



# PERSPECTIVES

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## **Cannabis & THC: Understanding the Effects & Liability**

Our perspectives feature the viewpoints of our subject matter experts on current topics and emerging trends.

## INTRODUCTION

State legalization of cannabis (i.e., marijuana) for medical and/or recreational use has spurred many questions regarding exposure concerns and drug testing concerns (e.g., what constitutes positive cannabis tests and how do results relate to impairment). Answers to these questions are applicable to:

1. Site inspectors, whose chance of encountering unintentional contact with cannabis has risen as both possession and cultivation (by individuals and commercial operations) has become permissible
2. Insurance carriers assessing grower and/or dispensary facilities policy applications for D&O, liability, and/or workers compensation coverage
3. Attribution of individual liability in forensic cases

Knowledge regarding the main psychoactive component of cannabis (tetrahydrocannabinol or THC) is essential to understanding these issues, especially those regarding intoxication and/or biological detection.

Cannabis contains more than 421 different chemical compounds, including a group of more than 60 bioactive compounds (called cannabinoids). Cannabinoids in raw (unprocessed) cannabis plants include tetrahydrocannabinolic acid (THCA), which, with heat, time, and/or light transforms into THC, the main psychoactive compound of cannabis products.

This paper provides general knowledge regarding THC, including how it is absorbed, metabolized, and distributed in the human body following oral and inhalation exposures, and the relationship between intoxication and detection in blood and urine. This paper is intended as a general overview, it is not comprehensive in nature, and readers are encouraged to contact J.S. Held toxicologists regarding specific questions and situations.

## CANNABIS IMPAIRMENT & REGULATIONS

Cannabis regulations are complicated: although individual states have legalized medical or personal use, it remains

federally illegal. Therefore, failing a THC drug test (i.e., presence of THC or metabolites in urine), regardless of potential impairment status, is sufficient to dismiss federal employees in applicable positions.

Regulations regarding impaired driving in states that have legalized THC use are generally based on “per se limits” (or the concentration that legally defines the minimum for a legally defined impaired status). For example, Colorado and Washington imposed per se limits for driving impairment of 5 ng/mL in whole blood.

The per se limits were established based on general correlations between elevated blood THC concentrations and periods of impairment following cannabis use. However, as described below, circulating levels do not correlate well with intoxication, and chronic, heavy users have been observed with elevated blood THC levels days following last use. Due to the complicated relationship between detection and impairment (and to prevent erroneous conclusions based on elevated blood levels in the absence of impairment), recommendations among non-federally employed workers established by the American College of Occupational and Environmental Medicine (ACOEM) involve testing of workers for potential THC impairment only after other medical signs of acute impairment have been observed in a worker. A conclusion that an employee, who was observed with medical signs of impairment, was likely acutely impaired by cannabis use is to be reached when subsequent testing shows plasma levels of 5 ng/mL or more THC (or THC plus THC-OH).

## THE HUMAN RESPONSE – FOLLOWING THC EXPOSURE

Sufficient THC exposure can induce both physiological and psychoactive effects (detailed in Table 1). Impairment is associated with a lack of coordination, muscle strength, and hand steadiness; lethargy; sedation; inability to concentrate; decreased psychomotor activity; slurred speech; and slow reaction time.

The chemical structure of THC causes it to be hydrophobic (“water-fearing”) and lipophilic (“fat-loving”), meaning when it enters the body, its chemical structure facilitates selective/preferential distribution into the body’s fat. In

PHYSICAL EFFECTS		PSYCHOACTIVE EFFECTS	
DECREASED	INCREASED	PSYCHOLOGICAL	COGNITIVE
Vascular resistance	Heart rate	Euphoria	Memory impairment
Intraocular (eyeball) pressure	Conjunctival injection (red eyes)	Garrulousness (excessive chattiness)	Decreased recall and word association
Airway resistance	Blood pressure	Feeling of floating	Slowed reading
Urinary retention (ability to empty the bladder)	Cerebral (brain) blood flow	Vivid visual imagery	Slowed comprehension
Testosterone (male hormone)			Impaired verbal expression
			Impaired mathematical ability

