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Hair Testing for Illicit Drugs
Do the Advantages of this Matrix Outweigh the Disadvantages?

By Kendra L. Palmer, MD, and Matthew D. Krasowski, MD, PhD

Hair has been used as a matrix for toxicology testing in various forms since the mid-1800s. For more than 100 years, testing was primarily limited to the detection of heavy metals. Advances in detection methods such as chromatography and mass spectrometry have allowed for the identification of many drugs and their metabolites.

Hair testing for drugs of abuse is common practice in forensic toxicology laboratories. Recently, the use of hair testing has increased in the clinical setting to detect therapeutic drugs and ethanol metabolites. Hair has several properties that make it a good alternative or complementary matrix to specimens such as urine or blood. These same properties can also present challenges during sample analysis and result interpretation.

Hair Anatomy and Physiology

Understanding the anatomy and physiology of hair is essential for the proper interpretation of hair toxicology results. Human hair originates from a follicle and is composed of a root and shaft (Figure 1). The follicle is embedded in the epidermis and contains the root, the portion of hair beneath the surface of the skin. Sebaceous glands secrete directly into the follicle, and sweat glands secrete to the skin surface near the follicle. Each follicle is closely associated with a vascular network that supplies nutrients and hormones.

As the hair grows beyond the surface of the skin, it forms the hair shaft, which is composed of an inner cortex and an outer cuticle. The cortex is made of cells tightly packed with alpha-keratin chains. Cortical cells also contain melanin, a pigment responsible for hair pigmentation, which is produced by melanocytes

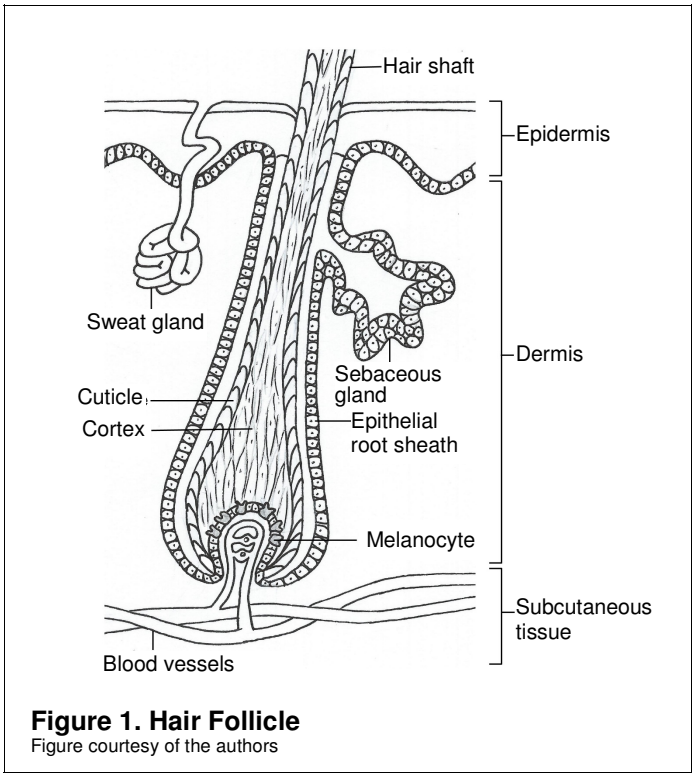

Figure 1. Hair Follicle
Figure courtesy of the authors

in the basal layer of the cortex, deep within the follicle (1).

The cuticle is a protective layer of epithelial cells that surrounds the cortex. The cuticle can degenerate toward the tip of the hair strand, leaving the cortex unprotected.

Each hair follicle independently cycles through three stages: anagen, catagen, and telogen. The duration of each stage varies depending on hair type, age,

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Hair Testing

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nutritional status, and season (2). The anagen phase, which typically lasts two to six years, is marked by increased metabolic activity resulting in hair growth. At any given time, about 85% of scalp hairs are in the anagen phase. On average, hair grows at a rate of one centimeter per month with a range of 0.6 to 3.4 cm (excluding young children, who have more variable growth rates). It takes seven to 10 days for growing hair to reach the surface of the scalp.

