Toxicology Update

Authored by ALFA International Attorneys:

Jim Jarrow
BAKER STERCHI COWDEN & RICE, LLC
Kansas City, MO
jarrow@bscr-law.com

Paul Robinson
MEYER, DARRAGH, BUCKLER, BEBENEK & ECK, P.L.L.C.
Pittsburgh, PA
probinson@mdbbe.com
Cannabis Terpenes

By Carla J. Kinslow, Ph.D.

Terpenes are plant-derived chemicals that are found in the sticky resin of the cannabis secretions from the female cannabis inflorescence (Booth et al., 2017). These chemicals have been well studied for decades, specifically related to their anti-bacterial or plant-protective characteristics; however, the role of terpenes in medicinal cannabis is a new field of strong scientific study. It’s the different ratios of terpene compositions, including monoterpenes and sesquiterpenes that provide each cannabis strain with its unique taste and smell (Booth et al., 2017). Interestingly, terpenes are what also what gives beer its “hoppy” smell and flavor (Booth et al., 2017). Botanists have been studying terpenes such as pinene (which give pine needles their scent) for decades.
These chemicals are also thought to influence the medicinal properties of the plant as well, specifically they are thought to convey anxiolytic, antibacterial, anti-inflammatory properties (Booth et al., 2017). By enlarge, the interest in cannabis-derived terpenes has been driven by anecdotal evidence claiming that these chemicals can be used to treat various conditions, including anxiety and appetite (Booth et al., 2017; Russo, 2011).

A terpene flavor profile chart¹, similar to the one to the left, is a common tool that is used by many cannabis Sommeliers to help match a customer’s terpene choice to the desired effects.

At least one terpene is known to bind to cannabinoid receptors in the human body and it is thought that terpenes may act in a synergistic manner with cannabinoids to produce many of the beneficial effects (Booth et al., 2017). The interplay between terpenes and cannabinoids to synergistically target cellular receptors and evoke specific effects is termed the “entourage effect” (Booth et al., 2017). Thus, it is suggested that the combinations of these plant compounds present in the resin in certain ratios of these chemical and, as such, convey strain specific effects.

In contrast to the relatively predictable concentrations of cannabinoids in various cannabis strains, terpene composition and concentrations in cannabis resins are also known to be highly variable. For example Booth et al. (2017), who studied only *C. sativa*, showed that terpene concentrations in this cannabis strain ranged from 3.6 to 389 µg/g. As such, terpene concentrations and compositions in the vast majority of

¹ https://emeraldviewmedia.com/terpenes-101/
cannabis strains are poorly characterized and in strains that are characterized, growing plants with a predictable terpene concentration poses an added challenge for producers.

The effect of cannabis terpenes on the human body

In general, terpenes are very potent, eliciting effects on animal and human behavior from inhalation of these chemicals from the ambient air (Russo, 2011). Terpenes at concentrations of at least 0.05% are considered to be of pharmacological interest (Russo, 2011; Pavlovic et al., 2018). For example, mice exposed to linalool and pinene terpenes in the ambient air for 1 hr showed a significant decrease or increase in their activity levels, respectively. This suggests that these terpenes had a rapid, direct pharmacological effect on the brain and may have a synergistic or direct opposite effects on behaviors (Russo, 2011; Pavlovic et al., 2018). Notably, it may not take a large amount of terpene to elicit a behavioral effect. Exposure to orange terpenes (primarily limonene) at undetectable levels in the blood increase mouse activity (Russo, 2011; Pavlovic et al., 2018). The lack of detectable levels may indicate that this chemical is rapidly taken up from the blood and redistributed to the brain, which would support why there is a rapid response at very low levels of exposure and the absence in the blood (Russo, 2011; Pavlovic et al., 2018).

Both animal and human studies have shown that terpenes can be rapidly absorbed or taken up into the body through both inhalation and dermal routes of entry. As much as 70% of linolene has been shown to be taken up upon inhalation in animal models, whereas peak blood concentrations of terpenes applied to the skin have been shown to occur within 19 minutes (Russo, 2011; Pavlovic et al., 2018).