**Table 1** - Acute (short-term) effects following THC exposure

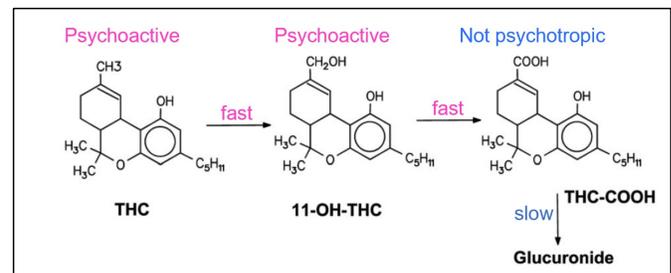
other words, fat within people’s bodies can be thought of as a THC-sponge, selectively absorbing THC from blood as it circulates throughout the body in blood, which is predominantly aqueous.

Following an acute exposure, elimination of THC from the bloodstream occurs as THC is either absorbed by body fat or is metabolized in the liver. Functionally this means that fat-laden organs (such as the brain) will increase in relative THC concentration as circulating levels start to decline, contributing to the phenomena that maximum psychoactive effects occur after blood levels have peaked (i.e., as blood levels are declining). In addition, this means that people with larger fat stores (i.e., those with increased body mass index or BMI) have different blood elimination profile/timelines following exposure than leaner individuals.

Brain sequestration of THC is responsible for the psychoactive acute effects and intoxication following exposure. Duration of THC intoxication depends on the dose consumed, the absorption rate, the rate of metabolism, and the time to loss of sensitivity to THC’s pharmacological actions. We help clients understand the complexities associated with timelines of use, timelines of intoxication, timelines of testing, and the intricacies involved in interpreting those relationships for

potential conclusions regarding potential health impacts, testing status, and/or intoxication status.

THC is metabolized in the liver into a series of more soluble compounds (see Figure 1), finally conjugating the THC-COOH metabolite with glucuronic acid, which is excreted in urine. The rapid metabolism of the psychoactive compounds (i.e., THC and 11-OH-THC) into the less-quickly metabolized non-psychoactive THC-COOH can result in an apparent buildup of the non-psychoactive THC-COOH in the blood following THC exposure.



**Figure 1** - THC metabolism (adapted from Musshoff and Madea, 2006)

THC’s fat-selective absorption results in a post-use reservoir in fat that slowly releases long after the psychoactive effects have ended (the small amount released over time is not associated with psychoactive effects). This is because, without subsequent THC exposures, THC stored in the fat is slowly released back into the bloodstream where it is metabolized and excreted in the urine. This slow release from fat results in an extended urinary excretion profile, causing THC metabolites to be detected in urine for days to months after last use, even though the individual is not impaired at the time of testing. Durations for urine detection primarily vary with dose consumed and use history (i.e., single use vs. chronic/daily consumption), but also can vary with other factors such as body mass, weight loss, and exercise. In addition, anecdotal reports have associated positive THC urine tests in former users that have lost dramatic amounts of weight after long periods of abstinence.

## KEY DIFFERENCES BETWEEN INHALATION & ORAL EXPOSURE

As demonstrated in Figure 2, timelines for effects are different for inhalation exposure compared to oral exposure (i.e., ingestion of edibles). Inhalation is associated with much faster effects, primarily because THC is rapidly absorbed into blood from air delivered into the lungs and the resulting THC-laden blood is pumped directly to the brain, which is the site of action for the resulting psychoactive effects. The quick absorption profile associated with inhalation is also associated with a faster decrease in blood concentration compared to oral exposures. In contrast, ingestion of THC-containing edibles delivers THC into the gastrointestinal tract (GI), where the rate of absorption into the blood stream is generally slower than inhalation exposures and also depends on what else has been eaten. The purpose of the GI tract is to absorb nutrients, and the function of the liver is to metabolize those ingested nutrients, and blood containing THC from the GI tract is pumped directly to the liver, which metabolizes it. This means that some of the ingested THC is absorbed but metabolized before it reaches systemic circulation and then gains entry into the brain. The slower absorption from the GI tract and then immediate metabolism results in a slower time frame for psychoactive effects compared to inhalation.