Hair growth stops at the beginning of the catagen phase, a short transitional stage lasting only a few days, when the root keratinizes and moves toward the epidermal surface. During the telogen phase, which lasts three to four months, the hair is shed. The follicle then re-enters the anagen phase.

Mechanisms of Incorporation and Detection

The mechanisms of drug incorporation into hair are not completely understood; however, it is thought to occur during the anagen phase (2). Drugs can reach the follicle through multiple routes, including the blood supplying its base. Other potential sources include sweat and sebum. It has also been proposed that hair can incorporate substances deposited from environmental contamination.

Melanin is one of several proposed drug-binding sites (2,3). If melanin is in fact involved in drug-binding, it would be a potential source of variability in test results because darker hair contains more melanin and therefore more sites for drug binding. Some factors that can affect drug binding include the drug's molecular size and structure, pH, and lipid solubility, as well as the ratio of ionized to non-ionized drug.

Testing Protocols

Hair toxicology testing protocols vary among laboratories but are generally similar (2,4). Most include the same basic steps of sample washing, homogenization, and extraction.

Washing removes substances, such as hair care products, that could interfere with extraction or analysis. It also removes potential environmental contaminants. Washing protocols vary, but ideally include the use of non-protic solvents, such as dichloromethane or acetone, which do not result in drug extraction (5). Protic solvents, such as methanol, can cause swelling of the hair and premature drug extraction.

Following washing, samples must be homogenized by the hair being cut into short segments or ground into a powder (although grinding does not improve extraction and may result in loss of sample). Incubation of the sample with methanol causes the hair to swell, allowing substances within the hair to be released into the solution via diffusion. The solution is then screened for specific drugs or drug classes using an enzyme-linked immunosorbent

Table 1. Assays Available in Hair Toxicology Testing

Drug Class	Example Analyte(s)
Amphetamines	Amphetamine, MDA, MDEA, MDMA, methamphetamine
Cannabinoids	Native THC, carboxy-THC
Cocaine	Benzoylecgonine, cocaethylene, cocaine, norcocaine
Dissociative anesthetics	Ketamine, norketamine, propofol glucuronide, phencyclidine
Opiates	6-Monoacetylmorphine (heroin metabolite), codeine, hydrocodone, hydromorphone, morphine, oxymorphone, oxycodone
Synthetic opioids	Normeperidine, methadone, EDDP (methadone metabolite), norfentanyl, tramadol, buprenorphine, norbuprenorphine, butorphanol, sufentanil, norsufentanil
Benzodiazepines	Alprazolam, diazepam, midazolam, nordiazepam, oxazepam, temazepam
Barbiturates	Amobarbital, butalbital, pentobarbital, phenobarbital, secobarbital
Other sedative-hypnotics	Zolpidem, zolpidem phenyl-4-carboxylic acid
Ethanol biomarker	Ethyl glucuronide

Abbreviations: MDA = methylenedioxyamphetamine; MDEA = methylenedioxyethamphetamine; MDMA = methylenedioxymethamphetamine; THC = tetrahydrocannabinol; EDDP = 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine
Source: References 2,4,6

assay (ELISA).

Positive ELISA results should be confirmed. Confirmatory testing requires a second extraction, with more extensive clean-up using either liquid-liquid or solid-phase extraction (4). Capillary gas chromatography-mass spectrometry (GC-MS) is the method used most frequently for confirmatory testing (2,5). GC-MS is highly specific for a large number of drugs and metabolites and is sensitive even at low drug concentrations. Table 1 summarizes some of the drug classes and analytes detectable in hair (2,4,6).

Environmental Exposure

Individuals may contest positive results on the claim that they did not use the drug, but their hair was contaminated by environmental exposure (5). Passive contamination can be differentiated from systemic exposure by using specific washing protocols and determining the ratio of drug concentration in the wash solution versus in the hair, although this practice is not used universally.

Analyzing the sample for drug metabolites is a better method for differentiating active from passive exposure. The detection of metabolites provides proof that a drug was in the subject's system, with the exception that some metabolites can be formed by hydrolysis. For example, the cocaine metabolites benzoylecgonine and ecgonine methyl ester can be formed by exogenous hydrolysis, whereas the metabolites norcocaine and cocaethylene (seen with simultaneous ethanol and cocaine consumption) are exclusively endogenous (5).

