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Marijuana, Workplace Drug Testing and the Adverse Drug Event - You are Fired!

Frank F Vincenzi*

Pharmacological Information and Consultation Service (PHICS), Arlington, WA, USA

***Corresponding Author**: Frank F Vincenzi, Pharmacological Information and Consultation Service (PHICS), Arlington, WA, USA.

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Abstract

Many workplace employment contracts include policies that result in the termination of any employee who tests positive for certain drugs of abuse. Screening of urine samples is by immunoassay. Such assays are non-quantitative and subject to false positives. If positive, then confirmatory laboratory analysis may detect prohibited substances. Prohibited drugs include marijuana with a short-acting compound, Δ-9-tetrahydrocannabinol (THC), whose intoxicating effects disappear rapidly. An inactive metabolite, 11-nor-Δ-9-tetrahydrocannabinol-9-carboxylic acid (THCA) is present in urine long after the effects of marijuana are gone but results in a positive test. Medical or recreational use of marijuana has become legal in some jurisdictions. An increasing number of individuals consume marijuana legally when not at work, but test positive hours or days later and are terminated from employment. It is proposed to replace urine testing with a two-step procedure that is non-invasive and less intrusive. First, screening by sampling oral fluid. Results are available in a few minutes. If, and only if the screening test is positive, then a finger-prick microsample of blood would be obtained by non-medical personnel. The dried blood spot sample would be analyzed by modern analytical techniques such as liquid chromatography, tandem mass spectrometry (LC/MS-MS) for identification and quantification of THC. If the blood concentration of THC is present at or above a defined the defined cutoff level, then the test will be positive. Until outdated ideas and methods are no longer used as a basis for workplace drug testing, many more individuals will be unjustly terminated from employment.

Keywords: *Marijuana; Workplace Drug Testing; Urine; Blood; Oral Fluid; Marijuana Metabolites; Employment Contracts*

Abbreviations

ADE: Adverse Drug Event; DBS: Dried Blood Spot; DOT: The U.S. Department of Transportation; DRUID: Driving Under the Influence of Drugs, Alcohol and Medicines in Europe; DUI: Driving While Under the Influence; EMIT: Enzyme Multiplied Immunoassay Technique; GC/MS: Gas Chromatography/Mass Spectrometry; LC/MS-MS: Liquid Chromatography/Tandem Mass Spectrometry; MS: Mass Spectrometry; OF: Oral Fluid; UDS: Urine Drug Screen; THC: Δ-9-tetrahydrocannabinol; THCA: 11-nor-Δ-9-tetrahydrocannabinol-9-carboxylic acid; VAMS: Volumetric Absorptive Microsampling

Introduction

Recently, the social impact of suspected adverse drug reactions was reported [1]. It was noted that there are few data on the social impact of adverse drug reactions related to medical care. I have always described pharmacology as a discipline with broad interests ranging from sub-molecular to societal. In this communication, I wish to discuss a problem that spans the range from molecular to societal. The non-medical use of at least one drug is a social impact issue that needs attention. Legal, pharmacodynamic and pharmacokinetic features underlie the matter. Changes will be suggested that may alleviate the adverse social and personal consequences of this problem.

The problem is the dismissal from employment as a consequence of an employee testing positive for 'marijuana' among so-called 'drugs of abuse'. Termination of employment is an adverse drug event (ADE). An ADE commonly refers to instances where patients are unintentionally harmed as a result of drug use [2]. Most individuals consider the loss of gainful employment to be a severe injury. Hence the intentionally provocative title of this communication.

There have been some significant changes in the legal status of marijuana (cannabis) in recent years in the United States and elsewhere. Although the Schedule I status of marijuana did not change at the federal (U.S.) level, in November 2012 the States of Washington and Colorado approved regulation of marijuana for recreational use. As of January 2019, recreational use of marijuana is legal in 10 states and the District of Columbia, and medical use is legal in 33 States [3]. Uruguay was the first country to legalize the production, sale and consumption marijuana in October 2014 [4]. Canada legalized marijuana as of 17 October 2018 [5].

