

FRANK PALLONE, JR., NEW JERSEY
CHAIRMAN

GREG WALDEN, OREGON
RANKING MEMBER

ONE HUNDRED SIXTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (202) 225-2927
Minority (202) 225-3641

October 14, 2020

The Honorable Stephen Hahn, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903

Dear Dr. Hahn:

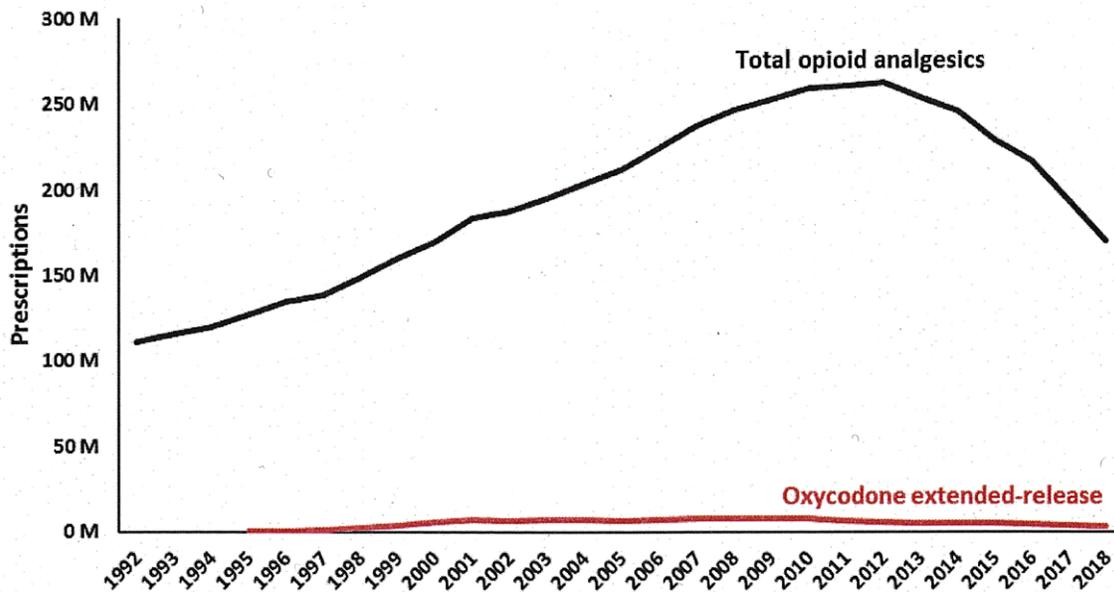
We write to request further information and clarification from the U.S. Food and Drug Administration (FDA) about information related to the role FDA's 2001 label change had in the opioid crisis and opioid manufacturing. On June 25, 2019, the bipartisan leadership of the Committee requested that the FDA provide a briefing to Committee staff on actions related to the FDA's decision in 2001 to approve changes in the label for Purdue Pharma's OxyContin. The label changes explicitly included language that covered chronic, long-term pain.¹ On January 13, 2020, the Republican leaders of the Committee reactivated an investigation concerning opioid manufacturers, including Purdue Pharma and one aspect of the investigation is the impact of the 2001 label change.²

On August 8, 2019, the FDA provided a briefing to bipartisan Committee staff in response to the June 25, 2019 request letter. During the briefing, the FDA maintained that the 2001 label change did not contribute to the worsening of the opioid crisis. In support of its contention, the FDA provided data showing the estimated number of prescriptions dispensed for extended release oxycodone generally did not increase after the 2001 label change, during the same time when prescription opioid use was increasing. The FDA data showed that the number of extended release oxycodone prescriptions made up a very small and decreasing fraction of opioid prescriptions. This data was presented in the following graph:

¹ Letter from The Honorable Frank Pallone, Jr. and The Honorable Greg Walden, Ranking Member, et al, House Energy and Commerce Committee to Acting FDA Commissioner Norman E. Sharpless, M.D. (June 25, 2019).

² Letter from The Honorable Greg Walden, Republican Leader, et al, House Energy and Commerce Committee to Dr. Craig Landau President and CEO, Purdue Pharma L.P. (January 13, 2020).

