comprehensive review of existing research programs and establish goals for pain management and addiction research (both prevention and treatment).

53. The Commission recommends Congress and the Federal Government provide additional resources to the National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), and National Institute on Alcohol Abuse and Alcoholism (NIAAA) to fund the research areas cited above. NIDA should continue research in concert with the pharmaceutical industry to develop and test innovative medications for SUDs and OUDs, including long-acting injectables, more potent opioid antagonists to reverse overdose, drugs used for detoxification, and opioid vaccines.

54. The Commission recommends further research of Technology-Assisted Monitoring and Treatment for high-risk patients and SUD patients. CMS, FDA, and the United States Preventative Services Task Force (USPSTF) should implement a fast-track review process for any new evidence-based technology supporting SUD prevention and treatments.

55. The Commission recommends that commercial insurers and CMS fast-track creation of Healthcare Common Procedure Coding System (HCPCS) codes for FDA-approved technology-based treatments, digital interventions, and biomarker-based interventions. NIH should develop a means to evaluate behavior modification apps for effectiveness.

56. The Commission recommends that the FDA establish guidelines for post-market surveillance related to diversion, addiction, and other adverse consequences of controlled substances.

The Drug Addiction and Opioid Crisis

The primary goal of the President's Commission on Combatting Drug Addiction and the Opioid Crisis is to develop an effective set of recommendations for the President to combat the opioid crisis and drug addiction in our nation. Many of the recommendations that follow will require appropriations from Congress into the Public Health Emergency Fund, for block grants to states and to DOJ for enforcement and judicial improvements. It is not the Commission's charge to quantify the amount of these resources, so we do not do so in this report.

The Commission urges Congress to respond to the President's declaration of a Public Health Emergency and fulfill their constitutionally delegated duty and appropriate sufficient funds to implement the Commission's recommendations. 175 Americans are dying every day. Congress must act. Notwithstanding this core mission, it is vital to address the influences that transformed the United States into the world leader of opioid prescribing, opioid addiction, and opioid overdose deaths.

Origins of the Current Crisis

The Current Crisis. In the mid- to late-19th century, the first national opioid crisis occurred; a detailed history is provided in Appendix 2. During this time, opioid use rose dramatically, fueled by physicians' unrestrained opioid prescriptions (morphine, laudanum, paregoric, codeine, and heroin) for pain or other ailments, and by liberal use of opioid-based treatments for injuries and diseases impacting Civil War combatants and veterans (see Appendix 2). In parallel with the current crisis, this nation-wide crisis extended across socio-economic statuses, and reached urban and rural areas. This first epidemic was eventually contained and reversed by physicians, pharmacists, medical education, and voluntary restraint, combined with federal regulations and law enforcement.

After the first crisis subsided, medical education emphasized the hazards of improper opioid prescribing, and by doing so, created a cultural mindset against the dangers of opioids. However, over 30 years ago, a sequence of events eroded fears of opioids, and the medical community once again relapsed into liberal use of medicinal opioids.

Triggered by excessive prescribing of opioids since 1999, the current crisis is being fueled by several factors that did not exist in the 19th century: the advent of large scale production and distribution of pure, potent, orally effective and addictive opioids; the widespread availability of inexpensive and purer illicit heroin; the influx of highly potent fentanyl/fentanyl analogs; the transition of prescription opioid misusers into use of heroin and fentanyl; and the production of illicit opioid pills containing deadly fentanyl(s) made by authentic pill presses. Prescription opioids now affect a wide age range, families both well-off and financially disadvantaged, urban and rural, and all ethnic and racial groups.

Historical precedent demonstrated that this crisis can be fought with effective medical education, voluntary or involuntary changes in prescribing practices, and a strong regulatory and enforcement environment. The recommendations of the Commission are grounded in this reality, and benefit from modern systematic epidemiological and large data analytics, evidence-based treatments, and medications to assist in recovery or rescue of an overdose crisis.

Contributors to the Current Crisis. A widely held and supportable view is that the modern opioid crisis originated within the healthcare system and have been influenced by several factors:

- **Unsubstantiated claims:** One early catalyst can be traced to a single letter to the Editor of the New England Journal of Medicine published in 1980, that was then cited by over 600 subsequent articles.[1,2] With the headline "Addiction Rare in Patients Treated with Narcotics," the flawed conclusion of the five-sentence letter was based on scrutiny of records of hospitalized patients administered an opioid. It offered no information on opioid dose, number of doses, the duration of opioid treatment, whether opioids were consumed after hospital discharge, or long-term follow-up, nor a description of criteria used to designate opioid addiction. Six years later, another problematic study concluded that "opioid maintenance therapy can be a safe, salutary and more humane alternative to the options of surgery or no treatment in those patients with intractable non-malignant pain and no history of drug abuse."[3] High quality evidence demonstrating that opioids can be used safely for chronic non-terminal pain did not exist at that time. These reports eroded the historical evidence (see Appendix 2) of iatrogenic addiction and aversion to opioids, with the poor-quality evidence that was unfortunately accepted by federal agencies and other oversight organizations.

- **Pain patient advocacy:** Advocacy for pain management and/or the use of opioids[4,5,6] by pain patients was promoted, not only by patients, but also by some physicians. One notable physician stated: "make pain 'visible'… ensure patients a place in the communications loop… assess patient satisfaction; and work with narcotics control authorities to encourage therapeutic opiate use… therapeutic use of opiate analgesics rarely results in addiction."[7]

- **The opioid pharmaceutical manufacturing and supply chain industry:** One pharmaceutical company sponsored over 20,000 educational events for physicians and others on managing pain with opioids, claiming their potential for addiction was low.[8] Yet, warning signs of the addictive potential of oxycodone and similar opioids long predated this period: in 1963, Bloomquist wrote that dihydrohydroxycodeinone (oxycodone, Percodan®), "although a useful analgesic retains addiction potential comparable to that of morphine. This fact should be considered when it is prescribed. Because of increasing numbers of addicts to this drug in the State of California, the California Medical Association Committee on Dangerous Drugs and the House of Delegates has recommended that oxycodone-containing drugs be returned to the triplicate prescription list as they were originally in 1949." This recommendation failed to pass the legislature.[9] Similar warnings followed.

  Aggressive promotion of an oxycodone brand from 1997-2002 led to a 10-fold rise in prescriptions to treat moderate to severe noncancer pain, and increases in prescribing of other opioids. Subsequently, the highest strengths permissible was increased for opioid-tolerant patients, likely contributing to its misuse. Extended-release (ER) formulations and delayed absorption were marketed as reducing abuse liability, but crushing the pills allowed users to snort or inject the drugs.[10,11] There are now at least five marketed opioids that carry abuse-deterrent labeling. It has been hypothesized that the marked rise in heroin and other illicit synthetic opioids is, in part, associated with unintended consequences of reformulation of OxyContin, and a reduced supply and greater expense of prescription opioids.[12,13]

  To this day, the opioid pharmaceutical industry influences the nation's response to the crisis.[14] For example, during the comment phase of the guideline developed by the Centers for Disease Control and Prevention (CDC) for pain management, opposition to the guideline was more

common among organizations with funding from opioid manufacturers than those without funding from the life sciences industry.[15]

- **Rogue pharmacies and unethical physician prescribing:** The key contributors of the large number of diverted opioids were unrestrained distributors, rogue pharmacies, unethical physicians, and patients whose opioid medications were diverted, or other patients who sold and profited from legitimately prescribed opioids.[16]

- **Pain as the 'fifth vital sign':** The phrase, "pain as the 'fifth vital sign,'" was initially promoted by the American Pain Society in 1995, to elevate awareness of pain treatment among healthcare professionals; "Vital Signs are taken seriously. If pain were assessed with the same zeal as other vital signs are, it would have a much better chance of being treated properly. We need to train doctors and nurses to treat pain as a vital sign. Quality care means that pain is measured and treated."[17]

  The Veteran's Administration (VA)[18] and then the Joint Commission on Accreditation of Healthcare Organizations (the Joint Commission) designated pain as a 'fifth vital sign.'[19,20] The Joint Commission accredits and certifies health care organizations. Certification has implications for objective assessment of clinical excellence, and for contracting and reimbursement. The Joint Commission's standards for pain assessment in 2000 "were a bold attempt to address widespread underassessment and undertreatment of pain,"[21] even though the health care community was not advocating for a regulatory approach to pain management.[22] The standards raised concerns that requiring all patients to be screened for the presence of pain and raising pain treatment to patients' rights issue could lead to overreliance on opioids.