In short, there is a growing population of individuals for whom the recreational or medical use of marijuana is legal. It is not the goal of this communication to document the rapidly changing landscape of the laws, but rather to consider a problem that arises from such changes. One glaring problem is the disparity between the U.S. Federal status of marijuana as a Schedule I Controlled Substance and its jurisdictional status in some States as legal for recreational or medical purposes. A Schedule I Controlled Substance is considered to "have no currently accepted medical use in the United States, a lack of accepted safety for use under medical supervision, and a high potential for abuse" [6]. Essentially, the use of marijuana is illegal under U.S. federal law but may be legal in certain jurisdictions. Laws in other countries may differ and are undergoing pressure for changes.

Analysis of drugs to detect impairment among employees has the justification of safety on the job. That is an appropriate goal, and it should be based on reliable analyses of active drugs that might cause impairment and thus endanger life or property. The U.S. Department of Transportation (DOT) routinely tests "safety-sensitive employees in aviation, trucking, railroads, mass transit, pipelines, and other transportation industries" {www.dot.gov/ost/dapc}. The drugs or drug classes routinely tested for by the DOT include:

- Marijuana metabolites/THC
- Cocaine metabolites
- Amphetamines (including methamphetamine, MDMA
- Opiates (including codeine, heroin (6-AM, morphine)
- Phencyclidine (PCP)

A DOT Drug and Alcohol Policy and Compliance notice states: "We want to make it perfectly clear that the state initiatives will have no bearing on the Department of Transportation's regulated drug testing program. The Department of Transportation's Drug and Alcohol Testing Regulation - 49 CFR Part 40 - does not authorize the use of Schedule I drugs, including marijuana, for any reason" [7].

Note that the DOT test is for marijuana metabolites/THC. Unfortunately, many employers have merely adopted the same policy. Thus, non-safety sensitive as well 'safety sensitive' employees are at risk of dismissal based on a single positive test of an inactive metabolite found in the urine many hours or days after the effects of marijuana have disappeared.

The method of testing for marijuana currently in wide use by employers in the United States (U.S.) is based on the presence in urine of 11-nor-Δ-9-tetrahydrocannabinol-9-carboxylic acid (THCA) an inactive metabolite of Δ-9-tetrahydrocannabinol (THC), the major active ingredient in marijuana. There are also a few minor metabolites, most of which are inactive, that may also be detected [8]. A urine screening test that indicates the presence of THCA at or above some cutoff limit (typically 50 ng/mL) results in a 'positive test' for 'marijuana'. In such cases, confirmation analysis is performed by gas chromatography/mass spectrometry (GC/MS) or similar techniques, including liquid chromatography/tandem mass spectrometry (LC/MS-MS) [9]. The 'confirmation' helps assure that the compound (THCA) is identified, and its concentration accurately quantified. Unfortunately, such confirmation is merely confirmation of an inactive metabolite in a body fluid with little or no relationship to possible drug-induced impairment of the individual near the time of sampling.

When mass spectrometry (MS) analysis is performed on a urine sample, it would be evident if THC were present along with THCA. MS analysis determines both the identities and the concentrations of compounds present in the sample. Confirmation of the presence of THCA by MS, unless otherwise noted, would also confirm the absence of THC. For an example, see the results of LC-MS/MS performed on a dried blood sample spiked with various natural and synthetic compounds related to THC [9].

I am not suggesting that drug testing for marijuana be eliminated but instead changed to a more rational way by which to assess possible impairment of employees. As is done by breath/blood analyses of alcohol, testing for 'drugs of abuse' should be based on measurement of a bodily fluid in which the concentration of that drug bears some relationship to impairment caused by the said drug; for example, blood and/or oral fluid (OF). Although commonly called saliva, OF is saliva from various salivary glands, mixed with other constituents of the mouth [10]. Drug testing should not be based on urine samples that may contain an inactive metabolite of a drug that was used hours, days, or weeks before. However, that is the unfortunate situation with marijuana.

