

Fentanyl Data in Fatalities and Impairment (DUID) Cases: a 5-year (2010 – 2016) Retrospective Study

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Abstract

Introduction: The Toxicology Department at the Cuyahoga County Medical Examiner's Office (CCMEO) and the Cuyahoga County Regional Forensic Science Laboratory, has observed an epidemic of fatal fentanyl deaths and an increase in Driving Under the Influence of Drugs (DUID) cases over the past 5 years (2010-2016 first quarter). Fentanyl, N-phenyl-N-[1-(2-phenylethyl) piperidin-4-yl] propanamide, is a potent, synthetic opioid with rapid onset and short duration of action. It is a strong mu opioid receptor agonist and 100 times more potent than morphine. Clinically used as an adjunct to surgical anesthetic and breakthrough pain, it is also produced in clandestine laboratories in powder and pill form. This has caused a resurgence of illicit use of fentanyl and its analogues. Data generated from postmortem cases received at the CCMEO over the past five years indicate there were 13 fentanyl related deaths in Cuyahoga County in 2010 (1.02 deaths per 100,000 people), in contrast to 77 fentanyl related deaths in the first quarter of 2016 (24.25 deaths per 100,000 people). Fentanyl related DUID cases have increased 100% since 2010. Interestingly, many of the recent DUID fentanyl blood concentrations fell into ranges generally recognized as toxic or fatal.

Objective: To present the demographics, results, incidence, and frequency of fentanyl deaths, including polysubstance abuse in postmortem, DUID and drug chemistry cases from 2010 to 2016 in Cleveland, Ohio (population ~396,815) and Cuyahoga County as a whole (population ~1,280,122)⁽¹⁾.

Method: In the 5-year period analyzed, there were 14,773 autopsies or death investigations performed at CCMEO with full toxicology requested on 9,932 cases and 1,832 DUID submissions. The CCMEO toxicology and drug chemistry departments performed standard comprehensive testing on multiple specimens and submissions using gas chromatography/mass spectrometry. Testing was performed, in the same manner, for DUID cases as requested by individual agencies. Fentanyl methodology and sensitivity levels were consistent throughout the study period with a LOD of 0.5 ng/mL and an LRL of 1.0 ng/mL.

Results: There has been a remarkable epidemiological change in the number of fentanyl related deaths and usage in Cuyahoga County, including Cleveland, Ohio and its suburbs. Postmortem fentanyl demographics are white (80%) males (75%) with ages evenly distributed among 19-60 years. Usage is equally dispersed between individuals in urban Cleveland and its suburbs.

In 2010, only 4.86% of poisoning deaths were due to fentanyl related intoxications. In 2014, this increased to 10.30% due to fentanyl related intoxications and dramatically increased in 2015 to 24.86%. Fatal fentanyl concentrations ranged from 1.0 to 80.0 ng/mL. Approximately, 20% of fentanyl fatalities were due to fentanyl alone. The majority were a result of polysubstance intoxications; primarily heroin/fentanyl, cocaine/fentanyl, ethanol/fentanyl, benzodiazepine/fentanyl, or a combination thereof. Similarly, fentanyl was pertinent in only 0.47% of the DUID cases in 2010 compared to 3.88% of cases in 2015 and 4.47% of cases in the first quarter of 2016.

Of the 41 total DUID cases positive for fentanyl, 7 were positive for fentanyl alone with concentrations ranging from 5.0 - 25.2 ng/mL with a median of 8.5 ng/mL and a mean of 10.2 ng/mL. A 25.2 ng/mL DUID fentanyl was reported in a 2015 case from a Cleveland suburb. In the remaining 34 DUID cases, fentanyl was present in conjunction with other substances. The fentanyl blood concentrations range from <1.0 - 11.0 ng/mL with a median of 4.1 ng/mL and mean of 4.8 ng/mL. Fentanyl was reported as positive for urine DUID cases. Drug chemistry fentanyl positive submissions increased from 0.01% in 2010 to 4.3% of positive submissions, for the first quarter of 2016.

Conclusion: This study demonstrates that there has been an increase in fentanyl related deaths and fentanyl related DUIDs in Cuyahoga County and surrounding counties. The increase in fentanyl follows the statistical increase of heroin abuse and is due to low cost and high availability of the clandestinely manufactured, illicit distribution of a non-traditional formulation of fentanyl. Fentanyl is also being sold fraudulently as heroin, oxycodone, benzodiazepine tablets, or compounded with other drugs to unsuspecting users.