  The Joint Commission received sponsorship for developing educational materials from an opioid pharmaceutical company, one of over 20,000 pain-related educational programs through direct sponsorship or financial grants. It was "unaware that the science behind their claims and the advice of experts in the field were erroneous."[23] This designation set in motion a growing compulsion to detect and treat pain, especially to prescribe opioids beyond traditional boundaries of treating acute, postoperative, procedural pain and end-of-life care. The surge in opioid supply escalated into opioid-related misuse, diversion, use disorder, and overdose deaths. Administrators, regulatory bodies, and insurers collectively pressured physicians to address patient satisfaction with aggressive pain management.[24] However, the concept that iatrogenic addiction was rare and that long-acting opioids were less addictive had been widely repeated, and studies refuting these claims were not published until years later. The Joint Commission has since eliminated the requirement that pain be assessed in all patients, except for patients receiving behavioral health care and established much stricter processes to review any corporate sponsorship of educational programs. In 2016, the Joint Commission began to revise its pain standards,[25] which will go into effect in January 2018.

- **Inadequate oversight by the Food and Drug Administration (FDA):** The FDA is the sole federal authority responsible for protecting public health by assuring the safety, efficacy, and security of human drugs, biological products, and medical devices. It approves medications to diagnose, treat, and mitigate illnesses, after assessing their safety and efficacy. It safeguards the nation's medications by setting standards for proper prescribing of approved drugs and post-approval surveillance. The FDA provided inadequate regulatory oversight. Even when overdose deaths mounted and when evidence for safe use in chronic care was substantially lacking, prior to 2001, the FDA accepted claims that newly formulated opioids were not

addictive, did not impose clinical trials of sufficient duration to detect addiction, or rigorous post-approval surveillance of adverse events, such as addiction.

The FDA also failed to assess the risks associated with deliberate diversion and misuse of opioids, risks that conceivably outweighed the intended benefits for patients if used as directed. They accepted the pharmaceutical industry's claim that iatrogenic addiction was "very rare" and that the delayed absorption of OxyContin reduced the abuse liability of the drug.[26] By 2001, the FDA removed these unsubstantiated claims from OxyContin's labeling. In March 2016, the FDA requested from the National Academies of Sciences, Engineering, and Medicine (NASEM) and received on July 13, 2017, a summary of the current status of science regarding prescription opioid abuse and misuse, and the role of opioids in pain management.[27] The current FDA Commissioner has stated a strong commitment to using the regulatory authority of the FDA to mitigate the adverse consequences of opioid use.[28]

- **Reimbursement for prescription opioids by health care insurers:** Sales of prescription opioids in the U.S. nearly quadrupled from 1999 to 2014,[29] largely paid for by insurance carriers. It is estimated that 1 out of 5 patients with non-cancer pain or pain-related diagnoses are prescribed opioids in office-based settings.[30] From 2007 to 2012, the rate of opioid prescribing steadily increased amongst specialists more likely to manage acute and chronic pain (pain medicine [49%], surgery [37%], physical medicine/rehabilitation [36%]). Insurance carriers, including Medicare Part D plans, did not serve as a stop-gap to the huge influx of opioid prescriptions.

- **Medical education:** Medical education has been deficient in pain management, opioid prescribing, screening for, and treating addictions.[31] During the 1990's, the pain movement should have alerted medical education institutions and creators of continuing medical education courses to address this issue. In some medical schools and some specialties, it remains inadequate to this day.[32] One strategy promoted 10 years ago to stratify patients' risk for opioid misuse and overdose was the screening of patients for substance use disorders (SUDs), especially pain patients.[33] Implementation of Screening, Brief Interventions, and Referral to Treatment (SBIRT) in healthcare systems was incentivized with billing codes.[34] SBIRT was mainstreamed into health care reform, but has yet to be incorporated nationally into medical curricula, or applied as routine care. Nor do core curricula necessarily address addictions, treatment options, or stress the need to screen for substance use and mental health.

- **Lack of patient education:** Patients and their families are not often fully informed regarding whether their prescriptions are opioids, the risks of opioid addiction or overdose, control and diversion, dose escalation, or use with alcohol or benzodiazepines.

- **Public demand evolves into reimbursement and physician quality ratings pegged to patient satisfaction scores:** Today, the use of opioids for chronic non-cancer pain remains controversial for the same reasons their use declined and was avoided at the turn of the 20th century: the potential for misuse and addiction, insufficient high-quality evidence of efficacy with long-term use, poor functional outcomes, overdose and death.

  Yet, a strong public demand for opioids continues to pressure clinicians to prescribe opioids persists. As an example, a recent survey of Emergency Department (ED) physicians indicated that 71% reported a perceived pressure to prescribe opioid analgesics to avoid administrative and regulatory criticism. Uniformly, they voiced concern about excessive emphasis on patient satisfaction scores by reimbursement entities as a means of evaluating their patient

management. The physician requirement to address pain as the "fifth vital sign" persists,[35] and reimbursement metrics based on patient satisfaction may have inadvertently created an environment conducive to exploitation by prescription opioid abusers.[36] There are legitimate circumstances for which opioids are an appropriate therapy. But many current institutional and societal issues continue to pressure physicians to prescribe opioids when they are not clinically appropriate.

Prior to this year, poor patient satisfaction with pain care could lead to reduced hospital reimbursement by Medicare through Value-Based Purchasing (VBP). There are often higher costs or no specific reimbursements for alternative pain management strategies, alternative pain intervention strategies, or spending time to educate patients about the risks of opioids. Further, failing to provide adequate pain relief can be grounds for malpractice claims or medical board action.

- **Lack of foresight of unintended consequences:** As prescription drugs came under tighter scrutiny and access became more limited (via abuse-deterrent formulations and more cautious prescribing), market forces responded by providing less expensive and more accessible *illicit* opioids. Increases in overdose death numbers due to prescription opioids have transitioned to overdoses largely due to heroin and, increasingly, fentanyl.[37] Locally, this trend may have been driven, in part, by tightening controls on prescription opioids. Physicians curtailed opioid prescriptions without guidelines on tapering and without determination of whether patients had developed an opioid use disorder (OUD), and if so, how to respond.[38]

  The availability of cheaper heroin also drove prescription opioid misusers to illicit opioids. Black market heroin is currently much less expensive than diverted prescription opioids, and fentanyl is even much less expensive per dose than heroin. Predictable from the economics of the two drug categories, the prescription drug overdose problem has decreased, but not the overall number of opioid-related deaths.

- **Treatment services insufficient to meet demand and to provide medication-assisted treatment (MAT):** As OUDs increased dramatically over the past 15 years, quality treatment services and the associated workforce did not expand in response to the growing crisis.

- **Lack of national prevention strategies:** Prevention strategies focusing on specific illicit drugs for vulnerable populations - adolescents, college age youth, pregnant women, unemployed men, and other - and for influencers, (parents, families) don't exist or have not been tested adequately.