As a resident of the State of Washington, and an occasional consultant on matters related to pharmacology, I am aware of this problem related to the differential pharmacokinetics and pharmacodynamics of THC (short half-life and short duration of action) one the one hand, and the pharmacokinetics of one of its inactive metabolites, THCA (long half-life, slow elimination from the body). THCA is eliminated from the body and is detectable in urine, hours, days, or even weeks after the last consumption of marijuana [8]. For a variety of reasons, some of which will be considered below, many employers have taken the position that detection in the urine of this inactive metabolite at or above some cutoff concentration (a 'positive' test) is, *per se,* evidence of marijuana-induced impairment ('under the influence') on the job. A test based on an inactive metabolite of a drug that an employee consumed legally for recreational or medical reasons long before reporting for work may result in termination. Three cases of employees who lived and worked in a State in which the recreational use of marijuana is legal are summarized below.

Cases

Case Number 1

Language from the employment contract of company A: "CORPORATE NON-DOT DRUG TESTING PROGRAM [THE COMPANY] is committed to providing a safe workplace for all employees. It is in the interest of the employees, the Company, the Local Union and the community that the [LOCATION] facility remains free from employees reporting for work or working under the influence of illegal drugs, controlled substances and/or alcohol. This policy is considered a living document and is subject to change as applicable with Federal and/or State law. The Union will be notified of changes, as they occur.

Elements of the Drug Testing plan include:

(1) An employee assistance plan

(2) A Medical Review Officer review of all positive results

(3) Random testing procedure, which may include oral fluids testing

(4) Reasonable suspicion, for cause, and post-accident testing

(5) All positive test results will result in termination.

Table 1 includes data provided by Laboratory X in a report on a urine sample collected after a minor accident on a Monday morning at work at Company A. The employee said that she had been to a weekend party at which she ate some brownies brought by a relative. The employee claimed not to be a marijuana user and did not know they were 'special' brownies. Co-workers at the scene of the accident observed no impairment and said the accident was not her fault. Nevertheless, the positive test result resulted in termination of employment.

Test(s)	Screening Cutoff	Confirm Cutoff	Quant	Unit	Result
Amphetamine(s)	1000	500		ng/mL	Negative
Cocaine^	2000	150		ng/mL	Negative
Marijuana Metab.	50	15	15	ng/mL	Positive*
Opiates	2000	2000		ng/mL	Negative
PCP	25	25		ng/mL	Negative

Table 1: *Results from laboratory X.*

**: Confirmation analyses are performed using Gas Chromatography/Mass Spectrometry*

^:as Benzoylecgonine

The screening test was considered to be positive - presumptively at or above 50 ng/mL. However, the confirmatory analysis found the concentration 'Marijuana Metab.' to be only 15 ng/mL. The results illustrate the non-quantitative nature of the screening test. They also show that quantification by GC/MS that resulted in a concentration just equal to the confirmatory cutoff resulted in a POSITIVE urine test - and thus termination of employment.

Case Number 2

Language in the employment contract of Company B was similar to that of Company A. Table 2 includes data provided by Laboratory Y in a report on a urine sample collected after an accident at Company B.

Test	Result	Quantitation	Screen Cutoff	Confirm Cutoff
Amphetamine	Negative		500 ng/mL	
Methamphetamine MDMA/MDA	Negative		500 ng/mL	
Cocaine metabolite	Negative		150 ng/mL	
6-acetylmorphine	Negative		10 ng/mL	
Opiates	Negative		200 ng/mL	
Phencyclidine	Negative		25 ng/mL	
Marijuana metabolites			50 ng/mL	
Marijuana Metabolite	Positive	1000 ng/mL		15 ng/mL
THCA > 1000 ng/mL				

Table 2: *Results from laboratory Y.*

Table notes that analyses for both cocaine and marijuana are based on metabolites. Since cocaine is not legal for recreational use in the U.S., I will not consider that issue further. The policy of Company B is that if the test for 'marijuana metabolites' is positive, then the employee will be terminated. The terminated employee (who lives and worked in a State where marijuana is legal) admitted that he was a regular user of marijuana, but that he only uses it to help him sleep. If so, by the time he reports to work the effects of the marijuana are probably gone. But the metabolite is not gone. Thus, after another employee (who was not terminated) drove a forklift into him causing bodily injury, a mandatory post-accident urine sample was obtained. Co-workers at the scene of the accident clearly stated that the accident was not the fault of the terminated employee and that they saw no signs of impairment. Nevertheless, the test for marijuana metabolites was positive, and the employee was terminated. Based on the high level of THCA in urine it is likely that this particular individual was a chronic high-level user.