Advantages of Hair Testing

Different sample matrices have distinct advantages and limitations (Table 2). Hair is unique in its ability to provide historical data of drug use and exposure. Once incorporated into hair, drugs are protected from metabolism and can remain stable for months or even years. Substances slowly leach out of hair over time, but normal daily hygiene has no significant effect. Drugs can undergo some decomposition by ultraviolet radiation and bleaching (5). Once collected, hair samples can be stored for long periods without refrigeration.

Hair provides a much longer detection window than blood or urine, which have detection windows ranging from hours to weeks (7). The longer detection window is helpful when the presentation for medical services is delayed, as can occur in cases of child abuse. It allows for drug detection even following short-term abstinence, which can be especially useful in alcohol abstinence monitoring. Ethyl glucuronide, an ethanol biomarker, is present long after ethanol has been metabolized (8). In some European countries, hair analysis for drugs of abuse is a part of the procedure for obtaining a driver's license (5).

Because growing hair takes seven to 10 days to reach the surface of the scalp, there is a delay between systemic drug exposure and detection in hair. Although this time lag can limit usefulness in some circumstances, it can avoid ambiguity in certain instances. For example, medications commonly administered immediately following trauma would not be detected in hair samples collected at the time of treatment (7).

As previously mentioned, hair can also provide data on passive exposure to a drug through analysis of external contaminants and by identification of parent drugs within the hair without the appropriate metabolites. This evidence can be useful in cases of suspected child endangerment, such as a home where methamphetamine is being synthesized (7).

Limitations of Hair Testing

As with any matrix, there are limitations to hair testing. Not all individuals (especially infants and younger children) have sufficient hair for testing. In

Table 2. Advantages and Disadvantages of Urine and Hair as Testing Matrices

Specimen	Advantages	Disadvantages
Urine	Well-standardized laboratory methods	Requires special facility for collection
	Easy matrix to work with	Easy sample adulteration if specimen collection is not observed
	Point-of-care screening tests available for drugs of abuse	Collection may be invasive
	Economical	Short detection window (days to weeks)
Hair	Long detection window (weeks to years)	Recent illicit drug use not detected
	Sample difficult to adulterate	Challenging matrix to work with
	Stable sample with long storage capability	Sample may not be available
	Recent medications not detected (e.g., opioids administered during acute event)	Laboratory methods less standardized
		Environmental contamination possible
		Potential hair color bias
		Requires expert interpretation

particular, this limits the applicability for newborn drug testing, for which specimens such as meconium, urine, or umbilical cord are more commonly used. In addition, drug stability can be a concern under some conditions. Although normal hair hygiene only mildly affects stability, cosmetic treatments with bleach, dye, or perming solutions can substantially decrease drug detection (2). Bleaching has the most significant effects. Even excessive exposure to light can decrease the stability of some substances, especially cannabinoids.

As with other reservoir matrices, the time, dosage, and frequency of drug use cannot be determined. The vast number of variables surrounding drug incorporation into hair, drug stability, and rates of hair growth, simply make this impossible.

There are substantial differences between the concentration of a drug in blood and the incorporation of that drug into hair. For example, cocaine, heroin, and 6-monoacetylmorphine (a metabolite of heroin) are not commonly detected in blood samples because of their poor stability or rapid metabolism, but they are the primary analytes detected in hair after cocaine and heroin use (1).

An additional limitation to hair testing is the potential for misinterpretation of results by those who are unfamiliar with the test. The long detection window can lead to the attribution of an acute event to previous, unrelated drug use. In addition, it can take months for hair to test negative after patients begin abstaining from some drugs.

Summary

Many substances can be detected in hair, and technological advances continue to improve sensitivity and specificity. Hair testing provides a detection window much longer than that of more conventional matrices, does not require specimen refrigeration, and can provide information on environmental exposure. It also has limitations. There is still limited understanding of the mechanism of drug incorporation into growing hair and different drugs incorporate at varied rates. These and other factors make it impossible to reliably determine the drug dosage or frequency of use. A solid understanding of the testing methods and variables reduces the risk of result misinterpretation.