Figure 3. Estimated Annual Number of Total Opioid Analgesics vs. Oxycodone Extended-Release Prescriptions Dispensed from U.S. Outpatient Pharmacies



Source: IQVIA National Prescription Audit. 1992-2018. Extracted March 2019. Includes outpatient retail and mail-order/specialty pharmacies. Does not include opioid-containing products used as part of medication-assisted treatment for opioid dependence, opioid-containing cough/cold products, or compounded bulk powder prescriptions. Of note, over time, there have been changes in the underlying data and methodology of the proprietary database, IQVIA NPA, including a recent change to manage prescription claims that are voided or reversed historically adjusted to January 2017, data prior to January 2017 have not been adjusted to this new methodology; therefore, changes over time must be interpreted in the context of the changes in methodology. For example, an estimated 2% of total prescription claims for oxycodone ER dispensed from U.S. retail pharmacies appears to have been voided or reversed in 2017.

The FDA data graph presents the number of prescriptions dispensed, but FDA did not provide data to the Committee on the dosages and durations of these prescriptions. When referring to different types of opioids, the FDA, the Centers for Disease Control and Prevention (CDC), Purdue and other manufacturers typically use the morphine milligram equivalent rate, or MME, a value assigned to represent the opioid’s relative potency.³ Standardizing data for comparison is important given that, while FDA believes it only intended to narrow the indication for OxyContin, the 2001 label change may have been used to help promote higher-dose, longer-term prescriptions, and thus could have facilitated prescriptions of Extended-Release and Long-Acting (ER/LA) oxycodone. Purdue internal documents indicate that the company may have viewed the effect of the label change as an opportunity to expand its market. For example, Purdue’s 2002 Budget Plan explained how they planned to take advantage of the new

³ U.S. Centers for Disease Control, Calculating Total Daily Dose of Opioids for Safer Dosage, *available at* https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf. See also David Armstrong and Jeff Ernsthausen, *Data Touted by OxyContin Maker to Fight Lawsuits Doesn’t Tell the Whole Story*, Pro Publica (Sept. 9, 2019) *available at* <https://www.propublica.org/article/data-touted-by-oxycotin-maker-to-fight-lawsuits-doesnt-tell-the-whole-story> (“‘All opioids are not created equal,’ said Len Paulozzi, a former medical epidemiologist at the Centers for Disease Control and Prevention who researched prescription opioid overdose risk. He said it is important to adjust for potency because ‘the risk of an overdose, whether fatal or nonfatal, is directly related to the dosage a person receives.’”)

language: “The action taken by the FDA to clarify the OxyContin Tablet labelling has created enormous opportunities. In effect, the FDA has expanded the indication for OxyContin Tablets to any patient with moderate to severe-around-the-clock persistent pain”⁴

D. OxyContin Future Opportunities

New Labeling Approved July 2001

The action by the FDA to clarify the OxyContin Tablets labeling has created enormous opportunities. In effect, the FDA has expanded the indication for OxyContin Tablets to any patient with moderate to severe around-the-clock persistent pain, provided that the pain is moderate to severe, and expected to be for an extended duration. This broad labeling is likely to never again be available for an opioid seeking FDA approval. This may give OxyContin Tablets a competitive advantage. This is a positive action which helps to combat the negative reports perpetuated by the media.