Magnitude and Demographics

National statistics on prescription opioid misuse and use disorder, 2016.[39] Weighted *National Survey on Drug Use and Health* (NSDUH) estimates suggested that, in 2016, 91.8 million (34.1%) or more than one-third of U.S. civilian, noninstitutionalized adults used prescription opioids; 11.5 million (4.3%) misused them. In 2015, 1.6 million (0.7%) had an OUD. Among adults with prescription opioid use, 12.2% reported misuse and 15.1% of misusers reported a prescription OUD.[40] The most commonly reported motivation for misuse was to relieve physical pain (63.6%). Misuse and use disorders were most commonly reported in adults who were uninsured, were

unemployed, had low income, or had behavioral health problems. Among adults with misuse, 62.2% reported using opioids without a prescription, and 40.6% obtained prescription opioids for free from friends or relatives for their most recent episode of misuse. The results suggest a need to improve access to evidence-based pain management and to decrease excessive prescribing that may leave unused opioids available for potential misuse.[41]

The NSDUH estimates that 3.4 million people aged 12 or older in 2016 were *current* misusers of pain relievers (1.2% of the population aged 12 or older).[42] In 2016, an estimated 239,000 adolescents aged 12 to 17 were *current* misusers of pain relievers (1.0% of adolescents) and 631,000 young adults aged 18 to 25 misused pain relievers in the past month (1.8% of young adults). Among adults aged 26 or older, 2.5 million are estimated to be current misusers of pain reliever (1.2%). Upwards of 1.8 million Americans harbor an OUD involving prescription opioids or 0.7% of people aged 12 or older. Among adolescents aged 12 to 17, 152,000 (0.6%) had a pain reliever use disorder in the past year, and 291,000 young adults aged 18 to 25 (0.8%) and 1.3 million adults aged 26 or older in 2016 (0.6%) had a pain reliever use disorder in the past year. These small percentages do not convey the massive personal and public health burden created by misuse of opioids.

National statistics on heroin use and use disorder, 2016.[43] The addictive and illegal opioid heroin has no accepted medical use in the United States. Past 30 day users of heroin (475,000) among people aged 12 or older or 0.2% of the population is probably an underestimate because NSDUH surveys households and does not capture heroin users in homeless shelters or transient populations with no fixed address, and the incarcerated. Despite its dangers heroin use continues to escalate and reflects changes in heroin use by adults aged 26 or older and, to a lesser extent, among young adults aged 18 to 25. Less than 0.1% of adolescents aged 12 to 17 were current or past year heroin users (3,000 and 13,000, respectively) and these numbers remained relatively stable. Among young adults aged 18 to 25, 0.3% were current heroin users (88,000) and this number rose since 2002. For past year and at minimum, 630,000 individuals have a heroin use disorder (HUD).[17] Among adults 26 and older 0.2% were current heroin users (383,000), a rise since 2015. About 626,000 people aged 12 or older reported an HUD (0.2%), an increase since 2002 to 2011. Less than 0.1% of adolescents aged 12 to 17 (1,000) had an HUD in the past year, but this rate was many times higher among 18-25-year-olds (152,000; 0.4%). Approximately 473,000 adults aged 26 or older had an HUD (0.2%)

Substance use disorder treatment needs, 2016.[44] For NSDUH, people are defined as needing substance use treatment if they had an SUD in the past year or if they received substance use treatment at a specialty facility in the past year. In 2016, 10.6% of people aged 12 or older (2.3 million people) who needed substance use treatment received treatment at a specialty facility in the past year. Among people in specific age groups needing substance use treatment, 8.2% of adolescents aged 12 to 17, 7.2% of young adults aged 18 to 25, and 12.1% of adults aged 26 or older received substance use treatment at a specialty facility in the past year. These percentages represent 89,000 adolescents, 383,000 young adults, and 1.8 million adults aged 26 or older who needed substance use treatment and received treatment at a specialty facility in the past year. Prior to 2016, NSDUH reported on the reasons people in need in treatment did not receive it. Approximately 90% self-reported they did not feel the need for treatment and did not seek it.

Special Populations. The Commission recognizes that, although many of the recommendations included in this report are generic for the population as a whole, subpopulations exist within our nation that conceivably require increased outreach, access to services, and more tailored or

intensive services. These special populations can be viewed from the perspective of race or ethnicity, residential location and population density, gender, age[45], mental[46] and physical health status (e.g. HIV-AIDS), income, employment, socio-economic status, education, veterans,[47,48] involvement in the criminal justice system (juveniles, parolees, incarcerated), family status (fetus[49], children of substance-using parents or other family members, pregnant women, living alone), healthcare insurance sources, behavioral health indicators[50] (other SUDs or history), type of opioid use (heroin/fentanyl, prescription opioid nonmedical or medical use, or combined use), and others.

According to the 2016 NSDUH, more males (4.8%) than females (3.8%) misused prescription opioid medications.[51] Young adults aged 18 to 25 years old had the largest proportion of misusers. In comparison to the national average for past year misuse of pain relievers by those 12 years and older, misuse was most common among Americans with two or more races (6.5%), American Indian or Alaska Natives (3.9%), Native Hawaiian or other Pacific Islanders (4.2%), and Hispanics (4.2%). The rate of non-medical use of prescription opioid medications was lowest among Asians (1.8%).

Scrutiny of the NSDUH and other data sources can reveal which populations are at highest risk. A recent study using 2010-2013 NSDUH data[52] revealed the prevalence of OUDs was highest among whites (72.29%), with lower prevalence among blacks (9.23%), Hispanics 13.82%, and others 4.66%. Other factors overrepresented among those reporting OUDs were adults aged 18–34 (55.95%), males (57.39%), low income (<$50,000; 67.12%), residents of large metropolitan areas (49.99%), with fewer privately insured persons (40.97%). Compared with whites, adolescents were overrepresented among mixed-race persons and Hispanics. In contrast, Native Americans included a higher proportion of older adults aged≥50.[53] Among mixed-race persons, the proportion of females was higher than males. The vast majority of blacks (83.78%), Native Americans (88.98%), and Hispanics (76.44%) were in the lowest income group. A high proportion of blacks, Native Hawaiians/Pacific Islanders/Asian Americans, and Hispanics resided in large metropolitan areas. A high proportion of native-Americans lived in nonmetropolitan areas. All non-white groups, except for Native Hawaiians/Pacific Islanders/Asian Americans, had higher proportions of public insurance than whites.

Among persons with OUD, the majority (80.09%) had another SUD, 28.74% had major depression, 53.02% had nicotine dependence, 40.93% had alcohol use disorder (AUD), and 43.22% had ≥1 other drug use disorder (cannabis 22.32%, tranquilizer 13.99%, cocaine 15.25%, stimulant 9.28%, hallucinogen 5.25%, sedative 3.51%, inhalant 2.22%), which was more prevalent among whites (83.39%) than Hispanics (72.04%). Major depressive episode was also common (28.74%). Most people with OUD report no use of OUD treatment, with only 26.19% using any alcohol or drug use treatment, 19.44% using opioid-specific treatment. Adolescents, the uninsured, blacks, Native Hawaiians/Pacific Islanders/Asian Americans, persons with prescription opioids only, and persons without depression episodes especially underutilized opioid-specific treatment. The treatment rate for adolescents among blacks with OUD was very low, unless they were involved with the criminal justice system. Among alcohol/drug use treatment users, self-help group and outpatient rehabilitation treatment were commonly used services.

Adolescent-onset OUD indicates a high risk for severe OUD. Low treatment rates, conceivably related to inadequate MAT data for adolescents, places this population at particular susceptibility. Native Hawaiians/Pacific Islanders/Asian Americans with OUD had the lowest prevalence of using alcohol/drug treatment (4.91%) or opioid-specific treatment (1.24%). Cultural-related

stigma toward addiction and a lack of culturally congruent addiction providers are unique barriers to seeking treatment. Residents in rural areas have relatively high rates of opioid overdoses, but they face substantial barriers to OUD treatment, including a shortage of mental/behavioral health providers.