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Learning Objectives

After reading this article, the reader will be able to identify situations in which hair as a testing matrix offers advantages compared with conventional matrices (such as urine and blood) as well as recognize the limitations of toxicology testing using hair.

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Cannabis and Driving Risk

Legalization Brings Urgent Need For More Evidence on Effects

By Marilyn A. Huestis, PhD

To date, 23 states have legalized medical marijuana (cannabis), and four states plus the District of Columbia have legalized adult recreational cannabis use. Recent nationwide surveys indicate that cannabis use is increasing and that the perception is growing among the public that cannabis is a safe drug with few health or safety risks. There is consequently an urgent need for objective scientific data about cannabis' impact on health, development, and safety to develop evidence-based drug policies.

As states struggle to set testing limits in blood and oral fluid to define what constitutes driving under the influence of cannabis, we need to clarify the acute and chronic effects of cannabis use on driving ability. There is a great deal of data available, including epidemiological studies of motor vehicle injuries and fatalities, roadside drug prevalence data, laboratory studies assessing cannabis' effects under well-controlled conditions, data from driving simulators, and on-the-road driving studies. Such studies provide an increasingly clear picture of cannabis' impact on the ability to drive an automobile safely.

Cannabis' Effects on Performance

Δ9-Tetrahydrocannabinol (THC) is the primary psychoactive component in cannabis. Cannabis intoxication causes sedation, memory loss, attention and executive function deficits, changes in perception (including time perception), euphoria, and often anxiety and paranoia. Acute cannabis intoxication also impairs judgment, cognitive function, and psychomotor function, sometimes contributing to risk-taking, but sometimes to heightened caution during driving (1). The quality and intensity of effects vary with dose, how the drug is administered (such as smoked, vaporized, or ingested), and the user's experience with the drug.

The effects that are most directly linked to driving ability include alterations in reaction time, perception, short-term memory, motor skills, divided attention, tracking, and executive function.

Frequency of use makes a difference. In a study comparing occasional with frequent cannabis smokers given the same dose, occasional users (less than twice a week) were more impaired on psychomotor tasks (including tracking errors, hits, false alarms, and reaction time) than more frequent users (more than 4 times a week). The occasional users were also more affected on subjective and physiological measures of intoxication, suggesting that partial tolerance occurs on some parameters (2).

Frequent cannabis users build up a large THC body burden over time because the drug is highly lipophilic and is stored especially in adipose tissues. Although half of the frequent smokers had no measurable blood THC 20 hours after the cessation of smoking, in some subjects THC could be detected for 30 days. These individuals experienced significant downregulation of CB1-cannabinoid receptors in their brains, which was accompanied by impairment in psychomotor tasks up to three weeks after last use (3). Other studies showed neurocognitive deficits in frequent cannabis users persisting weeks after the start of abstinence.

Epidemiological Data

After alcohol, cannabis is the drug found most frequently in the blood of impaired drivers and those involved in motor vehicle crashes. In the National Highway Traffic Safety Administration's 2013–2014 National Roadside Survey of Alcohol and Drug Use by Drivers, for the first time, the number of drivers testing positive for cannabis exceeded those testing positive for alcohol (4). In fact, there was a 48% increase in drivers positive for THC in blood or oral fluid compared with the 2007 National Roadside Survey.

Older epidemiological studies of cannabis effects on driving often had design weaknesses. Individuals stopped for erratic driving or involved in crashes are frequently not tested for drugs if they are above the legal limit for alcohol because that finding provides sufficient evidence for a driving-under-the-influence charge. This practice contributes to a lack of data on the frequency of driving under the influence of drugs (DUID).

Since the 1970s, the incidence of drunk driving has decreased, but drugged driving has increased, creating a serious public safety problem. When tested for multiple drugs, many drivers responsible for crashes are found to have both alcohol and cannabis (or other drugs) in their systems, making it difficult to determine cannabis' contribution to crash or fatality risk. In fact, THC is present much more frequently in combination with other psychoactive compounds than alone. Furthermore, THC concentrations drop rapidly after the end of cannabis smoking, and may fall below legislative limits in the 1.5 to 4 hours generally required to collect a blood specimen in these cases.

