In re Purdue Pharma LP, et al.

Joseph Hage Aaronson LLC

Counsel to Raymond Sackler Family ("Side B")

Defense Presentation Part 5: Underlying Claims Against Purdue, Effect of Criminal Plea, Deceptive Marketing, Preemption

April 27, 2021

Purdue Liability Is Necessary But Not Sufficient to Establish Director Liability

- All of the claims against the directors are dependent on Claimants' proving the underlying liability of Purdue
- The pre-petition claims against Purdue were weak but unmanageable — Purdue filed bankruptcy only because "the sheer number and scale of the Pending Actions is simply unmanageable" (Debtors' Informational Br. at 40 (Dkt. 17))
- Each Claimant must prove misrepresentation, causation, damage — all elements
- Each must establish the validity of the novel nuisance theory under its state's law
- Each must address overarching problems — *e.g.*, preemption, proximate cause
- Purdue's 2020 guilty plea does not help any Claimant establish a claim against Purdue

Purdue's 2020 Guilty Plea Does Not Help Any Claimant Establish A Claim Against Purdue

Purdue's 2020 Guilty Plea Does Not Help Any Claimant Establish A Claim Against Purdue

- Purdue pled guilty to a 3-count Information charging it with conspiracy to defraud the United States and violate the Food, Drug & Cosmetics Act
- Purdue admitted to:
  1. Fraud on the DEA and aiding and abetting prescribers in dispensing prescription drugs without a legitimate medical purpose (Count 1)
  2. Payments to two prescribers to induce them to write prescriptions in violation of the Anti-Kickback Statute (Count 2)
  3. Payments to Practice Fusion in violation of the Anti-Kickback Statute (Count 3)
- Nothing in Purdue's plea suggests that the former directors knew anything about Purdue's misconduct

(Purdue Plea Agmt., Schedule A, pp. 15-18)

Count 1: Fraud on The DEA – 1st Admission by PPLP

- **PPLP admitted that — in the sales data it provided to the DEA in support of its quota allocation requests — it included OxyContin prescriptions written by HCPs listed on Region Zero** (Purdue Plea Agmt., Schedule A, p. 16 ¶e)

Count 1: Fraud on The DEA – 1st Admission by PPLP

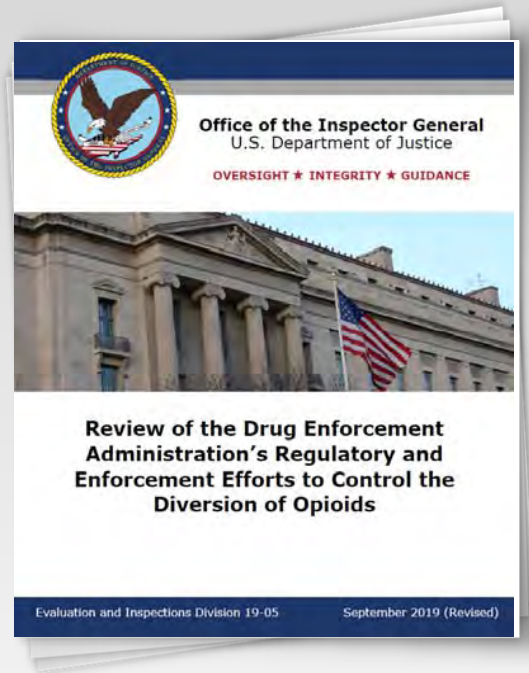
- **Claimants have no similar claims because quota allocation is determined exclusively by the DEA — no one else has quota-setting powers** (21 C.F.R. § 1303.21, *ff.)*
- PPLP did not have the power to stop Region Zero HCPs from prescribing OxyContin—but the State Claimants did have that power and had access to Region Zero information on request
- PPLP did not admit that inclusion of OxyContin prescriptions written by Region Zero HCPs actually affected the DEA's quota allocation in any year, **or did so in a way that affected any particular Claimant, or did so during a year within any applicable statute of limitations**
- The evidence shows that this misconduct had no effect on DEA quotas

DEA Was At All Times Well Aware That OxyContin Was Abused & Diverted

DEA's 2001 OxyContin National Action Plan:

DEA's Response to the OxyContin Crisis

To combat the growing OxyContin crisis, in the spring of 2001 DEA initiated an OxyContin National Action Plan. According to DEA, this was the first time in DEA's history that it developed a plan to target a brand-specific controlled substance with a focus on enforcement and regulatory investigations that targeted key points of diversion. The plan directed DEA field divisions and DEA's Office of Diversion Control (OD) to conduct in-depth investigations of OxyContin's manufacturer and distributors to determine their compliance with regulatory requirements designed to prevent diversion. The plan also sought to coordinate enforcement and intelligence sharing with federal, state, and local agencies; take regulatory and administrative action to limit abusers' access to OxyContin; and conduct outreach, awareness, and education initiatives to educate the public on the dangers of abusing OxyContin.



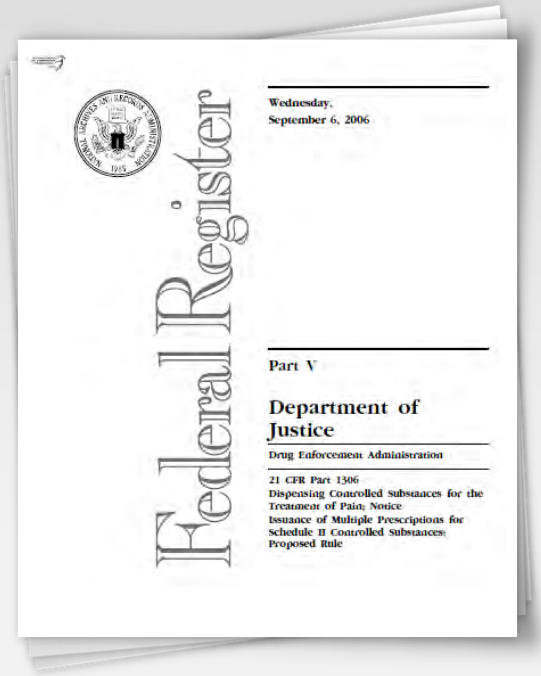
DOJ Office of Inspector General, OEI-19-05, *Review of DEA's Regulatory & Enforcement Efforts to Control the Diversion of Opioids*, at 4-5 (Sept. 2019) (https://oig.justice.gov/reports/2019/e1905.pdf)

DEA Was At All Times Well Aware That OxyContin Was Abused & Diverted

DEA 2006 Policy Statement: *Dispensing Controlled Substances for the Treatment of Pain*

Extent of Abuse in the United States of Controlled Prescription Drugs

The abuse (nonmedical use) of prescription drugs is a serious and growing health problem in this country. . . . A measure of the problem among young people is the 2005 Monitoring the Future (MTF) survey conducted by the University of Michigan. . . . For example, in 2005 ... 5.5 percent of [12th grade] students reported using OxyContin in the past year.



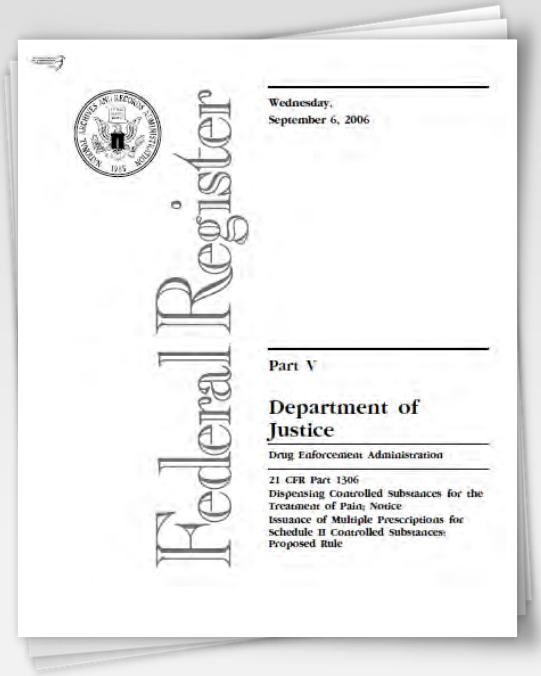
DEA Policy Statement, *Dispensing Controlled Substances for the Treatment of Pain*, 71 Fed. Reg. 52716, 52716 (Sept. 6, 2006)

DEA Was At All Times Well Aware That OxyContin Was Abused & Diverted

DEA 2006 Policy Statement: *Dispensing Controlled Substances for the Treatment of Pain*

- *Robert A. Smith, M.D.* (70 FR 33207)—Dr. Smith gave one patient seven to ten prescriptions of OxyContin per visit on a weekly basis. The prescriptions were written in the patient's name as well as the names of the patient's father and her fiancé. Each visit, the patient paid Dr. Smith a $65 fee for the office visit plus an additional $100 for the fraudulent prescriptions.

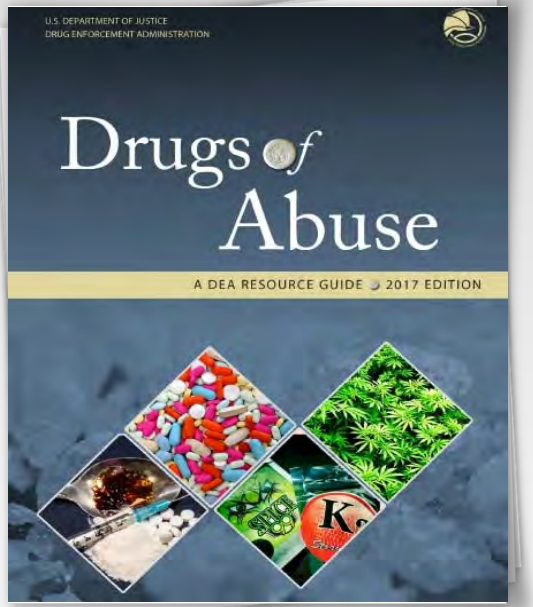
- *James S. Bischoff,, M.D.* (70 FR 12734)—
. . . Dr. Bischoff wrote the boy a prescription for 100 OxyContin, which Dr. Bischoff personally took to a pharmacy to be filled. Dr. Bischoff delivered only 20 tablets to the boy, unlawfully diverting the remaining 80 tablets.



DEA Policy Statement, *Dispensing Controlled Substances for the Treatment of Pain*, 71 Fed. Reg. 52716, 52720 (Sept. 6, 2006)

DEA Was At All Times Well Aware That OxyContin Was Abused & Diverted

DEA, *Drugs of Abuse* (2017 ed.)

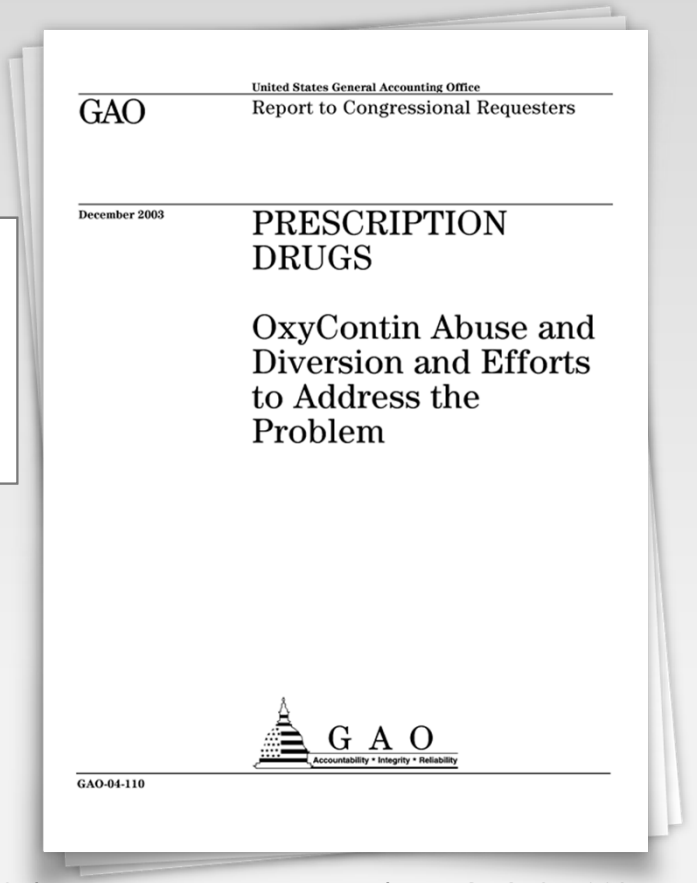


DEA, *Drugs of Abuse: A DEA Resource Guide* 38 (2017 ed.) - https://www.dea.gov/documents/2017/06/15/drugs-abuse

DEA Considered Abuse & Diversion in Setting Purdue's Quota

2003 GAO Report to Congress

In the last several years, DEA has taken the additional step of lowering the procurement quota requested by Purdue for the manufacture of OxyContin as a means for addressing abuse and diversion.



Dec. 2003 GAO Rept. to Congress at 38 (https://www.gao.gov/products/GAO-04-110)

DEA Considered Abuse & Diversion in Setting Purdue's Quota

From: Stedge, Barbara
Sent: Thursday, July 30, 2009 11:24 AM

Subject: FW: 2009 quota letter

Michael,

Can you provide DEA's rationale for granting less than the requested amount?
How is the inventory allowance being determined?

From: Morley, Michael J.
Date: Thursday, July 30, 2009 2:55 PM

Subject: RE: 2009 quota letter

Due to abuse and diversion of oxycodone products, DEA continues to authorize registered dosage form manufacturers a 30% inventory allowance. . . .

Your quota adjustment was assessed on many factors, including but not limited to . . .

* diversion/ abuse concerns

Message
From: Stedge, Barbara

Sent: 8/4/2009 6:03:06 PM
To: Morley, Michael J.
Subject: RE: 2009 quota letter
Attachments: image001.jpg; image002.gif

Michael:

I realize that there are various estimated values and as they change the Year-End projections will change. By updating the planned purchases with the actual quota granted and keeping all other factors the same, the total inventory allowance was 30.8%. Since DEA has applied an inventory allowance of 35.6% it would indicate that some other major factor[such as estimated commercial sales] in DEA's calculation was different.

My apologies if this wasn't clear, but I was trying to identify where the calculation differed. By revising the inventory projection and comparing the allowance to DEA's it was evident that the difference was the result of some other estimated value such as commercial demand as you indicated below.

Thank you for your time in this matter.

Regards,

Barbara Stedge

Director Controlled Substances/DEA Affairs

Purdue

973-837-5065

From: Morley, Michael J.
Sent: Tuesday, August 04, 2009 4:19 PM
To: Stedge, Barbara
Cc: Strait, Matthew J.; Carr, Susan M; Harper-Avilla, Stacy; Sannerud, Christine A
Subject: RE: 2009 quota letter

Good afternoon Barbara,

I'm not exactly sure what you are asking, but I will try to respond to your inquiry.

The tables provided have various estimated values and your calculations are based on these estimated values, i.e. forecasted sales, loss on assay, export requirements, etc.

Looking strictly at the data in your tables:

Your first table estimated 17,605 kg in sales with an estimated year-end inventory of 7,728 kg (44%)
Your second table estimated 17,605 kg in sales with an estimated year-end inventory of 5,409 kg (31%)

I suspect the difference lies in our offices estimated commercial demand vs. your estimated demand, but any difference in the various calculations or estimates will result in different calculated year-end inventory. As mentioned before, our office allows oxycodone dosage form manufacturers a 30% inventory allowance. In addition, due to the switch over to your new product line, our office considered your firm's request for an additional 5.6% inventory allowance.

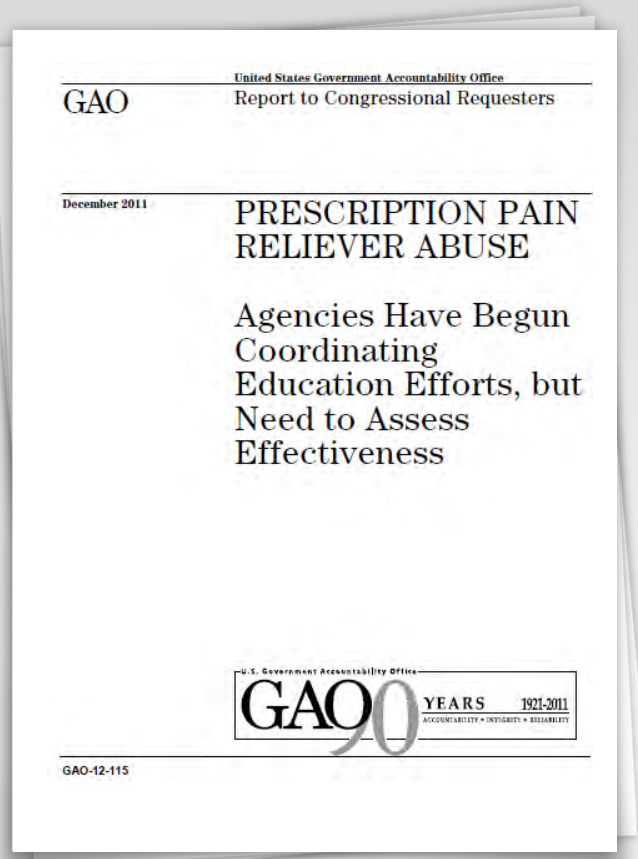
CONFIDENTIAL PWA001036221

July30-Aug. 4, 2009 Email Chain (PWA001036221)

DEA Has Determined That Establishing Quotas Based on Known Diversion "Will Not Appreciably Affect Diversion"

2011 GAO Report to Congress

While [DEA] officials said that they do seek to account for known diversion when setting [Aggregate Production Quotas], they said that establishing quotas based on known diversion for the purpose of reducing the availability of prescribed drugs will not appreciably affect diversion at the retail level and may prevent legitimate patients from having access to medication for legitimate medical needs.


United States Government Accountability Office
GAO
Report to Congressional Requesters

December 2011

PRESCRIPTION PAIN RELIEVER ABUSE

Agencies Have Begun Coordinating Education Efforts, but Need to Assess Effectiveness

U.S. Government Accountability Office
GAO 90 YEARS 1921-2011
ACCOUNTABILITY • INTEGRITY • RELIABILITY

GAO-12-115

Dec. 2011 GAO Rept. to Congress at 47 (https://www.gao.gov/assets/590/587301.pdf)

Count 1: Fraud on The DEA – 2nd Admission by PPLP

- Second, PPLP admitted that, with respect to "more than 100 HCPs," PPLP "failed to:

  (1) "report and provide complete and accurate information to DEA about HCPs after the HCPs were flagged by internal anti-diversion programs, in situations in which the Company possessed sufficient information that should have led to a report; and

  (2) "cease detailing HCPs after receiving information suggesting that those HCPs were prescribing opioid products without a legitimate medical purpose and outside the usual course of professional practice"

(Purdue Plea Agmt., Schedule A, p. 16 ¶f)

Count 1: Fraud on The DEA – 2nd Admission by PPLP

- Claimants do not and cannot advance similar claims
  - The States knew the ADD Program — most had insisted Purdue keep it in place
  - They knew that (1) "flagg[ing]" of an HCP did not give rise to a reporting requirement to the States, and (2) receipt of information suggesting that an HCP was misprescribing opioids did not trigger cessation of detailing
- There is no admission by PPLP as to the number or location of the "more than one hundred HCPs"
- There is no admission that any of these HCPs wrote any prescription for a medically unnecessary reason
- There is no admission that any of these HCPs did so during a year within any applicable statute of limitations

Count 1: Fraud on The DEA – 2nd Admission by PPLP

- There is no admission that Purdue's failure to report on or cease detailing these HCPs had any impact on DEA's quota allocation in any year
- There is no admission that any Claimant would have been affected if the unidentified HCPs been reported to DEA
- There is no admission that any prescription written by any of the "more than one hundred HCPs" caused any State to incur any cost
- There is no admission that — if Purdue had ceased detailing any of the HCPs — that would have had any effect on the HCPs' prescribing of Purdue opioids or had any impact on any Claimant

Count 1: Fraud on The DEA – 3rd Admission by PPLP

- PPLP admitted that it "fail[ed] to account for potential downstream diversion of its products in reporting sales numbers to DEA as part of its quota requests"

(Purdue Plea Agmt., Schedule A, pp. 16-17 ¶f)

  - **There is no admission that the failure to account for "potential downstream diversion" had any effect on DEA's quota allocation in any year or on any Claimant**
  - **There is no admission as to the location of any "potential downstream diversion"**
  - **There is no admission that the "potential downstream diversion" ever materialized or, if so, where, in what amount, and whether it occurred within the applicable statute of limitations**

Count 1: Fraud on The DEA – 4th Admission by PPLP

- PPLP admitted that it "knowingly and intentionally conspired and agreed with others to aid and abet HCPs' dispensing, without a legitimate medical purpose and outside the usual course of professional practice … prescription drugs"

  (Purdue Plea Agmt., Schedule A, p. 17 ¶g)

  - There is no admission as to
    - The number of unidentified HCPs
    - Their location
    - The amount or year of their illegal dispensing
    - Whether it affected any Claimant, let alone did so within the applicable statute of limitations

Count 2: Payments to Two HCPs

- In Count 2, PPLP admitted that, from June 2009 to March 2017, it unlawfully offered "payments in the form of speakers fees and other payments (*e.g.*, travel, lodging, consulting fees) to two HCPs with at least one purpose to induce those HCPs to write more prescriptions of Purdue opioid products, for which payment was made in whole or in part under a Federal healthcare program…."

  (Purdue Plea Agmt., Schedule A, p. 17 ¶h)

  - There is no suggestion that either HCP was deceived about the properties of Purdue's products
  - There is no admission that the payments actually affected the number of Purdue prescriptions the two HCPs wrote
  - There is no suggestion that either HCP prescribed Purdue products to a patient for medically unnecessary reasons

Count 2: Payments to Two HCPs

- There is no admission that either HCP prescribed Purdue products to a patient who, as a consequence, suffered from abuse, addiction or death
- There is no admission as to the location of the two HCPs
- There is no admission that any Claimant was financially affected by any prescription written, given that the prescriptions were paid for "in whole or in part under a Federal healthcare program"— and there is no indication that any Claimant paid for any other portion
- There is no admission as to the year in which the improper payments were made or whether they—or any consequent prescriptions—occurred within the applicable statute of limitations

Count 3: Practice Fusion

- In Count 3, PPLP admitted that, effective March 1, 2016, it entered into a one-year contract with Practice Fusion — a cloud-based electronic health records platform — to run a Clinical Decision Support program on its platform to alert HCPs to conduct pain assessments and document pain treatment plans
- PPLP admitted that "one purpose" of this was to increase Purdue's opioid sales, "portions of which were paid for by federal health care programs, in violation of the Anti-Kickback Statute" (Purdue Plea Agmt., Schedule A, pp. 17-18 ¶¶m, o)
  - There is no admission that any HCP was deceived by a Practice Fusion alert
  - There is no admission that any prescription written as a result of a Practice Fusion alert wrote lacked a legitimate medical purpose
  - There is no admission that any patient who received a prescription as a result of a Practice Fusion alert suffered from abuse, addiction or death

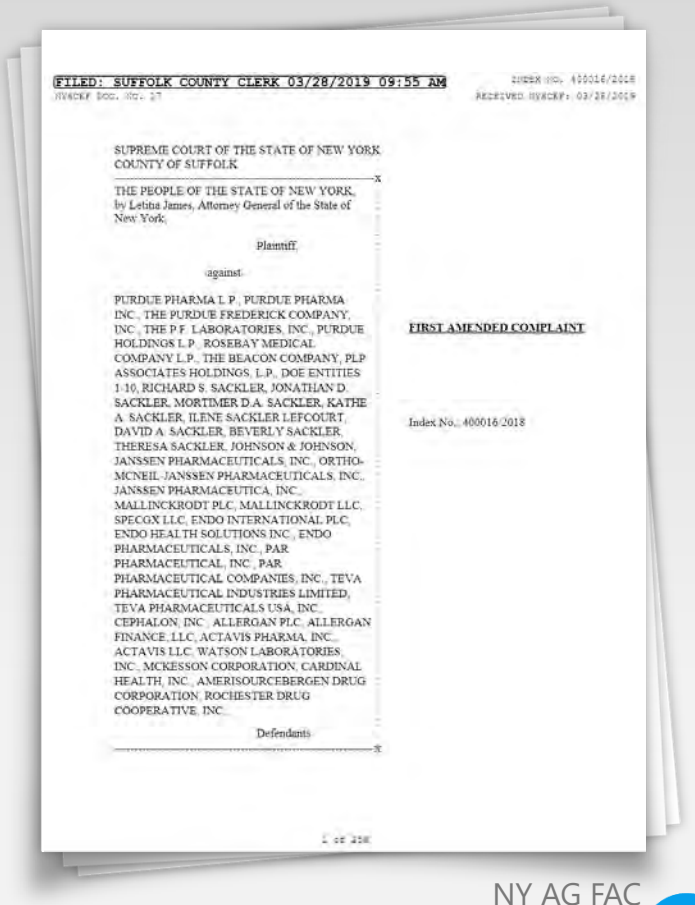
Count 3: Practice Fusion

- There is no admission that any prescription written as a result of a Practice Fusion alert had any impact on any Claimant, given that some portion of the prescriptions "were paid for by Federal healthcare programs"
  — and there is no indication that any Claimant paid for any other portion

Claimants' Deceptive Marketing Claims

Claimants' Deceptive Marketing Claims against Purdue

- New York alleges 10 representative misrepresentations
- DOJ adopted none of them in its criminal and civil settlements with Purdue and the family
- None supports a claim against the Individuals
- There is no allegation the Individuals approved, directed or encouraged any of the alleged Purdue misrepresentations
- Substantial evidence establishes that the supposed misrepresentations are in fact true
- The Claimants and the federal government made many of the same representations


FILED: SUFFOLK COUNTY CLERK 03/28/2019 09:55 AM

SUPREME COURT OF THE STATE OF NEW YORK
COUNTY OF SUFFOLK

THE PEOPLE OF THE STATE OF NEW YORK, by Letitia James, Attorney General of the State of New York,

Plaintiff,

against

PURDUE PHARMA L.P., PURDUE PHARMA INC., THE PURDUE FREDERICK COMPANY, INC., THE P.F. LABORATORIES, INC., PURDUE HOLDINGS L.P., ROSEBAY MEDICAL COMPANY L.P., THE BEACON COMPANY, PLP ASSOCIATES HOLDINGS, L.P., DOE ENTITIES 1-10, RICHARD S. SACKLER, JONATHAN D. SACKLER, MORTIMER D.A. SACKLER, KATHE A. SACKLER, ILENE SACKLER LEFCOURT, DAVID A. SACKLER, BEVERLY SACKLER, THERESA SACKLER, JOHNSON & JOHNSON, JANSSEN PHARMACEUTICALS, INC., ORTHO-MCNEIL-JANSSEN PHARMACEUTICALS, INC., JANSSEN PHARMACEUTICA, INC., MALLINCKRODT PLC, MALLINCKRODT LLC, SPECGX LLC, ENDO INTERNATIONAL PLC, ENDO HEALTH SOLUTIONS INC., ENDO PHARMACEUTICALS, INC., PAR PHARMACEUTICAL, INC., PAR PHARMACEUTICAL COMPANIES, INC., TEVA PHARMACEUTICAL INDUSTRIES LIMITED, TEVA PHARMACEUTICALS USA, INC., CEPHALON, INC., ALLERGAN PLC, ALLERGAN FINANCE, LLC, ACTAVIS PHARMA, INC., ACTAVIS LLC, WATSON LABORATORIES, INC., MCKESSON CORPORATION, CARDINAL HEALTH, INC., AMERISOURCEBERGEN DRUG CORPORATION, ROCHESTER DRUG COOPERATIVE, INC.,

Defendants

FIRST AMENDED COMPLAINT

Index No.: 400016/2018

NY AG FAC

Alleged Misrepresentation No. 1:
Risk of Addiction from Chronic Opioid Therapy Is Low

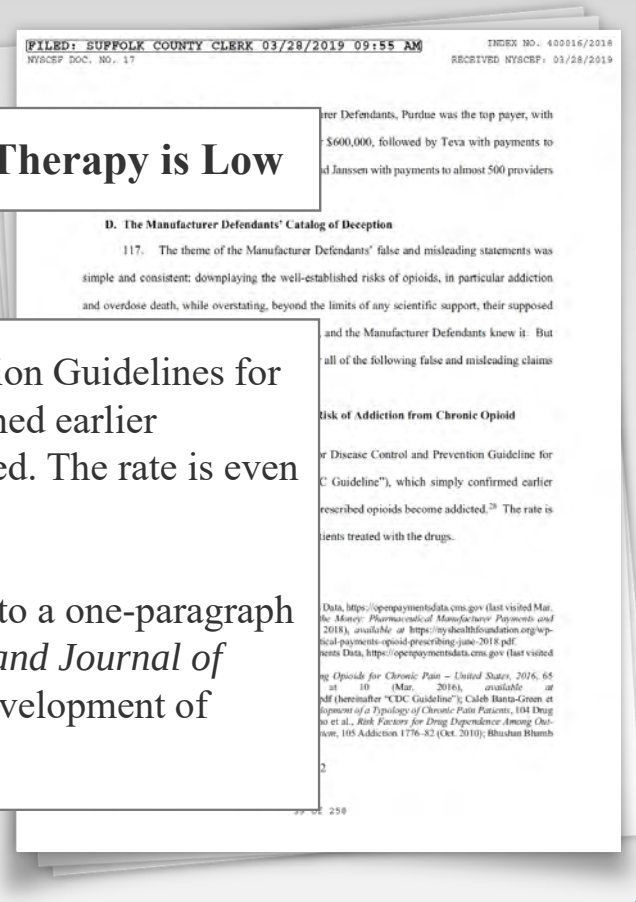
1. Misrepresentation #1: The Risk of Addiction from Chronic Opioid Therapy is Low

NY AG FAC, p. 32

118. According to the 2016 Centers for Disease Control and Prevention Guidelines for Prescribing Opioids for Chronic Pain (the "CDC Guideline"), which simply confirmed earlier scientific findings, up to 26% of people who are prescribed opioids becomes addicted. The rate is even worse—up to 40%—among chronic pain patients treated with the drugs.

119. To upend this hard reality, the Manufacturer Defendants turned to a one-paragraph letter to the editor from Dr. Hershel Jick and Jane Porter published in the *New England Journal of Medicine* ("NEJM") in 1980 (the "Porter/Jick letter"), which concluded that "the development of addiction is rare in medical patients with no history of addiction." . . . .