Case Number 3

Another example from Company B is shown below. Table 3 includes data provided by Laboratory Z in a report on a urine sample collected after a minor accident.

Drug Class	Result	Quantitation	Screen Cutoff	Confirm Cutoff
Amphetamines	Negative		500 ng/mL	
Benzoylecgonine (Cocaine)	Negative		150 ng/mL	
Opiates (Codeine/Morphine)	Negative		2000 ng/mL	
6-Monoacetylmorphine	Negative		10 ng/mL	
THC (Cannabinoids 50)	***Positive		50 ng/mL	
Delta-9-Carboxy THC	***Positive	44.1 ng/mL		
Marijuana Metabolite	Positive	1000 ng/mL		15 ng/mL
Phencyclidine	Negative		25 ng/mL	

Table 3: *Results from laboratory Z.*

In table 3, 'Confirmation of THC (Cannabinoids by GC/MS)' by GC/MS is not confirmation of active THC. It is confirmation of THCA, here labeled Delta-9-Carboxy THC. As in case number 2, the confirmation concentration was less than the screen cutoff value of 50 ng/mL. It must be emphasized that a POSITIVE test for 'THC (Cannabinoids 50)' does not demonstrate the presence of active THC, but only the metabolite THCA. This was confirmed by personal communication with the technician at Laboratory Z.

In the three cases shown above, there was no evidence of the presence of an impairment-producing compound in the urine samples. Furthermore, observers at the scene of the on-the-job accidents reported no apparent impairment of the employees. As noted, employee numbers 1 and 2 were terminated. Employee number 1 had a level of 'Marijuana Metab.' that was just at the cutoff concentration. Employee number 2 was almost certainly a chronic, heavy user. Chronic heavy users have substantial concentrations of THC in their blood long after any single smoking [11], or multiple oral ingestions [12] and may exhibit urinary excretion of THC over an extended period [13]. THC was not reported in the urine of employee number 2, thus it is unlikely that there was much of the active compound in his blood or urine at the time his co-worker ran into him with a forklift. For unclear reasons, employee number 3 was not terminated although the confirmation test reported a concentration of Delta-9-carboxy-THC above the cutoff value. Based on a lack of meaningful evidence, termination of employment may happen inequitably and for irrational reasons.

Discussion

Urine drug screens (UDSs) for marijuana (and other 'drugs of abuse') are routinely based on an initial screening - in which metabolites of THC are detected by immunoassay. The EMIT (enzyme multiplied immunoassay technique) assay is commonly employed in laboratories. The Syva Rapid Test® (Siemens Healthcare Diagnostics, Inc, 511 Benedict Avenue, Tarrytown, NY 10591-5097) that can detect a variety of 'drugs of abuse' is one trade name example [14]. Many manufacturers offer relatively inexpensive urine specimen collection cups that colorimetrically screen for various drugs within a few minutes, right in the cup. One such cup that tests for 5 drugs or drug classes lists them as: "Amphetamines (AMP) Cocaine (COC) Opiates (OPI) Phencyclidine (PCP) Marijuana (THC)" (TestCountry, 10123 Carroll Canyon Rd. San Diego, CA 92131) [15]. Of course, the test labeled "Marijuana (THC)" is NOT for THC, but inactive metabolites. In addition to alcohol (tested by breath), these are five classes of drugs that, as noted above, are part of the standard drug testing protocol of the DOT. Some urine collection cups screen for as many as 12 of drugs at once. And while such tests might indicate that a particular class of compounds may be present above a certain threshold (cutoff) concentration in the urine, there is no information on the actual concentration in the urine. Furthermore, certain non-related agents may cause false positive results in a UDS. False positive tests for marijuana may result from the ingestion of non-psychoactive compounds, such as non-steroidal anti-inflammatory drugs [16] or compounds that may be present in hemp seed bars or milk from cattle grazing on wild cannabis [17]. UDSs do not provide reliable information on the identity and concentrations of drug compound(s) that may be present in the blood or body. Thus, such tests are only presumptive.

