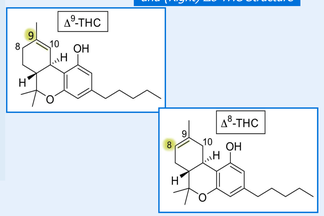
Δ-8- and Δ-9-THC-Carboxy Metabolites in Urine Drug Testing Specimens at CRL from April 2023 to January 2024

David Kuntz, Melissa Beals, Michael Clark, Martin Jacques, Rebecca Henkhaus. CRL, Lenexa, KS.

INTRODUCTION

Since gaining popularity in 2020, Δ8-THC has had a direct impact on the drug testing industry, creating potential analytical interference as well as negative confirmation results in tests with reporting criteria specific to Δ9-THC metabolite. As more states have passed legalization of Δ9-THC, the widespread usage of Δ8-THC has perpetuated as a means to pass drug tests when Δ9-THC use is still restricted.

Figures A and B: (Left) Δ9-THC Structure and (Right) Δ8-THC Structure



OBJECTIVE

Evaluate the presence of Δ8-COOH-THC in nonregulated urine drug testing samples being confirmed for Δ9-COOH-THC, and examine the prevalence of Δ8-COOH-THC among samples categorized by reason for test.

METHODS

From April 2023 through January 2024, a total of 108,131 urine specimens screened positive for cannabinoids by immunoassay and were analyzed by LC-MS/MS for confirmation. The confirmation assay, which had been optimized for separation of Δ8- and Δ9-COOH-THC, was validated in accordance with National Laboratory Certification Program guidelines, including interference studies involving numerous cannabinoids and other drugs. In addition to separating Δ8- and Δ9-COOH-THC, ions were collected and quantitative results were processed for each analyte in nonregulated specimens.

Figure C. Sample chromatogram from Δ9-COOH-THC confirmation

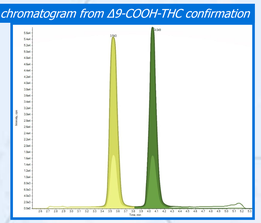


Table 1: Analyte Transitions and Elution Order

Analyte	Internal Standard	Precursor Ion	Product Ion Quantifier	Product Ion Qualifier	Elution Order	Assay LOD/LOQ (ng/mL)	Cutoff Concentration (ng/mL)	ULOL (ng/mL)
Δ9-COOH-THC	Δ9-COOH-THC-D9	343.1	299.2	245.1	Peak 4	3.0	15.0	5,000
Δ9-COOH-THC-D9		352.1	308.2	254.1	Peak 3			
Δ8-COOH-THC	Δ8-COOH-THC-D6	343.1	299.2	245.1	Peak 2	3.0	15.0	5,000
Δ8-COOH-THC-D6		349.1	305.2	251.1	Peak 1			

RESULTS / DISCUSSION

All specimens were de-identified and detached from client affiliation, with results reporting pursuant to client account and drug testing policy. The overall confirmation positivity rate for Δ9-COOH-THC was 82% with a 15 ng/mL cutoff, a significant decline from the almost 100% confirmation rates in years prior to 2020.

Samples screening positive but reporting negative with a 15 ng/mL cutoff included 6.2% that contained only Δ8-COOH-THC; 4.5% with Δ9-COOH-THC at a concentration greater than the assay LOQ of 3 ng/mL but less than 15 ng/mL; 4.8% that were positive for Δ8-COOH-THC at concentrations greater than the 15 ng/mL cutoff but had detectable levels of Δ9-COOH-THC less than 15 ng/mL; 1.4% with both Δ8- and Δ9-COOH-THC at detectable levels less than 15 ng/mL; and 1.1% of samples having both Δ8- and Δ9-THC metabolites less than 3 ng/mL.