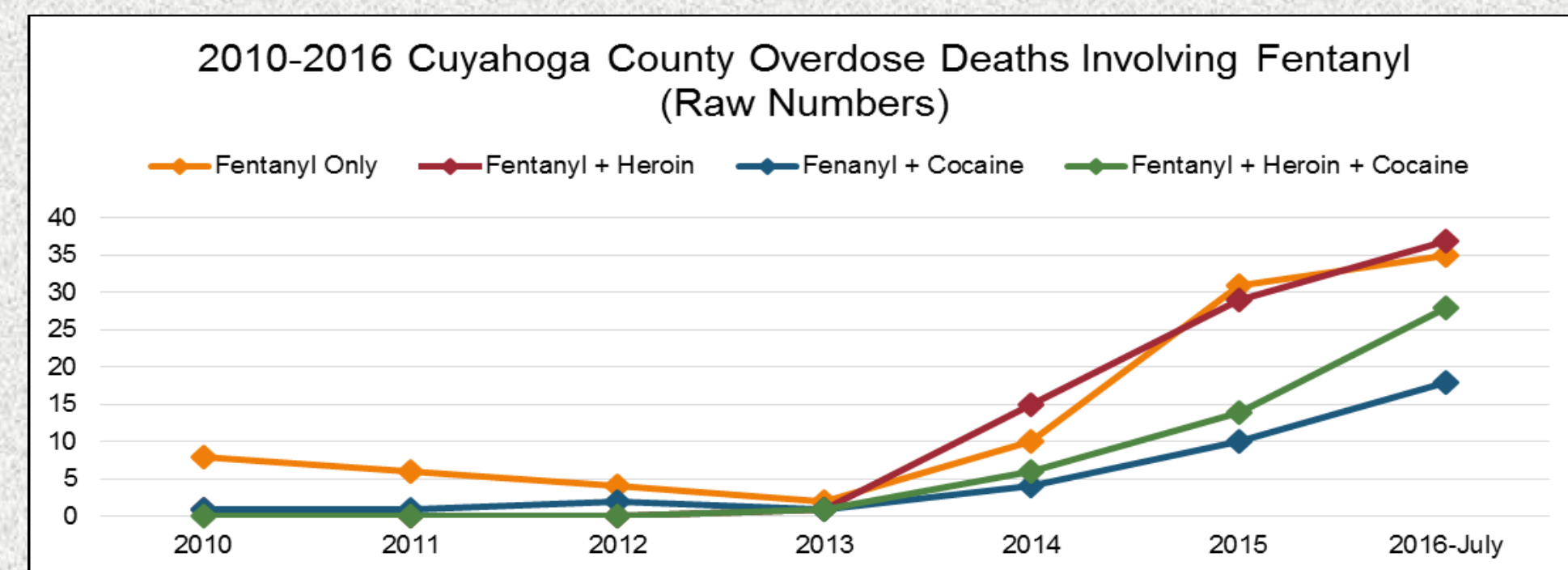
Keywords: Fentanyl, DUID, Medical Examiner, Demographic, Ohio

Objective

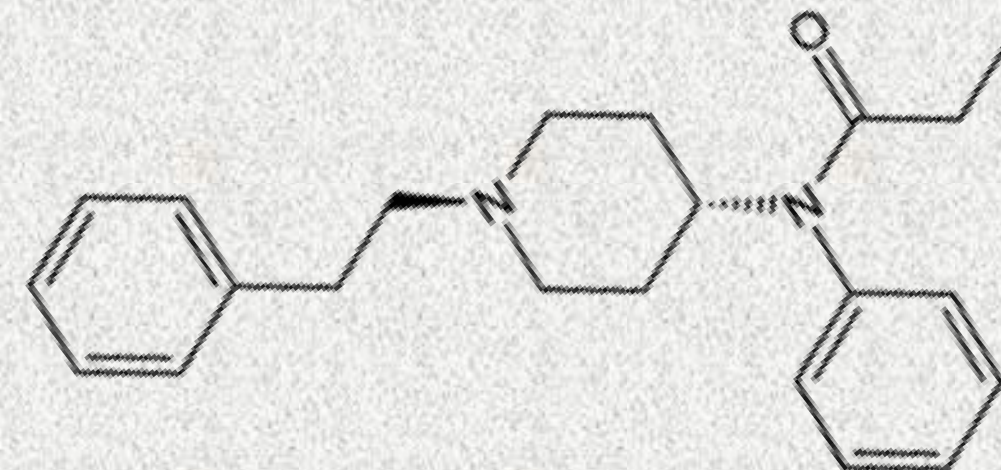
- To evaluate the frequency of fentanyl in fatal overdose cases and impaired DUID cases, as well as the range of fentanyl concentrations.
- To illustrate the demographics and incidence of fentanyl cases including polysubstance abuse.
- To present the drug paraphernalia submitted to drug chemistry relating to fentanyl cases.

