Department of Health and Human Services (HHS)
Substance Abuse and Mental Health Services Administration (SAMHSA)

Drug Testing Advisory Board

March 20, 2018
Minutes Summary – Open Session

SAMHSA's Drug Testing Advisory Board (DTAB) convened on March 20, 2018.

In accordance with the provisions of Public Law 92-463, the meeting was open to the public from 10:00 a.m. to 1:00 p.m.

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Board Members in Attendance

CAPT Sean J. Belouin, Designated Federal Official
Mr. Ronald R. Flegel, Board Chair
Ms. D. Faye Caldwell
Mr. Randall Clouette
Dr. Jennifer A. Collins
Dr. James L. Ferguson
Dr. David Green
Mr. Paul Harris
Mr. Tony Iannone
Ms. Patrice Kelly
Dr. Courtney Lias
Ms. Madeline A. Montgomery
Dr. Christine M. Moore
Dr. Buddha D. Paul
Dr. Michael Schaffer

Call to Order
CAPT Sean J. Belouin (DFO), DTAB, SAMHSA

CAPT Sean J. Belouin, the Designated Federal Official of SAMHSA's Drug Testing Advisory Board (DTAB) called the meeting to order at 10:00 a.m.

CAPT Belouin welcomed the Board members, Division of Workplace Programs (DWP) staff, federal partners (Department of Transportation – DOT, Department of Defense – DoD, Office of General Counsel – OGC, Nuclear Regulatory Commission - NRC, and the Office of National Drug Control Policy – ONDCP), contractors, invited guests, and members of the public. CAPT Belouin stated that the morning session was an open meeting with presentations from the Division of Workplace Program staff and from personnel at RTI International. Topics would include information about the synthetic opioid implementation, a review of the marijuana vaping studies, and a brief update on the Medical Review Officer Guidance Manual (and 2018 MRO Case Studies). The closed session would address the proposed Mandatory Guidelines for Federal Workplace Drug Testing programs for oral fluid.

CAPT Belouin announced that public comment was on the agenda, which was announced prior to the meeting. The remaining sessions of the two-day meeting would be closed. The closed session would address the proposed Mandatory Guidelines for Federal Workplace Drug Testing Programs for oral fluid. Only board members and invited guests may participate in the closed session. All information from the open session would be posted on the DTAB web site, including public comments.

CAPT Belouin invited Mr. Ron Flegel. Director of the Division of Workplace Programs and Chair of DTAB, to make opening remarks.

Welcome and Introductory Remarks, Ron Flegel, Chairman, Drug Testing Advisory Board

Ron Flegel, B.S., MT(ASCAP), M.S., Director of DWP and DTAB Chair, added his welcome to DTAB members, ex officio members, industry representatives and members of the public, expressing his appreciation for their contribution of time and expertise. He expressed his appreciation to those attending via teleconference and those attending in person, noting the uncertain weather conditions. He stated that there would be an update on the progress of the implementation of the Mandatory Guidelines for urine effective October 1, 2017. The proposed final oral fluid Mandatory Guidelines and the progress DWP is making on the hair Mandatory Guidelines will also be covered. Program initiatives will be briefly discussed, as will programmatic information collected by the HHS-certified laboratories, through RTI International, and federal agency updates.

There are several presentations from federal agencies about available testing data from the implementation of the urine Mandatory Guidelines, and on studies completed regarding marijuana. As mandated by public law, the Division of Workplace Programs develops and revises the Mandatory Guidelines for Federal Workplace Drug Testing reflecting the best available technology. DTAB was created to utilize experts in the drug testing fields of biochemistry, toxicology, laboratory operations, and alternative specimens, along with donor advocates to advise the Assistant Secretary for Mental Health and Substance Use on the development and revision of the Mandatory Guidelines. SAMSHA continues to pursue the improvement of quality of services for forensic workplace drug testing, regulated testing, and the private sector testing by assessing the science and technology used in drug analysis, and by improving the quality of related laboratory services and systems for drug testing, and to set standards for laboratory certification for federal workplace drug testing programs, which help guide national policy.