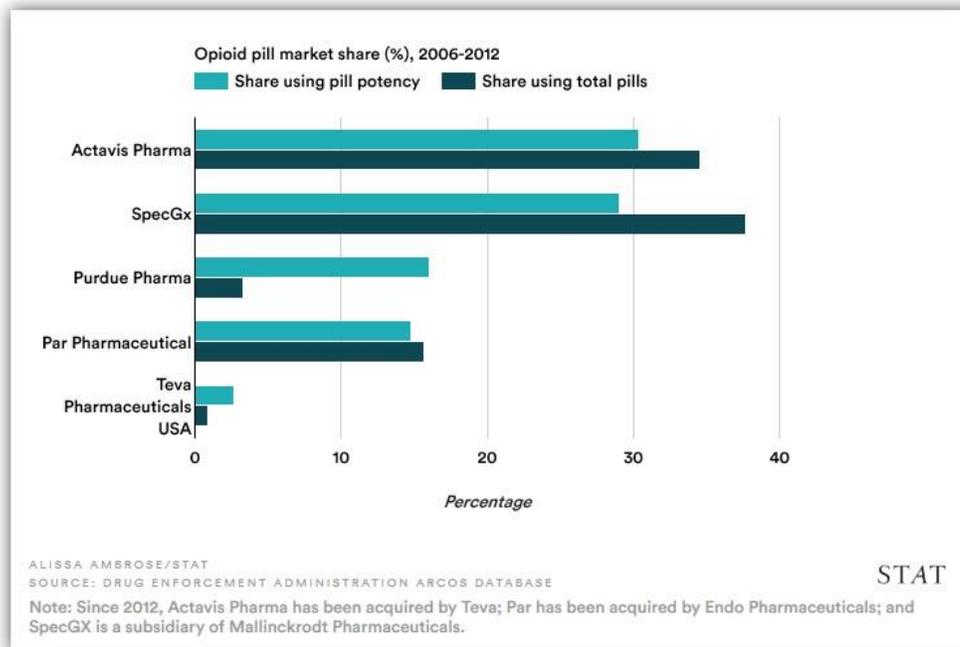
Source: CBS News

Thus, this additional context and customary data standardization should be taken into account in assessing the potential role the 2001 label change had on the opioid epidemic.

Studies, documents, and other data support these concerns related to higher dosage and longer duration in oxycodone prescribing (including OxyContin prescribing) that contributed to the opioid crisis. For example, a recent ProPublica analysis of Purdue Pharma data showed that for the 2006-2012 time period, when measured by number of prescriptions versus dosage strength of MME, Purdue’s market share increased from 3.3 percent to 16 percent, making Purdue the third-largest seller of opioids from 2006 to 2012.⁵

⁴ CBS News, 60 Minutes, (Feb. 24, 2019).

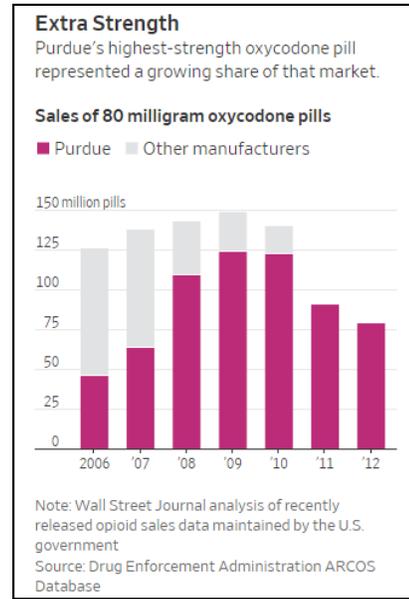
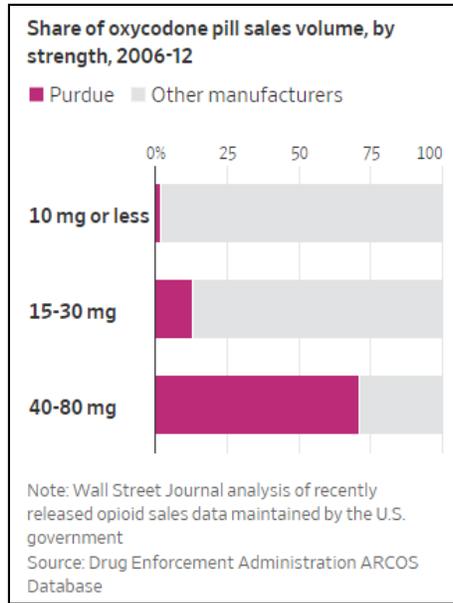
⁵ David Armstrong and Jeff Ernsthansen, *Data Touted by OxyContin Maker to Fight Lawsuits Doesn’t Tell the Whole Story*, Pro Publica (Sept. 9, 2019) available at <https://www.propublica.org/article/data-touted-by-oxycotin-maker-to-fight-lawsuits-doesnt-tell-the-whole-story>.