Newly Emerging Threats

New Psychoactive Substances. The term "new psychoactive substances" (NPS) can be defined as individual drugs in pure form or in complex preparations that are not scheduled under the *Single Convention on Narcotic Drugs* (1961) or the *Convention on Psychotropic Substances* (1971). NPS may be categorized by chemical structure, by psychoactive properties, by biological targets, or by source (plant, synthetic, or combined). The emergence of NPS that target opioid sites in the body is challenging public health and drug policies globally. Their novelty, ambiguous legal status, ability to evade toxicological tests, swift adaptation to legal restrictions, global internet marketing, and scant public knowledge of their adverse effects are among the key drivers of this 21st century phenomenon.

The designation "new" is not necessarily limited to newly-designed compounds with no historical precedent, but may also include compounds modified from substances previously used. The majority are chemical analogs of drugs in restricted categories and may elicit effects similar to the parent drug, or a more amplified response. Others may evoke unique or complex sensations because of their hybrid structures, or because several compounds with differing pharmacological profiles are combined and sold as a unit. Although synthetic cathinone analogs and synthetic cannabinoids occupy a major share of this market, synthetic opioids, especially fentanyl analogs, are by far the most problematic substances because they are emerging as a leading cause of opioid overdose deaths in the United States.[54]

Drivers of NPS. The rapid expansion of NPS in the past decade is fueled by a convergence of the information revolution, vague legal status, uncertain detectability, and financial incentives combined with guileful marketing.

The internet is a "global neural network" that can be exploited to disseminate promotion and distribution of these drugs instantly. The venues are chat rooms, blogs, instant messaging sites, social networking, or multimedia sites. At minimal cost, descriptions of new drugs, their positive psychoactive effects, doses, synthetic routes, and purchasing sites are accessible world-wide on computers or mobile devices such as smart phones or smart watches. Many of the marketing sites are impervious to legal sanctions, as it takes time to deliberate the evidence and move newly emerging drugs into a legally restrictive zone, especially internationally.

Imperfect international agreements and a gradual dissolution of international resolve to attenuate drug use compromise effective solutions to this unique problem. Often, substances that imitate controlled drugs are unscheduled, unregulated, and not under the auspices of international law. Their nebulous legal status is an incentive for entrepreneurs to introduce new drugs quickly into the global market.

The allure of NPS is magnified by current limitations in detecting them. Identifying these drugs for forensic, workplace, legal, and policy purposes is constrained by a lack of reference materials and the need for sophisticated detection methods which are not routinely available (e.g., mass

spectroscopy). The chemical structures of NPS are designed to keep one step ahead of federal and international laws that restrict distribution and sale of specific chemicals. The Drug Enforcement Administration (DEA) has emergency powers to temporarily schedule a drug for 36 months, a time frame to accumulate evidence for/against long-term drug scheduling.

New Psychoactive Opioids. Novel opioid receptor agonists, some of which are much more potent than morphine, are of particular public health concern, as they can be mixed with or substituted for heroin, and are more likely to be deadly.[55] As these novel opioids emerge, emergency responders, medical professionals, law enforcement personnel, death investigators, medical examiners, toxicologists, and prosecutors face the challenge of treating and investigating intoxications and deaths from novel compounds whose identities are often unknown and for which analytical standards do not exist.

In 2013, the rapid ascent of the potent opioid agonist fentanyl compelled a rethinking of public health and regulatory approaches to the opioid crisis.[56] Fentanyl and fentanyl analogs, including carfentanil, are becoming a major contributor to opioid overdose fatalities in specific states, especially in the eastern half of the nation.[57] Many have been identified, with some fentanyl analogs found as contaminants of other drugs, e.g. furanyl fentanyl has been identified as a contaminant in crack cocaine.[58,59,60,61,62] As many do not cross-react in routine assays, a simple analytic device to identify whether a street drug is unknowingly contaminated with fentanyl analogs may yield a false negative and a false sense of security.

Other opioid NPS compounds include U-50488, desomorphine, tapentadol, salvinorin A, and its analog herkinorin.[63] 'Krokodil,' the street name for a homemade cheap heroin substitute in Russia, is synthesized from codeine, iodine, and red phosphorus, with esomorphine claimed as the end product. A total of 54 morphinans were detected after detailed chemical analysis, highlighting the possibility that additional morphinans may contribute to the psychotropic effects of krokodil.[64]

Pathways to Opioid Use Disorder (Including Heroin) from Prescription Opioids

Prior History of Prescription Opioid Misusers Who Seek Treatment. In 2016, 91.8 million people (ages 12 or older) in the United States use pain relievers in the past year.[65] Of these, 11.5 million people reported misuse of pain relievers.

In an analysis of more than 4,400 patients entering drug treatment for opioid abuse, of individuals initially exposed to opioids through a physician's prescription to treat pain, 94.6% had used a psychoactive substance non-medically prior to or coincident with their opioid prescription. Alcohol (92.9%), nicotine and/or tobacco (89.5%), and marijuana (87.4%) were used by nearly all patients prior to, or coincident with, their first opioid prescription. If one excludes these drugs, 70.1% (n=2,913) still reported some psychoactive drug use of licit or illicit stimulants (77.8%), benzodiazepines (59.8%) or hallucinogens (55.2%).[66] Similar findings were observed in a study restricted to women.[67] The findings are consistent with concerns that persons with prior use of addictive substances are at considerably higher risk for prescription opioid misuse, with addiction to one substance alone uncommon.[68] It highlights the need for clinicians to screen patients for prior drug use histories and judicious monitoring of and intervention with these at-risk patients prior to or during opioid prescribing. There is abundant evidence is that increased risk of iatrogenic

addiction or nonmedical use of prescription drugs overlaps consistently with problematic drinking, marijuana use, and other forms of substance use or a history of substance use or use disorder.

Prescription Opioids and Transition to Prescription OUD. Understanding the risks factors that drive transition to an OUD are critical for developing effective policies to attenuate the process.[69,70] The specific opioid, the dose, number of doses, duration, route of administration, formulation, ER, or immediate-release (IR) can influence misuse and progression to addiction. Some opioids engender greater likability or abuse liability than others. In patients dependent on heroin, oxycodone was ranked highest of several opioids, while buprenorphine scored lowest.[71] Overall, the risk of transition from medical use for pain relief to dependence is especially high for opioids, especially with longer use, and high doses.

One study found that the probability of long-term prescription opioid use increased markedly in the initial period of therapy, especially after five days or one month.[72] One causative factor of addiction is the development of rapid tolerance which can progress to OUD, without careful tapering.

In a small study of a single population, patients self-reported five common pathways to OUD: (1) inadequately controlled pain; (2) initial exposure to opioids during acute pain, which triggered a unique positive response; (3) relief from emotional distress; (4) relapse to a prior opioid addiction triggered by prescription opioids; and (5) misuse of prescription opioids solely for psychoactive purposes.[73] This survey highlights the need for prescribing clinicians to screen patients for prior history of substance use.

Prescription Opioids and Heroin Use Disorder. The vast majority of patients who use prescription opioids, either short or long term, do not progress to misuse and are unlikely to transition to heroin use. If transition occurs, the reverse (heroin to prescription opioids) is rare, as heroin is less expensive, more euphoric by the intravenous route, and more accessible. Overprescribing is still considered a driver of increases in opioid-related consequences, addiction, overdose, and infections, as it sustains nonmedical use of prescription opioids.[74,75] However, heroin initiation occurs in a relatively small subgroup of nonmedical users of prescription opioids,[76,77,78] but nonmedical use is a key risk for conversion to heroin use.[79,80] Although the percent of annual conversions from the large number of prescription opioid users to new heroin users is low, approximately 80% of heroin users are estimated to have transitioned from misuse of prescription opioids in recent years.[81,82]

Transition to heroin use among young prescription opioid users was predicted by prescription OUD, use of prescription opioids at an early age, and recreational use for psychoactive purposes. More specifically, a nationally representative sample of U.S. adolescents (2004-2011 NSDUH; n = 223,534; aged 12-21 years), showed that a prior history of nonmedical use of prescription opioids was strongly associated with heroin initiation, with the highest risk being nonmedical use of prescription opioids at ages 10-12 years, regardless of race/ethnicity or income group.[83] Moreover, because the peak period of heroin initiation occurs later, efforts to prevent heroin use may be most effective if they focus on young people who already initiated nonmedical use of prescription opioids.