The SAMHSA DTAB provides advice to the Assistance Secretary for Mental Health and Substance Use based on the ongoing review of the direction, scope, balance and emphasis of the agency's drug testing activities and the drug testing lab certification program. The revised Mandatory Guidelines for Federal Workplace Drug Testing for urine had an effective date of October 1, 2017 for implementation. The tests have been going on for about six months. The major

changes in the urine Mandatory Guidelines were the inclusion of the semi-synthetic opioids, which includes oxycodone, oxymorphone, hydrocodone and hydromorphone, and increasing the lower cutoff range for indicating adulteration.

DWP continues to streamline the Annual Survey Report and has adjusted the annual reporting period for 2017 to early to mid-2018. The proposed oral fluid Mandatory Guidelines are under final review and will facilitate use of an alternative specimen. The guidelines will also serve to develop standards for laboratories, private employer testing and public-sector testing, and set standards for state agencies and law enforcement. DWP staff and the MRO working group have updated the Medical Review Officer Guidance Manual, and the review of the workplace prescription drug testing provisions were posted on the DWP web site last October. The MRO Guidance Manual and the MRO Case Studies will be posted in April. DWP continues to work with HHS-certified labs that are implementing the current 2017 Federal Custody and Control form (CCF). The 2014 CCF expires June 1, 2018. The newly approved CCF, which includes the semi-synthetic opioids, is now in use. DWP continues to focus on special projects, complete the extensive studies already undertaken through the National Laboratories Certification Program, the Behavioral Pharmacology Research Unit at John Hopkins School of Medicine, and with several subject matter experts in the field.

Finally, DWP's Prevention of Prescription Drugs in the Workplace Initiative is developing a new toolkit called "Substance Use Emerging Issues in the Workplace." It will be an online federal and non-federal prevention kit addressing opioid misuse and other emerging substance use issues. It should be available by September 2018. Mr. Flegel expressed appreciation for the interest in his presentation.

Division of Workplace Programs Overview, Ron Flegel

Mr. Flegel commented that in the Drug-Free Workplace Programs there are four areas that impinge on the individual employer. Each area has challenges – federal laws, state laws, testing issues related to cannabidiol (CBD) oil as a pain reliever, and contract/legal issues. DWP objectives and goals involve the present implementation of the revised urine Mandatory Guidelines on October 1, 2017, an ongoing process of final approval for oral fluid as an alternative specimen in Federal Workplace Drug Testing Programs; the current monitoring of semi-synthetic opioid testing in the regulated programs (hydrocodone, oxycodone, hydromorphone, oxymorphone); and the future goal of completing the proposed Mandatory Guidelines for hair.

Regarding the revised Urine Mandatory Guidelines, the changes were announced in the Federal Register published on January 23, 2017 (82 FR 7920, pp 7920-7970), and implemented on October 1, 2017. The revisions included the following changes:

- Added oxycodone, oxymorphone, hydrocodone, and hydromorphone;
- Removed MDEA;
- Added MDA as an initial testing analyte;
- Raised the lower pH cutoff level for adulterated specs [3 → 4].

The HHS certified labs met the October 1, 2017 effective date for providing qualifying performance testing samples, an accomplishment appreciated by the DWP. The Division is working with the Federal Agency Drug Program Coordinators who oversee the agencies Drug Free Workplace Programs, a requirement of the Mandatory Guidelines for testing of opioids. The HHS Secretary's priority has continued to be the opioid crisis, which is regularly mentioned in news media. Testing for synthetic opioids helps deter the illicit use of prescription opioids and supports treatment for employees in federal agencies. Finally, the new CCF is in effect for federal agencies. Use of the previous (2014) CCF has been extended to June 1, 2018, after which it cannot be used.

The oral fluid Mandatory Guidelines are progressing, and articles published in peer-reviewed journals are added to the DWP website. Mr. Flegel especially thanked Dr. Ed Cone and Dr. Ryan Vandrey for their work in developing the papers. When the Guidelines get through the federal review process, including the various federal agencies and OMB,

there will be a notice published in the Federal Register, hopefully in 2018. The inclusion of testing oral fluid as a new matrix will be the first since 1986. The synthetic opioids will be included in the matrix. The MRO Guidance Manual has been updated reflecting revisions to the urine Mandatory Guidelines.