Positive presumptive tests are followed by confirmatory 'gold standard' analyses such as GC/MS that can identify and quantify specific molecular species. Thus, with GC/MS one may identify and determine the respective levels of THC, 11-OH-THC (an active metabolite of THC) and THCA (an inactive metabolite) [18]. GC/MS can identify very low levels of such compounds. As noted by Couper and Logan, "Detection time is well past the window of intoxication and impairment" [19]. In other words, a confirmatory test of a THC metabolite (or even THC or 11-OH-THC) in the urine only indicates prior exposure. It does not prove impairment. Impairment results from active compounds circulating in the blood and to the brain, not from metabolites in the urine long after consumption of marijuana. Impairment caused by marijuana typically disappears in a few hours. The metabolite THCA may be detected in urine for up to a month or more [8,20]. For reasons discussed below, chronic users of marijuana may also have low, but detectable, levels of THC or 11-OH-THC in blood or urine for similar periods - long past the impairment caused by the most recent consumption of marijuana.

Urine tests for marijuana are likely to be positive for 3 days following a single use and for 5 - 7 days with moderate use (4/wk), 10 - 15 days for daily use and greater than 30 days for long-term heavy smokers [20]. A single use of marijuana can result in positive urine tests up to 1 week after administration, whereas long-term use can produce positive results in the urine up to 46 days after cessation [8].

Detection limits are so low that positive confirmatory tests for marijuana may result from 'passive smoking'. Passive inhalation of marijuana smoke has resulted in plasma THC levels of 1-7 mg/mL and urine THCA as high as 39 ng/mL [21]. Since the blood:plasma ratio is 0.5 - 0.6 [21], a test on blood obtained at a traffic stop on the way to work would not likely achieve the threshold THC level for *per se*

driving under the influence (DUI, 5 ng/mL of blood within 2 hours of driving in Washington State) [22]. On the other hand, because the confirmatory cutoff for THCA in urine is 15 ng/mL a subsequent random drug test at work would probably lead to a positive test and termination of employment.

As shown above, different laboratories (e.g., Laboratories X, Y, and Z) may screen for different sets of 'drugs of abuse'. While some of the so-called 'drugs of abuse' may be available by prescription, none is legally available for recreational use - with the exception of marijuana in a growing list of jurisdictions. Because many individuals are now legally consuming marijuana in their personal lives, and because termination of employment is based on a positive test for an inactive substance in urine, there is an urgent need for changes in company policies. Unless such changes are forthcoming, employees need to be warned that the employer basically owns their body and their behavior 24 hours per day, 7 days per week. I am not aware of published evidence regarding the number of terminations that have occurred as a consequence of positive tests for 'marijuana' based on urinary THCA. As a lone observer who only occasionally consults on such matters, I probably only see the 'tip of the iceberg', so to speak. I must assume that, unless employment contracts adopt a more rational approach to testing, such terminations will increase as the legal use of marijuana spreads.

Another approach is needed. When it comes to operating a motor vehicle - a topic that cannot be ignored in this context - a more rational approach is already in place. For example, in the State of Washington, timely blood drawing and laboratory analysis for THC (among other drugs) are performed [22]. According to Washington State law: "A person is guilty of driving while under the influence of intoxicating liquor, marijuana or any drug if the person drives a vehicle within this state:

(a) And the person has within two hours after driving an alcohol concentration of 0.08 or higher as shown by analysis of the person's breath or blood made under RCW 46.61.506; or

(b) The person has within two hours after driving, a THC concentration of 5.00 or higher as shown by analysis of the person's blood made under 46.61.506, or ...