An association between policies related to curtailing prescription opioids and heroin use or overdose mortality has yet to be definitively shown. Research has not yet shown whether restrictions on prescribing increased heroin use among those who had already initiated heroin. Yet,

past year heroin use among nonmedical opioid users has increased dramatically among young adults and emerging adults during the past six years.[84]

In one study of people in treatment, more persons (33.3%) in 2015 were experimenting with heroin as their first opioid exposure compared with 10 years prior (8.7%), although they may differ from the general population of opioid users.[85] In the same period, their endorsement of oxycodone and hydrocodone misuse declined. As supply side interventions reduce accessibility to commonly prescribed opioids, some initiates replace prescription opioids with heroin. Imprecise heroin dosing in users without a history of opioid use may contribute to overdose fatalities in novices. Fentanyl and analogues may be too strong for all but the most tolerant opioid users. Nearly half of patients entering treatment for OUD reported first exposure to opioids through a physician's prescription for pain management,[86] but these estimates may need revision in view of currently high availability of heroin and fentanyl.

Heroin Use. Heroin use also increased during the same period that witnessed a rise in prescription opioid misuse. Data from the 2001-2002 and 2012-2013 *National Epidemiologic Survey on Alcohol and Related Conditions-I and–III* (NESARC) showed prevalence of heroin use increased five-fold and use disorder tripled in the United States during the period between the two surveys.[87] The rise was greater among whites, unmarried respondents, males, young users, those with lower educational achievement, and those living in poverty. Prior exposure to nonmedical prescription opioids increased among white heroin users, reinforcing concerns and other reports that prescription opioid misusers were transitioning to heroin use. Evidence is accumulating that heroin is increasingly being used without prior to exposure to prescription opioids.[88]

Health, Financial, and Social Consequences

General Consequences of Opioid Misuse and Use Disorder. Heroin and other illicit opioids confer a high risk for medical consequences.[89] Nonmedical users of prescription pain relievers are 40 times more likely than the general population to use heroin or other injection drugs. Opioid addiction is a chronic difficult-to-treat disorder characterized by frequent relapses. Crude mortality rates and the risks of death of opioid users are substantially higher than the general population worldwide, although sample and country-level variables impact the extent and causes of mortality. Elevated causes of mortality among opioid users include overdose, traumatic and suicide deaths, and HIV-related mortality. Treatment, HIV-negative serostatus, and lower levels of injecting are protective factors against premature death.[90]

Powerful environmental factors can shape the course of heroin addiction. A study found that of the heroin-dependent soldiers who returned to the United States after the Vietnam War, only 12% were still drug dependent three years later.[91] Although more than half of the returning soldiers tried narcotics again, only a minority of them became re-addicted. These results illustrate that powerful environmental factors may influence the course of heroin addiction.[92]

Stable abstinence is less than 30% after 10-30 years, and even if abstinent, use of other drugs including alcohol is frequent.[93,94] Family, social support, and employment are associated with improved recovery rates, whereas a history of sexual or physical abuse and comorbid mental disorders correlate with persistent opioid use.[95,96,97]

A five-year abstinent period is associated with an increase in likelihood of stable abstinence. Mortality is 6-20 times higher than that of the general population, with deaths depending on country of origin. In the United States, the primary cause of mortality is overdose deaths.[98]

Medical Consequences. Opioid users are less healthy from the perspective of physical and mental health than drug users who do not use opioids.[99] They are also substantial users of medical services at higher costs than non-users and require chronic medical, psychiatric, and addiction care. Those using non-prescribed opioids differ from persons using opioids as prescribed, with more severe drug problems, as manifested by higher intravenous drug use and behavior that puts them at higher risk for HIV and Hepatitis C.

Opioid users have higher numbers of ED visits, more inpatient hospital stays, along with almost double the inpatient costs compared to their non-opioid using counterparts. Current data out of North Carolina indicates both a record number of overdose patients visiting EDs and that half, 49% of overdose survivors seen in the ED, do not have insurance.

Opioid users also have a higher mean number of outpatient medical visits and higher associated costs over the same time period. Their self-reported health status is lower, and they have a higher number of chronic medical comorbidities than their non-opioid using counterparts. They were also more likely to have been prescribed medication for psychological/emotional problems in their lifetime and to have a mental illness diagnosis.[100] Patients using opioids are more likely to be taking two or more illicit or non-prescribed drugs, to be taking non-prescribed benzodiazepines, and to report intravenous drug use. Compared to patients using opioids only as prescribed, those using any non-prescribed opioids were more likely to have been homeless, have more serious drug problems than those using opioids only as prescribed, engage in intravenous drug use, and have a higher HIV risk-taking score. Non-prescribed opioid users also had more problem alcohol use relative to their prescribed opioid user counterparts.

Infections and infectious diseases. Although overdose contributes most to drug-associated mortality, infections stemming from intravenous drug use are another major cause of death or an illness requiring hospitalization.[101,102,103] Injecting drug users are at risk for acquiring hepatitis C virus (HCV) and HIV, as well as invasive bacterial infections, including endocarditis.[104,105]

Brain Toxicity. Brain toxicity is a common finding for specific drugs of abuse.[106,107,108,109] Diagnostic imaging, especially magnetic resonance imaging (MRI) can detect a range of brain abnormalities associated with heroin use, including neurovascular complications related to inadequate blood supply such as stroke. A rare form of leukoencephalopathy has also been shown in people inhaling heroin vapors.

Children at risk. Children are at high risk in opioid-using environments. Pregnant women who continue to use opioids throughout the gestational period are likely to deliver a newborn with neonatal abstinence syndrome (NAS). The incidence of NAS is increasing in the United States, and carries an enormous burden in terms of hospital days and costs.[110] In comparing infants with a diagnosis of NAS with non-NAS infants between 2003 and 2012, NAS admissions increased more than fourfold, resulting in a surge in annual costs from $61 million and 67,869 hospital days in 2003 to nearly $316 million and 291,168 hospital days in 2012. For an infant affected by NAS, the hospital stay was nearly 3.5 times as long (16.57 hospital days compared with 4.98 for a non-NAS patient) and the costs more than three times greater ($16,893 compared to $5,610 for a non-affected infant).[111]

Children living in homes with drug abusers have numerous challenges, including the potential for exposure to drug production, chemicals, or equipment, neglect because the caregiver is using, abusive behavior towards the child,[112] risk of removal from their family, and/or exposure to the criminal sale or distribution of drugs.[113,114]

Labor Force. The Labor Force Participation Rate has declined since 2007, primarily due to an aging population and effects of the Great Recession. However, a recent Brookings Institution study examining the implications of the opioid crisis on the labor force suggests that the increase in opioid prescriptions could account for much of the decline in the labor force participation of "prime age men" (ages 25-54) during this same time.[115] The Bureau of Labor Statistics Time-Use Survey finds that 44% of prime age men not in the labor force acknowledged taking pain medications the previous day. The Brookings study found similar results (47% took pain medication the day before), however, nearly two-thirds of those men indicated it was *prescription* pain medication. Thus, on any given day, 31% of prime age men not in the labor force take prescription pain medication, most likely opioid based. These percentages are likely lower than the actual proportion of men who consume pain medication, due to the sigma and legal risk associated with narcotics.