Similarly, when the Wall Street Journal analyzed Drug Enforcement Administration (DEA) opioid sales data by dosage strength, Purdue’s oxycodone represented a much higher market share than would be indicated by calculating the number of prescriptions sold. When accounting for the dosage strength of each pill, Purdue was the top manufacturer of oxycodone pills. OxyContin represented a market-leading 27 percent of total oxycodone sold during 2006 – 2012.⁶ Internal Purdue documents revealed that in February 2008, a board member who previously served as Purdue’s president from 1999 to 2003 took an interest in measuring the company performance by prescription strength, giving higher measures to higher strengths, and instructed executives to provide detailed prescription projections by strength and month.⁷

⁶ Joseph Walker and Jared S. Hopkins, *Purdue Led Its Opioid Rivals in Pills More Prone to Abuse*, Wall Street Journal (Sept. 19, 2019) available at <https://www.wsj.com/articles/high-dose-opioid-pills-helped-fuel-purdue-pharmas-growth-11568914319>.

⁷*Id.*



Source: The Wall Street Journal⁸

Moreover, the average strength of OxyContin pills purchased by retail and mail-order pharmacies for 2006-2012 period was 41 milligrams, about three times greater than the second-highest average dose of 14 milligrams among the 10 largest oxycodone manufacturers. The average total MME for a Purdue pill sold was 61.5 compared to 11 MME per pill sold by the largest manufacturer, Actavis Pharma, and a 9.6 MME per pill from the second largest manufacturer at the time, SpecGx, according to the DEA database.⁹

FDA's own March 1, 2018 analysis of total leading opioid product MMEs sold reveals a markedly different comparison between oxycodone ER and oxycodone IR than from the graph FDA presented at the 2019 Committee staff briefing.¹⁰ According to several graphs in FDA's 2018 prescription opioid MME data analysis, sales of oxycodone ER MMEs increased from about \$22 billion sold in 2001 to a peak of about \$35 billion in 2010.¹¹

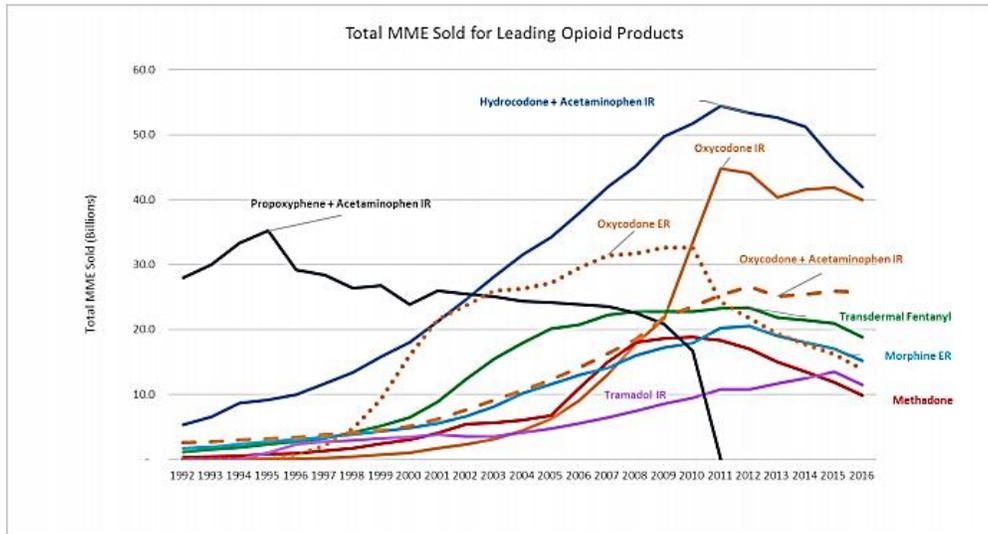
⁸ *Id.*

⁹ Armstrong, D, Ernsthauten, J, *Purdue Pharma touts data that downplay its role in the opioid epidemic, new analysis shows*, StatNews (Sept. 9, 2019) available at <https://www.statnews.com/2019/09/09/purdue-pharma-data-downplay-its-role-in-opioid-epidemic/>

¹⁰ United States Food and Drug Administration, *FDA Analysis of Long-Term Trends in Prescription Opioid Analgesic Products: Quantity, Sales, and Price Trends* (March 1, 2018), available at <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM598899.pdf>.