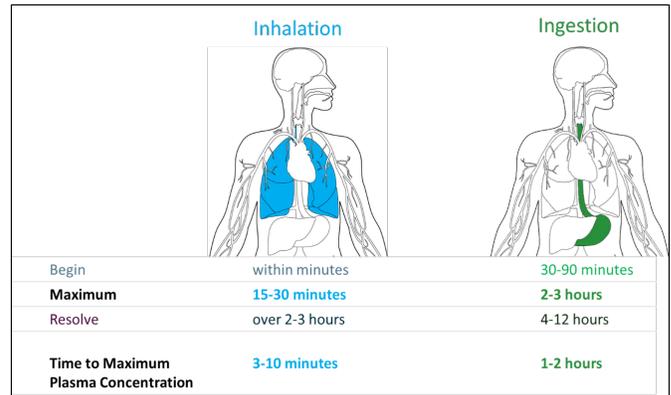


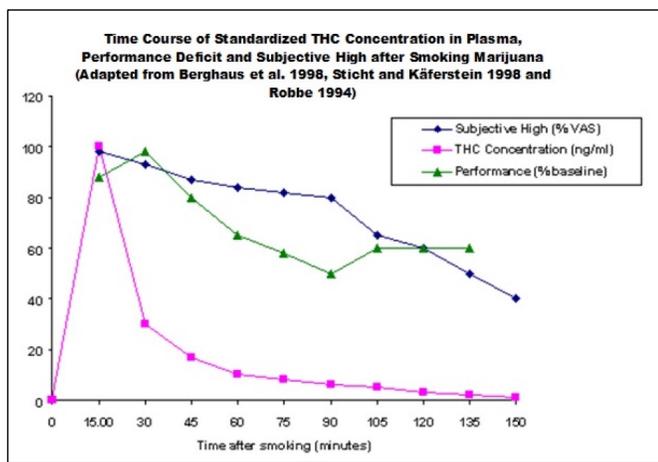
Figure 2 - Timelines for psychoactive effects following THC inhalation or ingestion

## DIFFICULTIES IN MEASURING THC EXPOSURE

The lipophilic nature of THC complicates conclusions regarding timelines of exposure and intoxication from biological samples. Knowledge regarding the type of analysis (i.e., urine vs. blood), type of method (screening vs. confirmatory), analytes assessed (THC, psychoactive metabolites, and/or non-psychoactive metabolites), timing of analysis compared to alleged event or exposure, and individual drug history (for THC and other potentially interfering compounds) is essential before any conclusions regarding test results and potential timelines for intoxication and/or use.

Urinary tests can be subject to false positive results (i.e., a positive test result occurs even though no THC was present) with use of cheaper screening tests, because they provide measurements of THC metabolites based on immunoassay methodology, which can generate false positives when urine contains nonsteroidal analgesic medication (i.e., ibuprofen or naproxen), efavirenz (HIV medication), promethazine (anti-nausea medication), or riboflavin (Vitamin B2). Generally urinary samples that test positive using immunoassay methods are reanalyzed using gas chromatography/mass spectrometry (GC/MS), which provides selective and accurate detection of THC metabolites. In order to assure accuracy of positive urinary test results, best practice is to ensure results were confirmed using GC/MS.

Blood sample collection is more invasive than urine collection; however, blood (or plasma or serum) samples analyzed using the selective gas chromatography/mass spectrometry accurately measure the amount of THC and THC-metabolites. Positive measurements of THC in blood generally correlate with recent exposure, although some research suggests heavy chronic users may have detectable THC in blood for days following last use (Odell et al., 2015). Conclusions regarding intoxication are complicated as blood concentrations reach maximum levels prior to maximum intoxication (i.e., blood concentrations are declining at the time of maximum impairment; see Figure 3).