NY AG FAC ¶¶118-19


FILED: SUFFOLK COUNTY CLERK 03/28/2019 09:55 AM INDEX NO. 400016/2018
NYSCEF DOC. NO. 17 RECEIVED NYSCEF: 03/28/2019

rer Defendants, Purdue was the top payer, with
$600,000, followed by Teva with payments to
d Janssen with payments to almost 500 providers

D. The Manufacturer Defendants' Catalog of Deception

117. The theme of the Manufacturer Defendants' false and misleading statements was simple and consistent: downplaying the well-established risks of opioids, in particular addiction and overdose death, while overstating, beyond the limits of any scientific support, their supposed and the Manufacturer Defendants knew it. But all of the following false and misleading claims

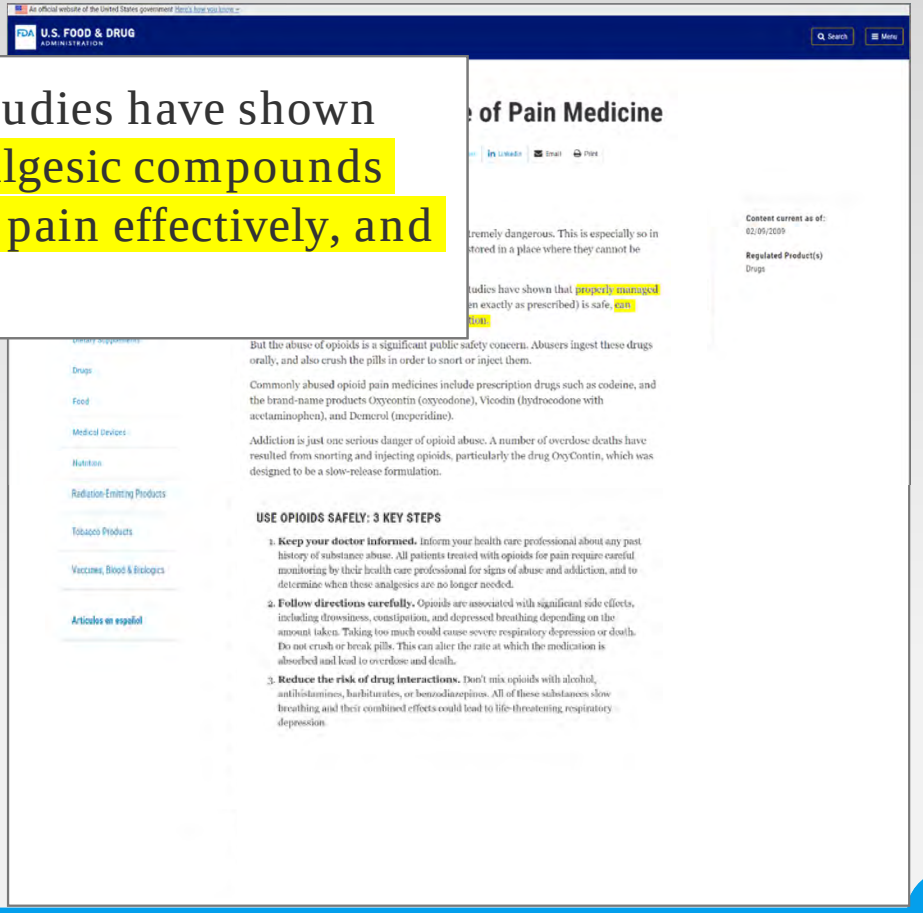
Risk of Addiction from Chronic Opioid

r Disease Control and Prevention Guideline for
C Guideline"), which simply confirmed earlier
rescribed opioids become addicted.[28] The rate is
ients treated with the drugs.

FDA: Medically-Managed Use of Opioids "Rarely Causes Addiction"

According to the National Institutes of Health, studies have shown that properly managed medical use of opioid analgesic compounds (taken exactly as prescribed) is safe, can manage pain effectively, and rarely causes addiction.

https://www.fda.gov/consumers/consumer-updates/guide-safe-use-pain-medicine
(last updated Feb. 9, 2009)



U.S. FOOD & DRUG ADMINISTRATION

Search Menu

of Pain Medicine

Content current as of: 02/09/2009

Regulated Product(s) Drugs

Drugs
Food
Medical Devices
Nutrition
Radiation-Emitting Products
Tobacco Products
Vaccines, Blood & Biologics
Articulos en español

But the abuse of opioids is a significant public safety concern. Abusers ingest these drugs orally, and also crush the pills in order to snort or inject them.

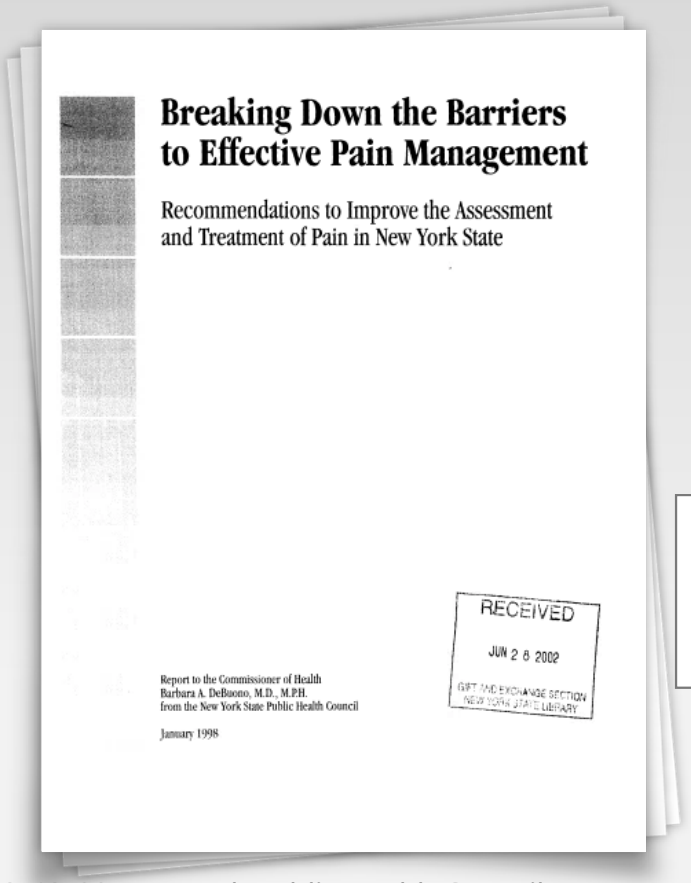
Commonly abused opioid pain medicines include prescription drugs such as codeine, and the brand-name products Oxycontin (oxycodone), Vicodin (hydrocodone with acetaminophen), and Demerol (meperidine).

Addiction is just one serious danger of opioid abuse. A number of overdose deaths have resulted from snorting and injecting opioids, particularly the drug OxyContin, which was designed to be a slow-release formulation.

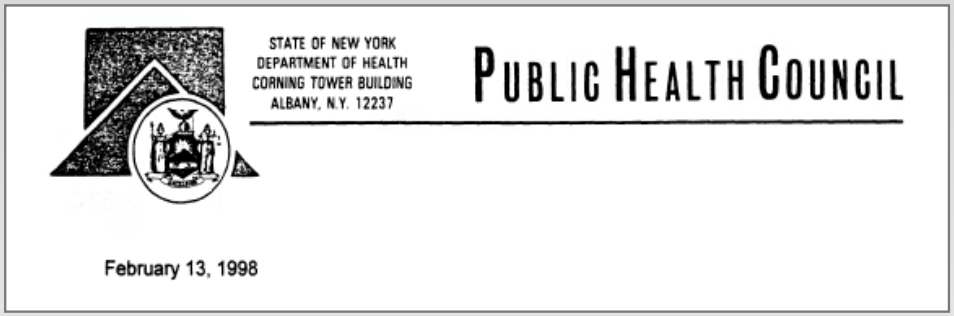
USE OPIOIDS SAFELY: 3 KEY STEPS

1. **Keep your doctor informed.** Inform your health care professional about any past history of substance abuse. All patients treated with opioids for pain require careful monitoring by their health care professional for signs of abuse and addiction, and to determine when these analgesics are no longer needed.
2. **Follow directions carefully.** Opioids are associated with significant side effects, including drowsiness, constipation, and depressed breathing depending on the amount taken. Taking too much could cause severe respiratory depression or death. Do not crush or break pills. This can alter the rate at which the medication is absorbed and lead to overdose and death.
3. **Reduce the risk of drug interactions.** Don't mix opioids with alcohol, antihistamines, barbiturates, or benzodiazepines. All of these substances slow breathing and their combined effects could lead to life-threatening respiratory depression.

New York Public Health Council in 1998: Medically-Managed Use of Opioids "Rarely Causes Addiction"



2/13/98 New York Public Health Council Report



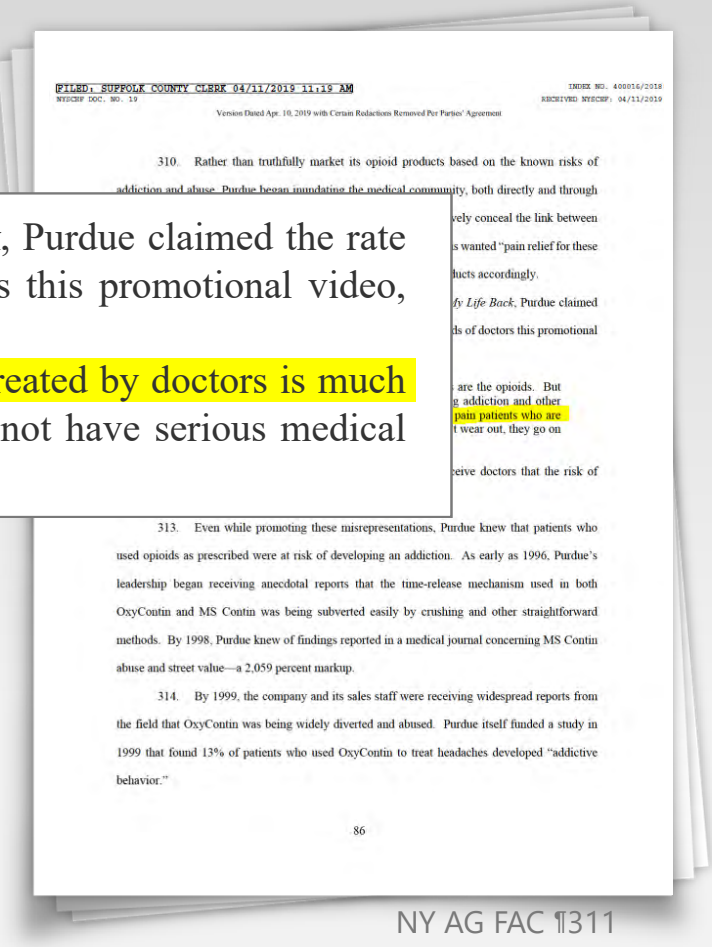
In 1998, the New York Public Health Council stated:

> "**Unfortunately, the public does not understand that opioid addiction when treating bona fide pain is rare**"

Alleged Misrepresentation in 1998 Video

311. For example, in its 1998 promotional video, *I Got My Life Back*, Purdue claimed the rate of addiction "is much less than 1%." Purdue mailed thousands of doctors this promotional video, where a physician asserts:

… Now, in fact, the rate of addiction amongst pain patients who are treated by doctors is much less than one percent. They don't wear out, they go on working, they do not have serious medical side effects.



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NYSCEF DOC. NO. 19 RECEIVED NYSCEF: 04/11/2019

Version Dated Apr. 10, 2019 with Certain Redactions Removed Per Parties' Agreement

310. Rather than truthfully market its opioid products based on the known risks of addiction and abuse, Purdue began inundating the medical community, both directly and through

311. For example, in its 1998 promotional video, *I Got My Life Back*, Purdue claimed

313. Even while promoting these misrepresentations, Purdue knew that patients who used opioids as prescribed were at risk of developing an addiction. As early as 1996, Purdue's leadership began receiving anecdotal reports that the time-release mechanism used in both OxyContin and MS Contin was being subverted easily by crushing and other straightforward methods. By 1998, Purdue knew of findings reported in a medical journal concerning MS Contin abuse and street value—a 2,059 percent markup.

314. By 1999, the company and its sales staff were receiving widespread reports from the field that OxyContin was being widely diverted and abused. Purdue itself funded a study in 1999 that found 13% of patients who used OxyContin to treat headaches developed "addictive behavior."

86

NY AG FAC ¶311

The New York Department of Public Health Was Saying Exactly the Same Thing at the Time

- **New York Health Department Task Force on Life and the Law Report — on New York Health Department website since 1994:**

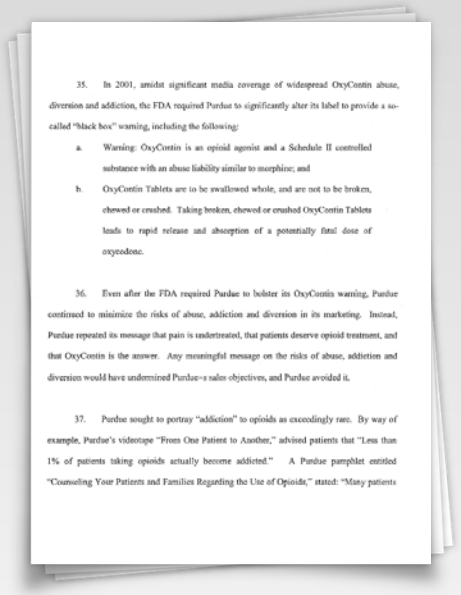
- "**Psychological dependence is extremely rare in patients receiving opioids or other medications for pain control**."
- "Studies also indicate that physicians and other health care professionals are excessively and unjustifiably concerned about the risk of addiction and respiratory depression, even though these responses to pain medication are extremely rare and can be prevented when treatment is appropriately monitored. In one study of 2,459 nurses, **only 24.8 percent knew that the rate of psychological dependence in patients treated with narcotic drugs for pain is less than one percent**"

https://www.health.ny.gov/regulations/task_force/reports_publications/when_death_is_sought/chap3.htm

This Alleged 1998 Misrepresentation Was Released in 2007

- **2007 Consent Judgments released these statements**

> 37. Purdue sought to portray "addiction" to opioids as exceedingly rare. By way of example, Purdue's videotape "From One Patient to Another," advised patients that "Less than 1% of patients taking opioids actually become addicted.



35. In 2001, amidst significant media coverage of widespread OxyContin abuse, diversion and addiction, the FDA required Purdue to significantly alter its label to provide a so-called "black box" warning, including the following:

a. Warning: OxyContin is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine; and

b. OxyContin Tablets are to be swallowed whole, and are not to be broken, chewed or crushed. Taking broken, chewed or crushed OxyContin Tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone.

36. Even after the FDA required Purdue to bolster its OxyContin warning, Purdue continued to minimize the risks of abuse, addiction and diversion in its marketing. Instead, Purdue repeated its message that pain is undertreated, that patients deserve opioid treatment, and that OxyContin is the answer. Any meaningful message on the risks of abuse, addiction and diversion would have undermined Purdue-s sales objectives, and Purdue avoided it.

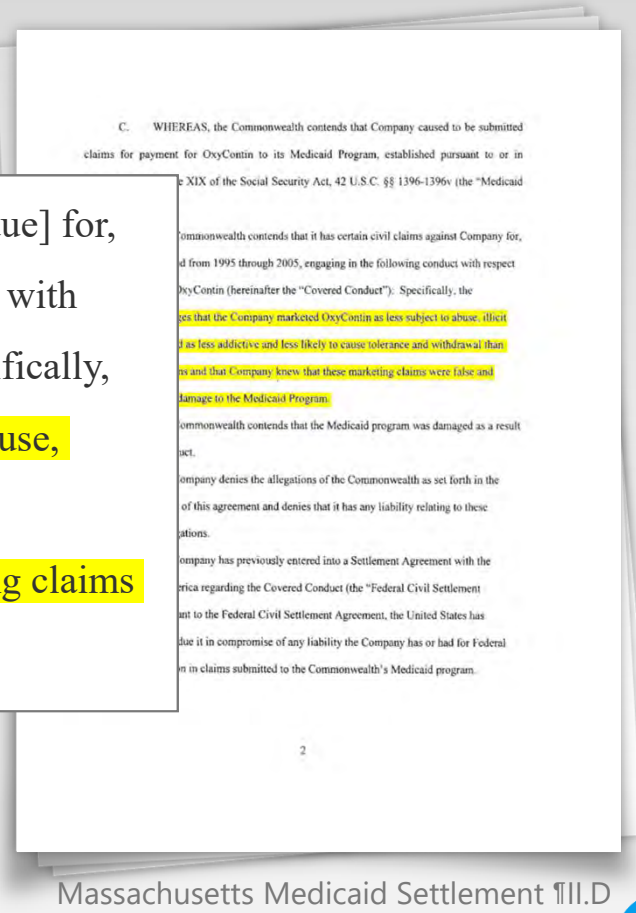
37. Purdue sought to portray "addiction" to opioids as exceedingly rare. By way of example, Purdue's videotape "From One Patient to Another," advised patients that "Less than 1% of patients taking opioids actually become addicted." A Purdue pamphlet entitled "Counseling Your Patients and Families Regarding the Use of Opioids," stated: "Many patients

2007 CT Complaint ¶37

This Alleged 1998 Misrepresentation Was Released in 2007

- **2007 Medicaid settlements released these statements**

D. The Commonwealth contends that it has certain civil claims against [Purdue] for, during the time period from 1995 through 2005, engaging in the following conduct with respect to the marketing of OxyContin (herein after the "Covered Conduct"): Specifically, the Commonwealth alleges that [Purdue] marketed OxyContin as less subject to abuse, illicit use and diversion and as less addictive and less likely to cause tolerance and withdrawal than other pain medications and that [Purdue] knew that these marketing claims were false and misleading, causing damage to the Medicaid Program.


C. WHEREAS, the Commonwealth contends that Company caused to be submitted
claims for payment for OxyContin to its Medicaid Program, established pursuant to or in
e XIX of the Social Security Act, 42 U.S.C. §§ 1396-1396v (the "Medicaid
Commonwealth contends that it has certain civil claims against Company for,
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l as less addictive and less likely to cause tolerance and withdrawal than
s and that Company knew that these marketing claims were false and
damage to the Medicaid Program.
Commonwealth contends that the Medicaid program was damaged as a result
act.
ompany denies the allegations of the Commonwealth as set forth in the
of this agreement and denies that it has any liability relating to these
ations.
ompany has previously entered into a Settlement Agreement with the
erica regarding the Covered Conduct (the "Federal Civil Settlement
ant to the Federal Civil Settlement Agreement, the United States has
due it in compromise of any liability the Company has or had for Federal
n in claims submitted to the Commonwealth's Medicaid program.
2

Massachusetts Medicaid Settlement ¶II.D

Alleged Misrepresentation No. 2:
Signs of Addictive Behavior May Be "Pseudoaddiction"

2. Misrepresentation #2: Signs of Addictive Behavior are "Pseudoaddiction," Potentially Requiring More Opioids

NY AG FAC, p. 34

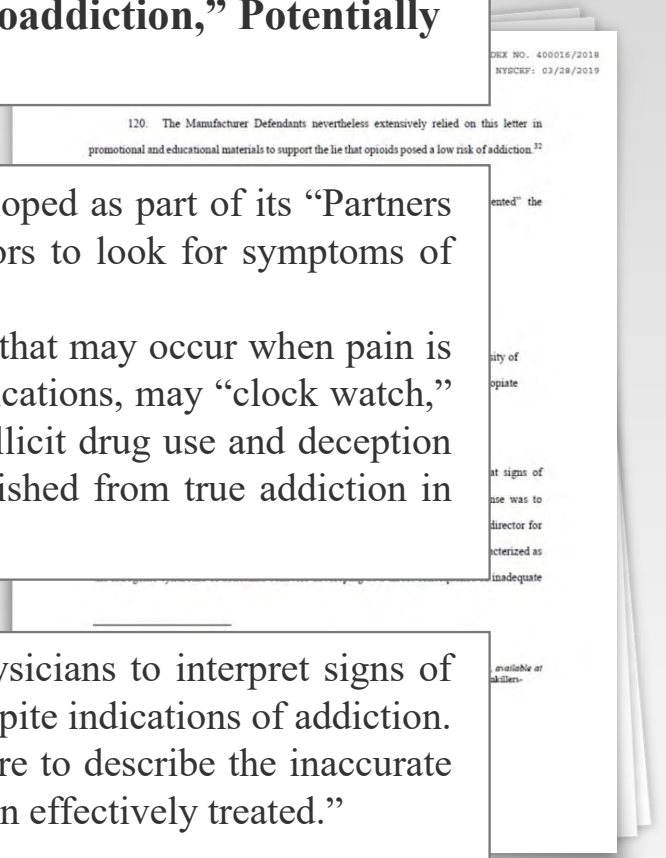
326. For example, Purdue widely distributed an unbranded pamphlet developed as part of its "Partners Against Pain" initiative, *Clinical Issues in Opioid Prescribing*, which urged doctors to look for symptoms of "pseudoaddiction:"

[Pseudoaddiction is a] term which has been used to describe patient behaviors that may occur when pain is undertreated. Patients with unrelieved pain may become focused on obtaining medications, may "clock watch," and may otherwise seem inappropriately "drug-seeking." Even such behaviors as illicit drug use and deception can occur in the patient's efforts to obtain relief. Pseudoaddiction can be distinguished from true addiction in that the behaviors resolve when the pain is effectively treated.

NY AG FAC ¶326

328. Purdue's other widely-distributed materials similarly encouraged physicians to interpret signs of addiction as under-treatment of pain and urged them to treat pain "aggressively" despite indications of addiction. One pamphlet . . . claimed: "The term pseudoaddiction has emerged in the literature to describe the inaccurate interpretation of [drug-seeking] behaviors in patients who have pain that has not been effectively treated."

NY AG FAC ¶328



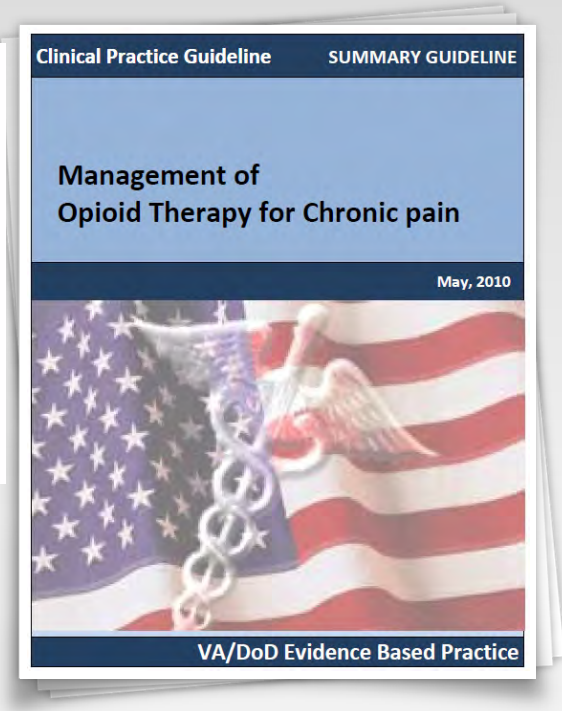
Alleged Misrepresentation No. 2:
Signs of Addictive Behavior May Be "Pseudoaddiction"

1. The Federal Government Recognizes Pseudoaddiction

Pseudoaddiction

Pseudoaddiction describes patient behaviors that may occur when pain is undertreated. Patients with unrelieved pain may become focused on obtaining medications, may "clock watch," and may otherwise seem to be inappropriately "drug seeking." Even such behaviors as illicit drug use and deception can occur in the patient's efforts to obtain pain relief. In contrast to true addiction, in pseudoaddiction the behaviors resolve when the pain is effectively treated (Definitions, 2001). Misunderstanding of this phenomenon may lead the clinician to inappropriately stigmatize the patient with the label 'addict.' In the setting of unrelieved pain, the request for increases in drug dose requires careful assessment, renewed efforts to manage pain, and avoidance of stigmatizing labels. Distinguishing addiction from pseudoaddiction can be difficult and often takes time and multiple patient encounters.

VA/Dept. of Defense, Clinical Practice Guideline,
Management of Opioid Therapy for Chronic Pain 13 (May 2010)



https://www.va.gov/painmanagement/docs/cpg_opioidtherapy_summary.pdf

Alleged Misrepresentation No. 2:
Signs of Addictive Behavior May Be "Pseudoaddiction"

2. The FDA-Approved Label for OxyContin Describes Pseudoaddiction

> Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control. Most chronic pain patients limit their intake of opioids to achieve a balance between the benefits of the drug and dose-limiting side effects.

1995 OxyContin Label, p. 2, (PDD150170001)

> Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control.

April 2013 OxyContin Label, p. 18, (PPLPC003000060503)

> Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control.

September 2018 OxyContin Label, p. 28, https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022272s039lbl.pdf

Alleged Misrepresentation No. 2:
Signs of Addictive Behavior May Be "Pseudoaddiction"

3. The FDA-Approved Label for Percodan Discusses Pseudoaddiction

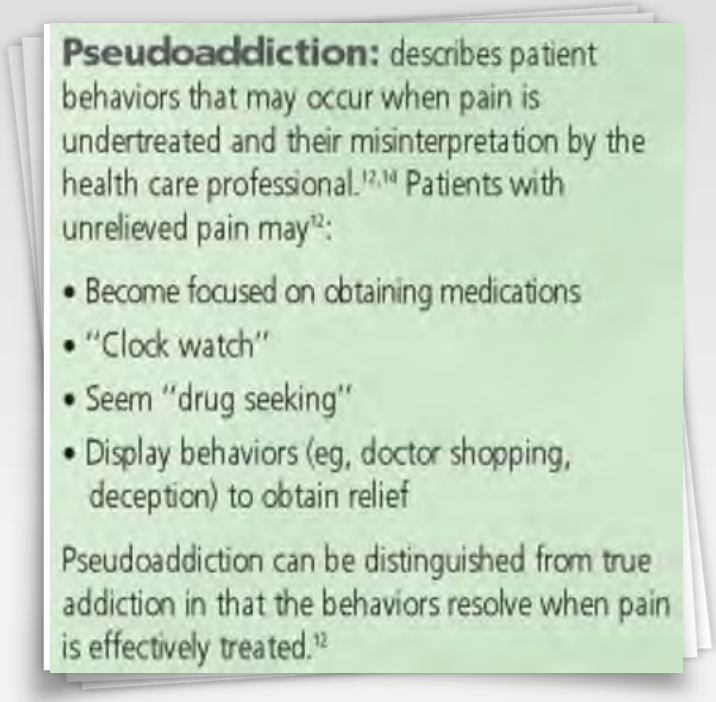
> Pseudoaddiction refers to pain relief seeking behavior of patients whose pain is poorly managed. It is considered an iatrogenic effect of ineffective pain management. The health care provider must assess continuously the psychological and clinical condition of a pain patient in order to distinguish addiction from pseudoaddiction and thus, be able to treat the pain adequately.

June 2010 Percodan Label, p. 17, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2004/07337slr029_percodan_lbl.pdf

Alleged Misrepresentation No. 2:
Signs of Addictive Behavior May Be "Pseudoaddiction"

4. The States Approved Educating HCPs About Pseudoaddiction

- ¶15 of the Consent Judgments required that Purdue provide all HCPs educational information about detecting and preventing abuse and diversion for 10 years (2007-2017)
- Purdue sent the materials to all Consent Judgment States on August 6, 2007 to ensure their consent (PPLPUCC004238887)
- The materials discussed pseudoaddiction at length
- Every state acquiesced — none objected



Pseudoaddiction: describes patient behaviors that may occur when pain is undertreated and their misinterpretation by the health care professional.[12,14] Patients with unrelieved pain may[12]:

- Become focused on obtaining medications
- "Clock watch"
- Seem "drug seeking"
- Display behaviors (eg, doctor shopping, deception) to obtain relief

Pseudoaddiction can be distinguished from true addiction in that the behaviors resolve when pain is effectively treated.[12]

Providing Relief, Preventing Abuse, PPLP003275282 at -288

Alleged Misrepresentation No. 2:
Signs of Addictive Behavior May Be "Pseudoaddiction"

5. Scientific Literature Acknowledges Pseudoaddiction

Green & Chambers, *Pseudoaddiction: Fact or Fiction? An Investigation of the Medical Literature*, CURRENT ADDICTION REPORTS at 310-317 (2015)

In a survey of medical literature, **224 papers were identified that discussed pseudoaddiction. Only 4 contended that it "remains untested and uncharacterized as an objectively confirmable diagnosis"** and **2 contended it was a "social rather than biological construct."**


Pseudoaddiction: Fact or Fiction? An Investigation of the Medical Literature

Scientific consensus is represented by 218 articles accepting the concept, not 6 questioning it

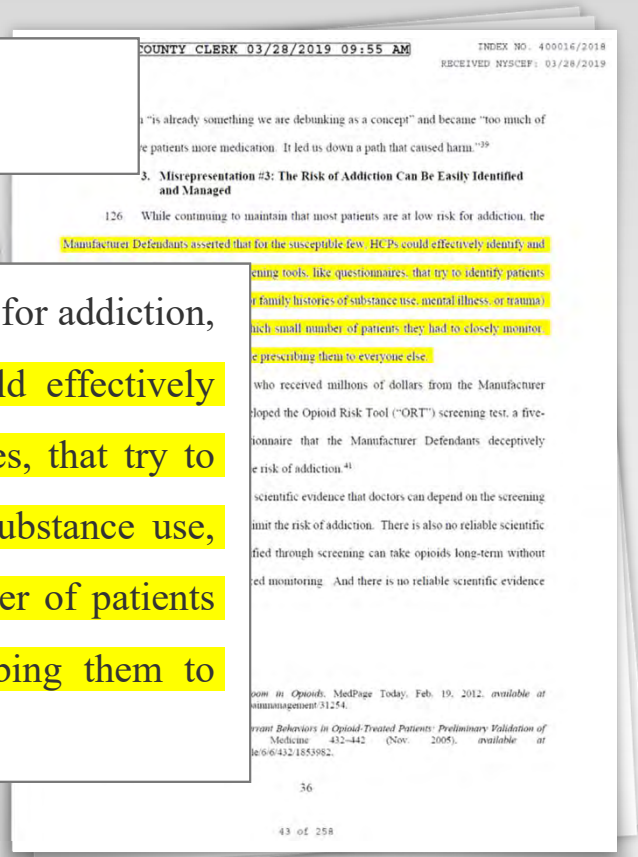
Alleged Misrepresentation No. 3:
Risk of Addiction Can Be Easily Identified And Managed

3. Misrepresentation #3: The Risk of Addiction Can Be Easily Identified and Managed

NY AG FAC, p. 36

126. While continuing to maintain that most patients are at low risk for addiction, the Manufacturer Defendants asserted that for the susceptible few, HCPs could effectively identify and manage the risk. They promoted screening tools, like questionnaires, that try to identify patients with addiction risks (such as personal or family histories of substance use, mental illness, or trauma) to make HCPs feel like they knew which small number of patients they had to closely monitor, thereby making them more comfortable prescribing them to everyone else.