Note that analysis of alcohol may be based on a breath test or analysis of blood. This is a point considered below. Note also that a threshold value of 5 ng/mL of THC (the major active compound in marijuana) in blood drawn within 2 hours of driving is *per se* evidence of DUI. Considering the short half-life of THC, blood must be drawn soon after an accident or traffic stop. So, drawing of a blood sample is a definitive way to establish impaired driving. Of course, invasive procedures, such as typical blood drawing, are not practical for on the job monitoring of employees for a variety of reasons. This is an issue considered below.

The vehicle threshold number for THC, like the 0.08% threshold for blood alcohol concentration (BAC), is an arbitrary number, but at least it is based on an active compound in the blood. In many European countries, the per se limit for alcohol is 0.05% (0.5 g/L), even lower in some. The DRUID Project (Driving Under the Influence of Drugs, Alcohol and Medicines in Europe) recommended a serum *per se* concentration of 3.8 ng/ml THC (≈ 2 ng/mL in whole blood). This level was found to be about as impairing as 0.5 g/L alcohol. They noted that some countries with lower alcohol limits might object, particularly those with a zero-tolerance approach [10]. For reasons considered below, the relationship between the concentration of THC in blood and the degree of impairment is more complicated than the concentration-effect relationship of alcohol. However, once tissues and blood have come to an equilibrium of sorts, there is a direct correlation between the blood concentration of THC and its effects [23].

Couper and Logan [19], noted that it is difficult to establish a relationship between a person's THC blood or plasma concentration and performance impairing effects. Concentrations of parent drug and metabolite are very dependent on the pattern of use as well as dose. THC concentrations typically peak during the act of smoking, while peak 11-OH-THC concentrations occur approximately 9-23 minutes after the start of smoking. Concentrations of both compounds decline rapidly and are often < 5 ng/mL at 3 hours. Significant (blood or plasma THC concentrations (7 to 18 ng/mL) are noted following even a single puff or 'hit' of a marijuana cigarette. Peak plasma THC concentrations ranged from 46-188 ng/mL in 6 subjects after they smoked 8.8 mg of THC over 10 minutes. Even 12 hours after use, chronic users can have mean plasma levels of THCA of 45 ng/mL. The corresponding THC levels are, however, less than 1 ng/mL. Couper and Logan [19] noted that it is "inadvisable to try and predict effects based on blood THC concentrations alone, and currently impossible to predict specific effects based on THCA concentrations" [19].

Thus, it is difficult to predict marijuana-induced impairment based on numbers alone. Most research on marijuana-induced impairment has been based on concentrations determined in plasma, and most forensic analysis is based on whole blood samples. The b:p ratio of 0.5 - 0.6 cited above [21], is a simplification. Schwilke., *et al.* [24] studied intrasubject and intersubject b:p ratios. Median ratios (and interquartile ranges) were: 0.39 (0.28 - 0.48) for THC, 0.56 (0.43 - 0.73) for 11-OH-THC and 0.37 (0.24 - 0.56) for THCA. The intrasubject coefficient of variability was18.1%-56.6% for THC, and 10.8 - 38.2% for THCA. In short, it is not a simple matter to predict the effects of marijuana in a given individual when the only information available is the quantification of THC and/or THCA in blood. Nevertheless, considering the growing contribution of marijuana to impaired driving [25,26], some *per se* value for THC is reasonable.

There is no doubt that high levels of THC and/or its active metabolite result in impairment of performance and contribute to traffic accidents and death [10,26]. This is indeed a substantial social impact and ADE related to marijuana use by drivers. THC-positive drivers, at high concentrations, are about three to seven times more likely to be responsible for their crash as compared to drivers that had not used drugs or alcohol [26]. The epidemiological data suggest that recent use of cannabis may increase crash risk, whereas past use of cannabis does not. In fact, the odds ratio of becoming involved in fatal or injurious traffic accidents under the influence of THC was less than 1 (less likely than drug free) in drivers with blood THC concentrations up to 2 ng/mL and in most studies was less than 1 in drivers positive for THCA only [26]. On the other hand, simultaneous use of THC and alcohol produces severe impairment of cognitive, psychomotor, and actual driving performance in experimental studies, and sharply increased the crash risk in epidemiological analyses [10,27].