**Figure 3** - Time course for THC concentration in plasma, performance deficits, and subjective high (from: Compton, 2017)

Due to the potential for THC to be detected in blood after impairment has ceased, guidelines published by the American College of Occupational and Environmental Medicine (ACOEM) indicate testing for potential THC impairment should never be assessed in isolation. Instead, testing should only follow observation and documentation of definable signs of impairment. An ACOEM panel reviewed data relating impairment and plasma levels of THC plus its active metabolite 11-OH-THC in casual vs. chronic users and subsequently categorized THC plasma levels with potential impairment. ACOEM concluded levels from 0-2 ng/mL cannot establish impairment in casual or chronic users; levels of 2-5 ng/mL correlate with “likely impaired” casual users and chronic users that “may be impaired;” and levels of 5+ ng/mL correlate with “likely impaired” casual and chronic users.

ACOEM recommended a serum level of 5 ng/mL or more of THC in serum or plasma as THC (or the sum of THC plus its active metabolite 11-OH-THC) would identify individuals most likely to be impaired due to THC (when those individuals have documented physical signs of impairment) (Phillips et al., 2015). These guidelines can be used with other factors (e.g., use history, dose, elapsed time since use, etc.) to understand applicability of test results in liability, litigation, or other matters.

States that have legalized cannabis use have taken a similar approach (e.g., using a cut-off or per se law concentration) to define driving under the influence (DUI). For example, Washington State motorists are guilty of DUI with detectable THC whole blood levels above 5 ng/mL (Revised Code of Washington RCW 46.61.502(1)(b)). Thus, a blood level above 5 ng/mL, which corresponds to about 10 ng/mL in serum or plasma, is the presumed level for DUI when accompanied by signs indicative of impairment. It is important to remember that while per se laws use a single number (e.g., 5 ng/mL in whole blood) to fit all cases, the value is not directly related to impairment. Instead, blood (or plasma) cut-off levels have been established for levels that correspond with recent exposure and acute impairment in most users; some heavy, chronic users may exhibit baseline levels that exceed cut offs in the absence of impairment.

As legislation continues to evolve, so do questions regarding unintentional or workplace exposures and their implications for health effects and testing status. Expert toxicologists work with employees, stakeholders, and other interested parties to evaluate, assess, and provide answers to these questions, including, but not limited to, providing general knowledge regarding THC exposure, use, and testing and deriving protective screening-values for specific situations, such as restoring a home previously used for a clandestine grow operation.

## CONCLUSION

There are complex relationships for exposure to THC-containing products and (1) subsequent intoxication timelines and (2) duration of positive drug testing. Although science is still attempting to characterize these relationships, contributing factors to both relationships that have been identified include both the dose consumed and use history. Routes of exposure also play a role (e.g., inhalation or oral) as well as differences

in absorption rates, metabolism rates, body mass, weight loss, and exercise. This white paper describes the complex relationships between THC use, intoxication, and detection in blood and urine.

J.S. Held toxicologists understand and are current with the evolving science regarding the complexities associated with timelines of use, timelines of intoxication, timelines of testing, and the intricacies involved in interpreting those relationships for potential conclusions regarding potential health impacts, testing status, and/or intoxication status and can help interpret test results for issues regarding liability, litigation, cleanup, and other matters.

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Dr. Nadia Moore is a Vice President and Principal Toxicologist in J.S. Held's Environmental, Health & Safety Practice. Her experience encompasses chemical and physical agents (including asbestos, pesticides, solvents, vapors, particulate matter, metals, and microbial agents), diverse exposure scenarios (including environmental, occupational, and residential), and all routes of exposure (including inhalation, oral/drinking water, and percutaneous). Nadia's practice also includes the determination of whether exposure to a chemical or physical agent has caused an injury, exposure assessment in diverse scenarios, determination of acceptable impurity levels in consumer products, and weight-of-evidence analysis of historical scientific data to gauge present-day conclusions.

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