Final studies and data collection for marijuana analytes are under review. There is no single immunoassay that detects both THC and THCA. The one commercial immunoassay (the ELISA) has significant cross reactivity with THC. Testing for THC is important for other purposes, including driving under the influence of drugs (DUID).

DWP staff is drafting proposed hair guidelines, and there is ongoing research on unique metabolites. DTAB recommended hair testing as an alternative, which is important for an effective testing program. For hair testing and the development of Hair Mandatory Guidelines, DTAB also recommended addressing decontamination of hair specimens and the impact of hair color. SAMHSA is continuing to develop the proposed Hair Mandatory Guidelines for Federal Workplace Drug Testing.

There are challenges: Implementing the Oral Fluid Mandatory Guidelines; reviewing the technical and scientific studies to support hair decontamination procedures and/or unique biomarkers/metabolites to rule out external contamination; and addressing emerging issues related to marijuana, opioids, synthetic drugs, legislation and state laws that are continually changing. However, there are also opportunities. Implementing the revised Urine Mandatory Guidelines expanded testing to include the semi-synthetic opioids and provide oversight and standardization of semi-synthetic opioids drug testing. That helps deter the illegal use of drugs and prescription opioids in the federal program, which would hopefully affect private employers. And implementing oral fluid drug testing as an alternative specimen should decrease the number of substituted and adulterated specimens and give the federal agencies a non-invasive alternative to urine testing.

Mr. Flegel described the 17 steps to achieve final approval of the Mandatory Guidelines and final announcement in the Federal Register and noted that a presentation on the updating of the MRO Guidance Manual is on the agenda for later in the program. He mentioned several ongoing studies, one on cannabidiols that should begin in June; a study of pharmacokinetics and pharmacodynamics of oral, smoked, and vaporized cannabis; and an effort to gather data on opioids for the Mandatory Guidelines (pH changes, invalid results, and substitutions). From driving under the influence of drugs testing, DWP has developed standards for oral fluid in federal workplace drug testing that may be helpful by other programs including law enforcement. Finally, marijuana continues to be an emerging issue (the passive inhalation study, the cannabis brownie/edibles study, and the cannabis vaping studies).

Agency Summary of Synthetic Opioid Testing Implementation, Paul Harris, U.S. Nuclear Regulatory Commission.

Mr. Harris expressed appreciation for the opportunity to make the presentation. He introduced Silas Kennedy, Chief, Fuel Cycle and Transportation Security Branch, who stated that the regulatory oversight and policy development for the Fitness for Duty Program (FDP) was the responsibility of his branch. That program includes drug and alcohol testing in the country's nuclear power plants. Mr. Harris commented that the branch has worked with the DTAB since 2015 and shortly thereafter, was made an ex-officio member. The DTAB has added four opioids to the testing panel, published draft oral fluid Mandatory Guidelines, and published a revision of the MRO Guidance Manual. DTAB continues to develop guidelines for the use of hair as a testing matrix, which would contribute to deterrence and expand the window for illegal drugs. DTAB also defined the justification for support for 10 CFR Part 26 drug testing requirements that are implemented in the nation's commercial nuclear power plants. Mr. Harris stated that he looks forward to many years of working with DTAB to assure public health and safety.

Mr. Harris stated that the NRC has about 3,000 staff located in Rockville, Maryland and provides oversight of the commercial nuclear industry. Drug testing is one of the important elements that assure that workers in the industry facilities can accomplish their work safely and competently. Brian Zaleski, a fitness for duty (FFD) expert at NRC,

discussed the defense in depth approach that is employed to assure safety. Because the rulemaking process can be lengthy, the NRC is considering additional methods to provide a level of assurance of safe facility operations, which is called, *Defense In Depth*. Joint testing is one element, coupled with behavioral observations.