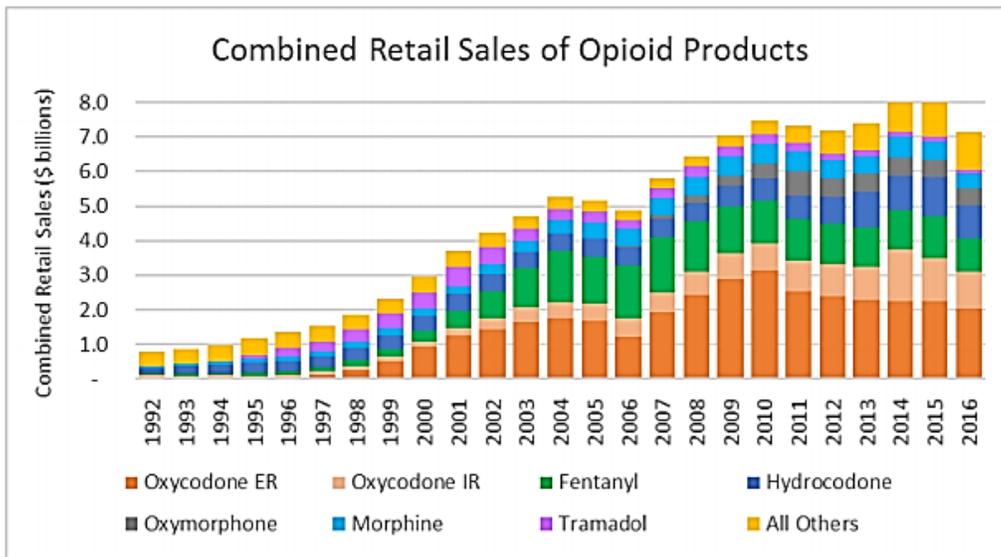
¹¹ *Id.*

Figure 3: Total MME Sold for Leading Opioid Products



Graph Source: FDA¹²

Figure 4: Combined Retail Sales of Analgesic Opioid Products

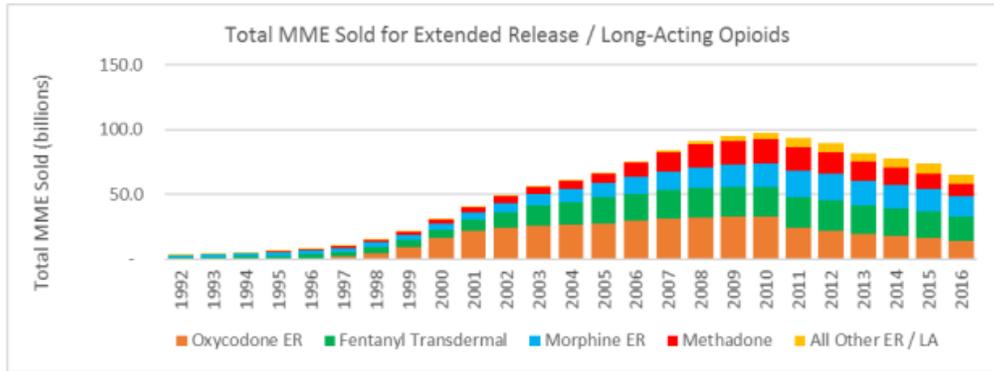


Graph Source: FDA¹³

¹² *Id.*

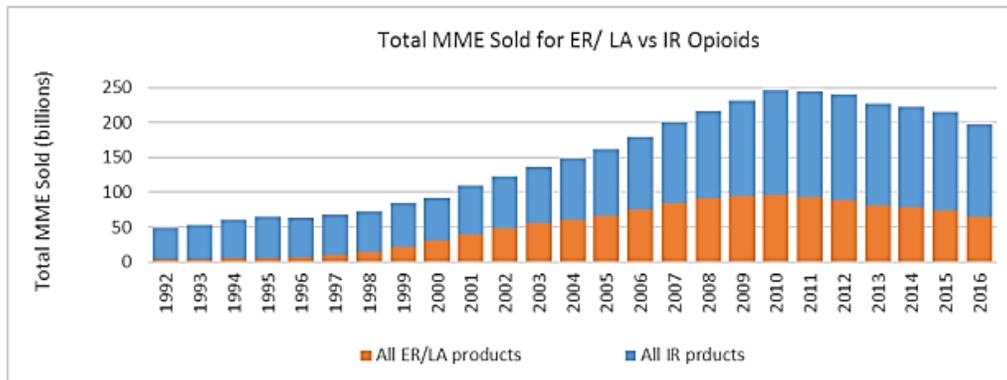
¹³ *Id.*

Figure 8b: Total MMEs sold for Extended Release / Long-Acting (ER/LA) Opioids



Graph Source: FDA¹⁴

Figure 8c: Total MMEs sold by IR and ER / LA



Graph Source: FDA¹⁵

There is substantial evidence showing OxyContin availability did not flatten out over the next few years after 2001. The high availability of OxyContin continued over the next few years; “by 2004 OxyContin had become a leading drug of abuse in the United States.”¹⁶ OxyContin sales more than doubled to \$2.3 billion in 2008 from a year earlier, its best year ever up to that point, according to data from IQVIA holdings.¹⁷ According to the DEA’s National Drug Threat Assessment, until 2010, OxyContin was “by far” the most commonly abused prescription painkiller in the country.¹⁸

¹⁴ *Id.*

¹⁵ *Id.*

¹⁶ Art Van Zee, The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy, 99 American Journal of Public Health 221 (February 2009).

¹⁷ Wall Street Journal, note 2.

¹⁸ 2015 Drug Threat Assessment 21 available at <https://www.dea.gov/sites/default/files/2018-07/2015%20NDTA%20Report.pdf>