Financial, Educational, Workplace, and Criminal Justice System. Prescription opioid overdose, abuse, and dependence carry high costs. In 2013, it was estimated that the total economic burden was $78.5 billion (in 2013 dollars).[116] Approximately one-third of the costs of the prescription opioid crisis are attributable to health care, and one-fourth of costs are borne by the public sector. Using data from various sources, the "monetized burden" of prescription opioid overdose, abuse, and dependence was estimated from a societal perspective, including direct healthcare costs, costs related to loss productivity, and costs to the criminal justice system. Total spending for health care and substance abuse was over $28 billion, most of which ($26 billion) was covered by insurance. In nonfatal cases, costs for lost productivity, including reduced productivity for incarcerated individuals, were estimated at about $20 billion. Fatal overdose costs related to healthcare and lost productivity were estimated at $21.5 billion. Approximately 25% of the economic burden was borne by public sector (Medicaid, Medicare, and veterans' programs) and other government sources for substance abuse treatment. Criminal justice-related costs were estimated at $7.7 billion expended by state and local governments in addition to lost tax revenue. The total estimated economic burden for prescription opioid abuse, addiction, and overdose death and heroin addiction would be approximately $111 billion (in 2013 dollars). Many costs are inestimable, including the social impact on opioid-dependent people, and the suffering of family members as witnesses to addiction or to fatal overdose.

Drug Overdose Deaths

The crisis in opioid overdose deaths has reached epidemic proportions in the United States (33,091 in 2015), and currently exceeds all other drug-related deaths or traffic fatalities. These data from the CDC are expected to rise even higher for 2016.[117] The risk of overdose resides primarily, but not exclusively, among those harboring a medical diagnosis of an OUD.[118] Of six risk markers (sex, age, race, psychiatric disorders, SUDs, urban/rural residence), SUDs have the strongest association with drug overdose death, followed by psychiatric disorders, white race, 35-44 year age group, and male sex.[119] Opioid-related death rates are higher among those who had recently been released from prison, those who doctor-shop and receive opioid prescriptions from multiple

pharmacies, and those who consume prescription opioids in combination with other scheduled medications, particularly benzodiazepines. From 1999 onwards, overdose deaths due to prescription opioids rose incrementally and consistently outpaced annual heroin death rates.

Heroin overdose deaths remained relatively low from 1999 onwards, and then escalated 4-fold from 2010-2015. Data from death certificates in 2015 revealed a disproportionate rise from the previous year in deaths attributable to fentanyl/analogs (72.2%) and heroin (20.6%), with prescription opioid-related deaths rising minimally (2.6%).

The overall death rate was higher for prescription opioids, but the most recent data show minimal increases in deaths involving prescription overdoses, while an increasing proportion now involves synthetic opioids, mainly fentanyl. Clearly, contamination of the heroin supply with fentanyl is currently driving recent increases in opioid-related overdose deaths. Reports from individual states in 2016 and 2017 confirm this emerging trend, as heroin and/or fentanyl currently account for more than 50% of the overdose deaths in specific states.[120]

Substance Use Treatment Availability

Among the many consequences of opioid misuse is the increasing need for SUD treatment services. SUD treatment facilities, particularly those providing MAT-enhanced opioid treatment programs (OTP), are uncommon in rural areas, as are physicians who can provide MAT from their offices.

Across all U.S. counties, 38% did not have a treatment facility for SUD in 2016 (Table 1).[121] Ten percent of large central metro counties did not have an SUD treatment facility. The data show that progressively larger proportions of counties did not have SUD treatment facilities as the level of urbanization decreased. Among the most rural counties, 55% did not have a substance use treatment facility.

Figure 1 below shows counties that did not have an SUD treatment facility as of 2014 by level of urbanization, and it is clear that the vast majority of counties is rural.

Table 1. Treatment Facilities for Substance Use Disorder by Level of Urbanization, 2016

Level of Urbanization	Number of Counties				Percent of Counties in Level of Urbanization			
	Total	No Treatment Facilities for Substance Use Disorder (SUD)	No SUD Treatment Facilities with Opioid Treatment Programs	No SUD Treatment Facilities that accept Medicaid	Total	No Treatment Facilities for SUD	No SUD Treatment Facilities with Opioid Treatment Programs	No SUD Treatment Facilities that accept Medicaid
Large Central Metro	68	7	8	7	100%	10%	12%	10%
Large Fringe Metro	368	88	259	104	100%	24%	70%	28%
Medium Metro	373	100	242	116	100%	27%	65%	31%
Small Metro	358	100	267	121	100%	28%	75%	34%
Micropolitan (non-metro)	641	157	586	204	100%	24%	91%	32%
Non-core (non-metro)	1,333	728	1,321	800	100%	55%	99%	60%
United States	3,141	1,180	2,683	1,352	100%	38%	85%	43%

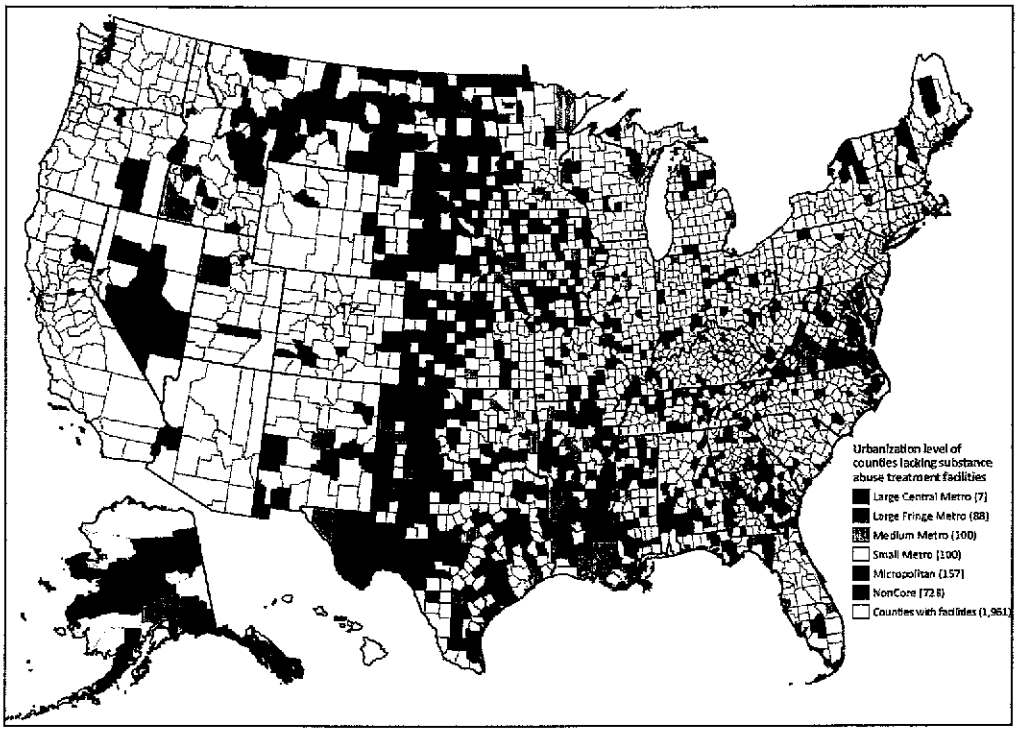

Figure 1. Counties with No Treatment Facilities for Substance Use Disorder by Level of Urbanization

Furthermore, 85% of all U.S. counties have no OTPs that provide MAT for people diagnosed with an OUD (Table 1). These facilities are concentrated in large central metropolitan areas, where 88% of these counties have at least one treatment facility offering OTP (only 12% of these central metropolitan counties do not have OTP facilities). For other metropolitan counties, 65 to 75% do not have OTP facilities, but among rural counties, almost all (91 to 99%) lack an OTP facility.

Figure 2 shows counties that did not have an OTP facility as of January 2016; as with SUD treatment facilities generally, the vast majority of these are rural counties. Many large fringe and medium metropolitan counties appear as doughnut-shaped areas around core locations where OTP facilities are located, but many rural counties are located far from OTP facilities.