Mr. Zaleski explained that his presentation would cover NRC's operating experience in 2017. He noted that the NRC has not implemented the 2017 HHS Guidelines, so the semi-synthetic opiates are not yet on the test panel. The reporting period for test results closed at the end of February and those results have not gone through quality assurance. The results presented are therefore preliminary. The Fitness for Duty program is more than just drug and alcohol testing. It collects data on every individual who tests positive and who works in an area where drugs and alcohol could negatively affect safety. The HHS-certified laboratories are required to report within 30 days, any event related to an unsatisfactory report.

The FFD program, in addition to drug and alcohol testing, includes an access authorization component (background investigations, psychological evaluations, credit reports). The latter is important in assuring reliability and trustworthiness of licensees. There is also a fatigue monitoring element, similar to the Federal Aviation Administration's pilot regulations that limit the number of hours in a specified period that an individual may work. Finally, there is a behavior observation protocol that requires individuals who work within NRC facilities to evaluate fellow workers and to identify impairment and report credible information that could affect behavior (there is training for that observational skill). The FFD program is a broader surveillance program than most drug/alcohol testing programs, even covering substances not specified in the various testing panels.

The broad objectives of the FFD program are to provide reasonable assurance that nuclear power plant personnel are trustworthy, reliable, and not under the influence of any substance, legal or illegal, or mentally or physically impaired from any cause, which in any way could adversely affect their ability to safely and competently perform assigned duties or be afforded unescorted access to the protected areas of nuclear power plants, sensitive information, or strategic special nuclear material. It applies to anyone who has unescorted access to the protected areas.

There are seven elements to Defense In Depth:

- Access authorization;
- Varied testing protocols - pre-access, random, for-cause, post-event, follow-up;
- Customized testing by individual licensee who may, for example, permit lower cutoff levels, enforced time-dependent blood alcohol concentration when dilution is suspected, and the ability to test for additional substances;
- Behavior observation on and offsite;
- Graduated sanctions (denial of employment) related to repeated violations;
- Annual refresher training;
- Specific reportimg requirements from 24-hour reports to 30-day reports, depending on the severity of the violation.

Mr. Zaleski reported the overall industry performance statistics for 2017, which were like the prior year. The NRC tested 148,357 individuals for drugs and alcohol. Of those, 1,143 tested positive or refused a test (64% at pre-access testing and 23% at random testing). The industry overall positive rate was 0.77%, broken down into 0.24% licensee employee and 1.01% contractor/vendor. Historically, positive licensee employees are typically less than 25% of the positives, and even less than the random positives.

Comparing test results over time, Mr. Zalesky pointed out that marijuana is the most prevalent positive drug (about 50%), followed by alcohol (about 22%). Detection of cocaine peaked in 2006 around 30%, then dropped significantly through 2013 to about 15%. Amphetamines and cocaine have had similar positive rates since 2013. In 2017, comparing licensee employees and contractors/vendors, the largest difference is alcohol positives among licensee

employees (35%) and contractors/vendors (16%). The gap is mainly because 19% of the latter refused a test, while less than 3% of the former refused a test. An important consideration is that refusal to take a test results in permanent dismissal for licensee employees, which is not the case for contractors/vendors. Finally, positives for marijuana, amphetamines and cocaine were similar in both groups.

Regarding allowing testing of additional drugs, a licensee may take local drug use customs and practices into account in testing for additional drugs; and a licensee may test for any substance an individual is suspected of having abused when performing follow-up, for-cause, and post-event tests. A few facilities each year conduct testing for one or more additional substances when ordered by the MRO. Positives in additional substance tests are rare, usually less than ten per year, and the predominant test that reveals positives for additional substances is the for-cause test. Although not yet in the NRC panel, 25% of the individuals tested for additional substances tested positive for the new semi-synthetic opiates, indicating some use of the drugs in the NRC workforce. Finally, most of those testing positives for the additional substances, also tested positive for a drug in the NRC test panel.

Mr. Zaleski stated that a large number of NRC employees and contractor/vendor individuals have been shown to have attempted to subvert the testing process, identified mainly with out-of-temperature specimens. First identified in 2012, it has been increasing slowly since, from 16% in 2012 to 26% in 2017. When alcohol positives are removed from the denominator (because virtually no one tries to subvert an alcohol test) the subversion percentage increases to about 30%.