Data provided by the CDC is consistent with concerns of increasing and substantially higher duration prescriptions for extended release oxycodone following the 2001 label change. The IQVIA prescription data specific to oxycodone shows that for ER oxycodone, in 2006, prescriptions averaged 270 days at 159.7 MME per day and 4203.6 MME per prescription compared to an average of 12.5 days at 62.9 MME per day and 726.7 MME per prescription for IR oxycodone. In 2009, the ER oxycodone MME prescriptions spiked at 169.9 MME per day and 4556.4 per prescription.¹⁹ In 2010, Purdue submitted and received FDA approval for a new drug application for reformulated ER oxycodone with abuse-deterrent properties.²⁰

Data provided by the CDC²¹

Oxycodone prescribing by immediate-release (IR) and extended-release (ER) formulations, United States, 2006-2018

Year	Day's supply		MME per day		MME per prescription	
	Oxycodone-ER	Oxycodone-IR	Oxycodone-ER	Oxycodone-IR	Oxycodone-ER	Oxycodone-IR
2006	27.0	12.5	159.7	62.9	4203.6	726.7
2007	27.2	13.1	160.9	65.4	4273.6	820.4
2008	27.2	13.8	166.7	67.8	4437.6	923.0
2009	27.2	14.4	169.9	70.3	4556.4	1021.0
2010	27.3	15.3	168.1	75.5	4554.2	1207.6
2011	27.4	16.0	154.1	78.8	4223.6	1338.4
2012	27.4	16.3	147.8	76.1	4076.2	1296.5
2013	27.4	16.6	140.1	73.1	3884.2	1264.2
2014	27.4	16.9	130.7	70.3	3629.4	1239.6
2015	28.5	16.1	122.9	68.0	3435.2	1215.1
2016	29.0	16.3	117.7	66.8	3297.1	1232.0
2017	27.7	18.3	109.5	64.7	3068.7	1226.2
2018	27.8	18.6	99.6	61.1	2782.3	1184.6