Study Limitations

Another major limitation to previous studies is the cannabinoid marker analyzed. Because THC is

distributed rapidly from the blood into the tissues, including the brain, some studies measure 11-nor-9-carboxy-THC, the inactive metabolite, which may be present in blood or oral fluid long after the impairing effects have ended.

In addition, many studies relied on self-reporting or urine test results, which have limited reliability in differentiating whether cannabis use occurred close enough in time to result in driving under its influence. The standardized field sobriety tests included in most police and drug recognition examiner evaluations were developed specifically for alcohol, not other drugs. Tolerance and residual THC in the blood pose challenges for correlating degree of intoxication to THC concentrations in blood or oral fluid. No single THC concentration works for identifying cannabis-impaired driving for frequent and occasional smokers.

Three recent meta-analyses found significant motor vehicle crash risk estimates associated with cannabis use, with increased risk ranging from 1.3 times more likely to 2.7 more likely (5–7). A French study of the role of alcohol and other drugs in auto fatalities found that drivers with THC in their blood (but no other drugs or alcohol) were 2.3 times more likely to be culpable than those without THC or alcohol (8). A nine-country study found no significant link between THC in blood and increased risk of being seriously injured or killed in a crash, although THC-positive drivers were 1.9 times more likely to be culpable for a fatal crash (9).

A recent large study by the National Highway Traffic Safety Administration found a significantly increased crash risk attributable to cannabis that was no longer significant after controlling for drivers' age, gender, race, and presence of alcohol (10). This was the largest and best-controlled epidemiological study of substance use and cannabis crash risk conducted to date, with blood or oral fluid collected from 3,095 drivers involved in crashes and 6,190 controls matched for location, day of the week, time, and direction of travel. Its weaknesses were that it was confined to one geographical area (Virginia Beach) and it had a bias toward less severe crashes.

Cannabis Legislation in U.S. States

Comparing crash and fatality statistics before and after cannabis legalization for medical or recreational use can provide valuable data. According to Fatality Analysis Reporting System data, in Colorado, the number of drivers involved in fatal crashes who tested positive for THC increased significantly after commercialization of medical cannabis in 2009, even after controlling for age and gender, and the proportion who tested positive for alcohol did not change (11).

In Washington state, cannabis was legalized for adults over 21 in December 2012, along with a legal blood limit for DUID of 5 µg/L THC. The number of suspected impairment cases positive for THC increased significantly in 2013 (12).

A recent California study compared roadside surveys in years before and after legalization of medical cannabis. It found no increase in THC-positive drivers, but did find a significant increase in fatally injured drivers who tested positive for cannabinoids (13).

Experimental Studies

The strength of experimental studies, including laboratory studies, driving simulators, and on-the-road investigations, is that they can control conditions better than epidemiological studies. They also offer the opportunity to select THC dose, to evaluate effects over time, and to compare the effects of THC in frequent and occasional users, with and without alcohol. Numerous experimental studies document impairment in various tasks relevant to driving ability, but direct relationships with blood THC concentration have not been easy to establish. In general, the greater the THC concentration, the greater the impairment.

Common effects of cannabis on driving ability include increased reaction time and increased weaving. Neurocognitive impairments relevant to driving ability, including diminished ability to draw on information from experience, are consistent with cannabis' well-known impact on memory and learning. Frequent smokers may compensate for their impairment by driving more slowly, but decrements remain in executive function, divided attention, and the ability to manage the multiple facets of driving (1).

In a recent study using the National Advanced Driving Simulator at the University of Iowa, National Institute on Drug Abuse researchers evaluated weaving within the lane, lane departures per minute, and maximum lateral acceleration. THC significantly impaired lateral control, whereas alcohol significantly impaired all measures (14). The study included six tests in which each driver was administered a lower THC dose alone, a higher THC dose alone, each THC

Driving Performance Study Video

To view a video interview with Marilyn Huestis discussing a recent study of the effects of cannabis on driving performance using the National Advanced Driving Simulator, visit https://www.drugabuse.gov/news-events/news-releases/2015/06/effects-marijuana-without-alcohol-driving-performance

dose with low-dose alcohol, alcohol alone, and neither drug.