Mr. Zaleski described five reports received in 2017. In general, there appears to be an increasing number of human performance errors in the labs compared to formulation issues with blind specimens. There is only one blind performance test sample supplier in the industry, an HHS-certified lab that creates the specimens. Specimen quality has improved thereby reducing poor formulations. The five reports involved:

- Specimen validity tests not performed on two donor specimens. The laboratory determined the data entry operator entered the incorrect testing profile;
- Two BPTS formulated to return "substituted" validity test results were reported as negative. Aliquoting is normally an automated process, manual aliquoting was performed for these specimens, which was deemed to be human error in the manual aliquoting step;
- BPTS formulated to test positive for marijuana was reported as negative. The laboratory determined that the THC screening reagent for one of the initial testing instruments was improperly prepared. The testing supervisor had directed staff to discard the reagent, but staff inadvertently missed the supervisor's direction;
- The confirmation assay was not interpreted accurately by the Certifying Scientist and should have been set up for re-extraction;
- A BPTS formulated to test positive for amphetamine and methamphetamine was reported as positive only for amphetamine. The scientist conducting the testing had failed to enter the data into the necessary computer reporting field for methamphetamine, which prevented the result from being recorded as positive.

Agency Summary of Synthetic Opioid Testing Implementation, COL Thomas Martin, Department of Defense

COL Martin stated that in the DoD's mission with regard to the Drug Demand Reduction Program (DDRP), is to maintain operational readiness, safety and security for the total force – active duty personnel, National Guard Reserve and the civilian workforce. The majority of the military service members are from the 18-25-year-old male population, the age group that scores about 20% of the drug abuse in the general population. The DoD Institute of Drug Testing in the

Vietnam era determined that about 5% of returning service members were returning with a heroin addiction. Then it was a treatment rehabilitation program. In 1981, the USS Nimitz aviation accident resulted in 14 killed, 48 injured, and loss or damage involving 18 aircraft. Of the deceased, six had measurable levels of marijuana on autopsy, and testing on the aircraft carrier revealed that half of the men on board had detectable levels of marijuana. Subsequently, changes were made such that the program became more punitive. There were significant penalties for testing positive, including court martial. In the past 15 years, there has been a significant increase in misuse or abuse of prescription pain medications. In 1984, the Department issued DoD Directive 1010.1 that formally defined forensic drug testing requirements and responsibilities for testing, and in 1986 an executive order expanded testing to DoD civilian employees.

The DDRP collects specimens for testing, conducts testing, maintains a prevention and outreach program, and maintains a joint service collaboration that includes centralized instrument procurement, military entrance processing (MEPS) drug testing for new recruits, and drug surveillance and testing methodology program at the Armed Forces Medical Examiners System at Dover Air Force Base. There are now 5 drug testing libraries. COL Martin shared the DoD opiate/opioid cutoff concentrations for the initial screening (by immunoassay) and the confirmation cutoffs assessed by lab analysis. For synthetic opioids, oxycodone and oxymorphone were added to the testing panel in 2006 (testing 25% of all samples), followed by synthetic opioids and benzodiazepines in 2010, and hydrocodone and hydromorphone in 2012, (testing 40% of samples). In 2013, testing was expanded to 100% testing for all opioids (codeine, morphine, hydrocodone, hydromorphone, oxycodone, oxymorphone).

With the 100% testing coverage, the program faced a potentially huge increase in the confirmation workload, which was mitigated by installing an electronic review, an automated MRO process by which valid prescriptions were tracked in a database against which positive tests could be electronically compared. The impact, for example, eliminated 80% of oxycodone positive tests (about 12,500 tests that did not have to be confirmed). There were similar, but less dramatic reductions in other drugs. The distribution of drugs that resulted in positive tests revealed that marijuana was the most prevalent (73%), followed by cocaine (15%) and opiates (12%). When the program was begun, a significant number of personnel tested positive, but since then the numbers have decreased significantly. One example is heroin, which peaked in 2013 with 197 individuals testing positive, and dropped each year thereafter until, in 2018, only 43 tested positive. The reasons for the drop include deterrence imposed by testing, and importantly, an improvement in policies and procedures governing prescriptions.