MME; morphine milligram equivalent

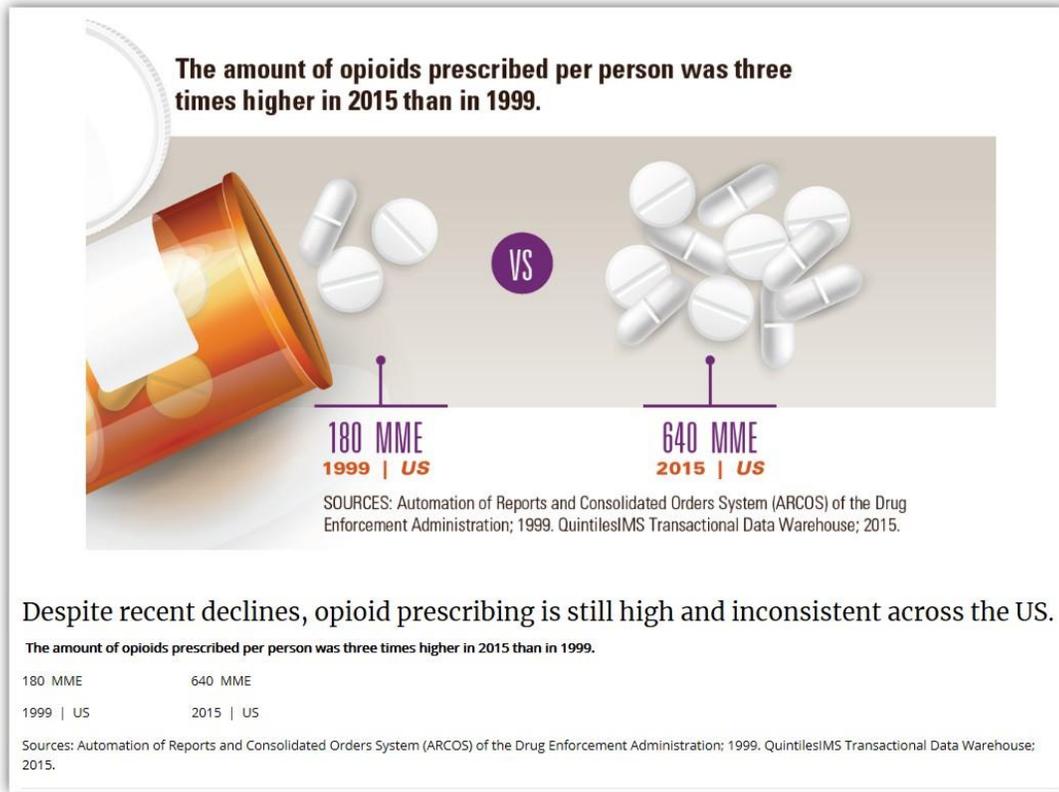
Data source: IQVIA Xponent 2006-2018. IQVIA Xponent is based on a sample of approximately 49,900 retail (non-hospital) pharmacies, which dispense nearly 92 percent of all retail prescriptions in the United States. For this database, a prescription is an initial or refill prescription dispensed at a retail pharmacy in the sample and paid for by commercial insurance, Medicaid, Medicare, or cash or its equivalent. This database does not include mail order pharmacy data.

Oxycodone was identified using the National Drug Code.

¹⁹ IQVIA Xponent data provided in CDC email to Minority Committee Staff (March 3, 2020).

²⁰ FDA Center for Drug Evaluation and Research, Office Director memo, "Abuse-Deterrent Properties of Purdue's Reformulated OxyContin (oxycodone hydrochloride) Extended-Release Tablets (2013), available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/022272Orig1s014_ODMemo.pdf

²¹ IQVIA Xponent data provided in CDC email to Minority Committee Staff by CDC (March 3, 2020).