The results showed again that, even given a standard THC dose, smokers can titrate it—by the number of puffs they take, the length and duration of inhalation, and more—to an individual level of comfort with subjective and cardiovascular effects. About half of participants had similar peak THC concentrations after the low and high THC doses. THC significantly increased the time of peak alcohol concentration. Low-dose alcohol significantly increased peak THC concentration compared with THC alone.

Blood THC concentrations of 8.2 and 13.1 μg/L increased within-lane weaving similar to 0.05 and 0.08 g/210L breath alcohol concentrations, respectively, the most common legal alcohol limits. The average time for blood collection after a traffic incident or stop is 1.5 to 4 hours. THC concentrations drop rapidly after smoking, so concentrations at the time of the blood draw may be much lower than at the time of driving, perhaps below per se driving limits.

Cannabis and Alcohol Together

Several studies indicate that cannabis in combination with alcohol presents a greater risk than either drug alone. Alcohol more profoundly affects executive than automatic behaviors. Several controlled experiments show that alcohol and cannabis additively or synergistically reduce performance on both cognitive tasks and simulated driving tasks relative to either substance alone (1). In our recent simulator study, cannabis-alcohol effects on in-lane weaving were additive rather than synergistic, with 5 μg/L THC and 0.05 g/210L alcohol showing an effect similar to that of 0.08 g/210L alcohol alone (14).

Epidemiological data have documented that combining alcohol and cannabis increases the risk of a fatal crash compared with using either substance alone (1). A recent analysis of blood tests including both THC and alcohol in the Fatality Analysis Reporting System found that the use of THC increased the risk of fatal crashes and that combining the two increased the risk compared with using either substance alone (15). This effect was more pronounced at lower blood alcohol concentrations, and the combined risk was primarily driven by alcohol. The French study of culpability in fatal crashes found that drivers with both THC and alcohol in their blood were 14.1 times more likely to be culpable than sober drivers, compared with 9.4 for alcohol alone (8). On the other hand, the recent National Highway Traffic Safety Administration study did not find an interactive effect; the increased risk of a crash after combined ingestion of THC and alcohol was attributable to alcohol (9).

THC in Body Fluids

Cannabinoid testing is particularly important for investigating DUID. There is tremendous interest in developing a cannabis-specific roadside test and cannabis markers in biological fluids that identify recent intake and differentiate residual THC release by tissues from new cannabis intake. Oral fluid is an effective alternative matrix for cannabis testing, offering noninvasive and directly observable sample collection, which reduces the potential for adulteration, lowers biohazard risk during collection, and increases the ease of multiple sample collections. The tests also offer better identification of recent exposure and correlation with blood than urine concentrations. Roadside oral fluid testing is an important new approach to identifying DUID.

A recent review examined the pharmacokinetics of cannabinoids in oral fluid from frequent and occasional cannabis users; detection windows; correlation with other biological matrices; onsite screening technologies; confirmatory methods; drug stability; and effects of sample collection procedures, adulterants, and passive environmental exposure (16). THC concentrations in oral fluid can be greater than 1000 μg/L immediately after smoking, but within hours drop to low concentrations that mirror blood concentrations. In contrast, the inactive metabolite is present in oral fluid in 1000-fold lower concentrations. Cannabinoid concentrations are influenced by administration route, dose, and cannabis use history.

The invention of a roadside THC "breathalyzer" similar to the one used for alcohol is not likely in the near future. THC can be measured in breath for a short time after controlled smoked cannabis administration: for up to four hours in some participants, for one to two hours in most, and not at all in others (17). But the measurement requires analysis by high-sensitivity liquid chromatography–tandem mass spectrometry, so a portable roadside device is not likely to be seen for some time.