With the introduction of synthetic opioid testing, MRO review has become more complicated. MROs need to be aware of metabolism pathways and ratios. The number of claims of innocent or accidental ingestion increased, and there was evidence of empathy as a decision factor in sharing prescription opioids. A significant challenge that has not been resolved is the definition of illicit or unauthorized use. It could involve use of a prescription for a different medical condition; use of a different dose than prescribed; using another person's prescription; use after expiration date (attempts within DoD to implement expiration dates had been unsuccessful). Today, DoD is only enforcing one finding: use of another person's prescription.

In conclusion, COL Martin mentioned four issues:

- Random urinalysis testing appears to be an effective deterrent to opioid drug abuse in concert with medical and education and outreach programs;
- Prevalence of opioids can result in large increases in workload, most of which is legitimate use;
- MRO review is more complicated and requires additional training, oversight, and quality assurance;
- Legal limits on possession and use of prescription drugs needed.

RTI Research #1, Marquita Brogdon, RTI

Ms. Brogdon stated that the Mandatory Guidelines for Federal Workplace Drug Testing Programs for Urine were published in the Federal Register on January 23, 2017, to be effective on October 1, 2017. The revised Mandatory

Guidelines allow federal agencies to test for additional Schedule II drugs specified in the Controlled Substances Act – oxycodone, oxymorphone, hydrocodone and hydromorphone. The Guidelines also removed MDEA from the drug testing profile and added MDA as an initial test analyte and raised the lower pH cutoff from 3 to 4 for identifying specimens as adulterated. The revision required MRO requalification training and re-examination at least every five years after initial MRO certification. The revision also revised pH cutoff for federal agency specimens and DOT-regulated specimens; discontinued testing federal agency specimens for MDEA, but did not affect continued testing of DOT-regulated specimens for MDEA. Also, the revision delayed until further notice, testing of federal agency specimens for the added opioids until the effective date specified by the federal agency, as was testing of DOT-regulated industry specimens for the added opioids.

Implementation of the revisions could be delayed by certain agencies unable to meet the October 1, 2017 effective date. SAMHSA directed agencies to notify their service providers of the date drugs could be submitted for testing. On January 1, 2018, DOT notified its service providers of implementation of testing of semi-synthetic opioids and removal of MDEA from its drug testing panel. Non-negative drug test results (not MRO certified) for reported drug positives, adulterated, substituted and/or invalid, revealed that the number of these tests has remained consistent month-by-month for the last few years. However, the trend departed from the typical path in October 2017 when the number of non-negative results for 2014 through 2016 declined significantly from the historical trend but held relatively steady in 2017. In part, this happened with the addition of the semi-synthetic opioids. That gap widened in January and February of 2018.

Since implementation of the revised drug testing panel on October 1, 2017, positivity rates for hydrocodone, hydromorphone, oxycodone and hydrocodone were slightly less than the positivity rates for THCA and amphetamines. Since some agencies were not prepared to implement the drug testing panel on October 1, the numbers are not necessarily representative of all federal testing pool agencies. With regard to adulteration of specimens, the revision raised the pH cutoff to 4.0 from 3.0, which now defines the adulterated threshold. Prior to the change, specimens in the 3.0-4.0 range would have been reported as invalid. Now they are reported as adulterated, resulting in an increase in adulterated specimens reported to about 25%.

In conclusion, Ms. Brogdon commented that there is evidence that the change in the pH cutoff resulted in detection of more donors trying to subvert the drug test, but the effect of adding the semi-synthetic opioids has not been determined. During discussion, Dr. Collins observed that the impact of the pH change does not, to her, seem significant. Mr. Flegel responded that urine sample manufacturers should be able to quickly change the pH of specimens. There was a significant peak of low pH reports in December followed by a rapid and dramatic decline to a level lower than any reported since January 2016. It could be overcompensation to what is being entered into the program and it implies that substitution/adulteration products must be closely monitored in all programs.