Optimally, evidence of drug-induced impairment rests on observations of performance as well as measured concentrations of active substances. The Standardized Field Sobriety Test provides only a moderate predictor of possible THC-induced driving impairment [28]. It is less sensitive for detecting marijuana impairment (mainly cognitive) than alcohol impairment (both cognitive and motor). In Norway, blood samples for drivers stopped for possible DUI were analyzed. Of approximately 30,000 samples, 589 were positive for THC (and not alcohol). Of these cases, 456 were assessed by police physicians who administered a clinical test for impairment. Of these, 46% were considered impaired, and 54% not impaired [29]. Impaired drivers had higher blood THC concentrations than drivers who were judged as not impaired (median; 2.5 ng/mL (range; 0.3 - 45.3 ng/mL) vs. median 1.9 ng/mL (range; 0.32 - 24.8 ng/mL), ($p < 0.05$). With blood THC concentrations above 3 ng/mL, drivers had an increased risk of being judged impaired when compared to drivers with lower concentration ranges. The authors concluded that the results support concentration-related effects, but also show substantial inter-individual differences. And there are some concentrations at which drivers are not measurably impaired.

It must be assumed that similar uncertainties exist on the job and that co-workers are not always able to judge impairment by casual observation. It would be useful if Drug Recognition Experts were available when workplace drug analyses are administered, but that may not be practical, particularly in small companies. Testing based on blood concentrations of THC rather than urine concentrations of THCA would provide a more equitable approach. Of course, traditional methods of drawing blood from employees is also not practical. However, there is some light at the end of this dark tunnel.

Considerable progress has been made in the last decade, in the use of oral fluid (OF, saliva) for drug testing. Desrosiers., *et al.* noted in 2012 that in many countries OF is collected at the roadside and tested by GC/MS or similar techniques [30]. In Europe, thirteen roadside testing devices were used in six countries by trained police officers in nearly 3000 roadside tests. As a result, eight devices were evaluated as 'promising' for roadside use by police officers, and these were then submitted for analytical evaluation [10]. In some cases, roadside screening tests of THC in blood or OF was confirmed by GC/MS or similar methods. But, at that time, roadside testing for THC was marginal at best [30]. Unfortunately, none of the OF tests reached the target value of 80% for sensitivity, specificity and accuracy [10].

Progress was being made in 2012 and has continued. The Dräger DrugTest® 5000 test cassette (Draeger, Inc., 7256 S. Sam Houston W Pkwy., Suite 100, Houston, TX 77085) [31] and the Quantisal™ device (Immunalysis Corp., 9975 Summers Ridge Rd, San Diego, CA 92121) [32] were evaluated by Desrosiers., *et al.* who tested OF of ten cannabis smokers that was collected prior to (-0.5 h), and 1, 2, 3, 4, and 6 h after smoking one cigarette containing ~ 54 mg of THC *ad libitum* for up to 10 minutes. They concluded that it "provided high diagnostic sensitivity for detection of cannabinoid exposure, and the selection of OF confirmation analytes and cutoffs provided appropriate windows of detection to meet the goal of different drug testing programs" [33].

As of December 2018, police in Canada are allowed to use approved oral fluid drug screening equipment to test for THC, methamphetamine and/or cocaine [34]. The advantages of oral fluid sampling include a non-invasive, onsite procedure with screening results available in a few minutes. A Standardized Field Sobriety Test can provide further or alternative evidence for impairment if screening equipment is not available, or the screen is negative. Identification and quantification of drug(s) by GC/MS or similar analyses is still needed for confirmation. Such analyses have typically been performed on blood drawn by qualified individuals and passed through a chain of evidence to a toxicology laboratory.

Recently, mass spectrometry has become so sensitive that reliable data can be obtained from a dried blood spot (DBS). This is a small volume (e.g. 10 microliters) of blood absorbed onto pre-marked circles on a matrix similar to filter paper. After drying, the sample can be placed in a plastic bag and mailed to the laboratory. A 10 mm diameter circle of the matrix is extracted, and mass spectrometry can distinguish THC, THCA, and a variety of synthetic compounds related to THC [9].