Legal Limits

On the question of a legal limit for THC in body fluids, many suggest that zero tolerance should be the standard. Mura and colleagues showed that THC is still measurable in the brain when it is no longer detectable in the blood (18), and our team showed that residual THC is associated with psychomotor impairment in frequent cannabis smokers for up to three weeks after their last intake (3). However, others believe that it is necessary to document impairment with sobriety tests, drug recognition examiner evaluations, or other objective measures to define cannabis-impaired driving.

Another approach is a two-tiered system of fi-

nancial penalties and points on a driving license for the per se limit of 1 or 2 µg/L THC in blood, and a more severe sanction for documented behavioral impairment. This approach has been used in Australia and some European Union countries for many years and been shown to deter cannabis-impaired driving.

Conclusions

A few conclusions can be drawn from the available data. Experimental studies clearly show that cannabis impairment reduces a driver's ability to safely operate an automobile. The epidemiological data are less consistent on crash risk and driver culpability, although most studies find that cannabis use significantly increases one or both.

Efforts are under way to evaluate driving data collected before and after legalization of medical or recreational cannabis. Currently in the U.S., state laws vary in the definition of THC-impaired driving, including zero tolerance (no blood THC permitted); per se concentrations of 1, 2, or 5 µg/L; or required documentation of driving impairment. The efficacy of these policies in reducing cannabis-impaired driving is not known and needs to be evaluated.

There is an urgent need to develop tools to identify drug-impaired driving at the roadside and to educate the public on the dangers of DUID. Roadside oral fluid tests are effective in Australia and Europe at deterring cannabis use and driving and are being evaluated in the U.S. On-site oral fluid tests are effective at identifying cannabis intake in occasional and frequent cannabis smokers after controlled cannabis administration. A sensitive cannabis breath test would be highly useful, but current technology cannot deliver the required sensitivity. Because no single blood THC concentration clearly identifies impairment in all cannabis users, a two-tiered system, similar to that used in Australia and Germany, may offer a reasonable approach.

Cannabis-impaired driving is a vitally important public health and safety issue. In the current environment of medical marijuana and legal cannabis use, research is critical for determining suitable evidence-based policies and testing methods to ensure the safety of drivers and passengers on America's roads.

Learning Objectives

After reading this article, the reader will be able to summarize the available data on the effects of cannabis use on driving and to describe the time course of THC in oral fluid after cannabis is smoked.

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The author has nothing to disclose.

SAMHSA Proposes Changes to Federal Drug-Test Guidelines

By Jennifer Collins, PhD

On May 15, the Substance Abuse and Mental Health Services Administration (SAMHSA) within the Department of Health and Human Services (DHHS) published two documents proposing changes to the federal workplace drug-testing guidelines. The proposed changes will affect laboratories certified under the National Laboratory Certification Program to perform workplace drug testing for federal employees and employees working in regulated industries such as transportation.

The first document proposes changes to the current guidelines for testing drugs of abuse in urine (94 FR 28101), and the second document establishes guidelines for use of oral fluid as an alternate matrix in federal workplace drug-testing programs (94 FR 28054) (1,2). The notices were published for public review with a 60-day comment period that closed on July 14.

Background

First published in April 1988, the Mandatory Guidelines for Federal Workplace Drug Testing Programs established the technical and scientific guidelines for drug testing of federal employees in compliance with Executive Order 12564, The Drug-free Federal Workplace (3). Effective in January 1990, the guidelines included requirements for employers, collection sites, laboratories, medical review officers (MROs), and other program participants. The guidelines established standards for certified laboratories to perform testing for regulated employees. The U.S. Department of Transportation is required by law to follow the DHHS drug-testing guidelines and publishes companion guidelines applicable to safety-sensitive employees in each of its operating administrations: Federal Aviation Administration, Federal Motor Carrier and Safety Administration, Federal Railway Administration, Federal Transit Administration, and Pipeline and Hazardous Materials Safety Administration (4).

The federal guidelines have been revised only four times since the original publication in 1988. Between 1994 and 2008, the changes included:

- The cutoff for the initial test for THC metabolite was lowered from 100 to 50 ng/ml (5).
- The initial and confirmatory cutoffs for opiates were raised from 300 ng/ml to 2000 ng/ml (6).
- New requirements for specimen validity testing were introduced (7).
- New compounds were added to the test panel (MDMA and the heroin metabolite 6-acetylmorphine) (8).
- Cutoffs were lowered for amphetamines and cocaine (8).