NY AG FAC ¶126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3. Misrepresentation #3: The Risk of Addiction Can Be Easily Identified and Managed

126 While continuing to maintain that most patients are at low risk for addiction, the

Manufacturer Defendants asserted that for the susceptible few, HCPs could effectively identify and

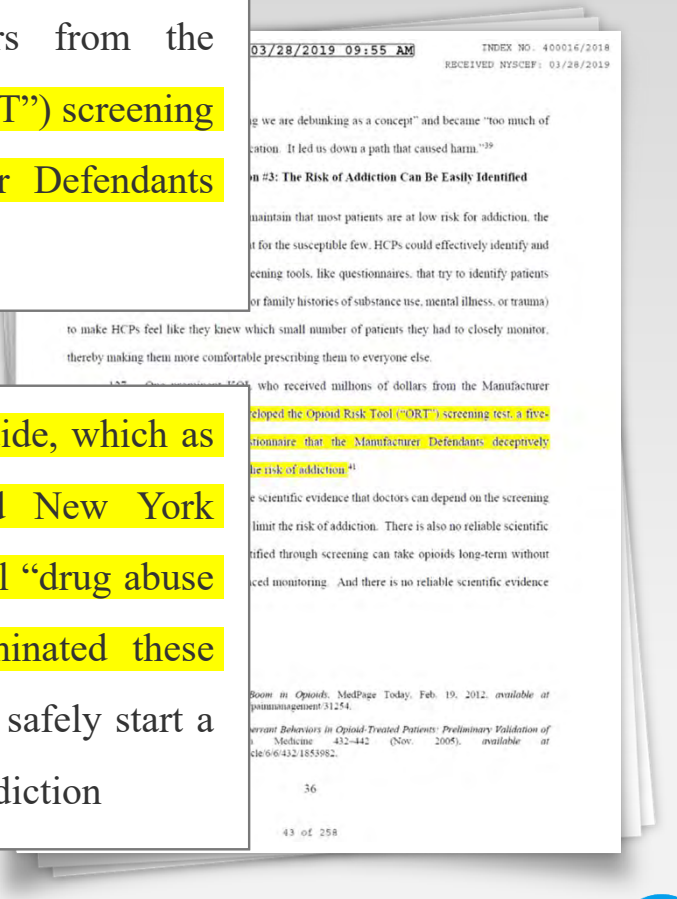
Alleged Misrepresentation No. 3:
Risk of Addiction Can Be Easily Identified And Managed

127. One prominent KOL who received millions of dollars from the Manufacturer Defendants, Dr. Lynn Webster developed the Opioid Risk Tool ("ORT") screening test, a five-question *self-reported* patient questionnaire that the Manufacturer Defendants deceptively represented could accurately predict the risk of addiction.

NY AG FAC ¶127

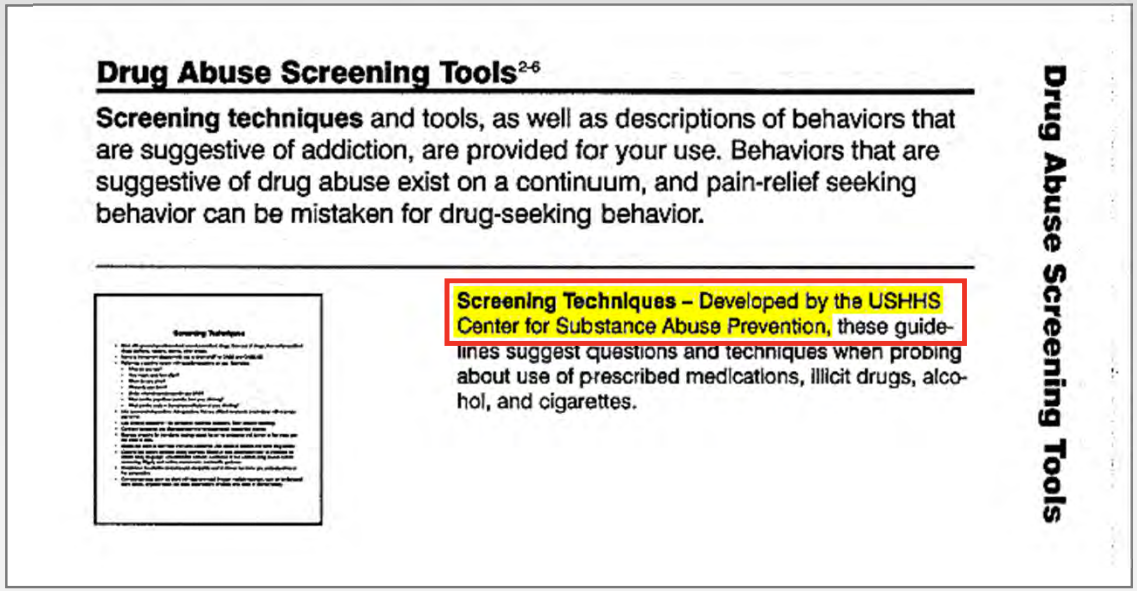
318. For example, Purdue distributed APF's Treatment Options guide, which as noted above, touted "opioid agreements." Purdue's detailers also provided New York prescribers a Partners Against Pain "Pain Management Kit" that contained several "drug abuse screening tools," including the "Opioid Risk Tool." Purdue actively disseminated these materials to misleadingly give providers a false sense of security that they could safely start a course of opioids with patients and effectively manage those with a high risk of addiction

NY AG FAC ¶318



Alleged Misrepresentation No. 3:
Risk of Addiction Can Be Easily Identified And Managed

- NYAG attacks screening tools developed by the U.S. Government

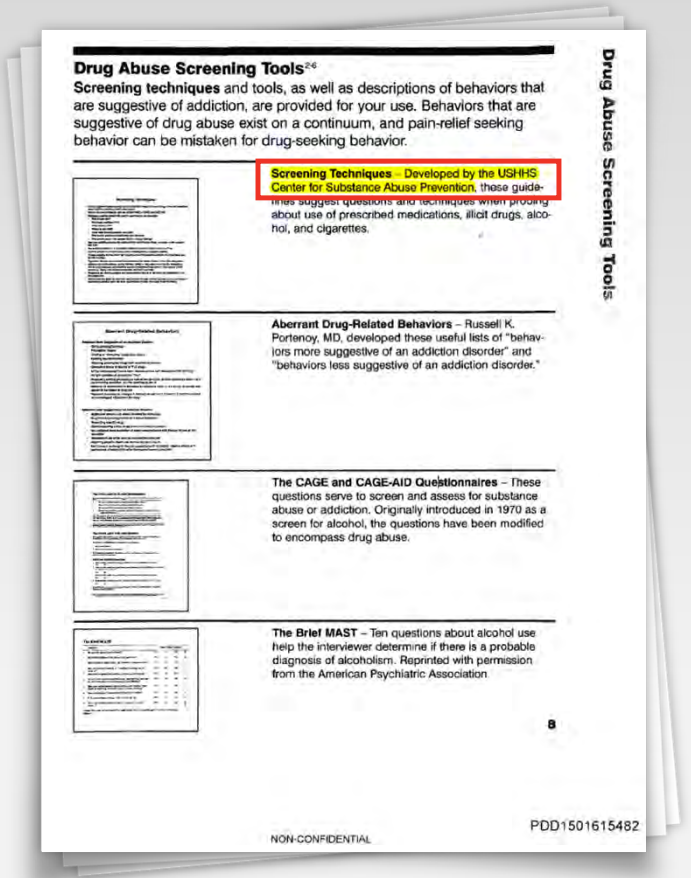


Drug Abuse Screening Tools[2-6]

Screening techniques and tools, as well as descriptions of behaviors that are suggestive of addiction, are provided for your use. Behaviors that are suggestive of drug abuse exist on a continuum, and pain-relief seeking behavior can be mistaken for drug-seeking behavior.

Screening Techniques – Developed by the USHHS Center for Substance Abuse Prevention, these guidelines suggest questions and techniques when probing about use of prescribed medications, illicit drugs, alcohol, and cigarettes.

Drug Abuse Screening Tools



Drug Abuse Screening Tools[2-6]

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Screening Techniques – Developed by the USHHS Center for Substance Abuse Prevention, these guidelines suggest questions and techniques when probing about use of prescribed medications, illicit drugs, alcohol, and cigarettes.

Aberrant Drug-Related Behaviors – Russell K. Portenoy, MD, developed these useful lists of "behaviors more suggestive of an addiction disorder" and "behaviors less suggestive of an addiction disorder."

The CAGE and CAGE-AID Questionnaires – These questions serve to screen and assess for substance abuse or addiction. Originally introduced in 1970 as a screen for alcohol, the questions have been modified to encompass drug abuse.

The Brief MAST – Ten questions about alcohol use help the interviewer determine if there is a probable diagnosis of alcoholism. Reprinted with permission from the American Psychiatric Association

8

Drug Abuse Screening Tools

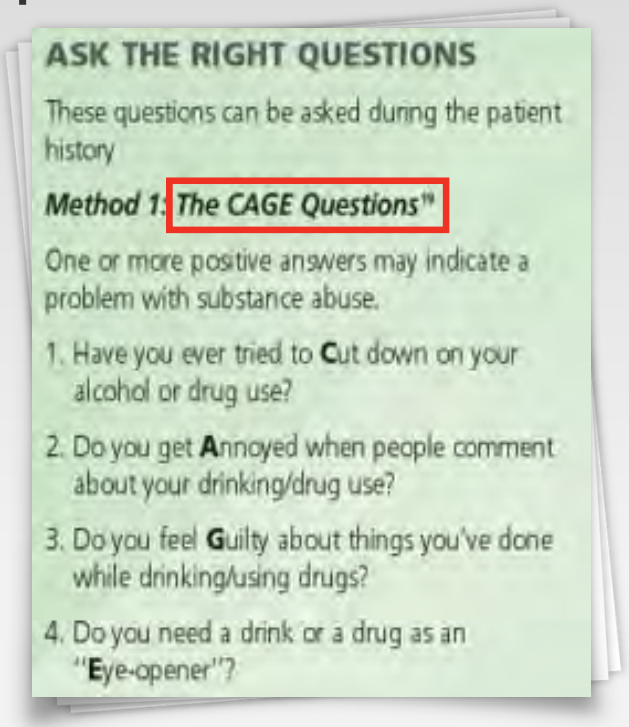
PDD1501615482

NON-CONFIDENTIAL

PARTNERS AGAINST PAIN, *Pain Management Kit* (2003) (PDD1501615472)

Alleged Misrepresentation No. 3:
Risk of Addiction Can Be Easily Identified And Managed

- **NYAG attacks advocating screening tools the States agreed that Purdue could use to educate HCPs — the CAGE questionnaire**
  - ¶15 of the Consent Judgments required that Purdue provide all HCPs educational information about detecting and preventing abuse and diversion for 10 years (2007-2017)
  - Purdue sent the materials to all Consent Judgment States on August 6, 2007 to ensure their consent (PPLPUCC004238887)
  - The materials recommended the CAGE questionnaire
  - Every state acquiesced—none objected



ASK THE RIGHT QUESTIONS

These questions can be asked during the patient history

***Method 1: The CAGE Questions*[19]**

One or more positive answers may indicate a problem with substance abuse.

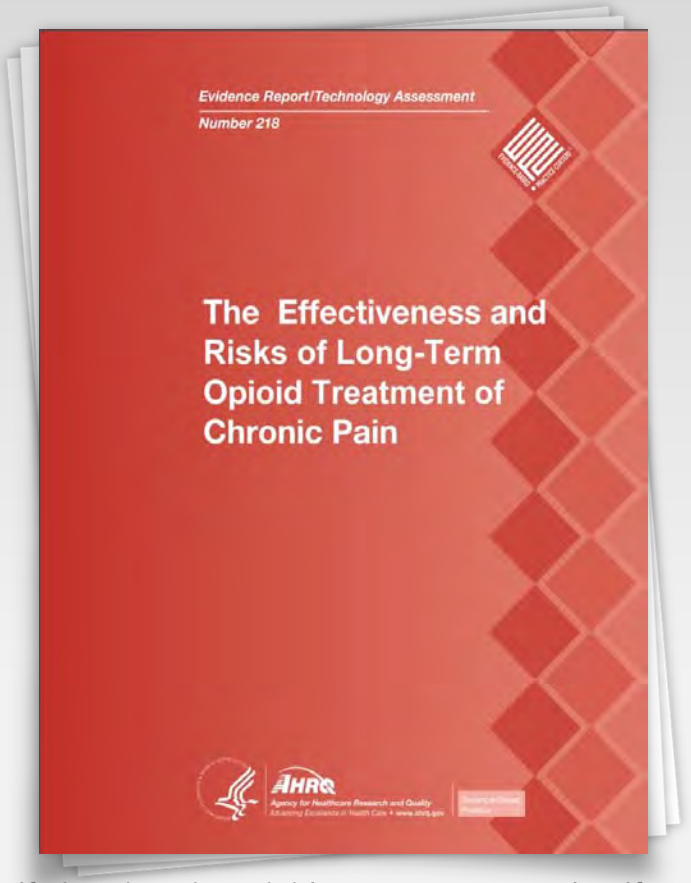
1. Have you ever tried to **C**ut down on your alcohol or drug use?
2. Do you get **A**nnoyed when people comment about your drinking/drug use?
3. Do you feel **G**uilty about things you've done while drinking/using drugs?
4. Do you need a drink or a drug as an "**E**ye-opener"?

Providing Relief, Preventing Abuse, PPLP003275282 at -292

Alleged Misrepresentation No. 3:
Risk of Addiction Can Be Easily Identified And Managed

- **NYAG relies on one 2014 study to claim risk assessment tools are deceptive** NY AG FAC ¶128 n.42
  - **The cited study did not determine that risk assessment tools were deceptive**
  - **It reviewed 4 studies that "examined the accuracy of instruments for predicting risk of opioid overdose, addiction, abuse or misuse."**
  - **It concluded that "[e]vidence … remains limited on the utility of opioid risk assessment instruments"**

See Roger Chou, et al., *The Effectiveness and Risks of Long-Term Opioid Treatment of Chronic Pain*, EVIDENCE REP./TECH. ASSESSMENT NO. 218, AGENCY FOR HEALTHCARE RESEARCH AND QUALITY, DEP'T OF HEALTH AND HUMAN SERVS., at ES-12, ES-20, ES-25 (2014)



https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/chronic-pain-opioid-treatment_research.pdf

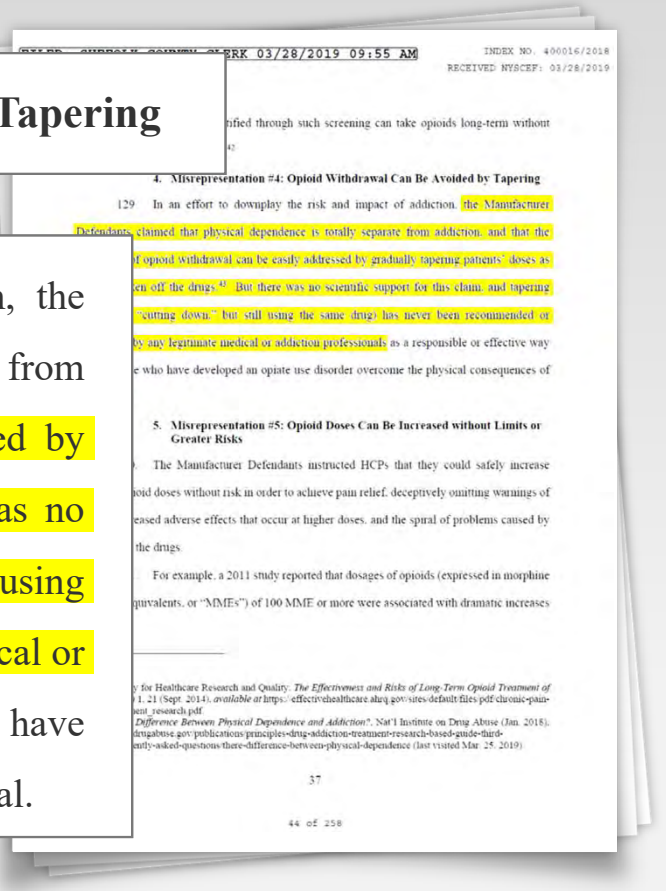
Alleged Misrepresentation No. 4:
Opioid Withdrawal Can Be Avoided by Tapering

4. Misrepresentation #4: Opioid Withdrawal Can Be Avoided by Tapering

NY AG FAC, p. 37

129. In an effort to downplay the risk and impact of addiction, the Manufacturer Defendants claimed that physical dependence is totally separate from addiction, and that the symptoms of opioid withdrawal can be easily addressed by gradually tapering patients' doses as they are taken off the drugs. But there was no scientific support for this claim, and tapering (essentially "cutting down," but still using the same drug) has never been recommended or recognized by any legitimate medical or addiction professionals as a responsible or effective way to help those who have developed an opiate use disorder overcome the physical consequences of withdrawal.

NY AG FAC ¶129



Tapering Is Identified As Useful to Avoid Precipitating Withdrawal on OxyContin's FDA-Approved Label

… it may be appropriate to taper the OxyContin dose, rather than abruptly discontinue it, due to the risk of precipitating withdrawal symptoms…

1995 OxyContin Label, p. 2, (PDD150170001)

When discontinuing OxyContin, gradually taper the dose *[see Dosage and Administration (2.4)]*. Do not abruptly discontinue OxyContin.

Apr. 2013 OxyContin Label, p. 10, (PPLPC003000060503)

When the patient no longer requires therapy with OXYCONTIN, taper the dosage gradually, by 25% to 50% every 2 to 4 days, while monitoring for signs and symptoms of withdrawal. If a patient develops these signs or symptoms, raise the dose to the previous level and taper more slowly, either by increasing the interval between decreases, decreasing the amount of change in dose, or both. Do not abruptly discontinue OXYCONTIN [*see Warnings and Precautions (5.14), Drug Abuse and Dependence (9.3)]*.

Sept. 2018 OxyContin Label, p. 10, https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022272s039lbl.pdf

Federal Law Requires Drug Promotion Be Consistent with the FDA Label

21 C.F.R. §201.100(d)(1)

Requires labeling to be "consistent with and not contrary to such approved and permitted labeling"

21 U.S.C. §321(m)

Defines "labeling" to include all "written, printed, or graphic matter" that accompanies the drug

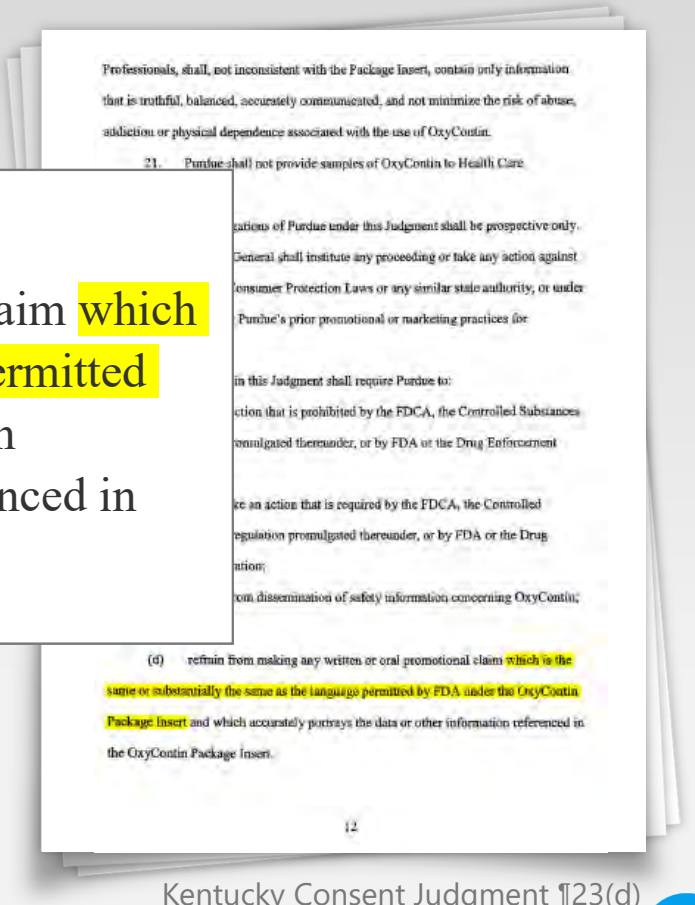
21 C.F.R. §202.1(l)(2)

Defines "labeling" to mean all materials "for use by medical practitioners … containing drug information … disseminated by or on behalf of [the] manufacturer"

Consent Judgments Permitted Marketing Consistent with the FDA-Approved Label

23. Nothing in this Judgment shall require Purdue to: …

(d) refrain from making any written or oral promotional claim which is the same or substantially the same as the language permitted by FDA under the OxyContin Package Insert and which accurately portrays the data or other information referenced in the OxyContin Package Insert.


Professionals, shall, not inconsistent with the Package Insert, contain only information that is truthful, balanced, accurately communicated, and not minimize the risk of abuse, addiction or physical dependence associated with the use of OxyContin.

21. Purdue shall not provide samples of OxyContin to Health Care

ations of Purdue under this Judgment shall be prospective only. General shall institute any proceeding or take any action against Consumer Protection Laws or any similar state authority, or under Purdue's prior promotional or marketing practices for

in this Judgment shall require Purdue to:
ction that is prohibited by the FDCA, the Controlled Substances promulgated thereunder, or by FDA or the Drug Enforcement

ke an action that is required by the FDCA, the Controlled regulation promulgated thereunder, or by FDA or the Drug ation;
om dissemination of safety information concerning OxyContin;

(d) refrain from making any written or oral promotional claim which is the same or substantially the same as the language permitted by FDA under the OxyContin Package Insert and which accurately portrays the data or other information referenced in the OxyContin Package Insert.

12

Kentucky Consent Judgment ¶23(d)

Consent Judgments Barred Promotion Inconsistent with the FDA-Approved Label

19-23649-rdd Doc 2251-3 Filed 01/11/21 Entered 01/11/21 23:33:24 03 Suppl.
Leventhal Ex. 003 Pg 2 of 25

RECEIVED
MAY 03 2007
FRANKLIN CIRCUIT COURT

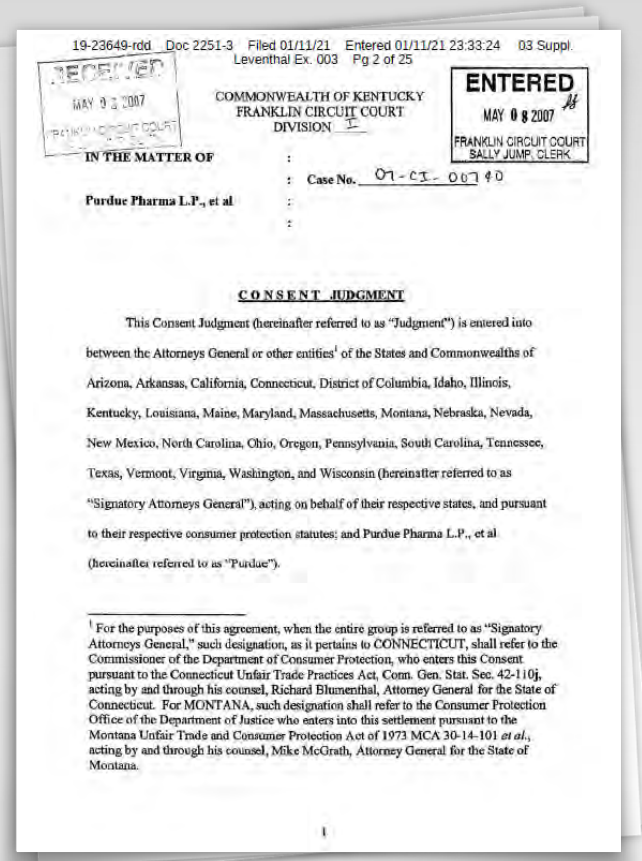
COMMONWEALTH OF KENTUCKY
FRANKLIN CIRCUIT COURT
DIVISION I

ENTERED
MAY 08 2007
FRANKLIN CIRCUIT COURT
SALLY JUMP, CLERK

IN THE MATTER OF :
: Case No. 07-CI-00740
Purdue Pharma L.P., et al :
:

CONSENT JUDGMENT

3. In the promotion and marketing of OxyContin, Purdue shall not market or promote OxyContin in a manner that is, directly or indirectly, inconsistent with the "Indication and Usage" section of the Package Insert for OxyContin. . . .



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Leventhal Ex. 003 Pg 2 of 25

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COMMONWEALTH OF KENTUCKY
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ENTERED
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FRANKLIN CIRCUIT COURT
SALLY JUMP, CLERK

IN THE MATTER OF :
: Case No. 07-CI-00740
Purdue Pharma L.P., et al :
:

CONSENT JUDGMENT

This Consent Judgment (hereinafter referred to as "Judgment") is entered into between the Attorneys General or other entities[1] of the States and Commonwealths of Arizona, Arkansas, California, Connecticut, District of Columbia, Idaho, Illinois, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Montana, Nebraska, Nevada, New Mexico, North Carolina, Ohio, Oregon, Pennsylvania, South Carolina, Tennessee, Texas, Vermont, Virginia, Washington, and Wisconsin (hereinafter referred to as "Signatory Attorneys General"), acting on behalf of their respective states, and pursuant to their respective consumer protection statutes; and Purdue Pharma L.P., et al (hereinafter referred to as "Purdue").

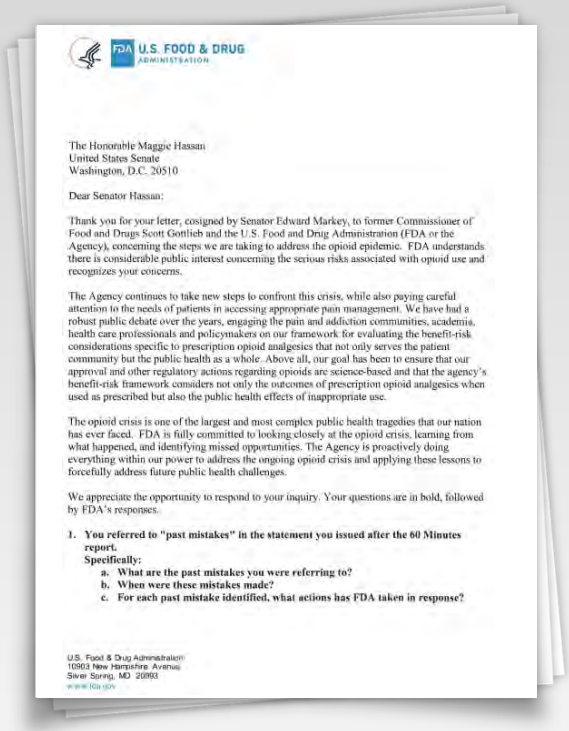
[1] For the purposes of this agreement, when the entire group is referred to as "Signatory Attorneys General," such designation, as it pertains to CONNECTICUT, shall refer to the Commissioner of the Department of Consumer Protection, who enters this Consent pursuant to the Connecticut Unfair Trade Practices Act, Conn. Gen. Stat. Sec. 42-110j, acting by and through his counsel, Richard Blumenthal, Attorney General for the State of Connecticut. For MONTANA, such designation shall refer to the Consumer Protection Office of the Department of Justice who enters into this settlement pursuant to the Montana Unfair Trade and Consumer Protection Act of 1973 MCA 30-14-101 *et al.*, acting by and through his counsel, Mike McGrath, Attorney General for the State of Montana.

Kentucky Consent Judgment ¶3

U.S. Government Still Recognizes Usefulness of Tapering

2020 FDA Letter to Senator Maggie Hassan:

- "[T]he HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics was published to further clarify **the need to judiciously provide individualized therapy, including slow tapering of opioids** … as well as recognition that there may be some patients who are unable to taper or discontinue opioid analgesic therapy." (Pages 13-14)



U.S. FOOD & DRUG ADMINISTRATION

The Honorable Maggie Hassan
United States Senate
Washington, D.C. 20510

Dear Senator Hassan:

Thank you for your letter, cosigned by Senator Edward Markey, to former Commissioner of Food and Drugs Scott Gottlieb and the U.S. Food and Drug Administration (FDA or the Agency), concerning the steps we are taking to address the opioid epidemic. FDA understands there is considerable public interest concerning the serious risks associated with opioid use and recognizes your concerns.

The Agency continues to take new steps to confront this crisis, while also paying careful attention to the needs of patients in accessing appropriate pain management. We have had a robust public debate over the years, engaging the pain and addiction communities, academia, health care professionals and policymakers on our framework for evaluating the benefit-risk considerations specific to prescription opioid analgesics that not only serves the patient community but the public health as a whole. Above all, our goal has been to ensure that our approval and other regulatory actions regarding opioids are science-based and that the agency's benefit-risk framework considers not only the outcomes of prescription opioid analgesics when used as prescribed but also the public health effects of inappropriate use.

The opioid crisis is one of the largest and most complex public health tragedies that our nation has ever faced. FDA is fully committed to looking closely at the opioid crisis, learning from what happened, and identifying missed opportunities. The Agency is proactively doing everything within our power to address the ongoing opioid crisis and applying these lessons to forcefully address future public health challenges.

We appreciate the opportunity to respond to your inquiry. Your questions are in bold, followed by FDA's responses.

1. **You referred to "past mistakes" in the statement you issued after the 60 Minutes report.**
   Specifically:
   a. **What are the past mistakes you were referring to?**
   b. **When were these mistakes made?**
   c. **For each past mistake identified, what actions has FDA taken in response?**

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

https://www.hassan.senate.gov/imo/media/doc/FDA%20RESPONSE%20HASSAN%201.21.20.pdf

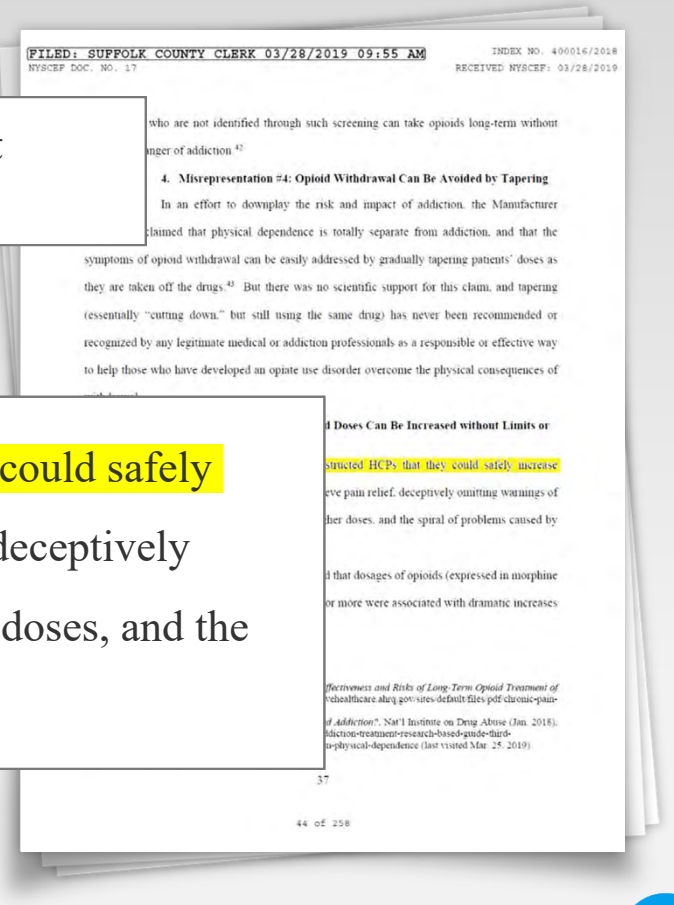
Alleged Misrepresentation No. 5:
Opioid Doses Can Be Increased without Limit or Greater Risk

5. Misrepresentation #5: Opioid Doses Can Be Increased without Limits or Greater Risks

NY AG FAC, p. 37

130. The Manufacturer Defendants instructed HCPs that they could safely increase patients' opioid doses without risk in order to achieve pain relief, deceptively omitting warnings of known, increased adverse effects that occur at higher doses, and the spiral of problems caused by tolerance to the drugs.