DBS can be problematic because of differences in blood hematocrit and a possibly variable relationship between the original volume of blood and the size of the dried spot. Development of volumetric absorptive microsampling (VAMS) appears to have overcome most or all of the uncertainties associated with placing a spot of dried blood on paper [35]. The VAMS sampler is a device similar to a laboratory pipette tip and can be handled by a variety of robotic pipetting systems. The tip of the device has a porous substrate that absorbs blood by wicking within about 2 - 4s. The amount absorbed is determined by the amount and nature of the substrate and was found to absorb a reproducible volume of blood irrespective of the hematocrit. The average volume of blood was 10.5 ± 0.1 microliter, with a coefficient of variation of 3.6% [35]. VAMS devices with the brand name Mitra™ (Neoteryx, 421 Amapola Ave. Torrance, CA 90501) [36] were used by Protti., *et al*. to collect blood microsamples to analyze THC, its two major metabolites and 10 different synthetic cannabinoids by LC-MS/MS.

Conclusion

In the following, I will consider only marijuana. I recognize that positive screens for other drugs may occur, and should be dealt with appropriately. It is suggested that recent advances in screening and analysis be employed to increase the reliability and rational basis for measuring THC (as well as active and inactive metabolites) in the blood of persons to be tested for marijuana in the workplace - somewhat like what is already being done on the road.

I propose that workplace policies adopt a two-step procedure for drug testing. Alcohol can continue to be determined by well-established breath analysis. For other drugs, OF will be screened onsite by one of the many devices currently being offered by various manufacturers [37]. Some countries specify such a screening approach. For example, in the Czech Republic, the employer is allowed to make a breath or saliva test, but 'biological samples' (presumably including blood) may only be taken by health care institutions [38]. THCA cannot be detected in oral fluid with commonly available toxicological methods [10]. Thus, compared to urine screening, the number of positive screening tests for marijuana is likely to substantially fewer if OF becomes the standard. If an OF screen is negative, then no further testing would be indicated. If the screen is positive, the result will be apparent within a few minutes. Then, and only then, will a finger prick blood sample be obtained. A blood microsample can be obtained using after a finger or heel prick by non-medical personnel [10].

The blood microsample (probably obtained by VAMS or similar technology) will be dried and submitted to a forensic toxicology laboratory for possible identification and quantification of a variety of active drug compounds, in particular, THC. If the blood level is at or above some agreed upon *per se* level, then the test would be positive. Different countries and jurisdictions are likely to have different *per se* levels, as they do for alcohol. In any event, if the THC level is below the cutoff level, then the test is negative. Most importantly, the result will be based on identification and quantification of THC in blood, not an inactive metabolite in urine. As noted by Protti., *et al.* (who tested for a wide variety of natural and synthetic cannabinoids) "All substances investigated in the presented studies could be determined in a DBS as reliably as in a whole blood specimen. Thus, the project demonstrated that DBS drug analysis can be regarded as a valuable and inexpensive alternative to the determination of substances in whole blood. Such use of DBS could greatly facilitate blood analysis in drug-driving cases in the near future" [9]. Use of DBS would also facilitate drug analysis in the workplace. Furthermore, compared to current practices, the two-step procedure will be less invasive than blood drawing and less intrusive than urine sampling. Finally, two-step procedure tests will be positive for very recent users and negative for users who consumed marijuana long before the test.

The legal (and illegal) use of marijuana is increasing throughout the world. Workplace drug testing is available in the UK [37,39]. Legalization of medical (but not [yet] recreational) use of marijuana in the UK will increase the need for rational testing. The legal status of workplace drug testing in many European countries has been reviewed [38]. The present communication was written from the point of view of a resident in a jurisdiction where the recreational and medical use of marijuana is legal. In similar jurisdictions, the need for timely modernization of workplace drug testing is particularly pressing. Until outdated ideas and methods are no longer used as a basis for workplace drug testing, many more individuals will be unjustly terminated from employment.

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Declaration of Conflicts of Interest

Various products were mentioned to illustrate methods of drug testing. I do not endorse any of these products. I have no financial interest in any of the companies so mentioned. The author declares no conflict of interest.

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