Introduction

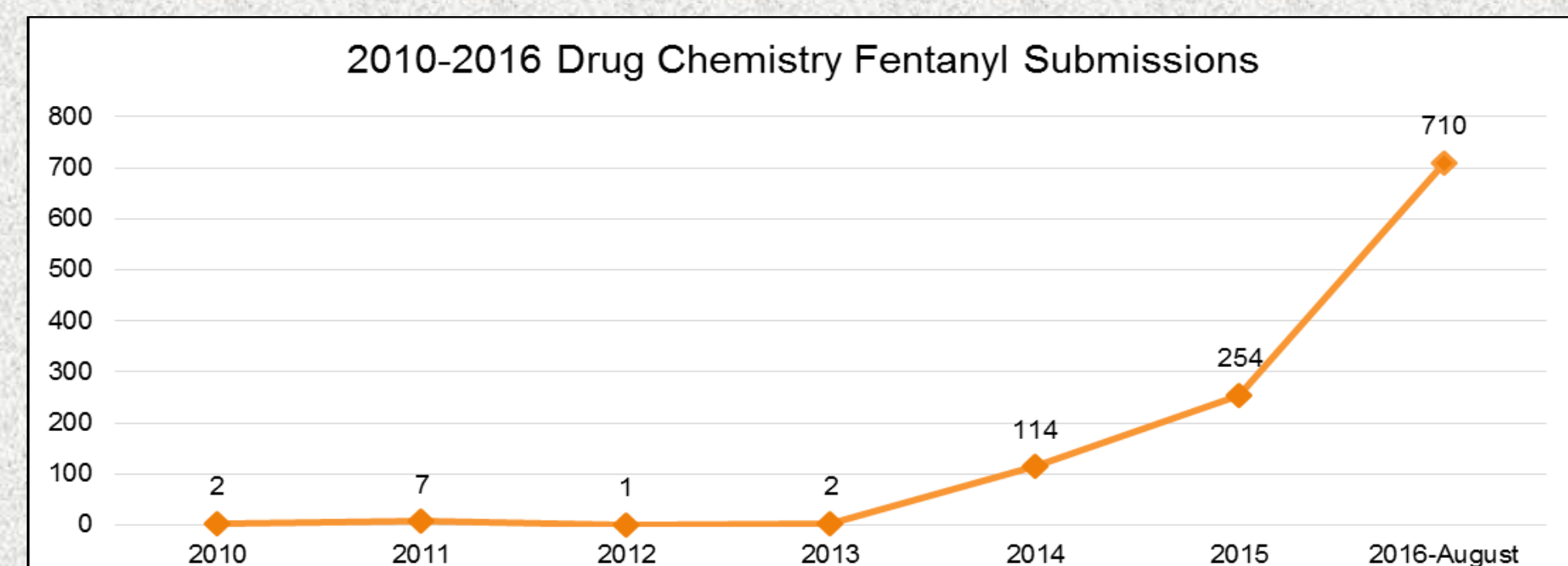
- Since 2010, CCMEO has experienced a large increase in fatal fentanyl overdoses and impaired DUID cases.
 - CCMEO is located in Cleveland, Ohio which is the most populated city in Cuyahoga County (population of ~1.2 million)⁽¹⁾.



- Fentanyl (N-phenyl-N-[1-(2-phenylethyl) piperidin-4-yl] propanamide) is a potent, synthetic opioid with rapid onset and short duration of action.
 - 100 times more potent than morphine.
 - Fentanyl is being produced in clandestine laboratories in powder and pill form.