NY AG FAC ¶130


FILED: SUFFOLK COUNTY CLERK 03/28/2019 09:55 AM INDEX NO. 400016/2018
NYSCEF DOC. NO. 17 RECEIVED NYSCEF: 03/28/2019

who are not identified through such screening can take opioids long-term without anger of addiction.[42]

4. Misrepresentation #4: Opioid Withdrawal Can Be Avoided by Tapering

In an effort to downplay the risk and impact of addiction, the Manufacturer claimed that physical dependence is totally separate from addiction, and that the symptoms of opioid withdrawal can be easily addressed by gradually tapering patients' doses as they are taken off the drugs.[43] But there was no scientific support for this claim, and tapering (essentially "cutting down," but still using the same drug) has never been recommended or recognized by any legitimate medical or addiction professionals as a responsible or effective way to help those who have developed an opiate use disorder overcome the physical consequences of

d Doses Can Be Increased without Limits or

structed HCPs that they could safely increase

eve pain relief, deceptively omitting warnings of

her doses, and the spiral of problems caused by

d that dosages of opioids (expressed in morphine

or more were associated with dramatic increases

ffectiveness and Risks of Long-Term Opioid Treatment of
vehealthcare.ahrq.gov/sites/default/files/pdf/chronic-pain-

d Addiction?, Nat'l Institute on Drug Abuse (Jan. 2018),
ddiction-treatment-research-based-guide-third-
n-physical-dependence (last visited Mar. 25, 2019).

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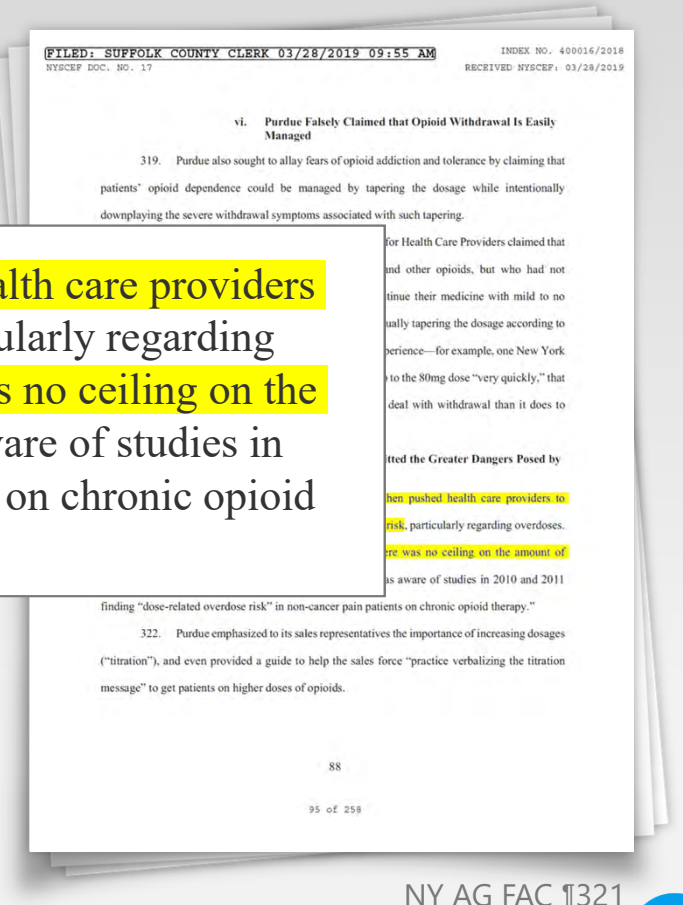
Alleged Misrepresentation No. 5:
Opioid Doses Can Be Increased without Limit or Greater Risk

Allegation: "No Ceiling" Statements Are Deceptive

321. Once patients started on opioids, Purdue then pushed health care providers to increase the dosages prescribed while omitting the increased risk, particularly regarding overdoses. Purdue trained its detailers to reassure prescribers that there was no ceiling on the amount of OxyContin a patient could be prescribed, even though it was aware of studies in 2010 and 2011 finding "dose-related overdose risk" in non-cancer patients on chronic opioid therapy."


FILED: SUFFOLK COUNTY CLERK 03/28/2019 09:55 AM INDEX NO. 400016/2018
NYSCEF DOC. NO. 17 RECEIVED NYSCEF: 03/28/2019

vi. Purdue Falsely Claimed that Opioid Withdrawal Is Easily Managed

319. Purdue also sought to allay fears of opioid addiction and tolerance by claiming that patients' opioid dependence could be managed by tapering the dosage while intentionally downplaying the severe withdrawal symptoms associated with such tapering.

for Health Care Providers claimed that
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to the 80mg dose "very quickly," that
deal with withdrawal than it does to

tted the Greater Dangers Posed by

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322. Purdue emphasized to its sales representatives the importance of increasing dosages ("titration"), and even provided a guide to help the sales force "practice verbalizing the titration message" to get patients on higher doses of opioids.

88

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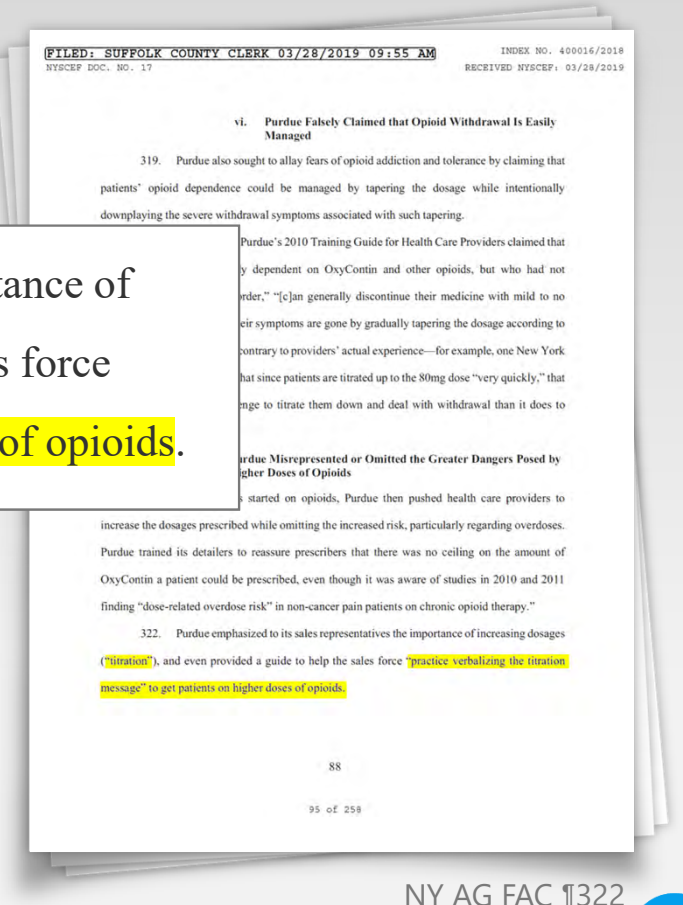
NY AG FAC ¶321

Alleged Misrepresentation No. 5:
Opioid Doses Can Be Increased without Limit or Greater Risk

Allegation: Emphasizing Titration Is Deceptive

322. Purdue emphasized to its sales representatives the importance of increasing dosages ("titration"), and even provided a guide to help the sales force "practice verbalizing the titration message" to get patients on higher doses of opioids.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Purdue's 2010 Training Guide for Health Care Providers claimed that

y dependent on OxyContin and other opioids, but who had not

rder," "[c]an generally discontinue their medicine with mild to no

eir symptoms are gone by gradually tapering the dosage according to

ontrary to providers' actual experience—for example, one New York

hat since patients are titrated up to the 80mg dose "very quickly," that

nge to titrate them down and deal with withdrawal than it does to

rdue Misrepresented or Omitted the Greater Dangers Posed by gher Doses of Opioids

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95 of 258

NY AG FAC ¶322

The FDA-Approved OxyContin Label States There Is No Ceiling Effect

1995 FDA-Approved OxyContin Label:

12.1 Mechanism of Action

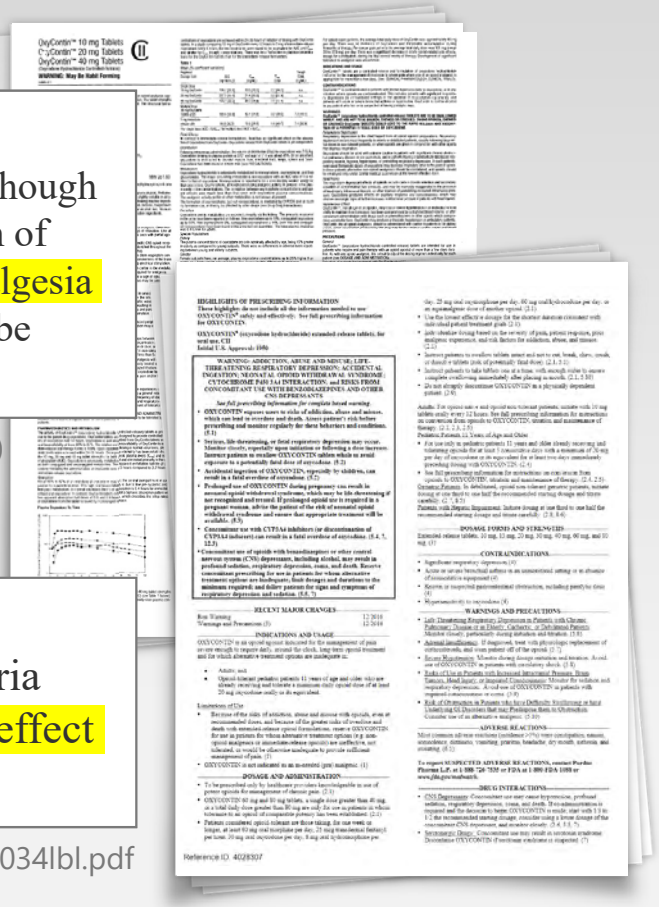
Oxycodone is a full opioid agonist and is relatively selective for the mu receptor, although it can bind to other opioid receptors at higher doses. The principal therapeutic action of oxycodone is analgesia. Like all full opioid agonists, there is no ceiling effect to analgesia for oxycodone. Clinically, dosage is titrated to provide adequate analgesia and may be limited by adverse reactions, including respiratory and CNS depression.

1995 OxyContin Label, p. 1, (PDD150170001)

2016 FDA-Approved OxyContin Label:

Oxycodone is a pure agonist opioid whose principal therapeutic action is analgesia. Other therapeutic effects of oxycodone include anxiolysis, euphoria and feelings of relaxation. Like all pure opioid agonists, there is no ceiling effect to analgesia, such as is seen with partial agonists or non-opioid analgesics.

2016 OxyContin Label, p. 33, https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/022272s034lbl.pdf

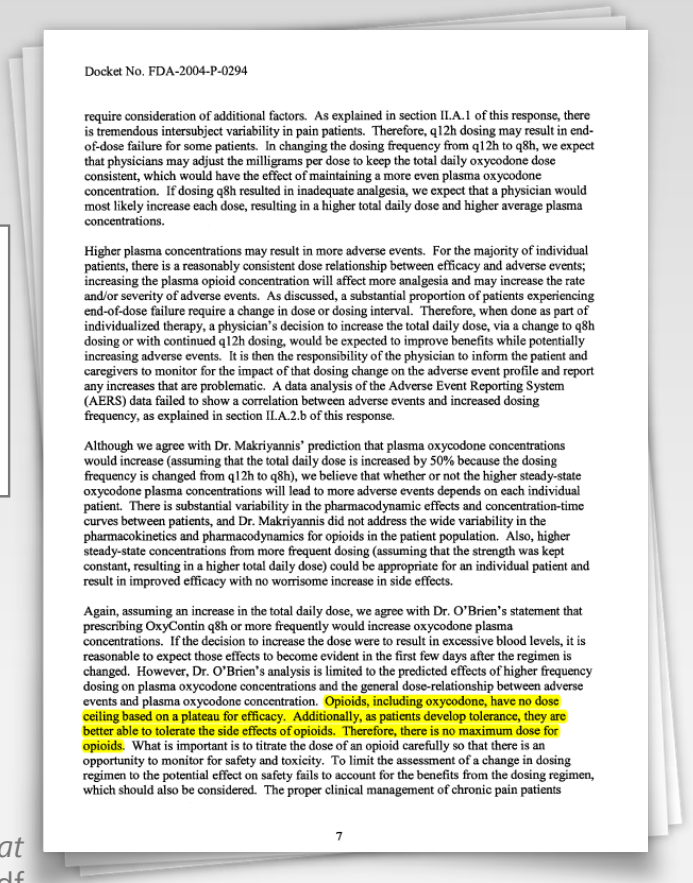


FDA Has Consistently Reaffirmed There Is No Ceiling Effect Or Maximum Dose For Opioids

FDA Letter to AG Richard Blumenthal (Sept. 9, 2008)

FDA Docket No. FDA-2004-P-0294, at p. 7

> **Opioids, including oxycodone, have no dose ceiling based on a plateau for efficiency**. Additionally, as patients develop tolerance, they are better able to tolerate the side effects of opioids. **Therefore, there is no maximum dose for opioids.**



Docket No. FDA-2004-P-0294

require consideration of additional factors. As explained in section II.A.1 of this response, there is tremendous intersubject variability in pain patients. Therefore, q12h dosing may result in end-of-dose failure for some patients. In changing the dosing frequency from q12h to q8h, we expect that physicians may adjust the milligrams per dose to keep the total daily oxycodone dose consistent, which would have the effect of maintaining a more even plasma oxycodone concentration. If dosing q8h resulted in inadequate analgesia, we expect that a physician would most likely increase each dose, resulting in a higher total daily dose and higher average plasma concentrations.

Higher plasma concentrations may result in more adverse events. For the majority of individual patients, there is a reasonably consistent dose relationship between efficacy and adverse events; increasing the plasma opioid concentration will affect more analgesia and may increase the rate and/or severity of adverse events. As discussed, a substantial proportion of patients experiencing end-of-dose failure require a change in dose or dosing interval. Therefore, when done as part of individualized therapy, a physician's decision to increase the total daily dose, via a change to q8h dosing or with continued q12h dosing, would be expected to improve benefits while potentially increasing adverse events. It is then the responsibility of the physician to inform the patient and caregivers to monitor for the impact of that dosing change on the adverse event profile and report any increases that are problematic. A data analysis of the Adverse Event Reporting System (AERS) data failed to show a correlation between adverse events and increased dosing frequency, as explained in section II.A.2.b of this response.

Although we agree with Dr. Makriyannis' prediction that plasma oxycodone concentrations would increase (assuming that the total daily dose is increased by 50% because the dosing frequency is changed from q12h to q8h), we believe that whether or not the higher steady-state oxycodone plasma concentrations will lead to more adverse events depends on each individual patient. There is substantial variability in the pharmacodynamic effects and concentration-time curves between patients, and Dr. Makriyannis did not address the wide variability in the pharmacokinetics and pharmacodynamics for opioids in the patient population. Also, higher steady-state concentrations from more frequent dosing (assuming that the strength was kept constant, resulting in a higher total daily dose) could be appropriate for an individual patient and result in improved efficacy with no worrisome increase in side effects.

Again, assuming an increase in the total daily dose, we agree with Dr. O'Brien's statement that prescribing OxyContin q8h or more frequently would increase oxycodone plasma concentrations. If the decision to increase the dose were to result in excessive blood levels, it is reasonable to expect those effects to become evident in the first few days after the regimen is changed. However, Dr. O'Brien's analysis is limited to the predicted effects of higher frequency dosing on plasma oxycodone concentrations and the general dose-relationship between adverse events and plasma oxycodone concentration. Opioids, including oxycodone, have no dose ceiling based on a plateau for efficacy. Additionally, as patients develop tolerance, they are better able to tolerate the side effects of opioids. Therefore, there is no maximum dose for opioids. What is important is to titrate the dose of an opioid carefully so that there is an opportunity to monitor for safety and toxicity. To limit the assessment of a change in dosing regimen to the potential effect on safety fails to account for the benefits from the dosing regimen, which should also be considered. The proper clinical management of chronic pain patients

7

FDA Docket No. FDA-2004-P-0294, at p. 7, *available at* https://www.purduepharma.com/wp-content/pdfs/fda_response_blumenthal_oxycontin.pdf

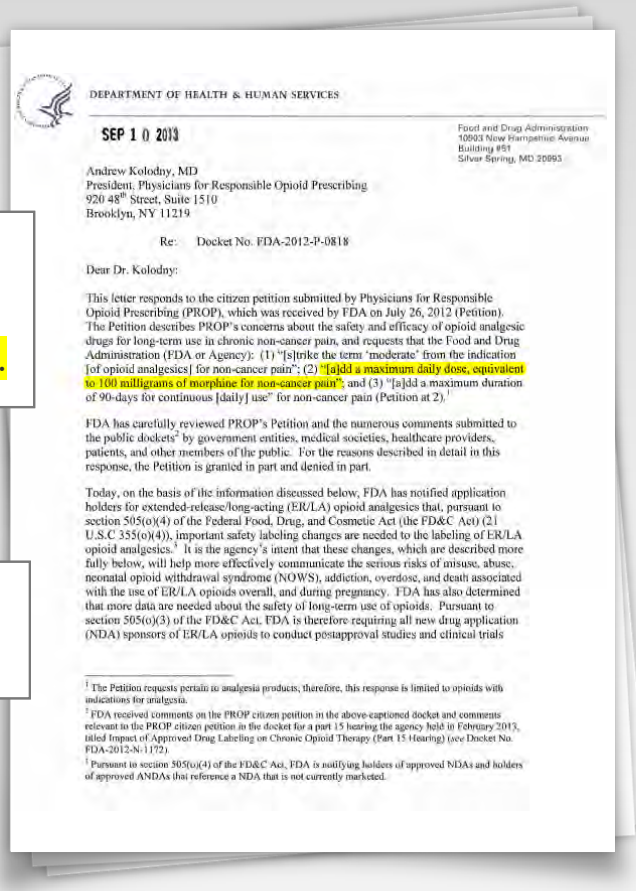
FDA Rejected a Maximum Daily Dose for OxyContin in 2013

In 2013 Physicians for Responsible Opioid Prescribing ("PROP") Petition asked the FDA to:

Add a maximum daily dose, equivalent to 100 milligrams of morphine for non-cancer pain . . . [because t]hree large observational studies published in 2010 and 2011 found dose-related overdose risk in CNCP patients on [chronic opioid therapy].

The FDA refused because:

… the scientific literature does not support establishing a maximum recommended daily dose of 100 mg MED.



DEPARTMENT OF HEALTH & HUMAN SERVICES

SEP 1 0 2013

Food and Drug Administration
10903 New Hampshire Avenue
Building #51
Silver Spring, MD 20993

Andrew Kolodny, MD
President, Physicians for Responsible Opioid Prescribing
920 48th Street, Suite 1510
Brooklyn, NY 11219

Re: Docket No. FDA-2012-P-0818

Dear Dr. Kolodny:

This letter responds to the citizen petition submitted by Physicians for Responsible Opioid Prescribing (PROP), which was received by FDA on July 26, 2012 (Petition). The Petition describes PROP's concerns about the safety and efficacy of opioid analgesic drugs for long-term use in chronic non-cancer pain, and requests that the Food and Drug Administration (FDA or Agency): (1) "[s]trike the term 'moderate' from the indication [of opioid analgesics] for non-cancer pain"; (2) "[a]dd a maximum daily dose, equivalent to 100 milligrams of morphine for non-cancer pain"; and (3) "[a]dd a maximum duration of 90-days for continuous [daily] use" for non-cancer pain (Petition at 2).[1]

FDA has carefully reviewed PROP's Petition and the numerous comments submitted to the public dockets[2] by government entities, medical societies, healthcare providers, patients, and other members of the public. For the reasons described in detail in this response, the Petition is granted in part and denied in part.

Today, on the basis of the information discussed below, FDA has notified application holders for extended-release/long-acting (ER/LA) opioid analgesics that, pursuant to section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C 355(o)(4)), important safety labeling changes are needed to the labeling of ER/LA opioid analgesics.[3] It is the agency's intent that these changes, which are described more fully below, will help more effectively communicate the serious risks of misuse, abuse, neonatal opioid withdrawal syndrome (NOWS), addiction, overdose, and death associated with the use of ER/LA opioids overall, and during pregnancy. FDA has also determined that more data are needed about the safety of long-term use of opioids. Pursuant to section 505(o)(3) of the FD&C Act, FDA is therefore requiring all new drug application (NDA) sponsors of ER/LA opioids to conduct postapproval studies and clinical trials

[1] The Petition requests pertain to analgesia products, therefore, this response is limited to opioids with indications for analgesia.

[2] FDA received comments on the PROP citizen petition in the above-captioned docket and comments relevant to the PROP citizen petition in the docket for a part 15 hearing the agency held in February 2013, titled Impact of Approved Drug Labeling on Chronic Opioid Therapy (Part 15 Hearing) (see Docket No. FDA-2012-N-1172).

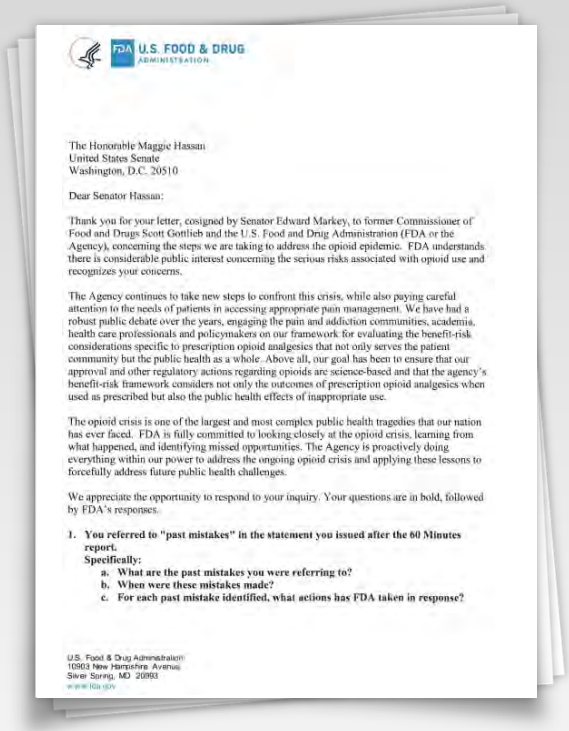
[3] Pursuant to section 505(o)(4) of the FD&C Act, FDA is notifying holders of approved NDAs and holders of approved ANDAs that reference a NDA that is not currently marketed.

9/10/13 2013 PROP Letter, pp. 1, 12, *available at* http://paindr.com/wp-content/uploads/2013/09/FDA_CDER_Response_to_Physicians_for_Responsible_Opioid_Prescribing_Partial_Petition_Approval_and_Denial.pdf

FDA Still Rejects A Maximum Dose for Opioids

2020 FDA Letter to Senator Maggie Hassan:

- "[T]he data do not suggest a threshold [dose] below which opioid use is 'safe' and above which it is 'too risky.'" (Page 13)



U.S. FOOD & DRUG ADMINISTRATION

The Honorable Maggie Hassan
United States Senate
Washington, D.C. 20510

Dear Senator Hassan:

Thank you for your letter, cosigned by Senator Edward Markey, to former Commissioner of Food and Drugs Scott Gottlieb and the U.S. Food and Drug Administration (FDA or the Agency), concerning the steps we are taking to address the opioid epidemic. FDA understands there is considerable public interest concerning the serious risks associated with opioid use and recognizes your concerns.

The Agency continues to take new steps to confront this crisis, while also paying careful attention to the needs of patients in accessing appropriate pain management. We have had a robust public debate over the years, engaging the pain and addiction communities, academia, health care professionals and policymakers on our framework for evaluating the benefit-risk considerations specific to prescription opioid analgesics that not only serves the patient community but the public health as a whole. Above all, our goal has been to ensure that our approval and other regulatory actions regarding opioids are science-based and that the agency's benefit-risk framework considers not only the outcomes of prescription opioid analgesics when used as prescribed but also the public health effects of inappropriate use.

The opioid crisis is one of the largest and most complex public health tragedies that our nation has ever faced. FDA is fully committed to looking closely at the opioid crisis, learning from what happened, and identifying missed opportunities. The Agency is proactively doing everything within our power to address the ongoing opioid crisis and applying these lessons to forcefully address future public health challenges.

We appreciate the opportunity to respond to your inquiry. Your questions are in bold, followed by FDA's responses.

1. **You referred to "past mistakes" in the statement you issued after the 60 Minutes report.**
   Specifically:
   a. **What are the past mistakes you were referring to?**
   b. **When were these mistakes made?**
   c. **For each past mistake identified, what actions has FDA taken in response?**

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

https://www.hassan.senate.gov/imo/media/doc/FDA%20RESPONSE%20HASSAN%201.21.20.pdf

Individualized Titration As Optimal Way to Find Lowest Effective Dose Is Explained in the OxyContin Label

1995 OxyContin Label:

As with all opioids, the minimum effective plasma concentration tor analgesia will vary widely among patients, especially among patients who have been previously treated with potent agonist opioids. As a result, patients need to be treated with individualized titration of dosage to the desired effect. The minimum effective analgesic concentration of oxycodone for any individual patient may increase with repeated dosing due to an increase in pain and/or the development of tolerance.

1995 OxyContin Label, p. 1, (PDD150170001)

2013 OxyContin Label:

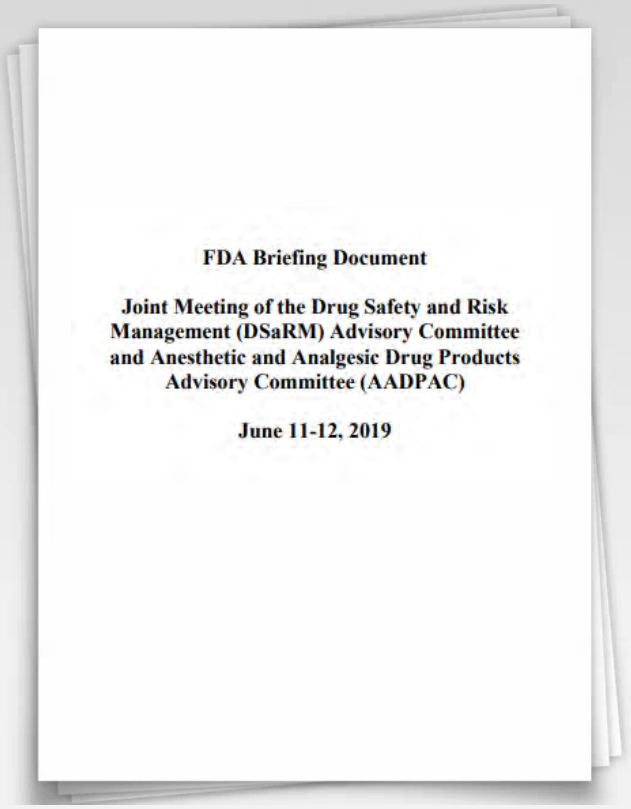
Individually titrate OxyContin to a dose that provides adequate analgesia and minimizes adverse reactions. Continually reevaluate patients receiving OxyContin to assess the maintenance of pain control and the relative incidence of adverse reactions. During chronic therapy, especially for non-cancer-related pain (or pain associated with other terminal illnesses), periodically reassess the continued need for the use of opioid analgesics.

April 2013 OxyContin Label, p. 7, (PPLPC003000060503)

Individualized Titration As Optimal Way to Find Lowest Effective Dose Is Explained in the OxyContin Label

FDA Briefing Book for June 11-12, 2019 Joint Meeting of the Drug Safety and Risk Mgmt. Advisory Comm. and Anesthetic and Analgesic Drug Products Advisory Comm.:

- "**With the consideration of individual variability, the clinician may individually titrate the [opioid] to a dose that provides adequate analgesia and minimizes adverse reactions based on the patient's response.**" (Page 14)
- "**The general approach is to initiate opioid treatment with a low dose and individually titrate to a tolerable dose that provides adequate analgesia.'"** (Page 14)



https://www.fda.gov/media/127780/download

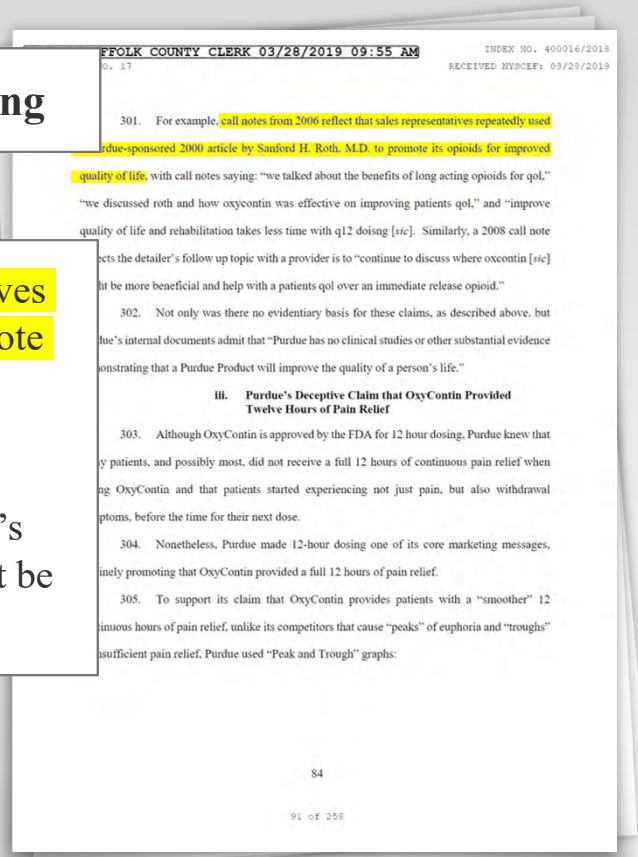
Alleged Misrepresentation No. 6:
Long-Term Opioid Use Improves Functioning

6. Misrepresentation #6: Long-Term Opioid Use Improves Functioning

NY AG FAC, p. 38

301. For example, call notes from 2006 reflect that sales representatives repeatedly used a Purdue-sponsored 2000 article by Sanford H. Roth, M.D. to promote its opioids for improved quality of life, with call notes saying: "we talked about the benefits of long acting opioids for qol," "we discussed roth and how oxycontin was effective on improving patients qol," and "improve quality of life and rehabilitation takes less time with q12 doisng [sic]. Similarly, a 2008 call note reflects the detailer's follow up topic with a provider is to "continue to discuss where oxcontin [sic] might be more beneficial and help with a patients qol over an immediate release opioid.".