RTI Research #2, Vaping Study, Dr. Ed Cone and Ryan Vandrey

Dr. Cone stated that vaping began a little more than a decade ago, and the technology of vaping has advanced to the point where it is in its fourth generation. Vaping has been applied to nicotine for some time, and the technology was promptly adopted by cannabis users. Vaping is considered by users as a safer alternative to smoking (combusting plant material). Toxins are significantly reduced by 95% by vaping. About 40% of cannabis users in Colorado are vaping exclusively. There are a wide variety of devices to facilitate ingestion of vaping products. They are portable or tabletop, can be used with cannabis as a plant material or extracts and oils. The devices can be used in public to hide the fact that a marijuana product is being used.

The study looked at vaping compared to smoking, since most of the literature is focused on the combustion process. It was a crossover study that recruited infrequent users (former drug users who were enrolled in a drug-free condition), healthy adults about equally divided between male and female (11 white, 3 black and 3 “other”), in their mid-twenties with a mean body weight of 26. The study consisted of six 8-hour sessions. Each subject inhaled vapor from zero, 10 and 25 milligrams equivalent of plant material that was vaped. They smoked the same amount as a cigarette.

There were three consecutive sessions, with random dose order within each route. Blood, oral fluid, urine and several pharmacodynamic measures were collected. NIDA provided the cannabis, 13% THC, 0.1% cannabidiol, 0.8% cannabinol. Specimens were analyzed by LC/MS. Limit of quantitation (LOQ) levels were 0.05 in blood and 1.0 in THC and 0.02 in carboxy acid. The assays were done in two ways, a liquid/liquid and a solid phase extraction. Although patterns of absorption were similar, vaped was more efficient than smoked. In oral fluid, the THC was also similar probably because vapors enter through the mouth with THC being laid down in the oral cavity and being absorbed or leached out. Carboxy acid appeared erratically a few times (over half of the subjects produced no detectable carboxy acid). CBN was present in fairly high levels (around 50 ng/ml), and CBD in much lower concentrations.

In summary, vaping is efficient and a fairly good way to obtain a relatively pure stream of vaporized THC without the toxin present in combustible products. Oral fluid concentrations were similar between vaping and smoking.

Dr. Vandrey discussed pharmacodynamic characteristics, showing comparisons of smoked and vaporized drug and their effect on several tasks using a visual analog scale. The drug effect of 10 micrograms of THC vaporized is about double the effect of vaporized, both peaking at about 1.6 hours and degrading steadily to baseline in eight hours. At 25 micrograms there is little difference in the drug effect peak, also at 1.6 hours. Heart rate also peaks in about 1.6 hours, with vaporized THC about twice the pulse rate of smoked THC, both returning to baseline in about two hours. In an assessment of a serial performance task that involves working memory and executive function there was little effect at the 10 microgram THC dose, but an immediate significant decline of function when 25 mcg was administered (with return to baseline after about 6 hours). The digit symbol substitution task resulted in a statistically significant degradation of performance with vaporization at both dose levels that lasted about two hours, followed by return to baseline in 3-5 hours. Finally, in the divided attention task (responding to two stimuli simultaneously), there was a greater negative performance with vaporization at both dose levels, a nominal change with smoking at 10 mcg and a slightly larger change at 25 mcg, but there was also a greater placebo effect.

Dr. Vandrey noted that, for both vaporized and smoked THC at the 25 mcg dose, blood THC peaked in 15-20 minutes but returned to baseline in less than two hours. However, the drug effect showed the same rapid peak, but a much slower return to baseline over the course of about six hours. Vaporized slightly exceeded smoked in both circumstances. When overlapping data from an oral versus smoked test, the blood THC did not show the dramatic peak, but did reveal a significant increase in drug effect after an hour that continued to eight hours before returning to baseline. In addition, there were higher ratings of adverse effects following vaporization – paranoia, dry mouth, red/irritated eyes, two cases of nausea indicating the 25-mcg dose was a very intoxicating dose, and one instance of hallucinations. All resolved within two hours, none required intervention. Additional studies are contemplated with other variables -- different doses, different types of cannabis, other routes of administration, etc.

In summary, Dr. Vandrey explained that vaporization appears to be a more efficient method of delivery (greater blood THC and subjective drug effects); that there are differences in the time course across assessments (blood THC and HR shorter than subjective DE and cognitive effects); correlations between pharmacokinetic and pharmacodynamic that appear to be modest at best; with THC in blood and oral fluid returning to zero within 4 hours of exposure.