- Deaths related to fentanyl increased from 4.8% to 24.8% of all poisoning deaths with concentrations ranging from 1.0 – 80.0 ng/mL*.
 - *2016: Fentanyl case = 180.0 ng/mL
- In 2016, CCMEO has seen fentanyl analogues, including carfentanil, acetyl fentanyl, furanyl fentanyl, and 3-methyl fentanyl.
- Positive DUID fentanyl cases are at levels that are historically considered fatal.
- Since 2010, the Drug Chemistry Department has seen a **34,400%** increase in submissions containing fentanyl and fentanyl analogues.



Methods

- Cases were screened for fentanyls using an ELISA blood screen.
- Positive or elevated fentanyl screens were confirmed by GC/MS.
- Fentanyls were extracted using a Solid Phase method with UCT Clean Screen® Solid Phase extraction columns ZSDAU20.
- Separate calibrators containing fentanyl, alfentanil and sufentanil were made from 100ug/mL Stock Cerilliant® solutions to create a five point calibration curve, with concentrations from 1 ng/mL – 25 ng/mL along with a deuterated internal standard.
- The Limit of Detection: 0.5 ng/mL.
- The Lower Reporting Limit: 1.0 ng/mL.
- The Quality Control containing fentanyl was made from a 25 ug/mL Alltech® stock solution.
- All calibrators, controls, negatives, and samples were prepared for solid phase extraction.
- After extraction and evaporation to dryness, samples were reconstituted with 50 µL of ethyl acetate.
- Analytes were separated and detected on an Agilent 7890 Gas Chromatograph equipped with a 5975C Agilent GC/MS using a Restek Rxi®-5ms capillary column.
- The GC/MS operating parameters were as follows: the injection port temperature was 250°C, run splitless; the initial oven temperature was 100°C with a ramp rate of 50°C/min to 200°C. Followed by a 20°C/min ramp which led to a final temperature 300°C, holding for 4 minutes. The total run time was 13.00 minutes. 1.0 µL of sample was injected on the GC/MS using a SIM method.
- Fentanyl was identified using retention time and SIM spectral match using ions m/z 245, 189, and 146.

Results

Table 1 – Total Poisonings Ruled at CCMEO

	2010	2011	2012	2013	2014	2015	2016*
Total Poisonings	267	304	307	337	352	371	137
% Fentanyl Poisonings	4.87%	2.63%	3.26%	1.48%	10.51%	24.53%	51.09%

Table 2 – Polypharmacy-Drugs of Abuse in Fentanyl Fatalities

	2010	2011	2012	2013	2014	2015	2016*
Fentanyl Only	30.77%	25.00%	20.00%	10.81%	20.68%	18.57%	18.57%
Fentanyl and Other Drugs	69.23%	75.00%	80.00%	89.19%	79.35%	81.43%	81.43%
Fentanyl and Heroin	7.69%	0.00%	0.00%	40.00%	59.46%	51.09%	50.00%
Fentanyl and Cocaine	7.69%	12.50%	40.00%	40.00%	27.03%	26.09%	27.14%
Fentanyl + Heroin + Cocaine	0.00%	0.00%	0.00%	20.00%	16.22%	15.22%	8.57%
Fentanyl and Benzodiazepines	23.08%	50.00%	10.00%	0.00%	18.92%	8.70%	18.57%
Fentanyl and Ethanol	7.69%	25.00%	0.00%	40.00%	21.62%	21.74%	20.00%

Table 3 – Polypharmacy-Drugs of Abuse in DUID Cases

	2010	2011	2012	2013	2014	2015	2016*
Total DUID Submissions	418	458	511	496	553	566	134
Fentanyl Only	0	0	0	1	1	3	2
Fentanyl and Other Drugs	2	0	1	0	8	19	31
Fentanyl and Heroin	0	0	1	0	2	2	4
Fentanyl and Cocaine	0	0	0	0	2	0	10
Fentanyl + Heroin + Cocaine	0	0	0	0	0	0	1
Fentanyl and Benzodiazepines	0	0	0	0	2	6	4
Fentanyl and Ethanol	1	0	0	0	1	1	1