NY AG FAC ¶301


FFOLK COUNTY CLERK 03/28/2019 09:55 AM INDEX NO. 400016/2018
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302. Not only was there no evidentiary basis for these claims, as described above, but lue's internal documents admit that "Purdue has no clinical studies or other substantial evidence onstrating that a Purdue Product will improve the quality of a person's life."

iii. Purdue's Deceptive Claim that OxyContin Provided Twelve Hours of Pain Relief

303. Although OxyContin is approved by the FDA for 12 hour dosing, Purdue knew that y patients, and possibly most, did not receive a full 12 hours of continuous pain relief when ng OxyContin and that patients started experiencing not just pain, but also withdrawal ptoms, before the time for their next dose.

304. Nonetheless, Purdue made 12-hour dosing one of its core marketing messages, inely promoting that OxyContin provided a full 12 hours of pain relief.

305. To support its claim that OxyContin provides patients with a "smoother" 12 inuous hours of pain relief, unlike its competitors that cause "peaks" of euphoria and "troughs" nsufficient pain relief, Purdue used "Peak and Trough" graphs:

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- Purdue expressly prohibited quality of life claims

Purdue Expressly Prohibited Quality of Life Claims

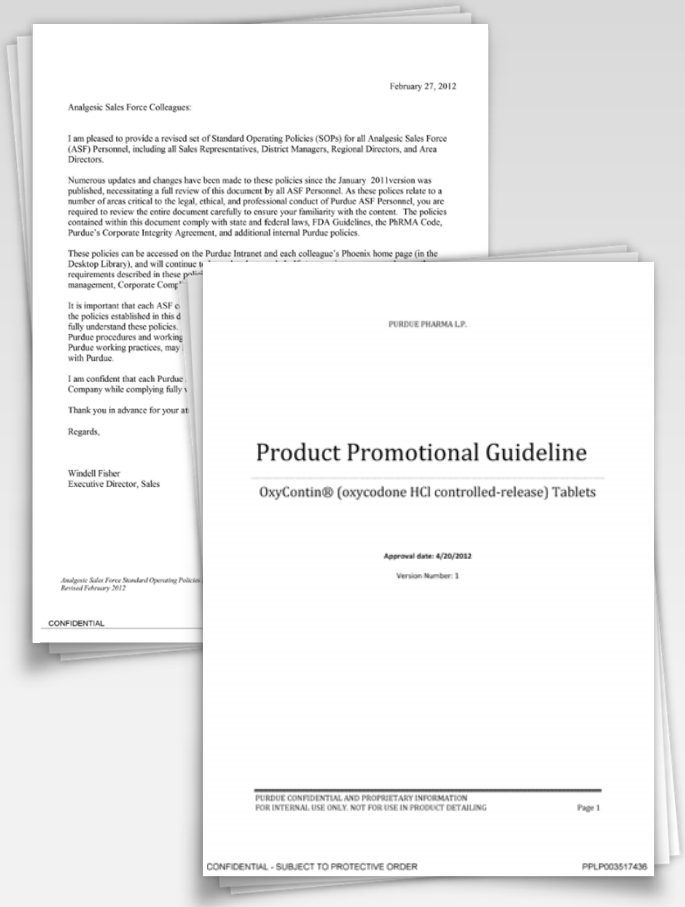
Quality of Life and Convenience Claims

Quality of life and convenience claims may be explicit or implied; both are to be avoided. All claims must be consistent with product labeling and Company Approved Material. As Purdue has no clinical studies or other substantial evidence demonstrating that a Purdue Product will improve the quality of a person's life or that taking a Purdue Product is more convenient than an alternative product, such claims cannot be made. Likewise, it is impermissible to ask a question of the customer that causes him/her to make a quality of life conclusion about a Purdue product.

5.0 TOPICS PRECLUDED FROM PROMOTION

The following topics are specifically excluded from promotional materials at this time.

- Efficacy claims or representations that suggest or imply that OxyContin is indicated for acute or mild chronic pain (or any other type of pain beyond moderate to severe chronic pain), pediatric patients, or pregnant women.
- Comparative efficacy or safety claims (e.g., "like all opioids…", "more effective than…").
- Any claim that suggests or implies that OxyContin can be used in pediatric patients.
- Pharmacoeconomic (PE) claims are not substantiated by competent and reliable scientific studies.
- Quality of Life (QoL) claims (e.g., improvements in functionality or sleep), including visual representations or pictorials that are not substantiated by patient reported outcomes (PROs) validated tools.



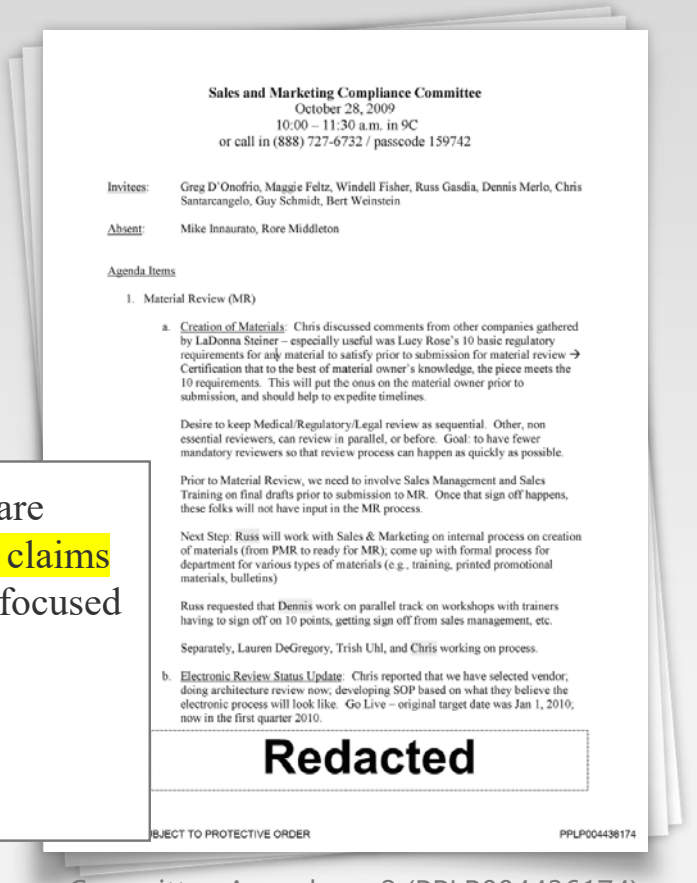
2/27/12 SOP for Analgesic Sales Force, p. 14 (PPLPC014000164042); 4/20/2012 Product Promotional Guidelines, p. 13 (PPLP003517436)

Purdue Retrained Or Disciplined Employees Who Made Quality of Life Claims

Sales and Marketing Compliance Committee
October 28, 2009
10:00 – 11:30 a.m. in 9C
or call in (888) 727-6732 / passcode 159742

2. Call Note Reviews: Litigation Support is thru July on key word searches; they are working to catch up on call note searches. Biggest issue = sleep and quality of life claims ➡ we trained on this issue in April and again in June 2009. This issue seems to be focused particularly in February timeframe.

Going forward, we will get reports on a monthly basis per Bert's agreement with Mike Panagrossi.



Sales and Marketing Compliance Committee
October 28, 2009
10:00 – 11:30 a.m. in 9C
or call in (888) 727-6732 / passcode 159742

Invitees: Greg D'Onofrio, Maggie Feltz, Windell Fisher, Russ Gasdia, Dennis Merlo, Chris Santarcangelo, Guy Schmidt, Bert Weinstein

Absent: Mike Innaurato, Rore Middleton

Agenda Items

1. Material Review (MR)

a. Creation of Materials: Chris discussed comments from other companies gathered by LaDonna Steiner – especially useful was Lucy Rose's 10 basic regulatory requirements for any material to satisfy prior to submission for material review → Certification that to the best of material owner's knowledge, the piece meets the 10 requirements. This will put the onus on the material owner prior to submission, and should help to expedite timelines.

Desire to keep Medical/Regulatory/Legal review as sequential. Other, non essential reviewers, can review in parallel, or before. Goal: to have fewer mandatory reviewers so that review process can happen as quickly as possible.

Prior to Material Review, we need to involve Sales Management and Sales Training on final drafts prior to submission to MR. Once that sign off happens, these folks will not have input in the MR process.

Next Step: Russ will work with Sales & Marketing on internal process on creation of materials (from PMR to ready for MR); come up with formal process for department for various types of materials (e.g., training, printed promotional materials, bulletins)

Russ requested that Dennis work on parallel track on workshops with trainers having to sign off on 10 points, getting sign off from sales management, etc.

Separately, Lauren DeGregory, Trish Uhl, and Chris working on process.

b. Electronic Review Status Update: Chris reported that we have selected vendor; doing architecture review now; developing SOP based on what they believe the electronic process will look like. Go Live – original target date was Jan 1, 2010; now in the first quarter 2010.

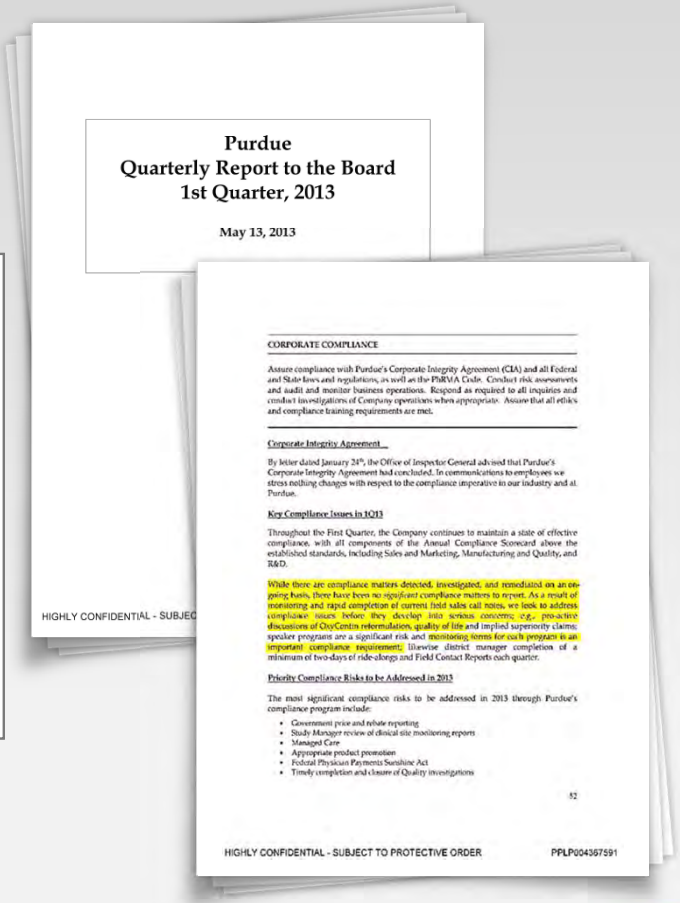
Redacted

BJECT TO PROTECTIVE ORDER PPLP004436174

10/28/09 Sales and Marketing Compliance Committee Agenda, p. 2 (PPLP004436174)

Board Was Informed Compliance Department Monitored And Remediated Quality of Life Claims

While there are compliance matters detected, investigated, and remediated on an ongoing basis, there have been no significant compliance matters to report. As a result of monitoring and rapid completion of current field sales call notes, **we look to address compliance issues before they develop into serious concerns; e.g.,** pro-active discussions of OxyContin reformulation, **quality of life** and implied superiority claims; speaker programs are a significant risk and monitoring forms for each program is an important compliance requirement; likewise district manager completion of a minimum of two-days of ride-alongs and Field Contact Reports each quarter.



Purdue
Quarterly Report to the Board
1st Quarter, 2013

May 13, 2013

CORPORATE COMPLIANCE

Assure compliance with Purdue's Corporate Integrity Agreement (CIA) and all Federal and State laws and regulations, as well as the PMWA Code. Conduct risk assessments and audit and monitor business operations. Respond as required to all inquiries and conduct investigations of Company operations when appropriate. Assure that all ethics and compliance training requirements are met.

Corporate Integrity Agreement

By letter dated January 24th, the Office of Inspector General advised that Purdue's Corporate Integrity Agreement had concluded. In communications to employees we stress nothing changes with respect to the compliance imperative in our industry and at Purdue.

Key Compliance Issues in 1Q13

Throughout the First Quarter, the Company continues to maintain a state of effective compliance, with all components of the Annual Compliance Scorecard above the established standards, including Sales and Marketing, Manufacturing and Quality, and R&D.

While there are compliance matters detected, investigated, and remediated on an ongoing basis, there have been no significant compliance matters to report. As a result of monitoring and rapid completion of current field sales call notes, we look to address compliance issues before they develop into serious concerns; e.g., pro-active discussions of OxyContin reformulation, quality of life and implied superiority claims; speaker programs are a significant risk and monitoring forms for each program is an important compliance requirement; likewise district manager completion of a minimum of two-days of ride-alongs and Field Contact Reports each quarter.

Priority Compliance Risks to be Addressed in 2013

The most significant compliance risks to be addressed in 2013 through Purdue's compliance program include:

- Government price and rebate reporting
- Study Manager review of clinical site monitoring reports
- Managed Care
- Appropriate product promotion
- Federal Physician Payments Sunshine Act
- Timely completion and closure of Quality investigations

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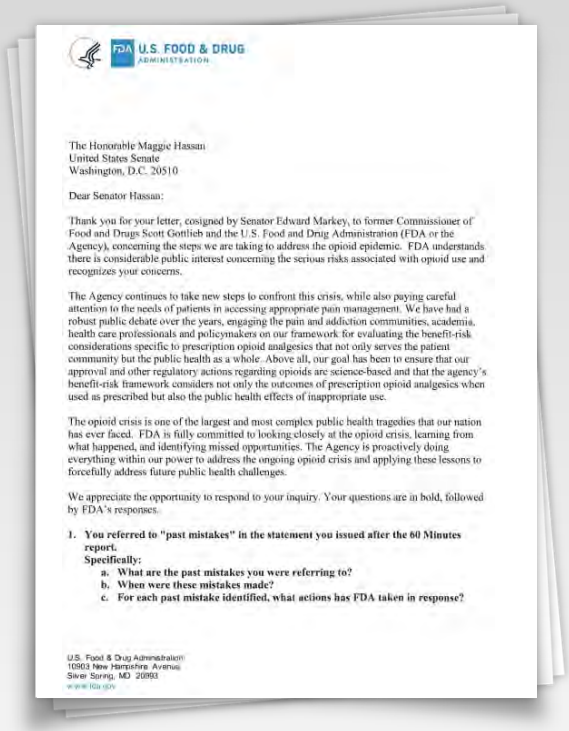
HIGHLY CONFIDENTIAL - SUBJECT TO PROTECTIVE ORDER PPLP004367591

May 2013 Board Report, p. 52 (PPLP004367540)

FDA Has Always Approved Long-Term Use of OxyContin

2020 FDA Letter to Senator Maggie Hassan:

- **"Chronic or long-term use (in appropriate situations), with no maximum duration, was always part of the approved use of OxyContin.'"** (Page 4)



U.S. FOOD & DRUG ADMINISTRATION

The Honorable Maggie Hassan
United States Senate
Washington, D.C. 20510

Dear Senator Hassan:

Thank you for your letter, cosigned by Senator Edward Markey, to former Commissioner of Food and Drugs Scott Gottlieb and the U.S. Food and Drug Administration (FDA or the Agency), concerning the steps we are taking to address the opioid epidemic. FDA understands there is considerable public interest concerning the serious risks associated with opioid use and recognizes your concerns.

The Agency continues to take new steps to confront this crisis, while also paying careful attention to the needs of patients in accessing appropriate pain management. We have had a robust public debate over the years, engaging the pain and addiction communities, academia, health care professionals and policymakers on our framework for evaluating the benefit-risk considerations specific to prescription opioid analgesics that not only serves the patient community but the public health as a whole. Above all, our goal has been to ensure that our approval and other regulatory actions regarding opioids are science-based and that the agency's benefit-risk framework considers not only the outcomes of prescription opioid analgesics when used as prescribed but also the public health effects of inappropriate use.

The opioid crisis is one of the largest and most complex public health tragedies that our nation has ever faced. FDA is fully committed to looking closely at the opioid crisis, learning from what happened, and identifying missed opportunities. The Agency is proactively doing everything within our power to address the ongoing opioid crisis and applying these lessons to forcefully address future public health challenges.

We appreciate the opportunity to respond to your inquiry. Your questions are in bold, followed by FDA's responses.

1. **You referred to "past mistakes" in the statement you issued after the 60 Minutes report.**
   Specifically:
   a. **What are the past mistakes you were referring to?**
   b. **When were these mistakes made?**
   c. **For each past mistake identified, what actions has FDA taken in response?**

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

https://www.hassan.senate.gov/imo/media/doc/FDA%20RESPONSE%20HASSAN%201.21.20.pdf

Alleged Misrepresentation No. 7:
Alternative Forms of Pain Relief Pose Greater Risks Than Opioids

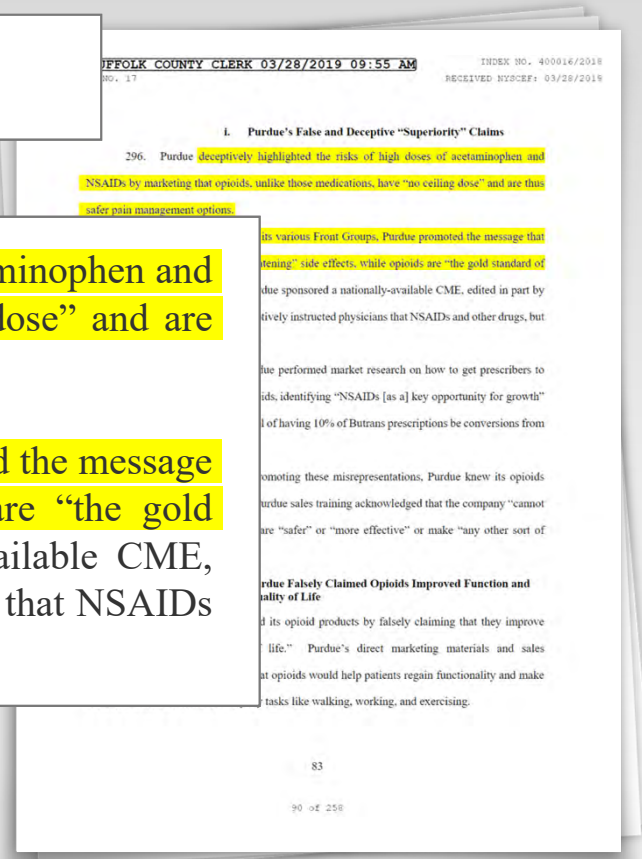
7. Misrepresentation #7: Alternative Forms of Pain Relief Pose Greater Risks than Opioids

NY AG FAC, p. 41

296. Purdue deceptively highlighted the risks of high doses of acetaminophen and NSAIDs by marketing that opioids, unlike those medications, have "no ceiling dose" and are thus safer pain management options.

297. Directly and through its various Front Groups, Purdue promoted the message that NSAIDs and Tylenol have "life-threatening" side effects, while opioids are "the gold standard of pain medications." For example, Purdue sponsored a nationally-available CME, edited in part by KOL Dr. Russell Portenoy, that deceptively instructed physicians that NSAIDs and other drugs, but not opioids, are unsafe at high doses.

NY AG FAC ¶¶296-97



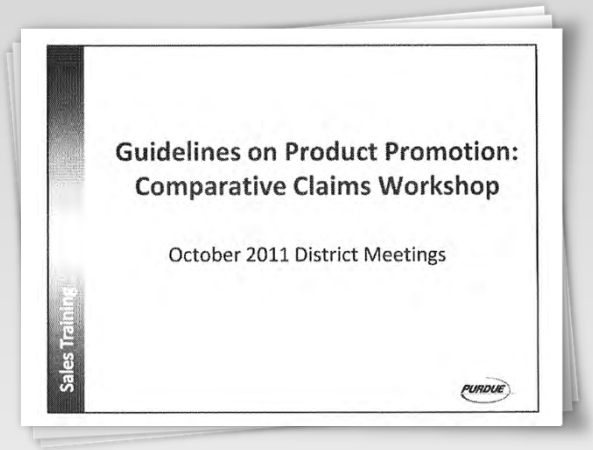
- Purdue expressly prohibited quality of life claims

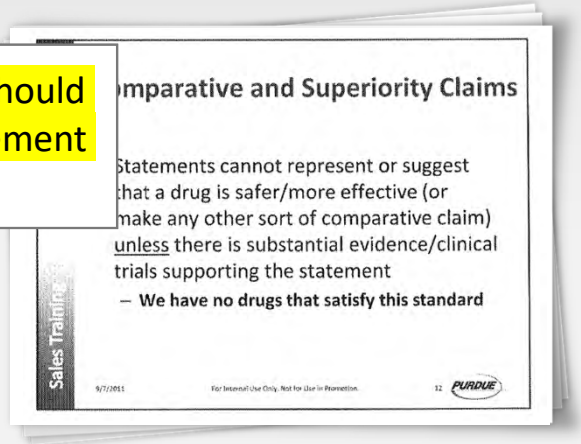
Purdue Prohibited Comparative Claims

Statements cannot represent or suggest that a drug is safer/more effective (or make any other sort of comparative claim) unless there is substantial evidence/clinical trials supporting the statement — We have no drugs that satisfy this standard

Be careful not to IMPLY superiority in your discussions with HCPs

What If It Is the HCP Who Is Making These Statements? . . . When this happens, what should you do? . . . There are circumstances where it is necessary to respond to the HCP's statement (e.g., when failure to do so might leave a misimpression about our products





10/11 Guidelines on Product Promotion: Comparative Claims Workshop (PPLP003439475)

Purdue Prohibited Comparative Claims

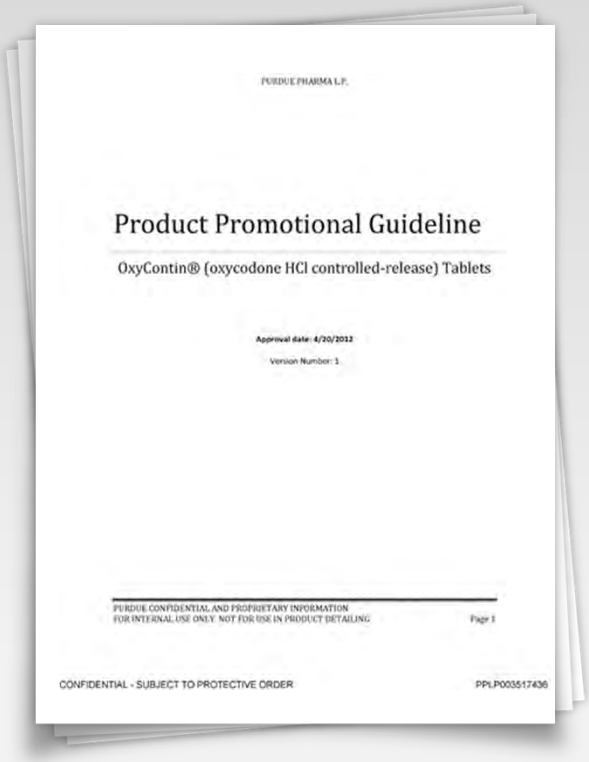
Product Promotional Guidelines (Apr. 20, 2012)**:**

- "**Care should be taken to avoid any comparative claims to other productions or classes of drugs.**" (Page 4)

***

"**5.0 TOPICS PRECLUDED FROM PROMOTION**"

- "**Comparative efficacy or safety claims**" (Page 13)


PURDUE PHARMA L.P.

Product Promotional Guideline

OxyContin® (oxycodone HCl controlled-release) Tablets

Approval date: 4/20/2012

Version Number: 1

PURDUE CONFIDENTIAL AND PROPRIETARY INFORMATION
FOR INTERNAL USE ONLY. NOT FOR USE IN PRODUCT DETAILING

Page 1

CONFIDENTIAL - SUBJECT TO PROTECTIVE ORDER

PPLP003517436

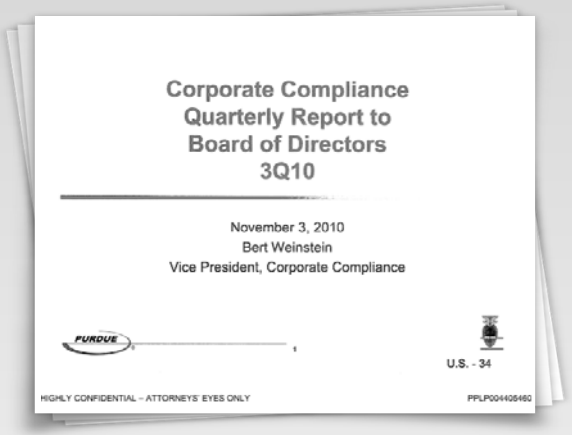
4/20/2012 Product Promotional Guidelines, pp. 4, 13 (PPLP003517436)

Board Was Advised Comparative Claims Were Monitored And Remediated

- Routine review of call notes revealed references that suggested potential comparative claims of superiority of Purdue products relative to competitors. Compliance conducted a broader review of all call notes entered after training on comparative claims in June 2009. A total of 75 potentially problematic notes were identified. Interviews were held with responsible sales representatives, and district managers who had reviewed, but not commented on those call notes.

- Follow up discipline included: termination of one representative for multiple compliance violations, **probation** for a second representative, and **written warning letters** for an additional 16 representatives. One manager received a written warning letter, and a second was provided with verbal coaching.

- **Additional procedures have been put in place**, to ensure that any training on promotional issues that a representative misses will be provided when the representative returns from leave (or joins the company if a new employee).


Corporate Compliance
Quarterly Report to
Board of Directors
3Q10

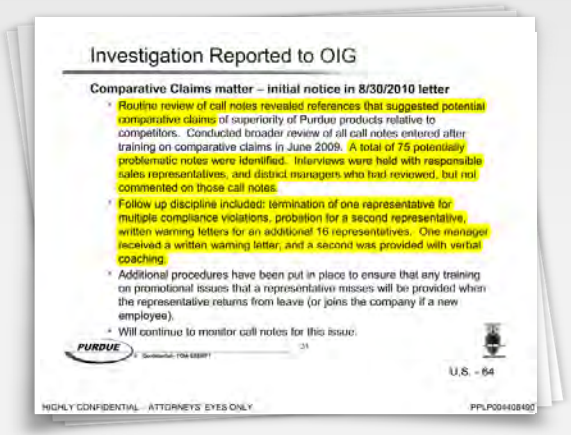
November 3, 2010
Bert Weinstein
Vice President, Corporate Compliance

PURDUE

U.S. - 34

HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY

PPLP004405460


Investigation Reported to OIG

Comparative Claims matter – initial notice in 8/30/2010 letter

- Routine review of call notes revealed references that suggested potential comparative claims of superiority of Purdue products relative to competitors. Conducted broader review of all call notes entered after training on comparative claims in June 2009. A total of 75 potentially problematic notes were identified. Interviews were held with responsible sales representatives, and district managers who had reviewed, but not commented on those call notes.
- Follow up discipline included: termination of one representative for multiple compliance violations, probation for a second representative, written warning letters for an additional 16 representatives. One manager received a written warning letter, and a second was provided with verbal coaching.
- Additional procedures have been put in place to ensure that any training on promotional issues that a representative misses will be provided when the representative returns from leave (or joins the company if a new employee).
- Will continue to monitor call notes for this issue.

PURDUE

U.S. - 64

HIGHLY CONFIDENTIAL – ATTORNEYS' EYES ONLY

PPLP004408490

3Q2010 Quarterly Compliance Report at slide 31 (PPLP004405460, -490)

Alleged Misrepresentation No. 8:
Extended-Release Drugs Provide 12 Or More Hours of Pain Relief

8. Misrepresentation #8: Extended-Release Drugs Provide Twelve or More Hours of Pain Relief

146. The Manufacturer Defendants misled doctors and patients about the original selling point of their "revolutionary" extended-release ("ER") opioids, making the knowingly false claim that such drugs would provide 12 or more hours of pain relief for most patients. This claim provided the basis for the Manufacturer Defendants' patents and their efforts to differentiate themselves from competitors, and facilitated their false claims that ER drugs have a more even, stable release mechanism that avoids peaks and valleys, and therefore the rush that fosters misuse and addiction.

147. The active ingredient in the Manufacturer Defendants' ER opioids does not enter the body at a linear rate. OxyContin, for example, works by releasing a greater proportion of oxycodone into the body upon administration, and the release gradually tapers. The reduced release of the drug over time means that the oxycodone no longer provides the same level of pain relief. As a result, in many patients, OxyContin does not last for the twelve hours promised. …

NY AG FAC p.43, ¶¶146-47

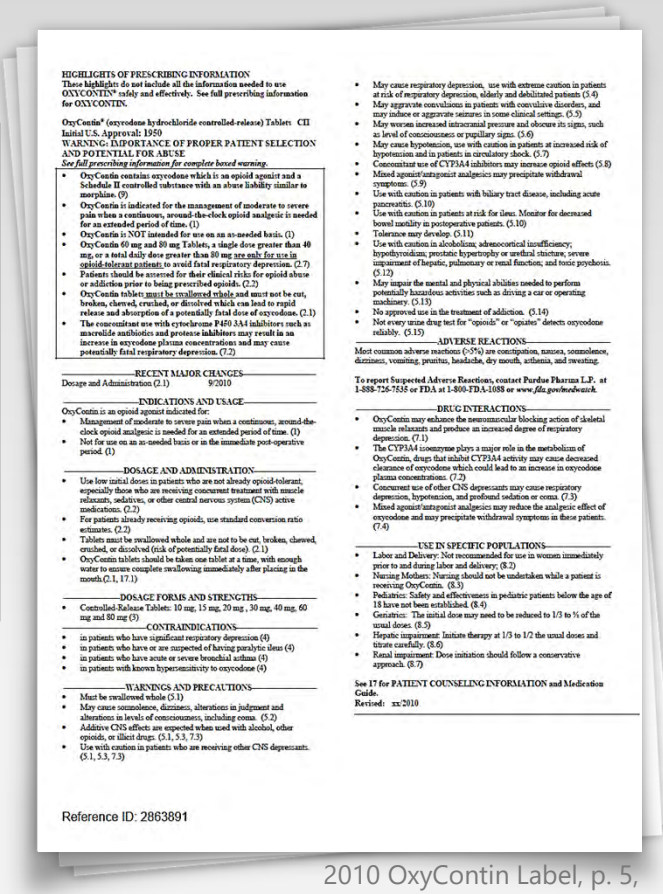
The FDA Approved OxyContin As A 12-Hour Drug

FDA-approved label:

2.2 Initiating Therapy with OxyContin

* * *

Experience indicates a reasonable starting dose of OxyContin for patients who are taking non-opioid analgesics and require continuous around-the-clock therapy for an extended period of time is 10 mg every 12 hours. Individually titrate OxyContin to a dose that provides adequate analgesia and minimizes adverse reactions while maintaining an every-twelve-hour dosing regimen.



HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OXYCONTIN® safely and effectively. See full prescribing information for OXYCONTIN.

OxyContin® (oxycodone hydrochloride controlled-release) Tablets CII
Initial U.S. Approval: 1950
WARNING: IMPORTANCE OF PROPER PATIENT SELECTION AND POTENTIAL FOR ABUSE
See full prescribing information for complete boxed warning.

- OxyContin contains oxycodone which is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine. (9)
- OxyContin is indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. (1)
- OxyContin is NOT intended for use on an as-needed basis. (1)
- OxyContin 60 mg and 80 mg Tablets, a single dose greater than 40 mg, or a total daily dose greater than 80 mg are only for use in opioid-tolerant patients to avoid fatal respiratory depression. (2.7)
- Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. (2.2)
- OxyContin tablets must be swallowed whole and must not be cut, broken, chewed, crushed, or dissolved which can lead to rapid release and absorption of a potentially fatal dose of oxycodone. (2.1)
- The concomitant use with cytochrome P450 3A4 inhibitors such as macrolide antibiotics and protease inhibitors may result in an increase in oxycodone plasma concentrations and may cause potentially fatal respiratory depression. (7.2)

RECENT MAJOR CHANGES
Dosage and Administration (2.1) 9/2010

INDICATIONS AND USAGE
OxyContin is an opioid agonist indicated for:

- Management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. (1)
- Not for use on an as-needed basis or in the immediate post-operative period. (1)

DOSAGE AND ADMINISTRATION

- Use low initial doses in patients who are not already opioid-tolerant, especially those who are receiving concurrent treatment with muscle relaxants, sedatives, or other central nervous system (CNS) active medications. (2.2)
- For patients already receiving opioids, use standard conversion ratio estimates. (2.2)
- Tablets must be swallowed whole and are not to be cut, broken, chewed, crushed, or dissolved (risk of potentially fatal dose). (2.1)
- OxyContin tablets should be taken one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth.(2.1, 17.1)

DOSAGE FORMS AND STRENGTHS

- Controlled-Release Tablets: 10 mg, 15 mg, 20 mg , 30 mg, 40 mg, 60 mg and 80 mg (3)

CONTRAINDICATIONS

- in patients who have significant respiratory depression (4)
- in patients who have or are suspected of having paralytic ileus (4)
- in patients who have acute or severe bronchial asthma (4)
- in patients with known hypersensitivity to oxycodone (4)

WARNINGS AND PRECAUTIONS

- Must be swallowed whole (5.1)
- May cause somnolence, dizziness, alterations in judgment and alterations in levels of consciousness, including coma. (5.2)
- Additive CNS effects are expected when used with alcohol, other opioids, or illicit drugs. (5.1, 5.3, 7.3)
- Use with caution in patients who are receiving other CNS depressants. (5.1, 5.3, 7.3)
- May cause respiratory depression, use with extreme caution in patients at risk of respiratory depression, elderly and debilitated patients (5.4)
- May aggravate convulsions in patients with convulsive disorders, and may induce or aggravate seizures in some clinical settings. (5.5)
- May worsen increased intracranial pressure and obscure its signs, such as level of consciousness or pupillary signs. (5.6)
- May cause hypotension, use with caution in patients at increased risk of hypotension and in patients in circulatory shock. (5.7)
- Concomitant use of CYP3A4 inhibitors may increase opioid effects (5.8)
- Mixed agonist/antagonist analgesics may precipitate withdrawal symptoms. (5.9)
- Use with caution in patients with biliary tract disease, including acute pancreatitis. (5.10)
- Use with caution in patients at risk for ileus. Monitor for decreased bowel motility in postoperative patients. (5.10)
- Tolerance may develop. (5.11)
- Use with caution in alcoholism; adrenocortical insufficiency; hypothyroidism; prostatic hypertrophy or urethral stricture; severe impairment of hepatic, pulmonary or renal function; and toxic psychosis. (5.12)
- May impair the mental and physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. (5.13)
- No approved use in the treatment of addiction. (5.14)
- Not every urine drug test for "opioids" or "opiates" detects oxycodone reliably. (5.15)

ADVERSE REACTIONS
Most common adverse reactions (>5%) are constipation, nausea, somnolence, dizziness, vomiting, pruritus, headache, dry mouth, asthenia, and sweating.

To report Suspected Adverse Reactions, contact Purdue Pharma L.P. at 1-888-726-7535 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

- OxyContin may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression. (7.1)
- The CYP3A4 isoenzyme plays a major role in the metabolism of OxyContin, drugs that inhibit CYP3A4 activity may cause decreased clearance of oxycodone which could lead to an increase in oxycodone plasma concentrations. (7.2)
- Concurrent use of other CNS depressants may cause respiratory depression, hypotension, and profound sedation or coma. (7.3)
- Mixed agonist/antagonist analgesics may reduce the analgesic effect of oxycodone and may precipitate withdrawal symptoms in these patients. (7.4)

USE IN SPECIFIC POPULATIONS

- Labor and Delivery: Not recommended for use in women immediately prior to and during labor and delivery; (8.2)
- Nursing Mothers: Nursing should not be undertaken while a patient is receiving OxyContin. (8.3)
- Pediatrics: Safety and effectiveness in pediatric patients below the age of 18 have not been established. (8.4)
- Geriatrics: The initial dose may need to be reduced to 1/3 to ½ of the usual doses. (8.5)
- Hepatic impairment: Initiate therapy at 1/3 to 1/2 the usual doses and titrate carefully. (8.6)
- Renal impairment: Dose initiation should follow a conservative approach. (8.7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.
Revised: xx/2010

Reference ID: 2863891

2010 OxyContin Label, p. 5, https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022272s006lbl.pdf.

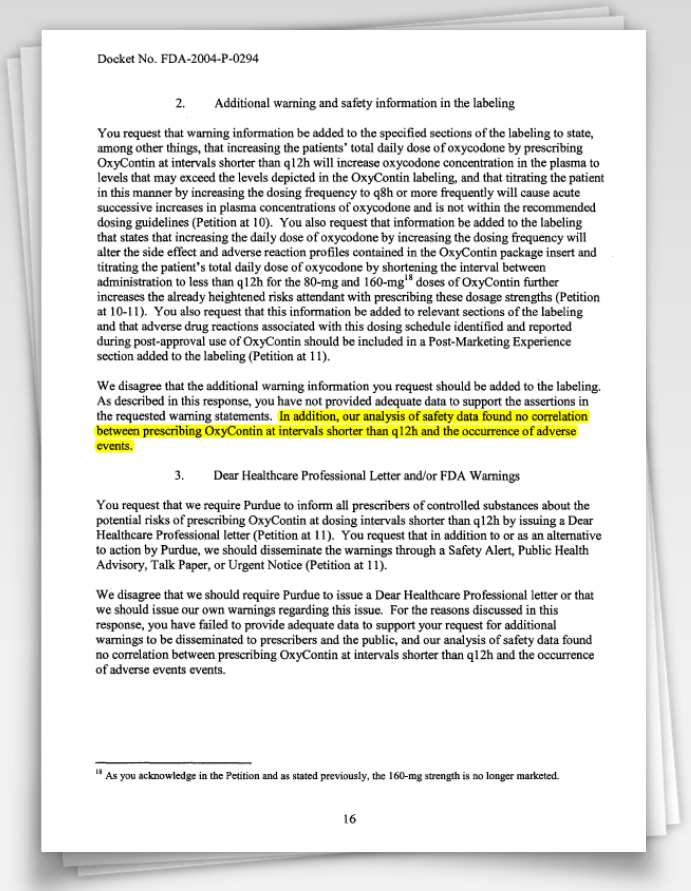
Purdue is therefore required to market OxyContin as a 12-hour drug (21 C.F.R. §201.100(d)(1); Consent Judgments ¶3)

FDA Found Dosing OxyContin More Often Than 12 Hours Was Not Associated with Adverse Events

FDA Letter to AG Richard Blumenthal (Sept. 9, 2008)

FDA Docket No. FDA-2004-P-0294, at p. 16

> **[O]ur analysis of safety data found no correlation between prescribing OxyContin at intervals shorter than q12h and the occurrence of adverse events.**



Docket No. FDA-2004-P-0294

2. Additional warning and safety information in the labeling

You request that warning information be added to the specified sections of the labeling to state, among other things, that increasing the patients' total daily dose of oxycodone by prescribing OxyContin at intervals shorter than q12h will increase oxycodone concentration in the plasma to levels that may exceed the levels depicted in the OxyContin labeling, and that titrating the patient in this manner by increasing the dosing frequency to q8h or more frequently will cause acute successive increases in plasma concentrations of oxycodone and is not within the recommended dosing guidelines (Petition at 10). You also request that information be added to the labeling that states that increasing the daily dose of oxycodone by increasing the dosing frequency will alter the side effect and adverse reaction profiles contained in the OxyContin package insert and titrating the patient's total daily dose of oxycodone by shortening the interval between administration to less than q12h for the 80-mg and 160-mg[18] doses of OxyContin further increases the already heightened risks attendant with prescribing these dosage strengths (Petition at 10-11). You also request that this information be added to relevant sections of the labeling and that adverse drug reactions associated with this dosing schedule identified and reported during post-approval use of OxyContin should be included in a Post-Marketing Experience section added to the labeling (Petition at 11).

We disagree that the additional warning information you request should be added to the labeling. As described in this response, you have not provided adequate data to support the assertions in the requested warning statements. In addition, our analysis of safety data found no correlation between prescribing OxyContin at intervals shorter than q12h and the occurrence of adverse events.

3. Dear Healthcare Professional Letter and/or FDA Warnings

You request that we require Purdue to inform all prescribers of controlled substances about the potential risks of prescribing OxyContin at dosing intervals shorter than q12h by issuing a Dear Healthcare Professional letter (Petition at 11). You request that in addition to or as an alternative to action by Purdue, we should disseminate the warnings through a Safety Alert, Public Health Advisory, Talk Paper, or Urgent Notice (Petition at 11).

We disagree that we should require Purdue to issue a Dear Healthcare Professional letter or that we should issue our own warnings regarding this issue. For the reasons discussed in this response, you have failed to provide adequate data to support your request for additional warnings to be disseminated to prescribers and the public, and our analysis of safety data found no correlation between prescribing OxyContin at intervals shorter than q12h and the occurrence of adverse events events.

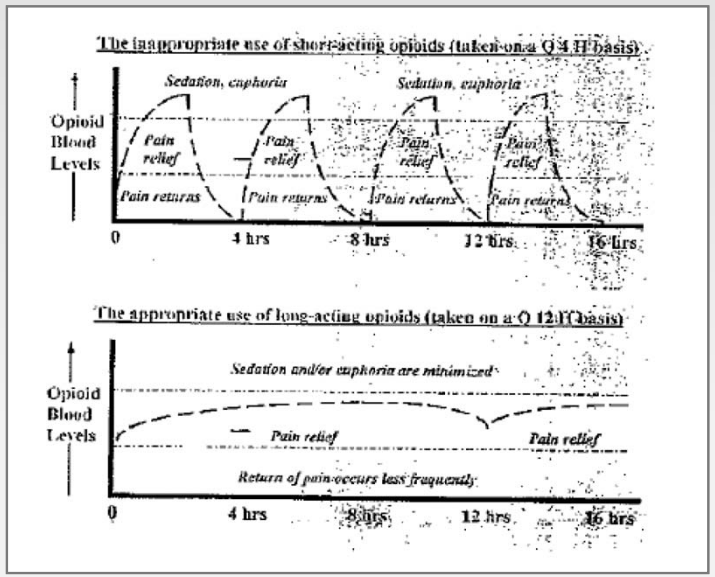
[18] As you acknowledge in the Petition and as stated previously, the 160-mg strength is no longer marketed.

16

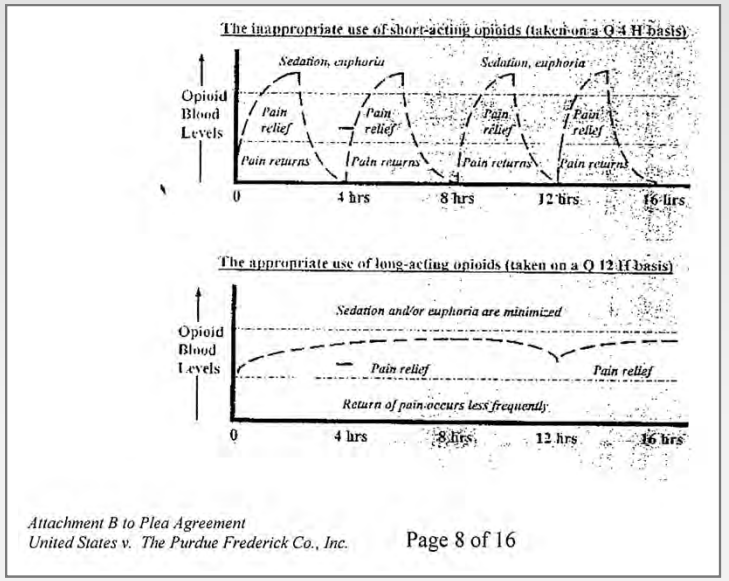
FDA Docket No. FDA-2004-P-0294, at p. 16, *available at available at* https://www.purduepharma.com/wp-content/pdfs/fda_response_blumenthal_oxycontin.pdf; *see also id.* at p.18

1998 Dosing Misrepresentations Are 23 Years' Old and Released

- NY AG's only example of Purdue overstating the dosing period is a graph from a 1998 training manual
- Purdue publicly admitted those graphs were deceptive when it pled guilty in 2007
- No evidence of post-2007 repetition



NY AG FAC, p. 85



Agreed Statement of Facts ¶¶25, 26, *United States v. Purdue Frederick Co.*, No. 1:07-cr-29 (JPJ) (W.D. Va. May 10, 2007)

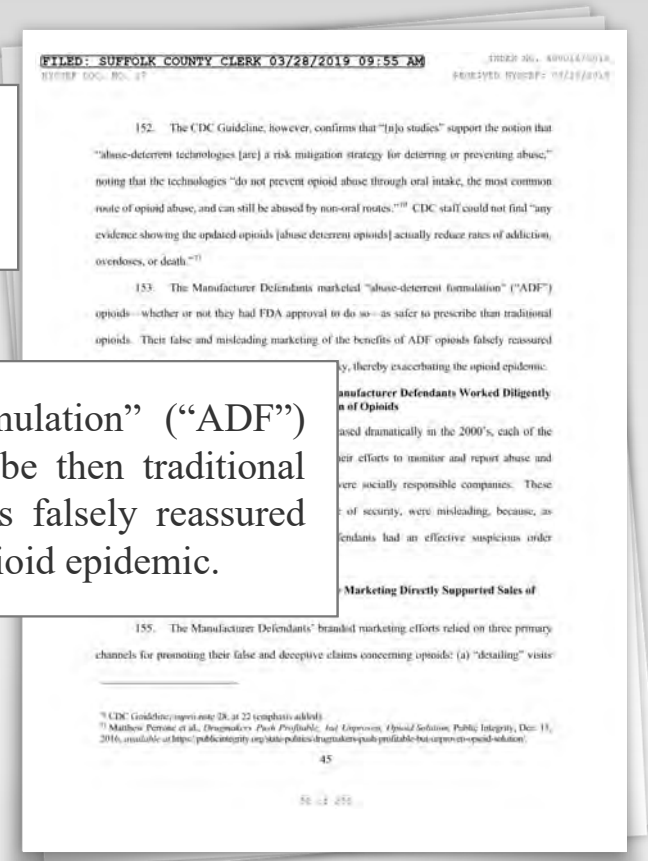
Alleged Misrepresentation No. 9:
OxyContin's 2010 Reformulation Successfully Deters Abuse

9. Misrepresentation #9: Newly-Developed but More Expensive Formulations of Opioids Successfully Deter Abuse

NY AG FAC p. 44

153. The Manufacturer Defendants marketed "abuse-deterrent formulation" ("ADF") opioids—whether or not they had FDA approval to do so—as safer to prescribe then traditional opioids. Their false and misleading marketing of the benefits of ADF opioids falsely reassured prescribers that prescribing such opioids was not risky, thereby exacerbating the opioid epidemic.

NY AG FAC ¶153


FILED: SUFFOLK COUNTY CLERK 03/28/2019 09:55 AM

152. The CDC Guideline, however, confirms that "[n]o studies" support the notion that "abuse-deterrent technologies [are] a risk mitigation strategy for deterring or preventing abuse," noting that the technologies "do not prevent opioid abuse through oral intake, the most common route of opioid abuse, and can still be abused by non-oral routes."[70] CDC staff could not find "any evidence showing the updated opioids [abuse deterrent opioids] actually reduce rates of addiction, overdoses, or death."[71]

153. The Manufacturer Defendants marketed "abuse-deterrent formulation" ("ADF") opioids—whether or not they had FDA approval to do so—as safer to prescribe than traditional opioids. Their false and misleading marketing of the benefits of ADF opioids falsely reassured

anufacturer Defendants Worked Diligently
n of Opioids

Marketing Directly Supported Sales of

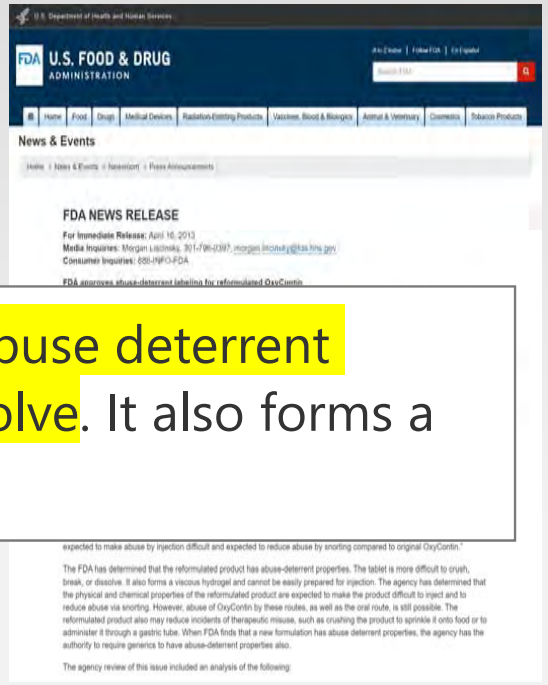
155. The Manufacturer Defendants' branded marketing efforts relied on three primary channels for promoting their false and deceptive claims concerning opioids: (a) "detailing" visits

45

Alleged Misrepresentation No. 9:
OxyContin's 2010 Reformulation Successfully Deters Abuse

1. **The only alleged misrepresentation is the abuse-deterrent language on the FDA-approved label**

2. **FDA determined reformulated OxyContin has abuse deterrent properties**


U.S. FOOD & DRUG ADMINISTRATION

News & Events

FDA NEWS RELEASE

For Immediate Release: April 16, 2013

Media Inquiries: Morgan Liscinsky, 301-796-0397, morgan.liscinsky@fda.hhs.gov

Consumer Inquiries: 888-INFO-FDA

FDA approves abuse-deterrent labeling for reformulated OxyContin

expected to make abuse by injection difficult and expected to reduce abuse by snorting compared to original OxyContin."

The FDA has determined that the reformulated product has abuse-deterrent properties. The tablet is more difficult to crush, break, or dissolve. It also forms a viscous hydrogel and cannot be easily prepared for injection. The agency has determined that the physical and chemical properties of the reformulated product are expected to make the product difficult to inject and to reduce abuse via snorting. However, abuse of OxyContin by these routes, as well as the oral route, is still possible. The reformulated product also may reduce incidents of therapeutic misuse, such as crushing the product to sprinkle it onto food or to administer it through a gastric tube. When FDA finds that a new formulation has abuse deterrent properties, the agency has the authority to require generics to have abuse-deterrent properties also.

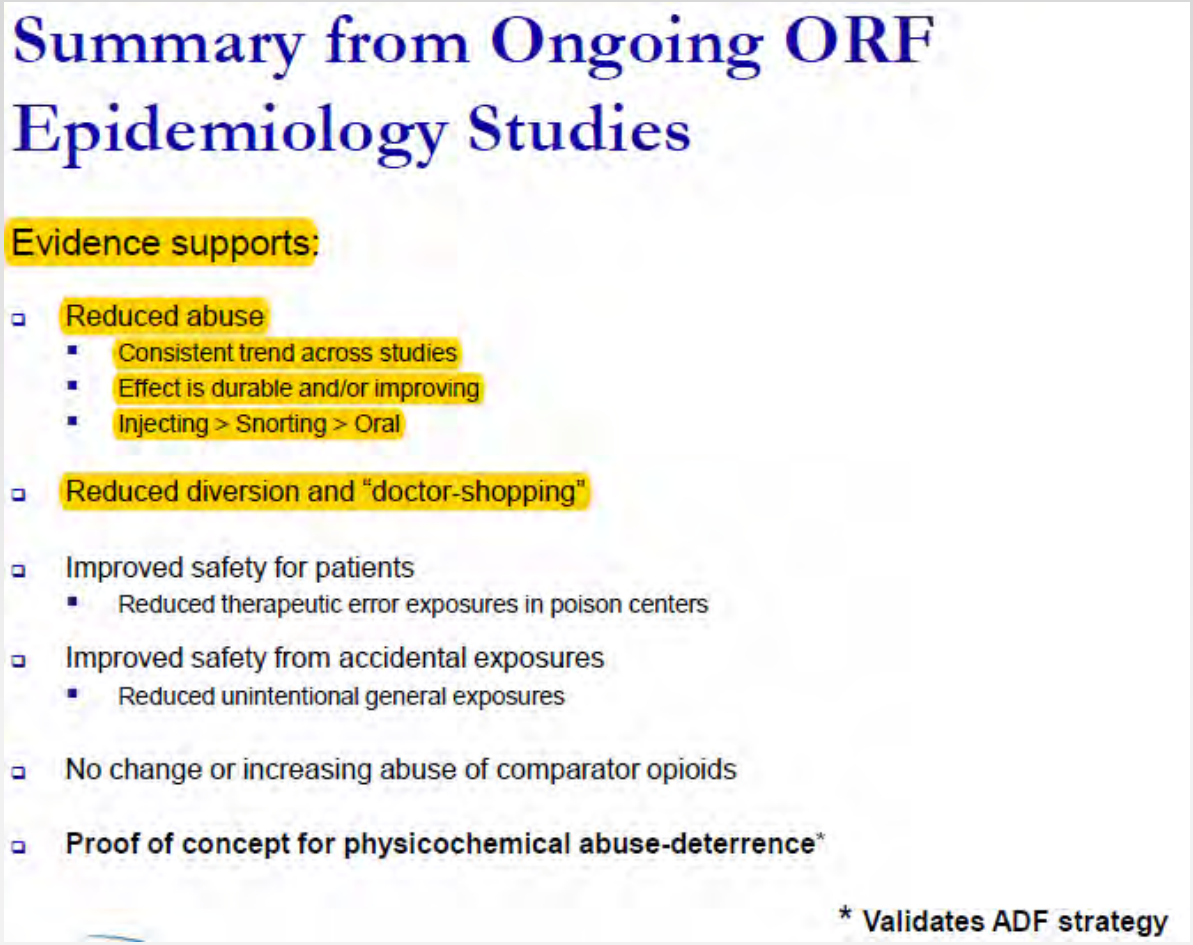
The agency review of this issue included an analysis of the following:

> The FDA has determined that the reformulated product has abuse deterrent properties. The tablet is more difficult to crush, break, or dissolve. It also forms a viscous hydrogel and cannot be easily prepared for injection. The agency has determined that the physical and chemical properties of the reformulated product are expected to make the product difficult to inject and to reduce abuse via snorting. However, abuse of OxyContin by these routes, as well as the oral route, is still possible. The reformulated product also may reduce incidents of therapeutic misuse, such as crushing the product to sprinkle it onto food or to administer it through a gastric tube. When FDA finds that a new formulation has abuse deterrent properties, the agency has the authority to require generics to have abuse-deterrent properties also.

April 16, 2013 FDA Press Release

https://web.archive.org/web/20130419012709/http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm348252.htm

Evidence Establishes That Abuse-Deterrent OxyContin Succeeded in Reducing Abuse



Summary from Ongoing ORF Epidemiology Studies

Evidence supports:

- Reduced abuse
  - Consistent trend across studies
  - Effect is durable and/or improving
  - Injecting > Snorting > Oral
- Reduced diversion and "doctor-shopping"
- Improved safety for patients
  - Reduced therapeutic error exposures in poison centers
- Improved safety from accidental exposures
  - Reduced unintentional general exposures
- No change or increasing abuse of comparator opioids
- **Proof of concept for physicochemical abuse-deterrence***

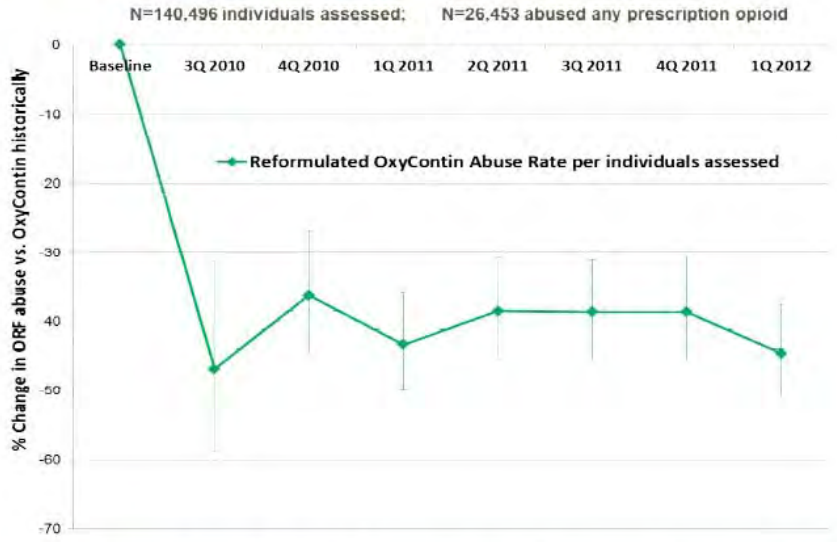
*** Validates ADF strategy**

PPLP004409195 (Nov. 3, 2012 Purdue Presentation to Beneficiaries)

Evidence Establishes That Abuse-Deterrent OxyContin Succeeded in Reducing Abuse

Abuse by Individuals Assessed for Substance Abuse Treatment

% Reduction from Baseline in NAVIPPRO® System
(Baseline is 14 months prior to ORF introduction)



95% confidence intervals shown; Baseline is average rate per individuals assessed over 14 months.

