K44 Plasma and Oral Fluid l-Methamphetamine Concentrations After Controlled Vicks VapoInhaler® Administration

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After attending this presentation, attendees will be able to describe *l*-methamphetamine (*l*-MAMP) pharmacokinetics in plasma and oral fluid (OF) after intranasal administration according to manufacturer's recommendations of over-the-counter Vicks® VapoInhaler™.

These findings will impact the forensic science community by improving interpretation of MAMP and amphetamine (AMP) OF results, guiding selection of MAMP OF screening tests, and performing chiral separation of MAMP and AMP for confirmation when needed.

AMPs are widely abused psychoactive substances included in drug testing programs in forensic, workplace, drug abuse treatment, and anti-doping settings. Consumption of over-the-counter Vicks® VapoInhaler™ can produce positive blood and urine MAMP results, requiring chiral separation of *d*- and *l*-enantiomers in positive cases. *l*-MAMP is the primary active component in Vicks, with the manufacturer reporting potential trace *d*-MAMP presence. To date, there are no published OF MAMP or AMP data following controlled Vicks® administration.

Thirteen healthy adults (ten male, three female) aged 19-54 years old participated in this National Institute on Drug Abuse Institutional Review Board-approved study; all provided written informed consent. Participants arrived the morning of the first dosing day (Day 1), when two sprays per nostril every 2h (manufacturer's dosing recommendation) were administered from 9:00 a.m. until 7:00 p.m. (six doses). A single dose was administered at 6:00 a.m. on Day 2. The manufacturer suggests that 0.16-0.6mg *l*-MAMP is administered with each dose. Plasma and OF specimens were collected before and up to 32h after the first dose throughout the two days. Plasma was collected with an indwelling venous catheter, and OF was collected with the Oral-Eze® collection device and was also collected for the Dräger DrugTest® 5000 on-site drug test. *d*- and *l*-MAMP and AMP enantiomers were confirmed in plasma and Oral-Eze® specimens by a Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) method after solid phase extraction and derivatization with 1-fluoro-2,4-dinitrophenyl-5-l-alanineamide (Marfey's reagent). The method's Limit Of Quantitation (LOQ) for all analytes in both matrices was 1µg/L.

A total of 351 plasma specimens from 13 participants and 324 OF specimens from 12 participants were collected. *d*-MAMP and *d*-AMP were not detected in any plasma or OF specimen. Only 2 participants were positive for *l*-MAMP in plasma, producing a combined 52 positive specimens at the method LOQ (14.8%). Maximum *l*-MAMP plasma concentrations did not exceed 10µg/L, and both participants were still positive 11h after the final dose. No *l*-AMP was present in plasma. The total number of OF specimens positive for *l*-MAMP at the method LOQ (1µg/L), and the 2004 proposed Substance Abuse and Mental Health Services Administration (SAMHSA) screening (AMPs 50µg/L) and confirmation (MAMP 50µg/L and AMP >LOD) cutoffs were 262 (80.9%, N=12 participants), 24 (7.4%, N=2), and 15 (4.6%, N=1), respectively. Suggestions were made to lower the screening and confirmation cutoffs to 25µg/L, similar to the Driving Under the Influence of Drugs, Alcohol, and Medicines (DRUID) cutoffs. At these lower 25µg/L cutoffs, there were 31 positive OF specimens (9.6%, N=3). The median (range) maximum *l*-MAMP concentration was 16.7 (8.4-182) µg/L. One participant had detectable OF *l*-AMP at the method LOQ, first detected 7h after the first dose. The maximum *l*-AMP concentration observed was 5.5µg/L. At the method LOQ, 7 participants (58.3% specimens) were still positive for *l*-MAMP 11h after the last dose; among the other 5, none were positive 9h after the last dose. At the proposed SAMHSA screening cutoff of 50µg/L, one participant was only *l*-MAMP positive in one sample immediately after the second dose (N=1), and another participant remained positive at the last OF specimen 11h after the last dose. At the confirmation cutoff, the last detection time was >11h after the last dose (N=1). The DrugTest 5000® utilizes a 35µg/L *d*-MAMP cutoff; all participants' OF specimens were negative on this test.

These data suggest that careful selection of an AMP's screening test for OF targeted toward *d*-MAMP may obviate the need for chiral separation and confirmation of presumptive positive AMPs tests. Furthermore, these data provide an LC-MS/MS confirmation method for *d*- and *l*-AMPs in OF that utilizes a

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chiral derivative rather than a chiral column. These data provide valuable new data for interpretation of OF AMPs tests.

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***L*-Methamphetamine, Oral Fluid, Chiral Separation**

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