Results

Figure 1 – Demographics: Gender & Race 2010 - 2016

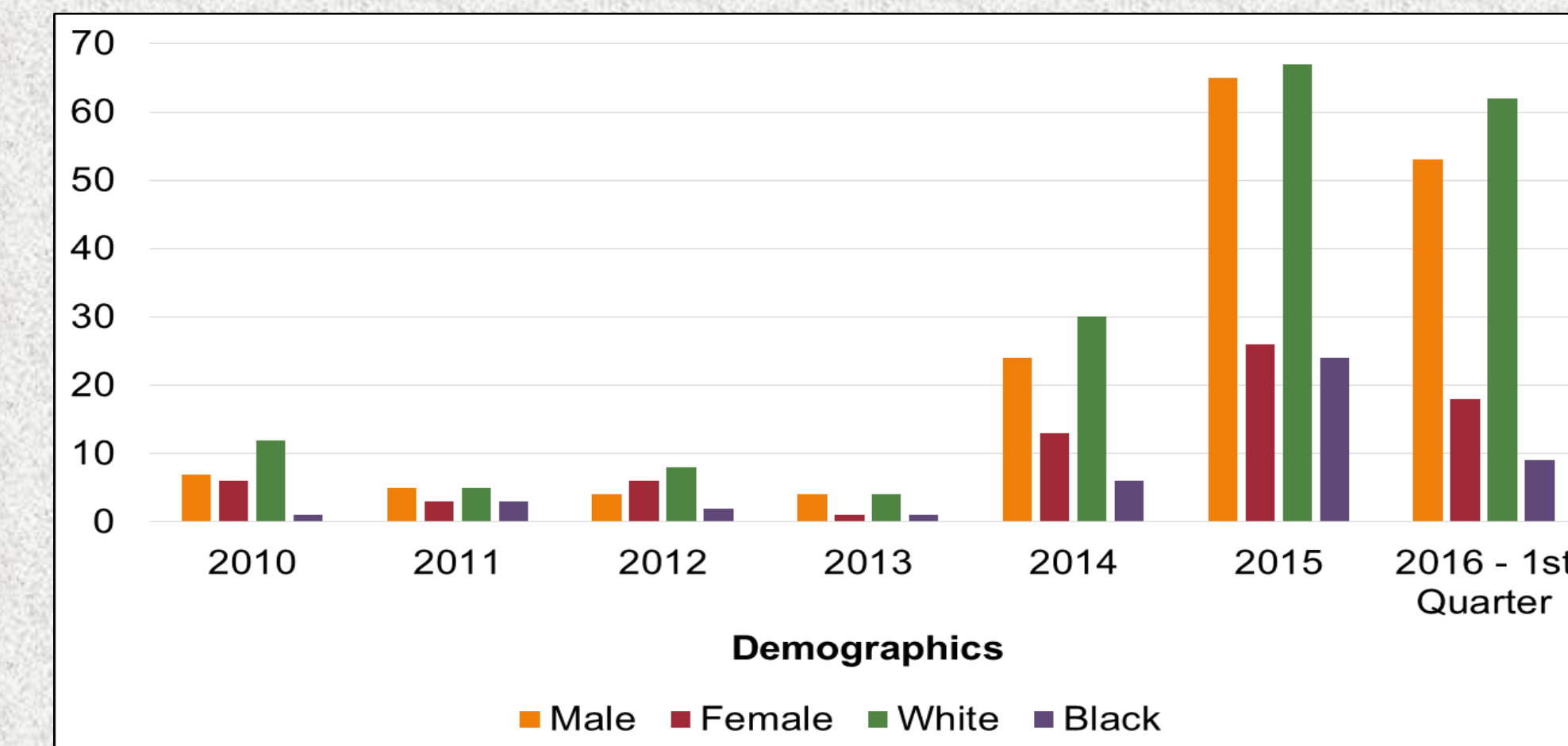


Figure 2 – Demographics: Age 2010 - 2016

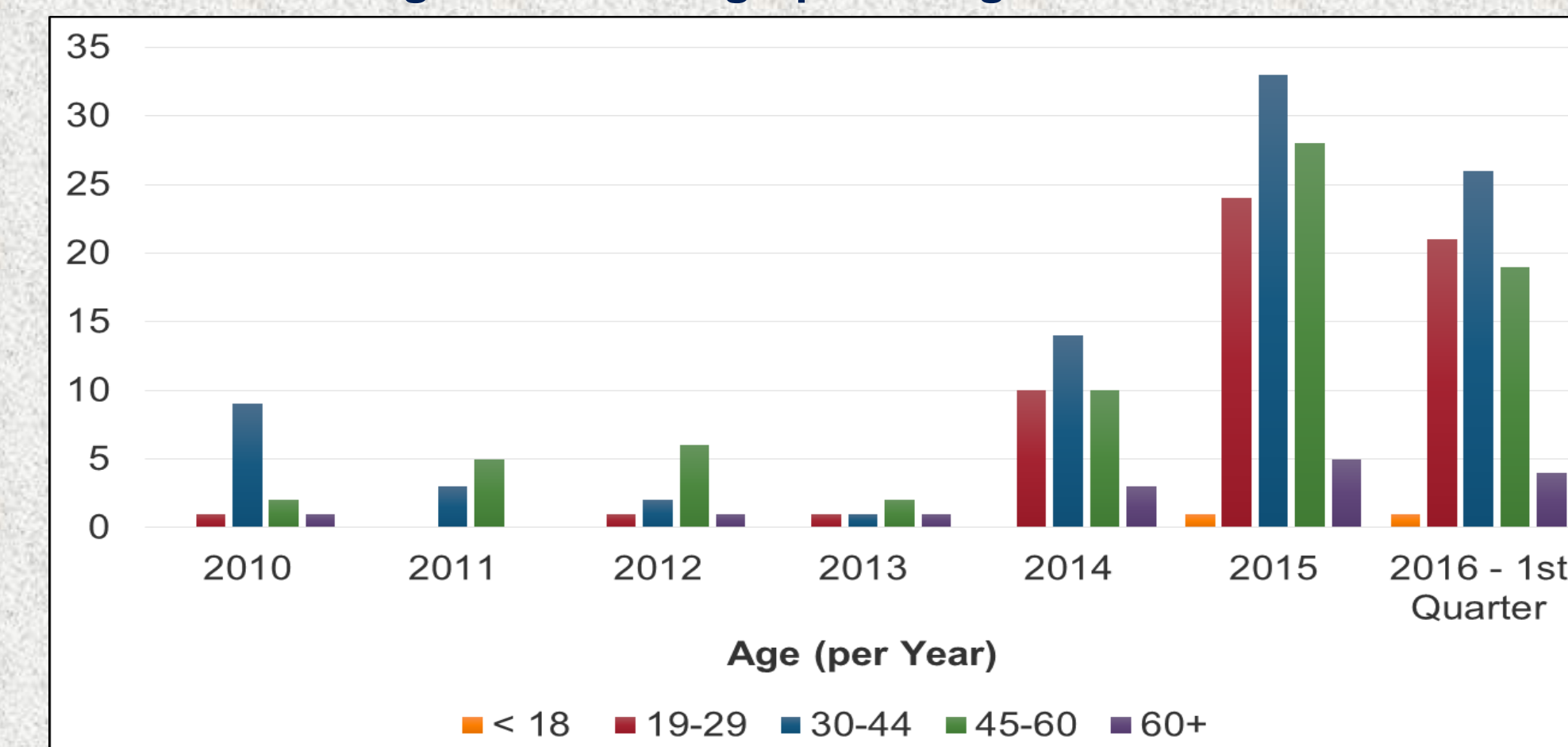


Figure 3 – DUID Police Department Submissions

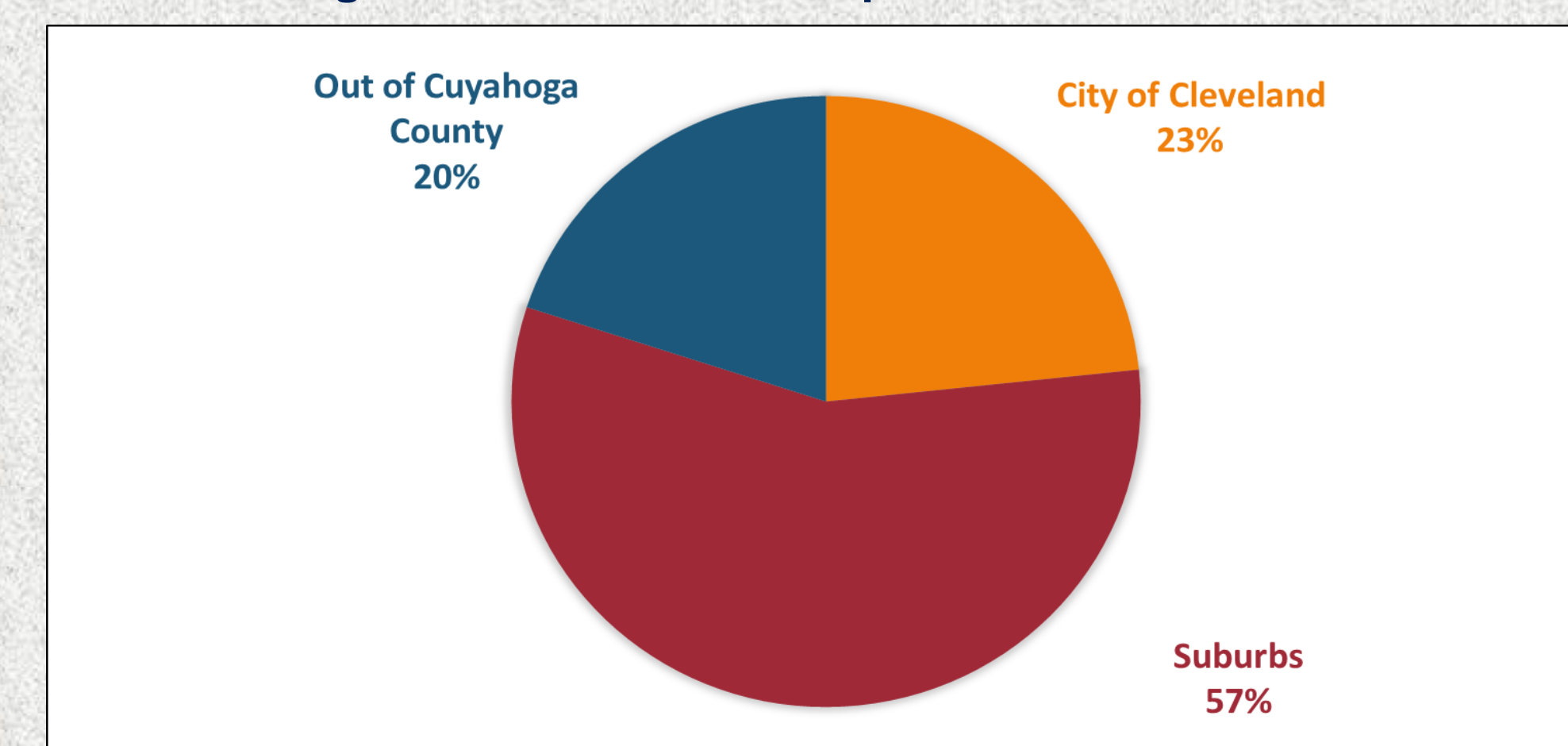


Figure 4 – Location of Incidence in Fentanyl Fatalities 2010 - 2016

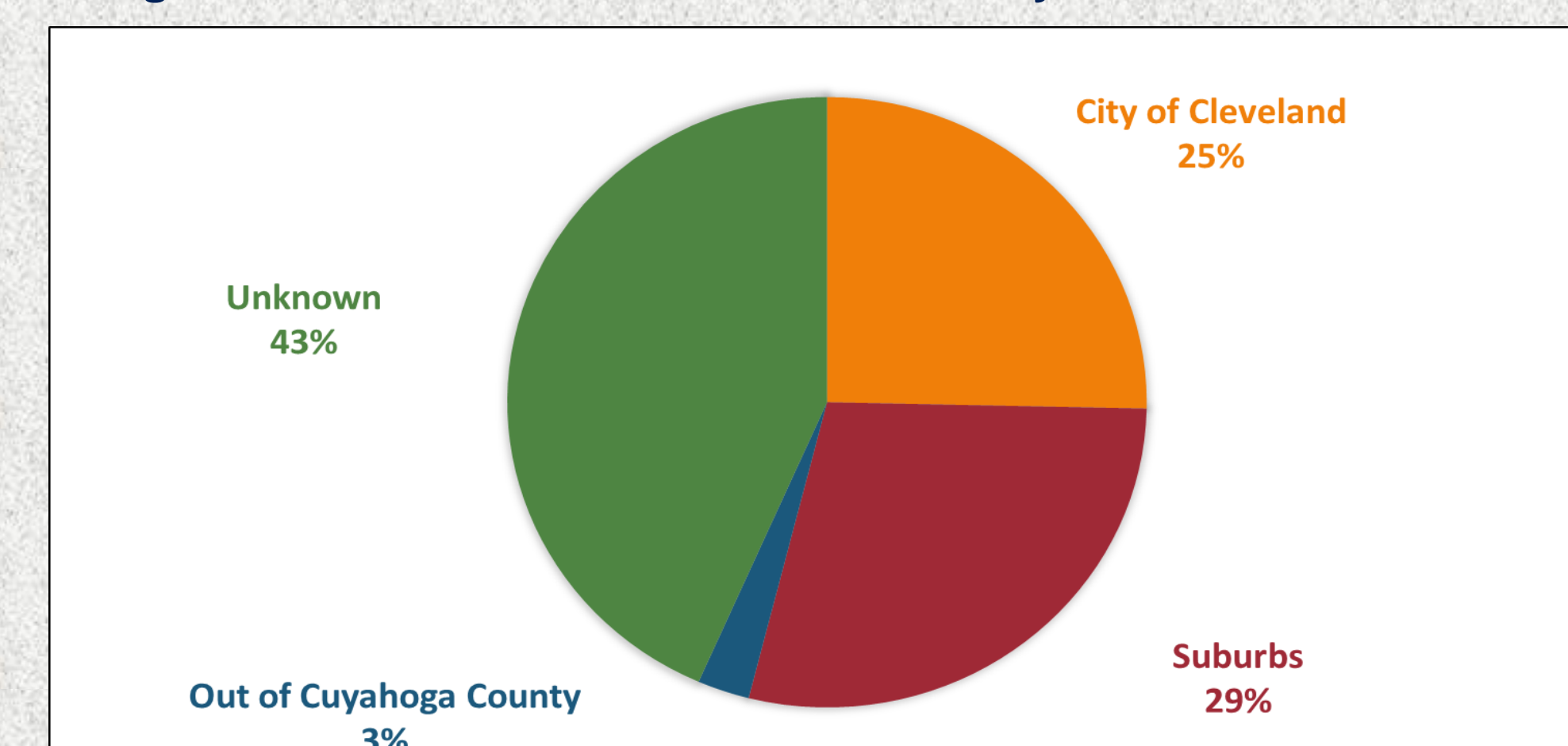


Table 4 – Number of Submissions to Drug Chemistry (January – August 2016)

	Fentanyl	Acetyl fentanyl	Furanyl fentanyl	Carfentanil	4-ANPP	3-Methyl fentanyl
Number of Submissions	710	47	16	10	6	5

Conclusions

- Fentanyl use has been on the rise in Cuyahoga County over the last 5 ½ years.