During discussion, there was an observation that administration of oils could be significantly more potent. Secondly, vaping oils produces very little detectable odor of marijuana. Dr. Vandrey agreed that THC levels in concentrates (like shatter and wax) are very high, but the user typically is exposed to much smaller amounts than raw plant materials. Also, when THC is extracted from raw plant material, it is not clear what other chemicals are extracted that could lead to pharmacokinetic or pharmacodynamic differences. He added that a visible vapor does appear from vaping, and in some cases a noticeable odor.

MRO Guidance Manual and 2018 MRO Case Studies Update, CAPT Sean J. Belouin

CAPT Belouin reported that the federal Mandatory Guidelines for urine were issued on January 23, 2017 and implemented on October 1, 2017. The Guidelines are continually monitored to add appropriate revisions and clarifications. The planned posting of the updates to the MRO Guidance Manual is April on the workplace.samhsa.gov website. As discussed earlier, four new prescription drugs have been added – oxycodone, oxymorphone, hydrocodone and hydromorphone. Hydrocodone products have been rescheduled to Schedule II effective October 6, 2014. CAPT Belouin displayed an extensive list of brand names for all four compounds.

The screening and confirmation cutoffs for the drugs plus MDMA/MDA are: hydrocodone 300/100, hydromorphone 300/100, oxycodone 100/100, oxymorphone 100/100, and MDMA/MDA 500/250. MDEA was deleted because it rarely tested positive. For a positive drug test result the specimen immunoassay result must be at or above the initial cutoff and the confirmatory test result (separate aliquot) must be at or above the confirmatory cutoff. Also mentioned before, the pH must be less than four to be reported as adulterated. A reported invalid specimen is one that has a pH greater or equal to 4.0 but less than 4.5. The addition of prescription opioids increases potential number of positive federally-regulated tests, involves MROs more proactively in addressing the "opioid dependency crisis;" and highlights potential issues of workplace safety in federal agencies.

Some of the revisions to the MRO Guidance Manual will include greater guidance in determining a legitimate medical explanation for a positive drug test, including the presumed definition of the length of time a prescription is valid. The MRO would also be able to determine if a positive test was the result of a legal administration of a drug, e.g., a pain medication administered by a hospital pharmacy following a medical procedure. In Section 6.3, concerning occupational and public safety, the MRO Guidance Manual does not require an MRO to determine whether a valid prescription can be used safely while performing work-related functions. Before an MRO discusses safety related to a valid prescription (legal drug use), the MRO should refer to any service agreement that may exist with a federal agency.

The 2018 MRO Case Studies have been completed. There are 32, covering a wide range of issues. They supplement the HHS MRO Guidance Manual. It should be remembered that the MRO Guidance Manual and 2018 MRO Case Studies do not apply to the DOT or NRC procedures. SAMHSA's program is a deterrent program, not a Fitness for Duty program. CAPT Belouin reiterated that the HHS MRO Guidance Manual and the 2018 MRO Case Studies should be posted on the website in April.

During the presentation, Dr. Schaffer submitted a question about the cannabis user population in the studies versus the population of daily users. In addition, can the study data be extrapolated to the latter, larger population. Finally, since the carboxy levels were inconsistent and rarely present in the study population, would that be significant when multiple doses are administered over long periods of time, and which population is more significant in determining the true drug user population, especially in a fitness-for-duty situation where impairment may be more relevant? Dr. Cone stated that these are two populations in very general terms. However, he added his opinion that the frequent user population is not most representative of the federal workplace program. Individuals would probably not test negative with that use pattern. For frequent users, the accumulation of carboxy acid will persist in urine and in oral fluid. The study data is not readily extrapolated. Dr. Vandrey agreed that in the federal environment, the infrequent user is most relevant, which was the rationale for their selection as study subjects. There are complicating factors from a regulatory standpoint because separate cutoffs, based on frequency of use, are not feasible.

Adjournment

CAPT Belouin determined that there were no members of the public who requested an opportunity to make a public comment. He declared the open session adjourned.