## K52 ∆9-Tetrahydrocannabinol, 11-Nor-9- Carboxy-Tetrahydrocannabinol, Cannabidiol, Cannabinol, and 11- Hydroxy-Tetrahydrocannabinol in Oral Fluid Following Controlled, Smoked Cannabis in Frequent and Occasional Smokers

*Sebastien Anizan, PhD*, National Institute on Drug Abuse, 251 Bayview Blvd, Baltimore, MD 21224; Garry Milman, PhD, National Institute on Drug Abuse, 251 Bayview Blvd, Ste 05A.505.16, Baltimore, MD 21224; Nathalie A. Desrosiers, MSc*, NIDA Intramural Research Program, 251 Bayview Blvd, Rm 05A721, Ste 200, Baltimore, MD 21224; Allan J. Barnes, BS, NIDA Intramural Research Program, 5500 Nathan Shock Dr, Rm 373, Baltimore, MD 21224; David A. Gorelick, MD, PhD, National Institute on Drug Abuse, 5500 Nathan Shock Dr, Baltimore, MD 21224; and Marilyn A. Huestis, PhD*, Chemistry & Drug Metabolism Section, Intramural Research, NIDA, NIH, 251 Bayview Blvd, Rm 05A721, Baltimore, MD 21224*

After attending this presentation, attendees will understand pharmacokinetic differences in Oral Fluid (OF) concentrations between chronic frequent and occasional cannabis smokers.

This presentation will impact the forensic science community by improving interpretation of oral fluid test results for different populations of cannabis smokers and may suggest recent cannabis use by selecting different analytes and cutoff concentrations.

In a previous study, additional cannabinoid analytes and cutoff concentrations were proposed to reduce the possibility of a positive cannabinoid OF test from environmental cannabis smoke contamination; however, the data only included chronic frequent cannabis smokers.[1] The objectives of the present study were to compare pharmacokinetic data from chronic frequent and occasional cannabis smokers, and to evaluate different cannabinoid analytes and cutoff concentrations to distinguish recent smoking from residual excretion in these populations.

This study consisted of healthy, 18 – 45-year-old cannabis smokers, who used cannabis at least four times per week (frequent smokers) or a maximum of two times per week (occasional smokers), provided written informed consent for this Institutional Review Board-approved study, and resided on the secure research unit for two days. OF specimens were collected with the Statsure™ device, 14 hr and 1 hr before and up to 30 hr after *ad libitum* smoking of a 6.8% ∆9-Tetrahydrocannabinol (THC) cigarette. Specimens were analyzed within 24 hr following collection. THC, 11-nor-9-carboxy-THC (THCCOOH), cannabidiol (CBD), cannabinol (CBN), and 11-hydroxy-THC (11-OH-THC) were quantified by 2D-GC/MS. Limits of quantification (LOQ) were 0.5 ng/mL for THC, CBD, CBN, and 11-OH-THC, and 15pg/mL for THCCOOH.

Eighteen subjects (eleven chronic frequent and seven occasional cannabis smokers) provided 306 OF specimens. Fourteen hours before smoking, all chronic frequent smokers' OF tested positive for THC (range 6-396.5ng/mL) and THCCOOH (23-124pg/mL), whereas all occasional smokers' OF specimens were negative for both analytes. One hour prior to dosing, nine chronic frequent smokers' OF specimens were still positive for THC (range 0.9 to 7ng/mL), while THCCOOH was always measurable in this population (range 2.0 – 13.6pg/mL).

No significant differences ($p>0.05$) in THC concentrations were observed 2h after cannabis smoking between chronic frequent and occasional smokers. OF THC concentrations were highly elevated for 2h with medians (range) of 517.3ng/mL (113.8 – 6,508), at 0.5 hr, 238.5ng/mL (28.4 – 6,362) at 1 hr and 72.5ng/mL (7.5 – 350.5) at 2 hr for the chronic frequent smokers. Medians (range) in occasional smokers were 481.8ng/mL (84.5 – 1471.3) 0.5 hr after smoking, 82.8ng/mL (48.4 – 561.5) at 1 hr, and 69.3ng/mL (23.4 – 213.7) at 2 hr. Eight of eleven chronic frequent smokers' OF specimens were still THC-positive at 30h (0.6 – 2.2ng/mL), whereas only one of seven occasional smokers was positive (0.5ng/mL). OF THCCOOH concentrations showed large differences between chronic frequent and occasional smokers at all time points: Results showed 83% of all specimens from occasional smokers were negative (all medians equal to 0) and 95% of OF specimens from chronic frequent smokers were positive. For both groups, CBD and CBN concentrations were maximal 0.5 hr after smoking, decreasing rapidly over time. The last positive OF CBD occurred 10.5 hr after smoking in two chronic frequent smokers (0.5 – 0.6ng/mL) and at 6 hr for one occasional smoker. For CBN, four chronic frequent and one occasional smokers' OF were still positive at 13.5 hr (0.6 – 1 and 0.6ng/mL, respectively). 11-OH-THC was not present in OF except when THC concentrations were greater than 1,000ng/mL.

At a cutoff concentration of 2ng/mL THC, proposed by the Substance Abuse and Mental Health Services Administration, 72% and 71% of chronic frequent and occasional smokers were positive for 21 hr and 10.5 hr, respectively.

These findings improve interpretation of cannabinoid OF concentrations in the workplace, cannabis dependence treatment, motor vehicle accidents, and doping in sports cases.

**Reference:**

1. Lee D, Schwope DM, Milman G, Barnes AJ, Gorelick DA, Huestis MA. Cannabinoid disposition in oral fluid after controlled smoked cannabis. Clin Chem. 2012;58:748-56.

**Oral Fluid, Tetrahydrocannabinol, Cannabinoids**

 ** Presenting Author*