Data were also obtained on the locations of physicians that can dispense buprenorphine from their offices.[122] Physicians can provide MAT for OUD treatment in settings other than OTP facilities, including dispensing buprenorphine from their offices. To prescribe or dispense buprenorphine for OUD treatment, qualified physicians must receive waivers from the DEA under the terms of the *Drug Addiction Treatment Act of 2000* (DATA 2000). As of February 2016, 47% of counties nationwide did not have a waived physician (Table 2). However, when classifying the county locations of waived physicians according to level of urbanization, the rural-urban disparities become clear. None of the large central metro counties, and 72% of the most rural counties, did not have a waived physician (Figure 3). The vast majority of counties without buprenorphine-waived doctors are rural. However, it is worth noting that the number of patients a physician can treat with buprenorphine is capped; so, having a waived physician within a geographic area is not necessarily indicative of sufficient access for county or city residents.

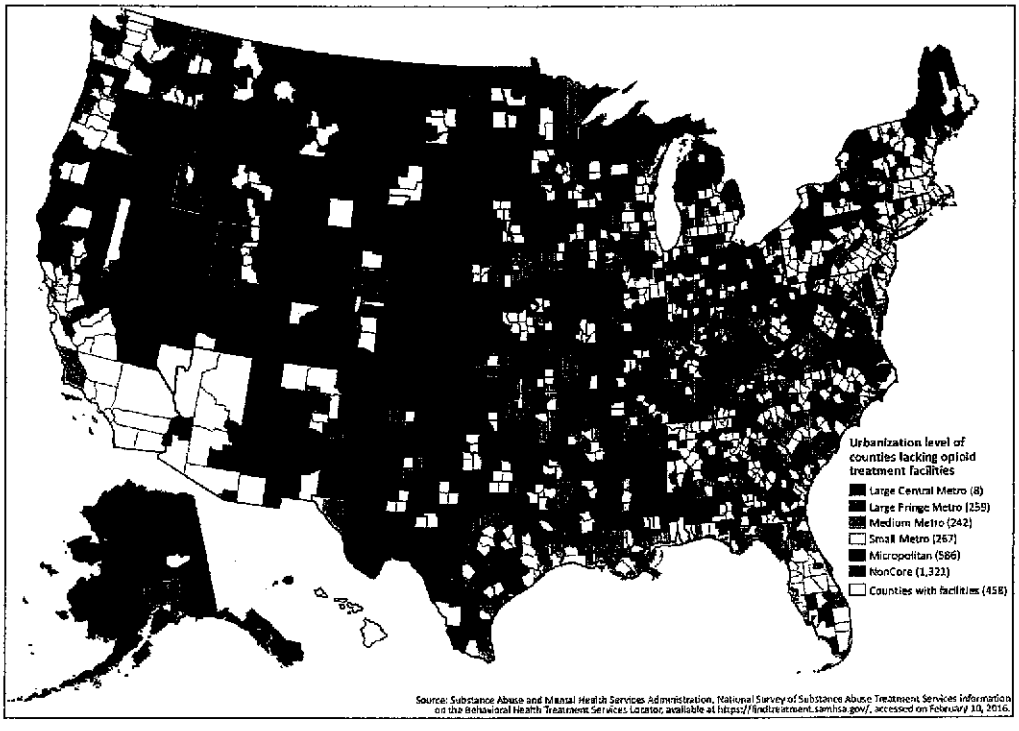

Figure 2. Counties with No Opioid Treatment Program Facilities by Level of Urbanization

While utilization of SUD treatment services in both rural and urban areas is challenged by many factors, the nature of these challenges varies. For example, findings from focus groups of counselors in rural areas noted a dearth of good facilities, poor access due to clients living far away from treatment centers, reliance on friends or family for transportation, and a need for basic medical and dental services. These factors were not mentioned by urban counselors.[123] A recent study of SUD treatment facilities that accept Medicaid also found that rural residents are less likely to have such a facility.[124]

Table 2. Physicians Waived to Dispense Buprenorphine by Level of Urbanization, 2016

Level of Urbanization	Number of Counties				Percent of Counties in Level of Urbanization			
	Total	No Waived Doctors	1-5 Waived Doctors	More than 5 Waived Doctors	Total	No Waived Doctors	1-5 Waived Doctors	More than 5 Waived Doctors
Large Central Metro	68	0	0	68	100%	0%	0%	100%
Large Fringe Metro	368	86	107	175	100%	23%	29%	48%
Medium Metro	373	107	86	180	100%	29%	23%	48%
Small Metro	358	113	103	142	100%	32%	29%	40%
Micropolitan (non-metro)	641	219	332	90	100%	34%	52%	14%
Non-core (non-metro)	1,333	964	340	29	100%	72%	26%	2%
United States	*3,141*	*1,489*	*968*	*684*	*100%*	*47%*	*31%*	*22%*

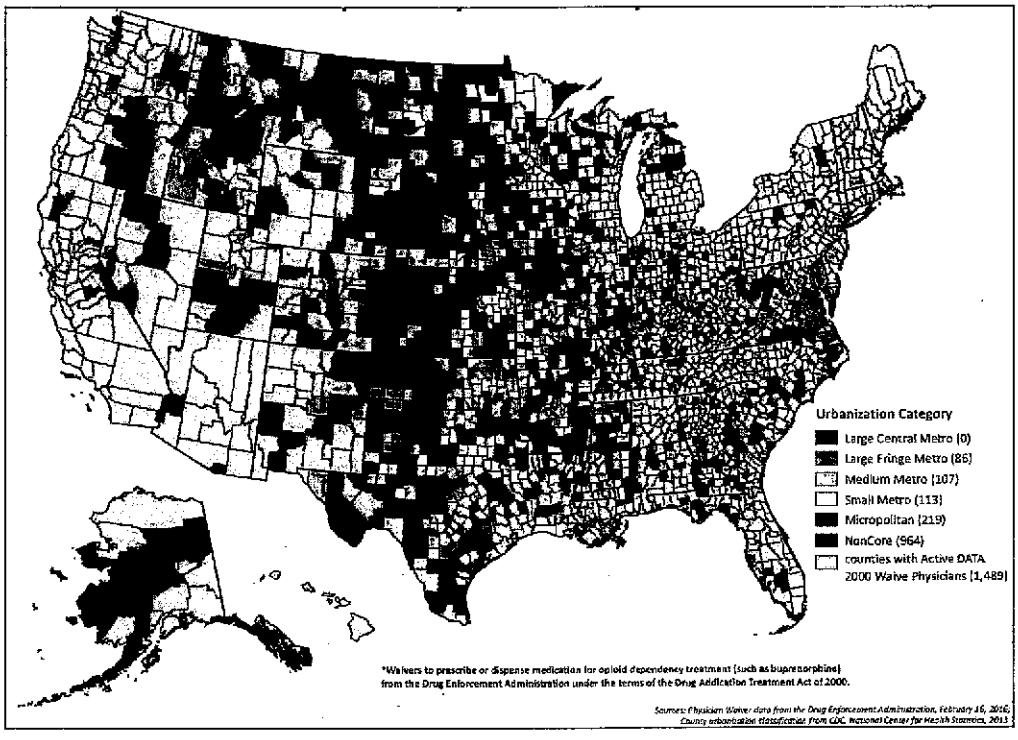

Figure 3. Counties with No Physicians with Buprenorphine Waivers by Level of Urbanization, 2016

Systems Approach to Solutions

There has never been a time more appropriate or opportune to develop effective and cost-effective policies for addressing substance use and disorders in our nation. A systems approach can facilitate development of recommendations and solutions to this dynamic and ever-shifting challenge. This report addresses solutions to each of the core components of the crisis, a trajectory which begins

with drug supply, attitudes towards drug use and knowledge of opioids, risk factors for misusing, and progresses to addiction, transition to heroin/fentanyl, situational factors in overdose, rescue, treatment, relapse prevention, recovery support, and continuum of care (Figure 4). Over the past decade, large databases have accumulated to inform policies and associated budgets.