In the revisions finalized in 2008, SAMHSA also proposed expanding the federal testing program to include the use of alternative specimens, including hair, oral fluid, and sweat. At the time, significant scientific, legal, and policy concerns were raised that lead SAMHSA to postpone the inclusion of alternate specimens pending further research (8).

SAMHSA's Drug Testing Advisory Board continued to review the science related to the use of alternative specimens and current drug use trends. In July 2011, the board recommended that SAMHSA include oral fluid as an alternative specimen for workplace drug testing and that the program include additional Schedule II prescription medications, such as oxycodone, oxymorphone, hydrocodone, and hydromorphone (9).

The guidelines proposed in May 2015 resulted from these 2011 recommendations.

Major Changes Proposed

Urine Mandatory Guidelines. Major proposed revisions include the following:

- Drug-test analytes are expanded to include four Schedule II prescription medications: hydrocodone, hydromorphone, oxycodone, and oxymorphone.

- MDA and MDEA, currently required components of confirmatory testing, are added as initial test target analytes.
- Permitted initial testing technology has been expanded from immunoassay-only to include alternative technologies such as spectrometry, as long as the required sensitivity, specificity, and accuracy are attained.
- The decision point for reporting a specimen as adulterated based on low pH has been changed from less than 3.0 to less than 4.0. In conjunction with this proposed change, the low decision point for reporting a sample as invalid changes from 3.0 to 4.0.
- The requalification requirements for being an MRO have been revised.

Oral Fluid Mandatory Guidelines. The revisions propose an entirely new set of guidelines that permit federal agencies to collect and test oral fluid specimens as a part of their testing programs. Major components of interest include the following:

- The guidelines' structure is similar to that of the urine testing guidelines, incorporating general requirements for chain of custody, security, initial and confirmatory testing methodologies, processes for review by an MRO, and federal agency actions.
- They establish standards and technical requirements specific to oral fluid, including collection devices and initial and confirmatory test analytes.
  * Collections must performed under observation.
  * Collections must be quantitative, at least 1.0 ml of oral fluid.
  * Split specimens are required, collected either simultaneously or serially.
  * Collection devices must meet performance criteria for quantitative accuracy and recovery.
- The test panel generally mirrors the components of the urine panel, including the additional Schedule II compounds indicated above. However, cutoffs are lower as relevant to oral fluid drug concentrations. In addition, the target analyte for cannabinoid testing is THC rather than the carboxy-THC metabolite target in urine testing.
- Initial instrumented test facilities—facilities where screening testing is performed with confirmation performed at a different site—are not permitted.
- Laboratories wishing to perform oral fluid testing for employees regulated under the federal guidelines must obtain a separate certification.

SAMHSA has requested additional input on selected issues such as validity testing in oral fluid, oral fluid split specimen collection procedures, MRO requalification requirements, and information regarding the use of carboxy-THC for detection of marijuana use (1,2). The full versions of both documents are available using the links in the references below.

Comments and Next Steps

At the close of the comment period on July 14, 800 comments had been submitted, 427 comments for urine and 373 comments for oral fluid (10). The comments were wide-ranging and can be viewed at www.regulations.gov.

The comments are currently under review at DHHS and will be presented to the Drug Testing Advisory Board, DHHS federal partners, and SAMHSA leadership. When finalized, the revised guidelines will be published in the Federal Register with an implementation timeline. Tentative timelines for the approval and implementation process were presented at the advisory board's August 7 meeting (10).

Summary

In summary, DHHS has proposed revising the Federal Workplace Drug Testing Guidelines to include additional analytes and matrices. The changes have been under consideration since 2011 based on recommendations by the Drug Testing Advisory Board. A public comment period on the proposed revisions ended in July and the comments are currently under review. Final guidelines will be published once all comments have been considered and resolved.

Learning Objectives

After reading the article, the reader will be able to summarize the proposed changes to the Mandatory Federal Workplace Drug Testing Guidelines and assess what laboratory changes may be required to comply with the revised guidelines.

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