K52 Abuse Deterrent Formulation (ADF) Oxycodone: A Ten-Year Study of Driving Under the Influence of Drugs (DUID) and Postmortem (PM) Oxycodone/Oxymorphone Blood Trends

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Learning Overview: After attending this presentation, attendees will be familiar with the formulation change to oxycodone tablets in 2010 and oxymorphone in 2012 and what impact(s), if any, the changes have had on oxycodone and oxymorphone blood concentrations in DUID and PM toxicology casework in the decade that followed.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by relaying information regarding oxycodone/oxymorphone blood concentrations and trends in DUID and PM populations following the drug tablet reformulation of oxycodone in 2010 and oxymorphone in 2012.

With the intent of deterring opioid abuse in the early 2000s, the pharmaceutical industry focused on developing ADFs for its products. In August 2010, the Food and Drug Administration (FDA) approved the first ADF product, commercial oxycodone tablets, which was soon followed by ADF oxymorphone in 2012. Both formulations made the tablets harder and more difficult to manipulate, crush, snort, and/or inject. Now more than ten years later, an FDA advisory committee recently concluded that while ADF oxycodone did reduce abuse by non-oral routes, the reformulation did not produce a meaningful reduction in overall opioid abuse, overdose, and death. The purpose of this work is to describe the trends of oxycodone and oxymorphone use in DUID and PM populations in the decade following oxycodone's reformulation.

Oxycodone- and/or oxymorphone-positive cases received at NMS Labs between January 2010 and July 2020 were reviewed. A total of more than 43,600 oxycodone and 16,000 oxymorphone cases were reported across all matrices, representing overall case positivity rates of approximately 4.7% and 1.7%, respectively. Cases were screened via immunoassay, Gas Chromatography/Mass Spectrometry (GC/MS), or Time-Of-Flight/Liquid Chromatography/Mass Spectrometry (TOF/LC/MS) depending on case type, matrix submitted, and year of analysis. For ease of discussion, this presentation will focus primarily on blood analysis results. Blood confirmation testing was performed via Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS) with reporting limits of 5.0ng/mL for oxycodone and 1.0ng/mL for oxymorphone.

Biennial snapshots of average free analyte concentration are reported below in Tables 1 (DUID blood) and 2 (PM blood–all types). Both case types show an approximate 2x decrease in average oxycodone blood concentrations and 6–7x decrease in oxymorphone blood concentrations over the ten-year time range. Following reformulation of oxycodone in 2010, DUID casework trends indicate a steady six-year decrease in average oxycodone blood concentrations before plateauing near 60ng/mL. In contrast, DUID oxymorphone concentrations saw a sharp drop of nearly 75% in average blood concentration after the 2012 reformulation. Furthermore, average PM blood concentrations of both oxycodone and oxymorphone abruptly dropped by 55%–60% in the first two years following reformulation of their respective tablets before plateauing. This data supports the idea that ADF reformulations reduced some but not all routes of oxycodone/oxymorphone abuse.

Table 1 – DUID Blood		**2010**	**2012**	**2014**	**2016**	**2018**	**2020 (Jan-July)**
Oxycodone – free (ng/mL)	N	120	860	970	1800	730	240
	Average (±SD)	120 (± 130)	100 (± 120)	90 (± 120)	70 (± 100)	60 (± 90)	50 (± 80)
Oxymorphone - free(ng/mL)	N	10	70	330	770	240	60
	Average (±SD)	10 (± 10)	20 (± 10)	5.0 (± 7.0)	7.0 (± 60)	4.0 (± 6.0)	2.0 (± 3.0)

Table 2 – PM Blood (all)		**2010**	**2012**	**2014**	**2016**	**2018**	**2020 (Jan-July)**
Oxycodone - free (ng/mL)	N	2600	3700	4000	5100	5000	2800
	Average (±SD)	810 (± 9200)	460 (± 2300)	400 (± 1700)	450 (± 4100)	310 (± 1300)	340 (± 3600)
Oxymorphone - free (ng/mL)	N	810	1100	2300	3500	3200	1600
	Average (±SD)	100 (± 610)	70 (± 230)	40 (± 240)	20 (± 90)	10 (± 90)	10 (± 70)

Note: Average ± SD values have been truncated to simplify reporting.

From this data, oxycodone/oxymorphone prevalence appears to be declining with maximum DUID and PM positive reports being issued in 2016 and 2017, respectively. While this is good news, prevalence and concentrations cannot be the sole indicators for measuring abuse. Additional explanations for oxycodone decline include restrictions and/or hesitations by medical professionals to prescribe opioids and the rise of abuse in both heroin and synthetic opioids. Given this information, it is difficult to attribute the impact that ADF reformulations alone have had on opioid use and abuse over the past ten years.

ADF Oxycodone, Oxycodone, Opioid Abuse

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