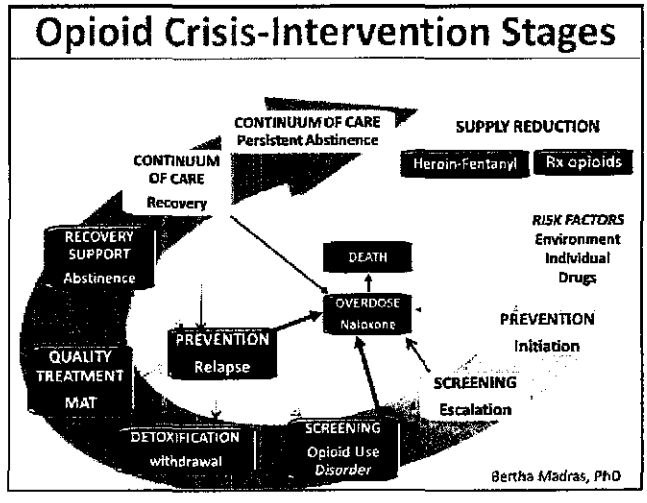

Figure 4. Opioid Crisis-Intervention Stages

The most urgent goals and readily quantifiable achievements will be a reduction in overdose episodes and deaths, increased entry into and adherence to high quality treatment, and a reduction in prescribed opioids. More complex models are needed to address whether prescribing policies result in time-dependent reductions in prescription opioid diversion or increase heroin/fentanyl use, who is at risk for transitioning to heroin or fentanyl, the incidence and prevalence of OUD, and others. The opioid epidemic defies standard medical and legal models for addressing addiction and trafficking. Limited data exists to track the crisis and identify weaknesses in current responses (e.g. prescribing practices, treatment availability, individuals at risk), but is held in different databases across a multitude of public and private organizations, and significant proportion is not in real-time.

Building a secure data foundation that promotes cross-entity collaboration while protecting privacy is a challenging but necessary step to save lives, expand treatment options, and effectively prevent further spread of this deadly epidemic. The data exists but resides in agency silos, or in the private sector providing analytics for specific industries (e.g. pharmaceutical or healthcare insurers), making it difficult to act upon the information. **The Federal Government should create an integrated data environment that brings together publicly available data with agency-specific data to help address this epidemic.** Often, the same data viewed through a different lens can support multiple parts of the problem. For example, doctors can use prescription drug monitoring programs (PDMPs) to check patient records, while law enforcement can use PDMPs to identify prolific opioid prescribers and public health agencies can use it to identify and intervene in a potential victim pool before overdoses occur – different, but all valuable uses of the same data.

This kind of effort would not require a new data warehouse or standardization initiative; the integrated data environment can immediately integrate existing data sources.

Federal Funding and Programs

On page 87 of the report, there is a full breakdown of federal funding sources for drug-related activities, including interdiction, prevention, and treatment. As shown in that section, the federal funding landscape is complex, exists in silos, potentially duplicative, and supports hundreds of on the ground programs.

Streamlining Federal Funding for Opioids and Consideration of State Administrators

One of the first activities the Commission Chair undertook was a series of calls with Governors' Offices in nearly all 50 states. A number of themes emerged from those calls that are reflected in this report and the recommendations. Regarding funding, many Governors and senior staff members expressed concern at how addiction and opioid-related funding coming from the Federal Government was fragmented; provided by many different agencies and funding sources which each had their own application requirements, reporting mechanisms, and preferred outcomes.

It is clear that each federal agency has goals related to reducing drug use and misuse and provides funding for such activities. However, from the vantage points of states, this funding is not well coordinated, and applying for funding from the many different agencies, is a tremendous administrative burden for states.

The SAMHSA block grants provide a formula-based grant to states for treatment activities; if additional funding opportunities could be rolled into the SAMHSA block grant, or combined to form larger block grants that required one application and one set of reporting requirements, that would free up state resources to focus on implementation activities, rather than paperwork.

Some states have identified a State Administrator to coordinate opioid and addiction activities. Others may use their Single State Authorities for substance abuse services to serve as an effective point of contact or liaison regarding most federally-supported demand reduction efforts in a state—although they may not always have up-to-date information on Department of Health and Human Services (HHS) or Department of Justice (DOJ) discretionary grant activities not directly involving the state. Regardless of the single entity that is identified by the state, the Federal Government should have a comparable single entity point of contact to help track activities related to discretionary grants with a demand reduction focus.

The Office of National Drug Control Policy's (ONDCP) core function is to develop and coordinate the implementation of national drug policy, but it does not have appropriate staff or organizational units to track federally supported demand reduction funding and activities at the program or grant level (versus the overarching policy level). The tasks of making and tracking grant awards fall squarely within the responsibility of the Departments and agencies that manage grant programs, including HHS's Regional Offices and the more recently established Substance Abuse and Mental Health Services Administration (SAMHSA) Regional Directors stationed in these offices. It therefore would seem reasonable for HHS to support ONDCP in this function by serving as an intermediary with Single State Authorities in the 50 states, the District of Columbia, and the territories. By so leveraging HHS and SAMHSA regional infrastructure, ONDCP could maintain timely accounting and ongoing awareness of the current allocation of federal demand reduction funding and the coordination of federally supported initiations, their contribution to activities

funded at the state and local level, duplication or inefficiencies that may need to be addressed, and timely scrutiny the program effectiveness of federally-or-state-funded programs. This would assist ONDCP to become aware of promising practices emerging at the state level.

1. **The Commission urges Congress and the Administration to block grant federal funding for opioid-related and SUD-related activities to the states, where the battle is happening every day. There are multiple federal agencies and multiple grants within those agencies that cause states a significant administrative burden from an application and reporting perspective. Creating uniform block grants would allow more resources to be spent on administering life-saving programs. This was a request to the Commission by nearly every Governor, regardless of party, across the country.**
2. **The Commission believes that ONDCP must establish a coordinated system for tracking all federally-funded initiatives, through support from HHS and DOJ. If we are to invest in combating this epidemic, we must invest in only those programs that achieve quantifiable goals and metrics. We are operating blindly today; ONDCP must establish a system of tracking and accountability.**

Funding Effective Opioid-Related Programs

As stewards of taxpayer dollars, the Federal Government must ensure that programs demonstrate effectiveness in achieving the desired policy outcomes. While various assessments have demonstrated that treating and preventing substance use are effective in reducing the costs associated with health care, the workplace, and criminal justice system, these costs-benefit analyses were done at the system, not program, level.

At the program level, the Federal Government has a long history of undertaking a variety of efforts, varyingly referred to as strategic planning, performance management, program evaluation, or performance budgeting, to inform management decisions for program and policy officials. These efforts have contributed to significant investments being made in the development of an evidence base for effective programs. However, comparing the effectiveness of programs has proven more elusive, and looking at system-wide cost effectiveness is rare. Research studies in addition to private and public-sector analyses may be of value to Federal efforts to develop and implement cost-benefit evaluations. For example, the Washington State Institute for Public Policy maintains a list of available, evidence-based public policy options and ranks them by return on investment.[125] While not a complete list, such ranked lists provide policymakers with a better understanding of the likelihood of which, of the many policy options available, are most likely to produce more benefits at lower costs.

Given the substantial challenges of the heroin and prescription opioid epidemic, it is critically important that the Federal Government maximize the impact of its response by supporting the most effective programs and policies to reduce the number of individuals affected by OUDs and end the nation's opioid epidemic. A thorough review of programs and policy options would assist the Director of ONDCP in making recommendations on how to best allocate scarce federal resources to achieve the objectives of the *National Drug Control Strategy*.

3. **To achieve accountability in federal programs, the Commission recommends that ONDCP review is a component of every federal program and that necessary funding is provided for implementation. Cooperation by federal agencies and the states must be mandated.**