- Our study found that the fentanyl decedents tended to be **white, males** between the ages of **19-60** years.
- Decedents' location of incident was evenly distributed between the City of Cleveland and its suburbs.
- DUID cases have increased **> 100%** since 2010 with case concentrations as high as **25.2 ng/mL** of fentanyl. This is much higher than what is considered fatal.
 - Therapeutic concentrations are 1-3 ng/mL and toxic concentrations are 3-28 ng/mL^(2,4).
- DUID fentanyl cases were predominately received from the suburbs (57%) over the City of Cleveland (23%).
- Since the first quarter of 2016, there has been an enormous increase in fentanyl fatalities and DUID cases. Several cases have included fentanyl analogues: acetyl fentanyl, 3-methyl fentanyl, and furanyl fentanyl.
- Drug chemistry has seen a significant spike in fentanyl submissions since 2010 from **2** submissions to **710** submissions in 2016.
- Since July 2016, **carfentanil** has become a serious concern, with several deaths due to the emergence of the drug, in Cuyahoga County and the State of Ohio.
- The largest fentanyl fatality was seen in Cuyahoga County after the first quarter of 2016. Fentanyl was confirmed in the femoral blood at a concentration of **180.0 ng/mL**.
- Fentanyl use has escalated in Cuyahoga County and the State of Ohio over the last two years. The increase has led to the highest number of overdoses recorded in Cuyahoga County during the month of August 2016⁽³⁾.
- Possible causes of fentanyl incidence include:
 - Low cost and high availability of clandestinely produced fentanyl and its precursors.
 - Fraudulent sales of fentanyl to buyers as prescription pills or heroin.
 - Increase in tolerance and addiction of opiate users.
 - The Mexican cartels switch to trafficking heroin and fentanyl from marijuana for a greater profit margin.
- One case from 2016 contained only fentanyl analogues acetyl fentanyl and furanyl fentanyl, not fentanyl itself.
- Referring to Figure 4, the Unknown Location of Incidence could not be determined due to circumstances of the cases.

References

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