Figure D: Δ9-COOH-THC Confirmation Positivity

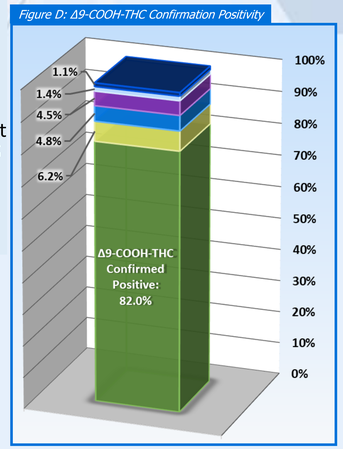
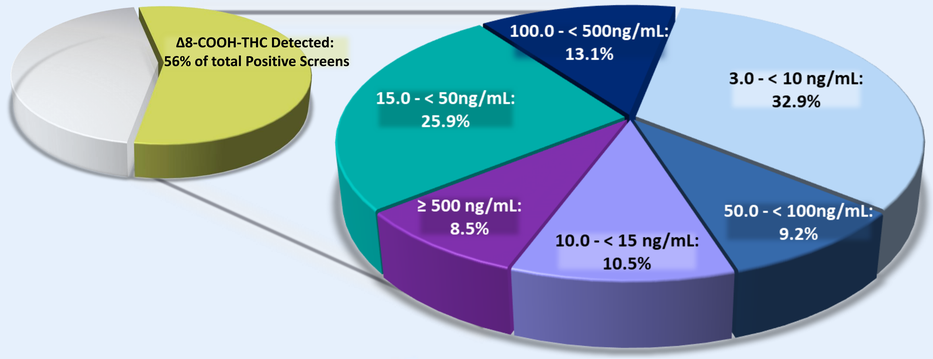


Table 2: Breakdown of Non-Confirming Positive Screens

Δ9-, Δ8-COOH-THC not detected:	**1.1%**
Δ9-, Δ8-COOH-THC both detected but less than cutoff:	**1.4%**
Δ9-COOH-THC detected but less than cutoff, no Δ8-COOH-THC detected:	**4.5%**
Δ8-COOH-THC Positive, Δ9-COOH-THC detected but less than cutoff:	**4.8%**
Δ8-COOH-THC Positive, no Δ9-COOH-THC detected:	**6.2%**

Figure E: Concentration Ranges of Δ8-COOH-THC



Δ8-COOH-THC was detected in 56.0% of the samples that screened positive, and Δ8- and Δ9-COOH-THC were both detected in 49.8% of the positive screens. For samples with detectable levels of Δ8-COOH-THC, 8.5% had concentrations greater than 500 ng/mL, with the highest concentration reaching almost 70,000 ng/mL.

Figure F. Percentage of screened-positive samples containing Δ8-COOH-THC, only Δ8-COOH-THC, and both Δ8-COOH-THC and Δ9-COOH-THC

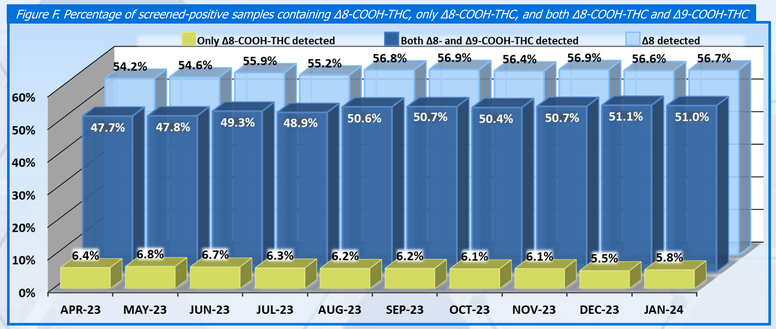


Figure G. Percentage of screened-positive samples containing Δ8-COOH-THC, categorized by Collection Reason

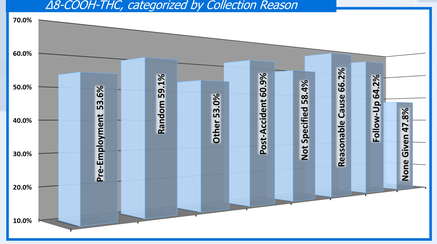


Figure H. Percentage of samples containing only Δ8-COOH-THC, and samples positive for Δ8-COOH-THC but negative for Δ9-COOH-THC , by Reason for Test