Source: Opioid Prescribing, CDC²²

The elevated levels of ER oxycodone prescription duration and potency in the U.S. occurred against a backdrop of excessive oxycodone consumption when evaluated on a worldwide scale. Even though the U.S. only has about 5 percent of the world’s population, data from the United Nations International Narcotics Control Board shows that the U.S. consistently consumed a disproportionate share of the global oxycodone market from 2000-2018.²³ Despite a recent decline, the U.S. consumed an average of nearly 80 percent of the world’s oxycodone, the highest amount of any country. By contrast, the second highest ranking oxycodone consumption countries averaged less than six percent of global consumption during the same time span.²⁴

²² Centers for Disease Control and Prevention, VialSigns infographic, available at <https://www.cdc.gov/vitalsigns/opioids/infographic.html#graphic-a>

²³ International Narcotics Control Board, Narcotic Drugs – Technical Reports 2001-2009, available at https://www.incb.org/incb/en/narcotic-drugs/Technical_Reports/narcotic_drugs_reports.html.

²⁴ *Id.*

Year	Total Global Consumption	U.S. Consumption	U.S. % of Global Consumption	U.S. Consumption (kg)	#2 Country Name	#2 Country Tons	#2 Country % of Global Consumption	#2 Country (kg)
2000	18.6 tons	17.3 tons	93%	17272	Canada	.6 tons	3%	589
2001	31.4 tons	28 tons	90%	21871	Canada	.9 tons	2.80%	915
2002	27.6 tons	24.4 tons	88%	24407	Canada	1.7 tons	6.16%	1,679
2003	34 tons	30 tons	88%	29966	Canada	1.8 tons	5.29%	1,766
2004	37 tons	31 tons	85%	31456	Canada	2.6 tons	7.03%	2553
2005	42.6 tons	35 tons	83%	35041	Canada	3.3 tons	7.75%	3284
2006	42.6 tons	34 tons	80%	34243	Canada	3.5 tons	8.22%	3487
2007	51.6 tons	42.4 tons	82%	42445	Canada	3.7 tons	7.17%	3689
2008	52.5 tons	40.5 tons	77%	40523	Canada	4.5 tons	8.57%	4513
2009	77 tons	32 tons	81%	62380	Canada	4.8 tons	6.23%	4799
2010	74 tons	58.9 tons	80%	58987	Canada	5.6 tons	7.57%	5609
2011	81.6 tons	66 tons	81%	66199	Canada	5 tons	6.13%	5012
2012	94.9 tons	77 tons	82%	77405	Canada	4.9 tons	5.06%	4899
2013	82 tons	63.7 tons	78%	63713	Canada	4 tons	4.90%	4041
2014	84.8 tons	61.9 tons	73%	61921	United Kingdom	5.9 tons	6.96%	5904
2015	83.3 tons	62.6 tons	69%	62556	Canada	3.5 tons	4.20%	3500
2016	79.7 tons	58 tons	72.90%	58118	Canada	3.6 tons	4.52%	3643
2017	62.6 tons	42.2 tons	67.70%	42380	Canada	3.5 tons	5.60%	3463
2018	59.8 tons	37.9 tons	63.40%	37946	Germany	3.5 tons	5.80%	3473

Graph Data Source: International Narcotics Control Board ²⁵

To facilitate our understanding of what factors contributed to the opioid crisis over the last two decades and how such a public health disaster can be avoided in the future, please provide the following by November 12, 2020:

1. FDA's analysis of the information presented in this letter discussing the factors the FDA believes impacted opioid marketing and prescribing after the 2001 labeling change, and whether FDA can rule out the possibility that the text of the 2001 labeling change may have been used by Purdue Pharma in a way that contributed to the worsening of the ongoing opioid crisis.
2. What are the lessons learned for FDA in ensuring FDA-approved labeling is not misinterpreted and misused by drug manufacturers in the future?

Your assistance is appreciated. If you have any questions, please contact Alan Slobodin or Diane Cutler of the Minority Committee staff at (202) 225-3641.

²⁵This table was prepared by Minority Committee staff from data presented in individual annual INCB reports.

Sincerely,



Greg Walden
Republican Leader
Committee on Energy and Commerce



Brett Guthrie
Republican Leader
Subcommittee on Oversight and
Investigations



H. Morgan Griffith
Member of Congress

cc: The Honorable Frank Pallone, Jr., Chairman

The Honorable Diana DeGette, Chair

Subcommittee on Oversight and Investigations