PURDUE

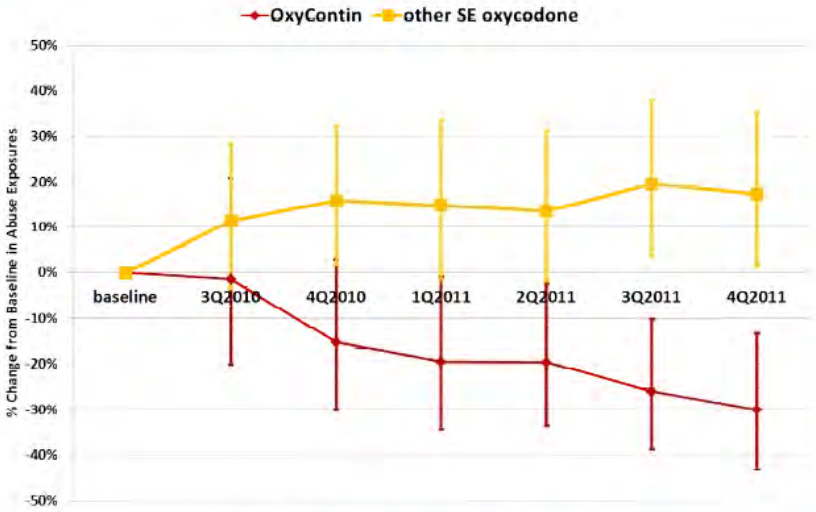
Confidential

PPLPC044000041897, -961 (Mar. 21, 2013 Presentation to Board)

Evidence Establishes That Abuse-Deterrent OxyContin Succeeded in Reducing Abuse

Poison Center Data from National Poison Data System

% Reduction from Baseline in Number of Intentional Abuse Exposures
(Baseline is 12 months prior to ORF introduction)



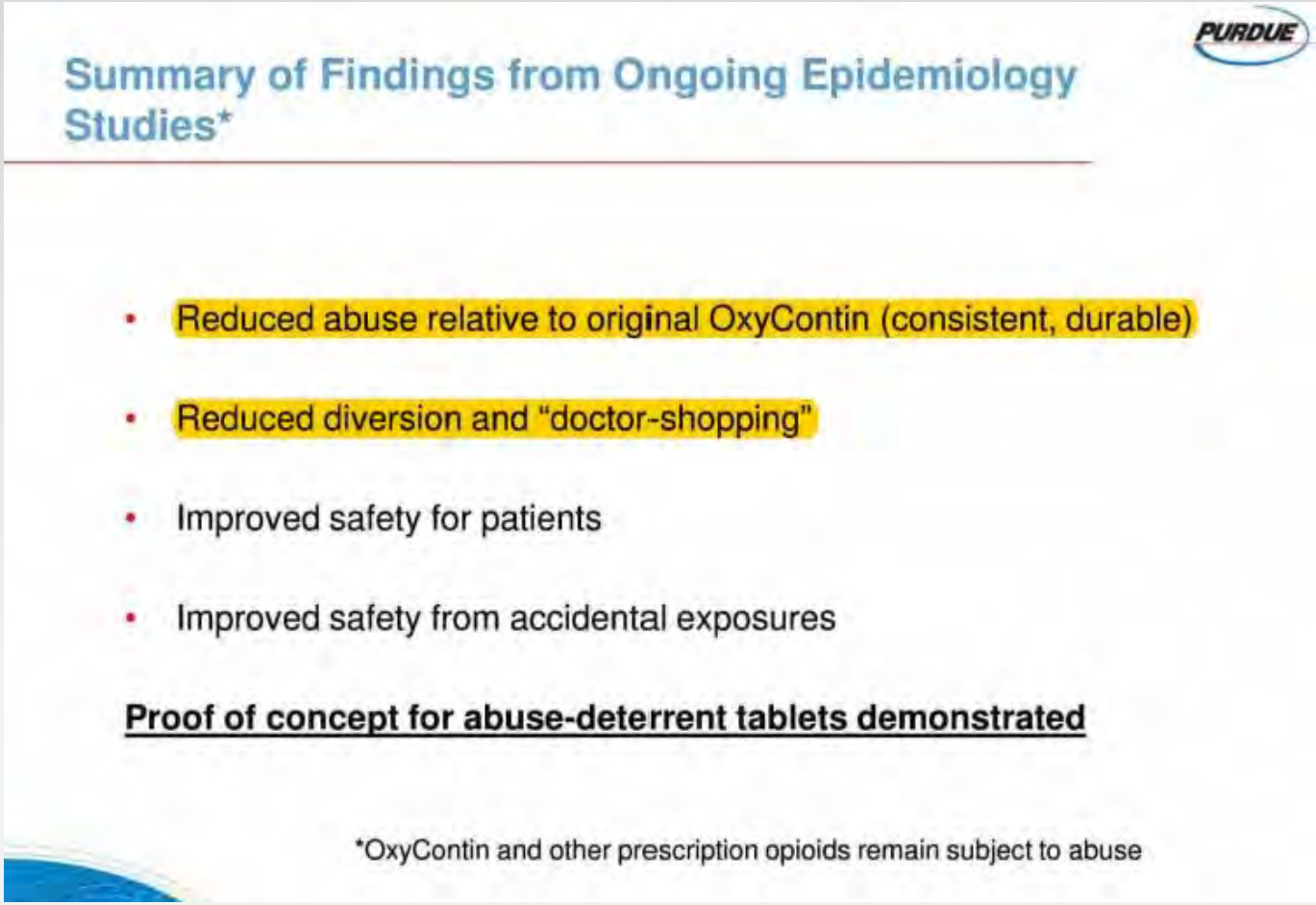
Source: National Poison Data System. Note: Baseline is average of 4 quarters from 3Q2009 to 2Q2010. 95% CI shown

PURDUE

Confidential

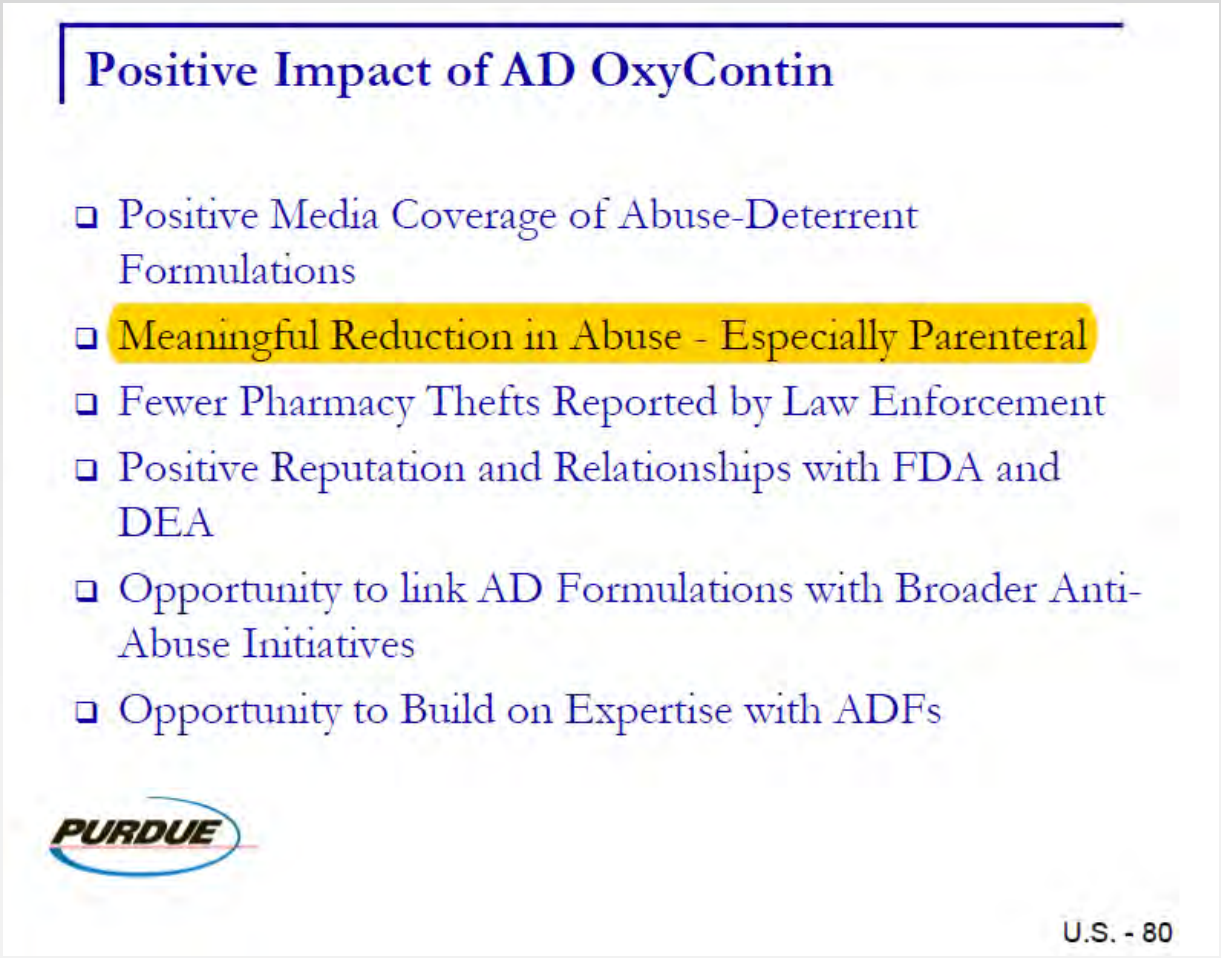
PPLPC044000041897, -962 (Mar. 21, 2013 Presentation to Board)

Evidence Establishes That Abuse-Deterrent OxyContin Succeeded in Reducing Abuse



PPLPC044000041968
(Mar. 21, 2013
Presentation to Board)

Evidence Establishes That Abuse-Deterrent OxyContin Succeeded in Reducing Abuse



PPLP004409860 (July 25, 2013 Presentation to Board)

FDA Still Encourages Development of Abuse-Deterrent Opioids

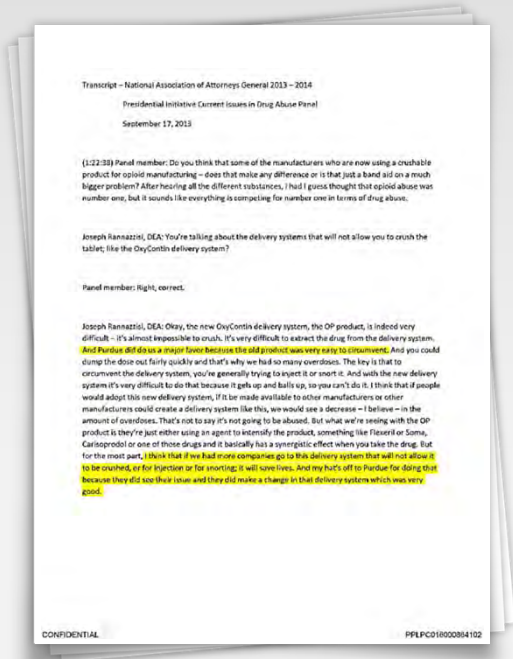
The FDA is encouraging the development of prescription opioids with abuse-deterrent formulations (ADFs) to help combat the opioid crisis. The agency recognizes that abuse deterrent opioids are not abuse- or addiction-proof but are a step toward products that may help reduce abuse.

https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/abuse-deterrent-opioid-analgesics

DEA Praised Abuse-Deterrent OxyContin, Encouraged Emulation

Quote from Jose Rannazzisi, former head of the DEA's Office of Diversion Control, at the National Association of Attorneys General in 2013:

Joseph Rannazzisi, DEA: Okay, the new OxyContin delivery system, the OP product, is indeed very difficult - it's almost impossible to crush. It's very difficult to extract the drug from the delivery system. And Purdue did do us a major favor because the old product was very easy to circumvent. And you could dump the dose out fairly quickly and that's why we had so many overdoses. The key is that to circumvent the delivery system, you're generally trying to inject it or snort it. And with the new delivery system it's very difficult to do that because it gels up and balls up, so you can't do it. I think that if people would adopt this new delivery system, if it be made available to other manufacturers or other manufacturers could create a delivery system like this, we would see a decrease - I believe - in the amount of overdoses. That's not to say it's not going to be abused. But what we're seeing with the OP product is they're just either using an agent to intensify the product, something like Flexeril or Soma, Carisoprodol or one of those drugs and it basically has a synergistic effect when you take the drug. But for the most part, I think that if we had more companies go to this delivery system that will not allow it to be crushed, or for injection or for snorting; it will save lives. And my hat's off to Purdue for doing that because they did see their issue and they did make a change in that delivery system which was very good.


Transcript – National Association of Attorneys General 2013 – 2014

Presidential Initiative Current Issues in Drug Abuse Panel

September 17, 2013

(1:22:33) Panel member: Do you think that some of the manufacturers who are now using a crushable product for opioid manufacturing – does that make any difference or is that just a band aid on a much bigger problem? After hearing all the different substances, I had I guess thought that opioid abuse was number one, but it sounds like everything is competing for number one in terms of drug abuse.

Joseph Rannazzisi, DEA: You're talking about the delivery systems that will not allow you to crush the tablet; like the OxyContin delivery system?

Panel member: Right, correct.

Joseph Rannazzisi, DEA: Okay, the new OxyContin delivery system, the OP product, is indeed very difficult – it's almost impossible to crush. It's very difficult to extract the drug from the delivery system. And Purdue did do us a major favor because the old product was very easy to circumvent. And you could dump the dose out fairly quickly and that's why we had so many overdoses. The key is that to circumvent the delivery system, you're generally trying to inject it or snort it. And with the new delivery system it's very difficult to do that because it gels up and balls up, so you can't do it. I think that if people would adopt this new delivery system, if it be made available to other manufacturers or other manufacturers could create a delivery system like this, we would see a decrease – I believe – in the amount of overdoses. That's not to say it's not going to be abused. But what we're seeing with the OP product is they're just either using an agent to intensify the product, something like Flexeril or Soma, Carisoprodol or one of those drugs and it basically has a synergistic effect when you take the drug. But for the most part, I think that if we had more companies go to this delivery system that will not allow it to be crushed, or for injection or for snorting; it will save lives. And my hat's off to Purdue for doing that because they did see their issue and they did make a change in that delivery system which was very good.

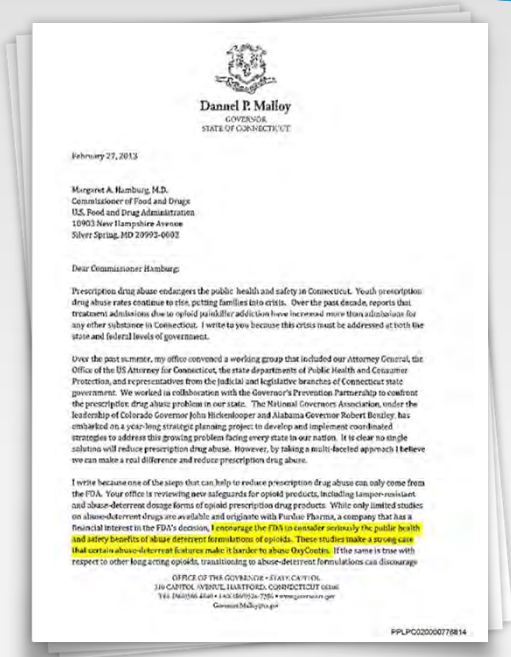
CONFIDENTIAL PPLPC018000884102

9/17/13 J. Rannazzisi, DEA (Presidential Initiative Current Issues In Drug Abuse Panel) (PPLPC018000884102)

Connecticut Governor Praised Abuse-Deterrent OxyContin, Encouraged Emulation

Dannel P. Malloy
GOVERNOR
STATE OF CONNECTICUT

I write because one of the steps that can help to reduce prescription drug abuse can only come from the FDA. Your office is reviewing new safeguards for opioid products, including tamper-resistant and abuse-deterrent dosage forms of opioid prescription drug products. While only limited studies on abuse-deterrent drugs are available and originate with Purdue Pharma, a company that has a financial interest in the FDA's decision, I encourage the FDA to consider seriously the public health and safety benefits of abuse deterrent formulations of opioids. These studies make a strong case that certain abuse-deterrent features make it harder to abuse OxyContin. If the same is true with respect to other long acting opioids, transitioning to abuse-deterrent formulations can discourage the abuse of extended release opioid prescription drugs while still making opioid drugs available to the patients who need them.


Dannel P. Malloy
GOVERNOR
STATE OF CONNECTICUT

February 27, 2013

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Commissioner Hamburg:

Prescription drug abuse endangers the public health and safety in Connecticut. Youth prescription drug abuse rates continue to rise, putting families into crisis. Over the past decade, reports that treatment admissions due to opioid painkiller addiction have increased more than admissions for any other substance in Connecticut. I write to you because this crisis must be addressed at both the state and federal levels of government.

Over the past summer, my office convened a working group that included our Attorney General, the Office of the US Attorney for Connecticut, the state departments of Public Health and Consumer Protection, and representatives from the judicial and legislative branches of Connecticut state government. We worked in collaboration with the Governor's Prevention Partnership to confront the prescription drug abuse problem in our state. The National Governors Association, under the leadership of Colorado Governor John Hickenlooper and Alabama Governor Robert Bentley, has embarked on a year-long strategic planning project to develop and implement coordinated strategies to address this growing problem facing every state in our nation. It is clear no single solution will reduce prescription drug abuse. However, by taking a multi-faceted approach I believe we can make a real difference and reduce prescription drug abuse.

I write because one of the steps that can help to reduce prescription drug abuse can only come from the FDA. Your office is reviewing new safeguards for opioid products, including tamper-resistant and abuse-deterrent dosage forms of opioid prescription drug products. While only limited studies on abuse-deterrent drugs are available and originate with Purdue Pharma, a company that has a financial interest in the FDA's decision, I encourage the FDA to consider seriously the public health and safety benefits of abuse deterrent formulations of opioids. These studies make a strong case that certain abuse-deterrent features make it harder to abuse OxyContin. If the same is true with respect to other long acting opioids, transitioning to abuse-deterrent formulations can discourage

OFFICE OF THE GOVERNOR • STATE CAPITOL

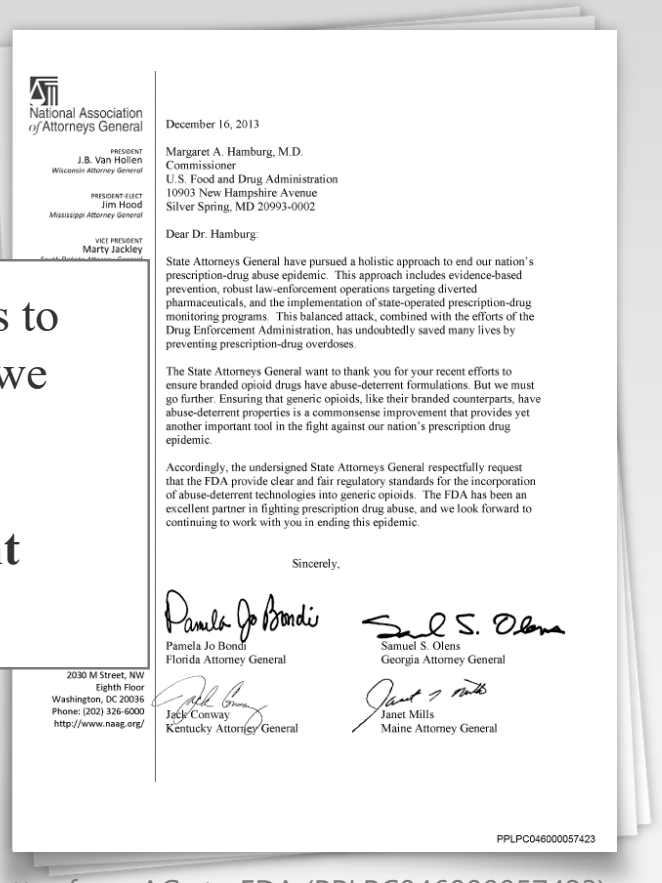
PPLPC020000776814

2/27/13 Letter from D. Malloy (PPLPC020000776814)

42 State AGs Encouraged Abuse-Deterrent Formulations

National Association of Attorneys General

The State Attorneys General want to thank you for your recent efforts to ensure branded opioid drugs have abuse-deterrent formulations. But we must go further. **Ensuring generic opioids, like their branded counterparts, have abuse-deterrent properties is a commonsense improvement that provides yet another important tool in the fight against our nation's prescription drug epidemic**.



National Association of Attorneys General

PRESIDENT
J.B. Van Hollen
Wisconsin Attorney General

PRESIDENT-ELECT
Jim Hood
Mississippi Attorney General

VICE PRESIDENT
Marty Jackley

2030 M Street, NW
Eighth Floor
Washington, DC 20036
Phone: (202) 326-6000
http://www.naag.org/

December 16, 2013

Margaret A. Hamburg, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Dr. Hamburg:

State Attorneys General have pursued a holistic approach to end our nation's prescription-drug abuse epidemic. This approach includes evidence-based prevention, robust law-enforcement operations targeting diverted pharmaceuticals, and the implementation of state-operated prescription-drug monitoring programs. This balanced attack, combined with the efforts of the Drug Enforcement Administration, has undoubtedly saved many lives by preventing prescription-drug overdoses.

The State Attorneys General want to thank you for your recent efforts to ensure branded opioid drugs have abuse-deterrent formulations. But we must go further. Ensuring that generic opioids, like their branded counterparts, have abuse-deterrent properties is a commonsense improvement that provides yet another important tool in the fight against our nation's prescription drug epidemic.

Accordingly, the undersigned State Attorneys General respectfully request that the FDA provide clear and fair regulatory standards for the incorporation of abuse-deterrent technologies into generic opioids. The FDA has been an excellent partner in fighting prescription drug abuse, and we look forward to continuing to work with you in ending this epidemic.

Sincerely,

Pamela Jo Bondi
Florida Attorney General

Samuel S. Olens
Georgia Attorney General

Jack Conway
Kentucky Attorney General

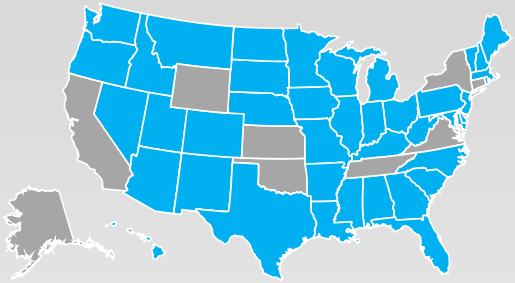
Janet Mills
Maine Attorney General

PPLPC046000057423

12/16/13 Letter from AGs to FDA (PPLPC046000057423)

42 State AGs Encouraged Abuse-Deterrent Formulations

National Association of Attorneys General



Pamela Jo Bondi
Florida Attorney General

Samuel S. Olens
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Jack Conway
Kentucky Attorney General

Janet Mills
Maine Attorney General

Chris Koster
Missouri Attorney General

Luther Strange
Alabama Attorney General

Tom Horne
Arizona Attorney General

Dustin McDaniel
Arkansas Attorney General

John Suthers
Colorado Attorney General

Joseph R. "Beau" Biden III
Delaware Attorney General

Lenny Rapadas
Guam Attorney General

David Louie
Hawaii Attorney General

Lawrence Wasden
Idaho Attorney General

Lisa Madigan
Illinois Attorney General

Greg Zoeller
Indiana Attorney General

Tom Miller
Iowa Attorney General

James "Buddy" Caldwell
Louisiana Attorney General

Douglas F. Gansler
Maryland Attorney General

Martha Coakley
Massachusetts Attorney General

Bill Schuette
Michigan Attorney General

Lori Swanson
Minnesota Attorney General

Jim Hood
Mississippi Attorney General

Tim Fox
Montana Attorney General

Jon Bruning
Nebraska Attorney General

Catherine Cortez Masto
Nevada Attorney General

Joseph Foster
New Hampshire Attorney General

John Hoffman
Acting New Jersey Attorney General

Gary King
New Mexico Attorney General

Roy Cooper
North Carolina Attorney General

Wayne Stenehjem
North Dakota Attorney General

Mike DeWine
Ohio Attorney General

Ellen Rosenblum
Oregon Attorney General

Kathleen Kane
Pennsylvania Attorney General

Peter F. Kilmartin
Rhode Island Attorney General

Alan Wilson
South Carolina

Marty J. Jackley
South Dakota Attorney General

Greg Abbott
Texas Attorney General

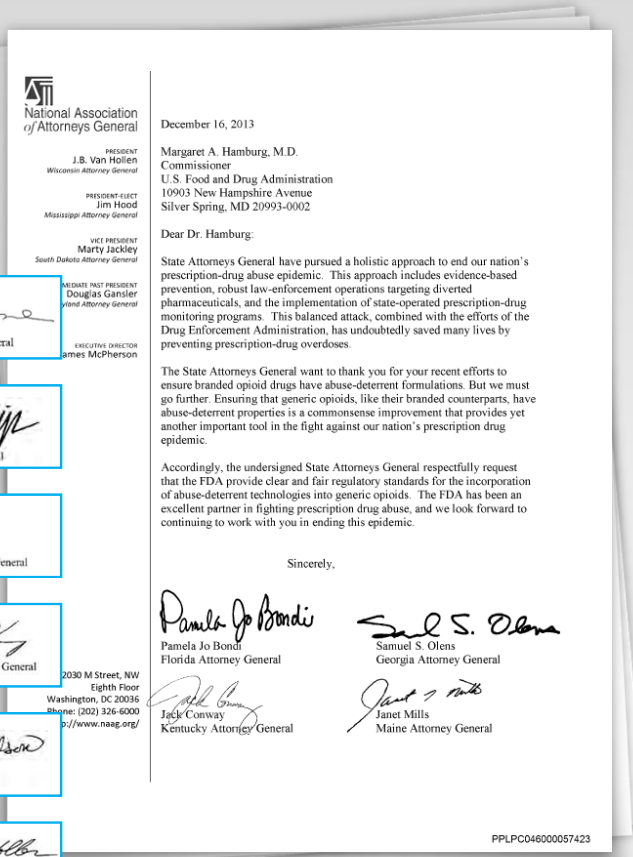
Brian Tarbet
Acting Utah Attorney General

William H. Sorrell
Vermont Attorney General

Robert W. Ferguson
Washington Attorney General

Patrick Morrisey
West Virginia Attorney General

J.B. Van Hollen
Wisconsin Attorney General



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Maine Attorney General

PPLPC046000057423

12/16/13 Letter from AGs to FDA (PPLPC046000057423)

FDA-Approved Label for Abuse-Deterrent OxyContin Discloses Continuing Risk of Addiction And Abuse

WARNING: ABUSE POTENTIAL, LIFE-THREATENING

RESPIRATORY DEPRESSION, and ACCIDENTAL EXPOSURE

See full prescribing information for complete boxed warning.

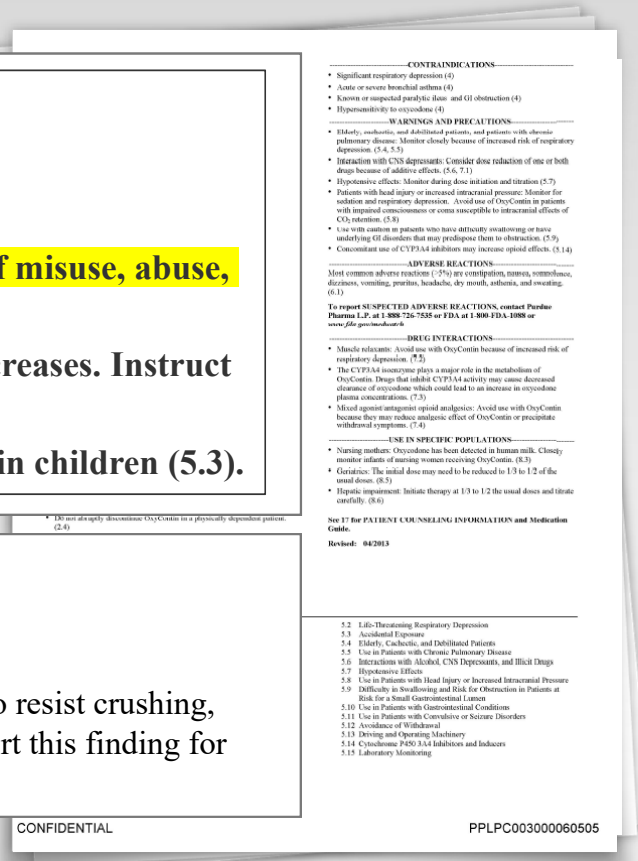
- **OxyContin contains oxycodone, a Schedule II controlled substance. Monitor for signs of misuse, abuse, and addiction during OxyContin therapy (5.1, 9).**
- **Fatal respiratory depression may occur, with highest risk at initiation and with dose increases. Instruct patients on proper administration of OxyContin tablets to reduce the risk (5.2).**
- **Accidental ingestion of OxyContin can result in fatal overdose of oxycodone, especially in children (5.3).**

Abuse Deterrence Studies

* * *

In Vitro Testing

Results support that, relative to original OxyContin, there is an increase in the ability of OxyContin to resist crushing, breaking, and dissolution using a variety of tools and solvents. The results of these studies also support this finding for OxyContin relative to an immediate-release oxycodone.


CONTRAINDICATIONS

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

USE IN SPECIFIC POPULATIONS

CONFIDENTIAL PPLPC003000060505

Apr. 2013 OxyContin Label, pp. 1, 18-19, (PPLPC003000060503)

FDA-Approved Label for Abuse-Deterrent OxyContin Discloses Continuing Risk of Addiction And Abuse

5.1 Abuse Potential

OxyContin contains oxycodone, an opioid agonist and a Schedule II controlled substance. Oxycodone can be abused in a manner similar to other opioid agonists legal or illicit. Opioid agonists are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing OxyContin in situations where there is concern about increased risks of misuse, abuse, or diversion. Concerns about abuse, addiction, and diversion should not, however, prevent the proper management of pain.

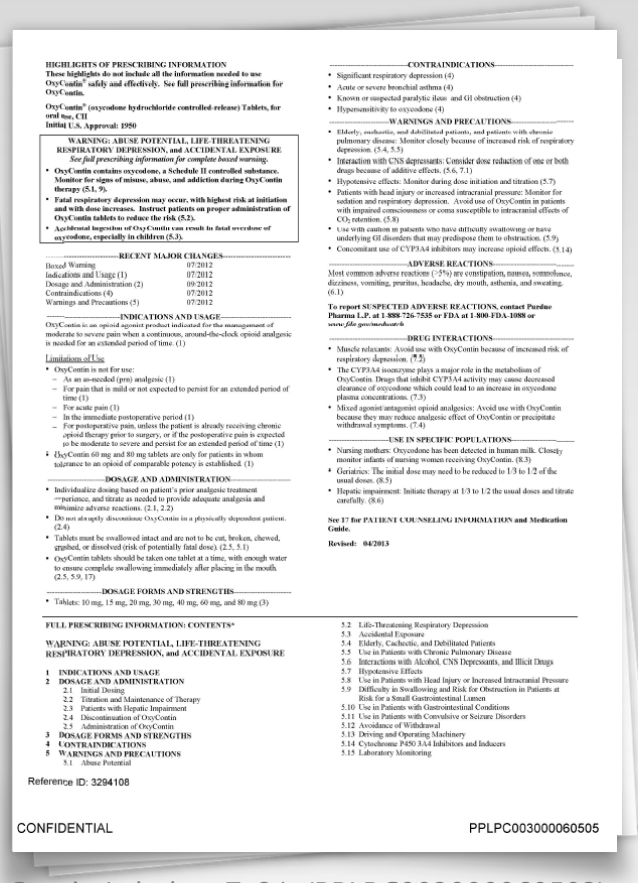
* * *

Misuse or abuse of OxyContin by crushing, chewing, snorting, or injecting the dissolved product will result in the uncontrolled delivery of the opioid and pose a significant risk that could result in overdose and death [see Drug Abuse and Dependence (9) and Overdosage (10)].

Contact local state professional licensing board or state controlled substances authority for information on how to prevent and detect abuse or diversion of this product.

Summary

The in vitro data demonstrate that OXYCONTIN has physicochemical properties expected to make abuse via injection difficult. The data from the clinical study, along with support from the in vitro data, also indicate that **OXYCONTIN has physicochemical properties that are expected to reduce abuse via the intranasal route. However, abuse of OXYCONTIN by these routes, as well as by the oral route, is still possible.**



HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OxyContin® safely and effectively. See full prescribing information for OxyContin.

OxyContin® (oxycodone hydrochloride controlled-release) Tablets, for oral use, CII

Initial U.S. Approval: 1950

WARNING: ABUSE POTENTIAL, LIFE-THREATENING RESPIRATORY DEPRESSION, and ACCIDENTAL EXPOSURE

See full prescribing information for complete boxed warning.