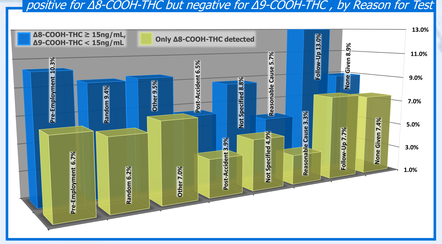
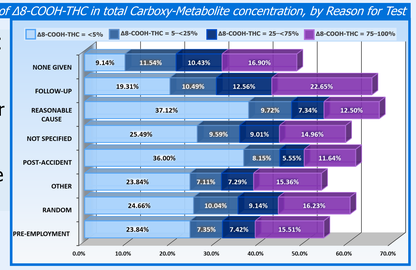


Figure I. Percentage of Δ8-COOH-THC in total Carboxy-Metabolite concentration, by Reason for Test



When categorized by reason for test, Δ8-COOH-THC was detected in more than 60% of Post-Accident, Reasonable Cause, and Follow-Up tests. However, Post-Accident and Reasonable Cause tests had lower concentrations of Δ8-THC metabolite overall, with Δ8-COOH-THC comprising less than 5% of the total Carboxy-THC in more than 35% of screened positive samples in these categories.

Among reason for test groups with sample populations exceeding 1,000, the highest percentages of samples with only Δ8-COOH-THC, as well as samples reporting negative for Δ9-COOH-THC having Δ8-COOH-THC concentrations greater than 15 ng/mL, were attributed to Follow-Up tests. Δ8-COOH-THC made up 75% or more of the Carboxy-THC metabolite concentrations for more than 20% of Follow-Up tests with detectable Δ8-THC metabolite.

Figure J: Relevant Δ8-COOH-THC statistics, categorized by Collection Reason

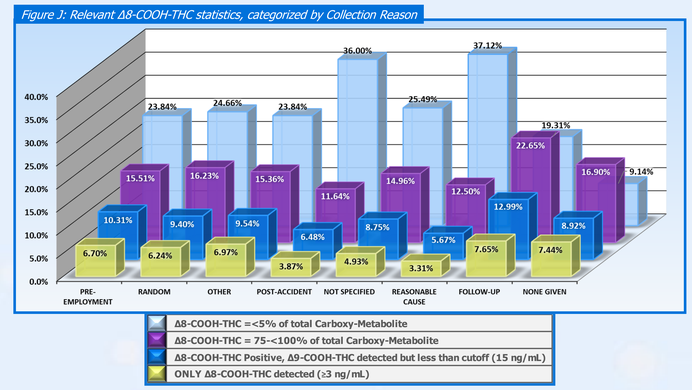
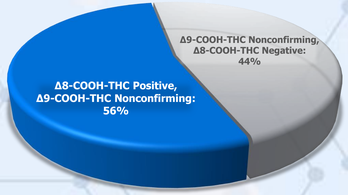
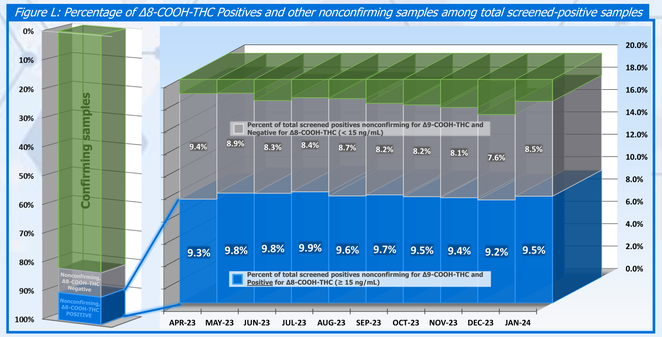


Figure K: Percentage of Δ8-COOH-THC Positives among nonconfirming samples



Almost 10% of samples screening positive for cannabinoids report negative for Δ9-COOH-THC concentrations less than the 15 ng/mL cutoff, but in fact have Δ8-COOH-THC concentrations greater than 15 ng/mL; this means that more than half of nonconfirming samples would actually report positive for Δ8-COOH-THC.

Figure L: Percentage of Δ8-COOH-THC Positives and other nonconfirming samples among total screened-positive samples



CONCLUSION

The presence of Δ8-COOH-THC in urine drug testing samples continues to reveal a threat to public safety that is going largely unaddressed. Because Δ8-THC is intoxicating, inexpensive, and ambiguously legal, it will likely continue in popularity until corporate and federal policy include Δ8-THC testing in addition to Δ9-THC.

DISCLOSURE

No relevant financial or nonfinancial relationships to disclose.