- **OxyContin contains oxycodone, a Schedule II controlled substance. Monitor for signs of misuse, abuse, and addiction during OxyContin therapy (5.1, 9).**
- **Fatal respiratory depression may occur, with highest risk at initiation and with dose increases. Instruct patients on proper administration of OxyContin tablets to reduce the risk (5.2).**
- **Accidental ingestion of OxyContin can result in fatal overdose of oxycodone, especially in children (5.3).**

RECENT MAJOR CHANGES

Boxed Warning	07/2012
Indications and Usage (1)	07/2012
Dosage and Administration (2)	09/2012
Contraindications (4)	07/2012
Warnings and Precautions (5)	07/2012

INDICATIONS AND USAGE

OxyContin is an opioid agonist product indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. (1)

Limitations of Use

- OxyContin is not for use:
  - As an as-needed (prn) analgesic (1)
  - For pain that is mild or not expected to persist for an extended period of time (1)
  - For acute pain (1)
  - In the immediate postoperative period (1)
  - For postoperative pain, unless the patient is already receiving chronic opioid therapy prior to surgery, or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time (1)
- OxyContin 60 mg and 80 mg tablets are only for patients in whom tolerance to an opioid of comparable potency is established. (1)

DOSAGE AND ADMINISTRATION

- Individualize dosing based on patient's prior analgesic treatment experience, and titrate as needed to provide adequate analgesia and minimize adverse reactions. (2.1, 2.2)
- Do not abruptly discontinue OxyContin in a physically dependent patient. (2.4)
- Tablets must be swallowed intact and are not to be cut, broken, chewed, crushed, or dissolved (risk of potentially fatal dose). (2.5, 5.1)
- OxyContin tablets should be taken one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth. (2.5, 5.9, 17)

DOSAGE FORMS AND STRENGTHS

- Tablets: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, and 80 mg (3)

CONTRAINDICATIONS

- Significant respiratory depression (4)
- Acute or severe bronchial asthma (4)
- Known or suspected paralytic ileus and GI obstruction (4)
- Hypersensitivity to oxycodone (4)

WARNINGS AND PRECAUTIONS

- Elderly, cachectic, and debilitated patients, and patients with chronic pulmonary disease: Monitor closely because of increased risk of respiratory depression. (5.4, 5.5)
- Interaction with CNS depressants: Consider dose reduction of one or both drugs because of additive effects. (5.6, 7.1)
- Hypotensive effects: Monitor during dose initiation and titration (5.7)
- Patients with head injury or increased intracranial pressure: Monitor for sedation and respiratory depression. Avoid use of OxyContin in patients with impaired consciousness or coma susceptible to intracranial effects of CO_2 retention. (5.8)
- Use with caution in patients who have difficulty swallowing or have underlying GI disorders that may predispose them to obstruction. (5.9)
- Concomitant use of CYP3A4 inhibitors may increase opioid effects. (5.14)

ADVERSE REACTIONS

Most common adverse reactions (>5%) are constipation, nausea, somnolence, dizziness, vomiting, pruritus, headache, dry mouth, asthenia, and sweating. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Purdue Pharma L.P. at 1-888-726-7535 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

DRUG INTERACTIONS

- Muscle relaxants: Avoid use with OxyContin because of increased risk of respiratory depression. (7.2)
- The CYP3A4 isoenzyme plays a major role in the metabolism of OxyContin. Drugs that inhibit CYP3A4 activity may cause decreased clearance of oxycodone which could lead to an increase in oxycodone plasma concentrations. (7.3)
- Mixed agonist/antagonist opioid analgesics: Avoid use with OxyContin because they may reduce analgesic effect of OxyContin or precipitate withdrawal symptoms. (7.4)

USE IN SPECIFIC POPULATIONS

- Nursing mothers: Oxycodone has been detected in human milk. Closely monitor infants of nursing women receiving OxyContin. (8.3)
- Geriatrics: The initial dose may need to be reduced to 1/3 to 1/2 of the usual doses. (8.5)
- Hepatic impairment: Initiate therapy at 1/3 to 1/2 the usual doses and titrate carefully. (8.6)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 04/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

Reference ID: 3294108

CONFIDENTIAL PPLPC003000060505

Apr. 2013 OxyContin Label, p. 7, 21, (PPLPC003000060503)

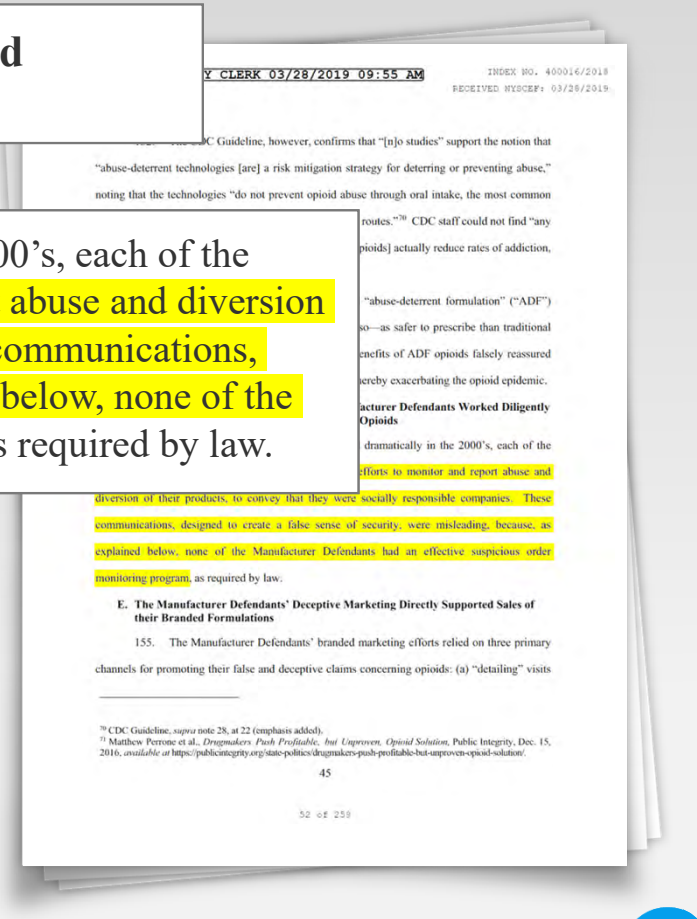
Alleged Misrepresentation No. 10: The Manufacturer Defendants Worked Diligently to Detect And Prevent Diversion of Opioids

10. Misrepresentation #10: The Manufacturer Defendants Worked Diligently to Detect and Prevent Diversion of Opioids

NY AG FAC p. 45

154. After the diversion of opioids increased dramatically in the 2000's, each of the Manufacturer Defendants extensively advertised their efforts to monitor and report abuse and diversion of their products, to convey that they were socially responsible companies. These communications, designed to create a false sense of security, were misleading because, as explained below, none of the Manufacturer Defendants had an effective suspicious order monitoring program, as required by law.

NY AG FAC ¶154



1. **Irrelevant: No marketing based on anti-diversion initiatives**
2. **Purdue spent hundreds of millions of dollars on anti-diversion initiatives**
   https://www.purduepharma.com/addressing-the-crisis/select-initiatives/

Purdue Spent Hundreds of Millions of Dollars on Anti-Diversion Initiatives

Previously available at https://www.purdueopioidinfo.com/app/uploads/2019/05/purdue-80-actions-taken-timeline-10.pdf

PURDUE

Timeline of Select Initiatives

2001

Purdue developed the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) system to detect and study abuse, misuse, and diversion on a nationwide basis. Purdue transferred ownership of RADARS in 2006 to not-for-profit Denver Health and Hospital Authority's Rocky Mountain Poison and Drug Center. Purdue transferred the system to an independent third party which allowed pharmaceutical companies and government agencies to more readily access valuable data on opioid abuse and diversion.

2002

Purdue voluntarily developed a risk management plan (RiskMAP) in coordination with the FDA to help detect and prevent opioid abuse and diversion.

Purdue provided more than $4 million to develop "Painfully Obvious," a prescription drug abuse awareness program for pre-teens, parents, and middle school teachers.

Purdue began a program to provide tamper-resistant prescription pads at no cost to healthcare professionals. These prescription pads were ordered by more than 16,000 DEA-registered healthcare professionals.

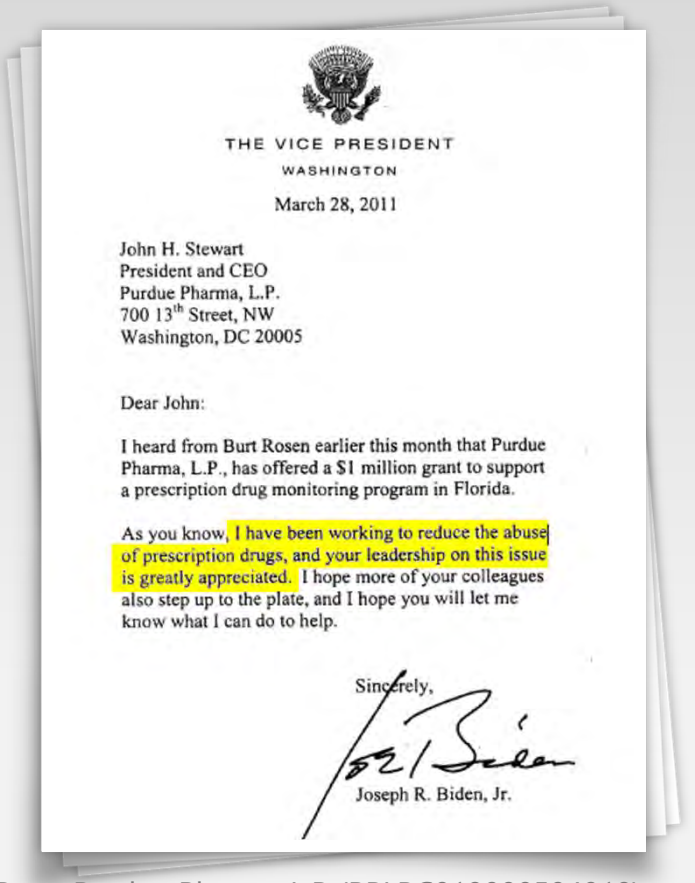
Purdue worked with The Governor's Prevention Partnership in

Vice President Biden Praised Purdue for Its Leadership on Anti-Abuse Efforts

THE VICE PRESIDENT
WASHINGTON
March 28, 2011

I heard from Burt Rosen earlier this month that Purdue Pharma, L.P., has offered a $1 million grant to support a prescription drug monitoring program in Florida.

As you know, I have been working to reduce the abuse of prescription drugs, and your leadership on this issue is greatly appreciated. I hope more of your colleagues also step up to the plate, and I hope you will let me know what I can do to help.



THE VICE PRESIDENT
WASHINGTON
March 28, 2011

John H. Stewart
President and CEO
Purdue Pharma, L.P.
700 13th Street, NW
Washington, DC 20005

Dear John:

I heard from Burt Rosen earlier this month that Purdue Pharma, L.P., has offered a $1 million grant to support a prescription drug monitoring program in Florida.

As you know, I have been working to reduce the abuse of prescription drugs, and your leadership on this issue is greatly appreciated. I hope more of your colleagues also step up to the plate, and I hope you will let me know what I can do to help.

Sincerely,

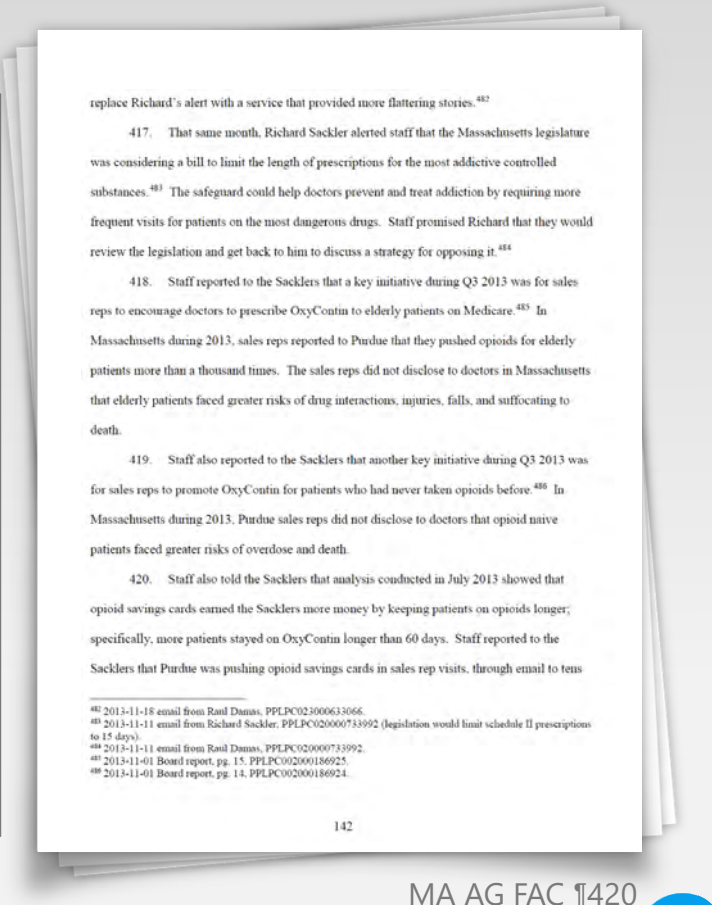
Joseph R. Biden, Jr.

3/28/11 Letter from Joe Biden, Vice President of the Untied States, to John H. Stewart, Pres., Purdue Pharma L.P. (PPLPC018000504018)

Allegation: Savings Cards Deceptively Kept Patients on Opioids Longer

Massachusetts AG Complaint ¶ 420:

420. Staff also told the Sacklers that analysis conducted in July 2013 showed that opioid savings cards earned the Sacklers more money by keeping patients on opioids longer; specifically, more patients stayed on OxyContin longer than 60 days. Staff reported to the Sacklers that Purdue was pushing opioid savings cards in sales rep visits, through email to tens of thousands of health care providers, and online. In Massachusetts during 2013, sales reps reported to Purdue that they promoted opioid savings cards to prescribers more than a thousand times. The sales reps did not tell doctors in Massachusetts that savings cards led patients to stay on opioids longer than 60 days, or that staying on opioids longer increased the risk of addiction and death.



replace Richard's alert with a service that provided more flattering stories.[482]

417. That same month, Richard Sackler alerted staff that the Massachusetts legislature was considering a bill to limit the length of prescriptions for the most addictive controlled substances.[483] The safeguard could help doctors prevent and treat addiction by requiring more frequent visits for patients on the most dangerous drugs. Staff promised Richard that they would review the legislation and get back to him to discuss a strategy for opposing it.[484]

418. Staff reported to the Sacklers that a key initiative during Q3 2013 was for sales reps to encourage doctors to prescribe OxyContin to elderly patients on Medicare.[485] In Massachusetts during 2013, sales reps reported to Purdue that they pushed opioids for elderly patients more than a thousand times. The sales reps did not disclose to doctors in Massachusetts that elderly patients faced greater risks of drug interactions, injuries, falls, and suffocating to death.

419. Staff also reported to the Sacklers that another key initiative during Q3 2013 was for sales reps to promote OxyContin for patients who had never taken opioids before.[486] In Massachusetts during 2013, Purdue sales reps did not disclose to doctors that opioid naive patients faced greater risks of overdose and death.

420. Staff also told the Sacklers that analysis conducted in July 2013 showed that opioid savings cards earned the Sacklers more money by keeping patients on opioids longer; specifically, more patients stayed on OxyContin longer than 60 days. Staff reported to the Sacklers that Purdue was pushing opioid savings cards in sales rep visits, through email to tens

[482] 2013-11-18 email from Raul Damas, PPLPC023000633066.
[483] 2013-11-11 email from Richard Sackler, PPLPC020000733992 (legislation would limit schedule II prescriptions to 15 days).
[484] 2013-11-11 email from Raul Damas, PPLPC020000733992.
[485] 2013-11-01 Board report, pg. 15, PPLPC002000186925.
[486] 2013-11-01 Board report, pg. 14, PPLPC002000186924.

142

MA AG FAC ¶420

Savings Cards Carried OxyContin's Black Box Warning

WARNING:
OxyContin® is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.

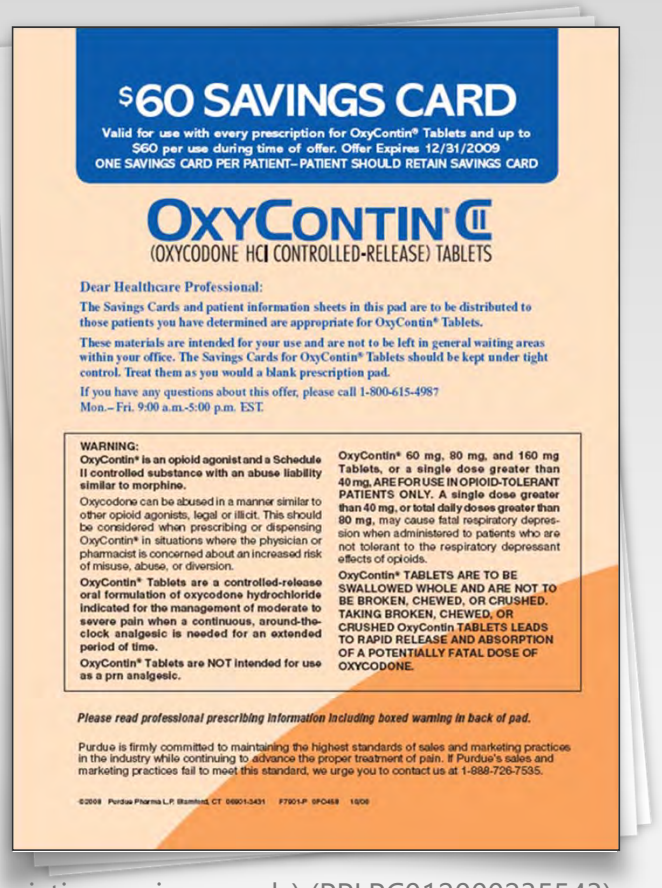
Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OxyContin® in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

OxyContin® Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

OxyContin® Tablets are NOT intended for use as a prn analgesic.

OxyContin® 60 mg, 80 mg, and 160 mg Tablets, or a single dose greater than 40 mg, ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. A single dose greater than 40 mg, or total daily doses greater than 80 mg, may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory depressant effects of opioids.

OxyContin® TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OxyContin TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.



$60 SAVINGS CARD

Valid for use with every prescription for OxyContin® Tablets and up to $60 per use during time of offer. Offer Expires 12/31/2009
ONE SAVINGS CARD PER PATIENT–PATIENT SHOULD RETAIN SAVINGS CARD

OXYCONTIN® CII
(OXYCODONE HCl CONTROLLED-RELEASE) TABLETS

Dear Healthcare Professional:

The Savings Cards and patient information sheets in this pad are to be distributed to those patients you have determined are appropriate for OxyContin® Tablets.

These materials are intended for your use and are not to be left in general waiting areas within your office. The Savings Cards for OxyContin® Tablets should be kept under tight control. Treat them as you would a blank prescription pad.

If you have any questions about this offer, please call 1-800-615-4987
Mon.–Fri. 9:00 a.m.-5:00 p.m. EST.

WARNING:
OxyContin® is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.

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Please read professional prescribing information including boxed warning in back of pad.

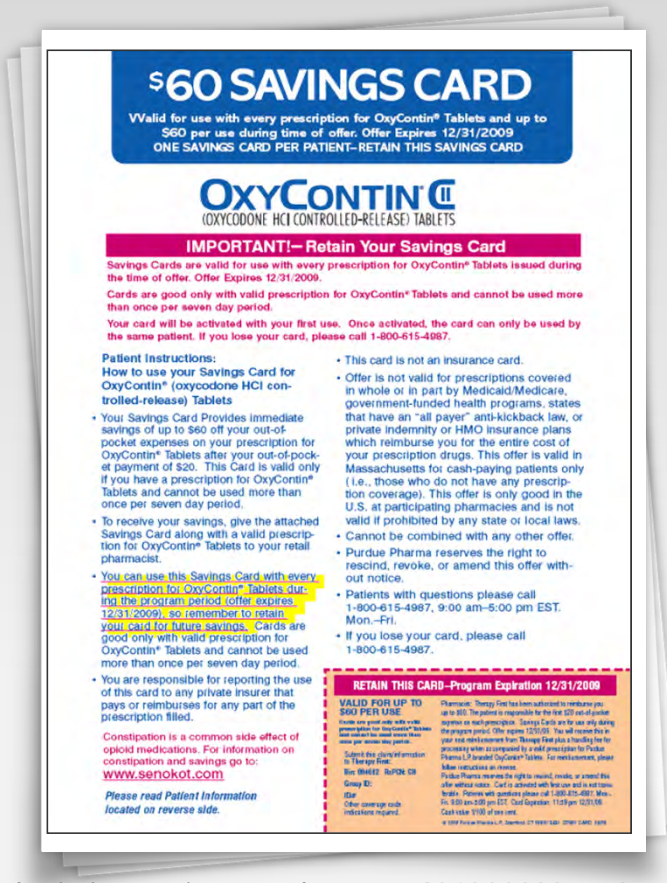
Purdue is firmly committed to maintaining the highest standards of sales and marketing practices in the industry while continuing to advance the proper treatment of pain. If Purdue's sales and marketing practices fail to meet this standard, we urge you to contact us at 1-888-726-7535.

©2008 Purdue Pharma L.P. Stamford, CT 06901-3431 F7901-P 6PO459 10/08

Board Presentation, p. 14 (depicting savings cards) (PPLPC012000235543)

Savings Cards Could Be Used Only With A Prescription

- To receive your savings, give the attached Savings Card along with a valid prescription for OxyContin® Tablets to your retail pharmacist.
- You can use this Savings Card with every prescription for OxyContin® Tablets during the program period (offer expires 12/31/2009), so remember to retain your card for future savings. Cards are good only with valid prescription for OxyContin® Tablets and cannot be used more than once per seven day period.



- **There is nothing deceptive about a savings card**

Board Presentation, p. 14 (depicting savings cards) (PPLPC012000235543)

Preemption

The Three Preemption Doctrines

State law is preempted if:

1. It is impossible to comply with both state and federal law ("Impossibility Preemption")

   Merck Sharp & Dohme Corp. v. Albrecht, 139 S. Ct. 1668, 1678–79 (2019)
   (state law failure to warn claims might be preempted if the FDA would have rejected the proposed warnings)

2. It conflicts with the federal regulatory scheme created by Congress ("Conflict Preemption")

   Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 350–51 (2001)
   (state law claims that defendant committed fraud on the FDA were preempted)

3. It "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress," or otherwise conflicts with federal law ("Obstacle Preemption")

   Hines v. Davidowitz, 312 U.S. 52, 67 (1941)

Federal Law Requires Drug Promotion Be Consistent with the FDA-Approved Label

21 C.F.R. §201.100(d)(1)

Requires labeling to be "consistent with and not contrary to such approved and permitted labeling"

21 U.S.C. §321(m)

Defines "labeling" to include all "written, printed, or graphic matter" that accompanies the drug

21 C.F.R. §202.1(l)(2)

Defines "labeling" to mean all materials "for use by medical practitioners … containing drug information … disseminated by … [the] manufacturer"

Many Alleged Misrepresentations Are Consistent with the Label and Preempted — Impossibility Preemption

ALLEGATION	CORRESPONDING LABEL PROVISION
"No ceiling" NY AG FAC ¶¶321, 322	"Like all full opioid agonists, there is no ceiling effect to analgesia for oxycodone." October 2019 OxyContin Label, p. 35, https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022272s043lbl.pdf
"Tapering . . . has never been recommended or recognized by any legitimate medical or addiction professionals" NY AG FAC ¶129	"When discontinuing OxyContin, gradually taper the dosage …." October 2019 OxyContin Label, p. 33, https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022272s043lbl.pdf
"Signs of Addictive Behavior are Pseudoaddiction" NY AG FAC p. 34	"Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control." October 2019 OxyContin Label, p. 29, https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022272s043lbl.pdf

The equivalent of the above appear in earlier labels

Claimants' Claims That Purdue Should Have Added Warnings Rejected By The FDA Are Preempted — Impossibility Preemption

State law failure to warn claims are preempted if (1) they are based on information known by the FDA at the time of approval, or (2) the FDA would have rejected the warning

Merck Sharp & Dohme Corp. v. Albrecht,
139 S. Ct. 1668, 1678–79 (2019)

State law failure to warn claims would be preempted if the FDA would have rejected the proposed warnings.

In re Celexa & Lexapro Mktg. & Sales Practices Litig.,
779 F.3d 34, 43 (1st Cir. 2015)

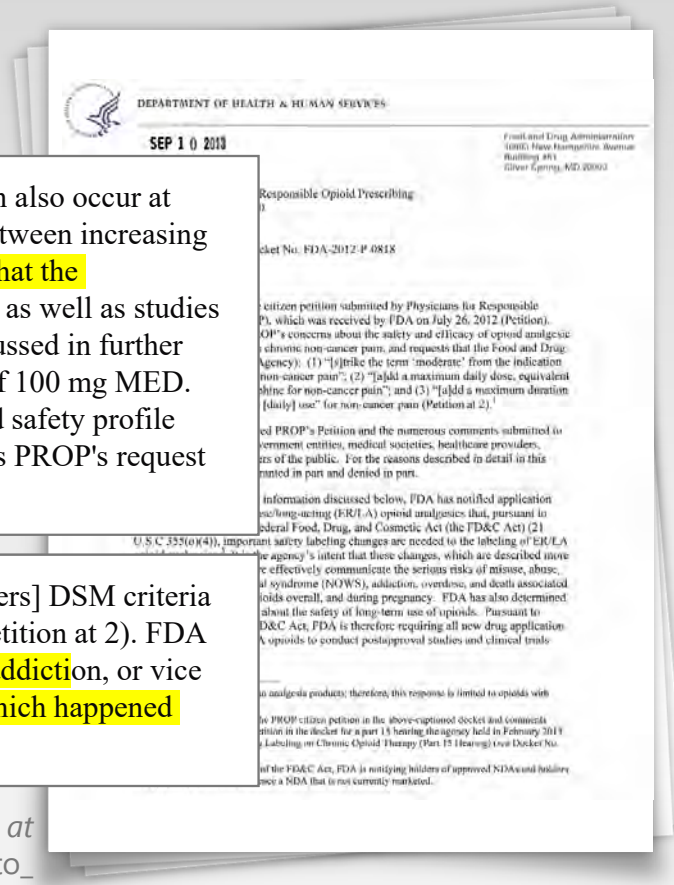
Preemption where alleged omission *"was known to the FDA at the time of the approval."*

Maze v. Bayer Healthcare Pharm. Inc.,
2019 WL 1062387, at *3 (E.D. Tenn. Mar. 6, 2019)

"[T]o impose state-law tort liability based on information known to the FDA at the time of approval is strictly prohibited under the Supremacy Clause and Wyeth."

In 2013, The FDA Expressly Rejected Warnings Claimants Seek

In 2013, FDA rejected PROP's request to impose a maximum dose or limit the duration of treatment


DEPARTMENT OF HEALTH & HUMAN SERVICES

SEP 1 0 2013

Responsible Opioid Prescribing

cket No. FDA-2012-P-0818

FDA agrees that adverse events and substance abuse of opioids occur at high doses-but adverse events can also occur at doses less than 100 mg MED. FDA also acknowledges that the available data do suggest a relationship between increasing opioid dose and risk of certain adverse events. However, the available information does not demonstrate that the relationship is necessarily a causal one. FDA has reviewed the studies cited in support of PROP's request, as well as studies cited in comments to the Petition docket and other studies described in the literature. For the reasons discussed in further detail below, the scientific literature does not support establishing a maximum recommended daily dose of 100 mg MED. Further, creating a maximum dose of 100 mg MED, or another dose ceiling, could imply a superior opioid safety profile under that set threshold, when there are no data to support such a conclusion. The Agency therefore denies PROP's request that opioid labeling specify a maximum daily dose.

The Petition also asserts that "[r]ecent surveys using [Diagnostic and Statistical Manual of Mental Disorders] DSM criteria found high rates of addiction in [chronic non-cancer pain] patients receiving [chronic opioid therapy]" (Petition at 2). FDA agrees with this assertion. However, the cited surveys did not suggest that chronic opioid therapy causes addiction, or vice versa. Both addiction and chronic opioid therapy were measured at one, point in time, so it is unknown which happened first: addiction or chronic opioid therapy.

9/10/13 2013 PROP Letter, pp. 12, 16, *available at* http://paindr.com/wp-content/uploads/2013/09/FDA_CDER_Response_to_Physicians_for_Responsible_Opioid_Prescribing_Partial_Petition_Approval_and_Denial.pdf

FDA Implicitly Rejected Many Studies Claimants Rely on When It Approved the Reformulated OxyContin Label in 2010

- **Purdue could not unilaterally change label to address studies available to the FDA when the label was approved**
- **Most studies cited in the complaints were available when the FDA approved the reformulated OxyContin label in 2010**

21 C.F.R. §201.57(c)(6) and 21 C.F.R. §314.70(c)(6)

Only "newly acquired information" showing a "causal" relationship between the drug and a "clinically significant hazard" could justify a unilateral change. Which FDA can still reject.

FDA Implicitly Rejected Many Studies Claimants Rely on When It Approved the Reformulated OxyContin Label in 2010

Examples of old studies Claimants' failure-to-warn claims rely on:

- **2008:** Jeffrey Dersh et al., *Prescription Opioid Dependence is Associated with Poorer Outcomes in Disabling Spinal Disorders*, 33 SPINE 2219, 2219-27 (2008)
- **2002:** Thomas R. Kosten & Tony P. George, *The Neurobiology of Opioid Dependence: Implications for Treatment*, 1 SCI. & PRAC. PERSPS. 13, 13-20 (July 2002)
- **2009:** Caleb Banta-Green et al., *Opioid Use Behaviors, Mental Health and Pain—Development of a Typology of Chronic Pain Patients*, 104 DRUG ALCOHOL DEPENDENCE 34, 34-42 (2009).

Claimants' Fraud-on-the-FDA Claims Are Preempted — Conflict Preemption

Claimants' claims that the FDA should never have approved OxyContin for 12 hour dosing are fraud-on-the-FDA claims and are preempted

Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 350–51 (2001)

- Under *Buckman v. Plaintiffs' Legal Committee*, 531 U.S. 341, 350–51 (2001), **a claim that the FDA should not have approved a drug or medical device for a particular use or indication is preempted as a fraud-on-the-FDA claim**.
- The FDA approved OxyContin for 12 hour dosing.
  - It adhered to that decision in response to Connecticut AG's citizens petition.
- Claimants' claims that OxyContin should not have been approved for 12 hour dosing are essentially fraud-on-the-FDA claims and are therefore preempted.

Claimants' Claims That Science Approved by the FDA Is False Are Preempted — Obstacle Preemption

Wyeth v. Levine,
555 U.S. 555 (2009)

Merck Sharp & Dohme Corp. v. Albrecht,
139 S. Ct. 1668 (2019)

Wyeth v. Levine, 555 U.S. 555 (2009), and *Merck Sharp & Dohme Corp. v. Albrec*ht, 139 S. Ct. 1668 (2019), address ways in which state and federal laws can be **complementary**.

- But they are limited to "failure to warn claims" which complement the FDA's labelling requirements.

State law cannot **conflict** with federal law.

- A state law claim is preempted if it will "**frustrate** the achievement of congressional objectives." *Levine*, 555 U.S. at 581.
- State law is preempted if it "stands as an **obstacle** to the accomplishment and execution of the full purposes and objectives of Congress." *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941).

Claimants' Claims That Science Approved by the FDA Is False Are Preempted — Obstacle Preemption

- **Some of Claimants' claims pit federal and state law against each other:**
- **To prevail, Claimants must show that a statement that the federal regulator said is *true* and must appear on the label is in fact *false*. For example:**
  - The FDA label says that, as a scientific fact, OxyContin has **no ceiling dose**.
    - The NY AG's claim that, under state law, this statement is "false[]" is therefore preempted. *See* NY AG FAC ¶190.
  - The FDA label says that drug-seeking behavior **may not be a sign of addiction**.
    - The NY AG's claim that under state law it is false to say that drug seeking behavior may not be a sign of addiction is preempted. *See* NY AG FAC ¶¶325-29.

Those claims pose an obstacle to the federal scheme and are preempted.

In re Purdue Pharma LP, et al.

Joseph Hage Aaronson LLC

Counsel to Raymond Sackler Family ("Side B")

Defense Presentation Part 5: Underlying Claims Against Purdue, Effect of Criminal Plea, Deceptive Marketing, Preemption

April 27, 2021