The citrus-based terpenes (such as limonene) are the most ubiquitous in nature, found in most citrus fruits, and has been associated with several positive health endpoints. When depressed patients were exposed to citrus fragrance in a hospital setting through the ambient air, they found subsequent reduction or discontinuation of
prescribed antidepressant medication as well as the presence of increased stimulation of the immune system (Russo, 2011; Pavlovic et al., 2018). Direct application of limonene to breast cancer cells induces a self-destruction response (apoptosis) and the metabolite of limonene (perillic acid) has been shown to have anti-stress responses in mice (Russo, 2011; Pavlovic et al., 2018).

While some studies indicate positive endpoints for these terpene compounds, much of the research on terpenes as they relate to their effect in humans is quite limited. The mechanisms of each individual chemical are far from being understood, much less how they act together or with other compounds such as cannabinoids is even more of a mystery. Although there is an agreement that terpenes play a role in eliciting an effect, the lack of our understanding of terpene exposure and how it affects the targeted receptors in the brain is a major concern. The fact that these compounds act on humans at very low levels and that there may also be ubiquitous or background exposures from our environment or our food complicates the interpretation of terpene-specific effects.

Product Consistency and Safety

Due to the synergistic nature of cannabinoids and terpenes, a primary route of terpene consumption is through the use of CBD oil. In a recent study that evaluated the chemical fingerprint of 15 commercially available CBD oils, the researchers found as many as 48 individual terpenes in the CBD preparations (Pavlovic et al., 2018). Of these, myrcene and limonene accompanied by beta-ocimene and trans-caryophyllene were found in all samples; however, the concentrations of each of these varied by as much as 1000x across the different oils in this study (Pavlovic et al., 2018). Some oils contained numerous terpenes and others contained only a few. Such variability adds to the complexity in trying to understand the contribution of these chemicals to the overall effect of these products.
With regard to the safety of terpenes, many terpenes are common flavor and fragrance components used in several foods and that have been designated Generally Recognized as Safe (GRAS) by the US Food and Drug Administration (FDA) and other regulatory agencies (Russo, 2011). An FDA database search at the time of this publication did not find any terpene-specific product recalls.\(^2\) However, the GRAS designation is specific for a route of exposure at specific concentrations. Most of the terpenes in cannabis have not been well characterized and there are no label requirements to list each of these and their concentrations for a specific cannabis strain or their respective concentrations in a preparation of cannabis oil.

Side effects reported in the scientific literature from surveyed consumers of cannabis include anxiety, paranoia, dry mouth, short term memory issues, and respiratory issues (Kamal et al., 2018).

**Summary**

Cannabis is being used across ages, races, with inconsistent concentrations and uncharacterized compounds. The short- and long-term effects of this drug are not well understood and should be appreciated upon choice to use this drug. Terpenes are an inherent component of the cannabis plant that has been associated with medicinal benefits, some of which have been studied for decades. However, the body of solid scientific literature regarding cannabis-derived terpenes is lacking, specifically in the areas of dose and response relationships. Furthermore, concentrations of these chemicals are highly variable across cannabis strains, and terpene-containing products. As such, this area of science as well as this industry has a considerable amount of growth ahead of itself before accurate doses and consistent product concentrations can be provided to the consumer.

\(^2\) [https://www.fda.gov/safety/recalls/](https://www.fda.gov/safety/recalls/)
References


Opioids
By Carla J. Kinslow, Ph.D.

Opioids are a very powerful class of pain-relieving drugs that many of us may have been prescribed at some time in our lives. If you’ve taken: Tylenol-3 (with codeine), Fentanyl (Actiq®, Duragesic®, Fentora®, Abstral®, Onsolis®), Hydrocodone (Hysingla®, Zohydro-ER®), Hydrocodone/acetaminophen (Lorcet®, Lortab®, Norco®, Vicodin®), Hydromorphone (Dilaudid®, Exalgo®), Meperidine (Demerol®), Oxycodone, Morphine, or Methadone, you have taken opioids. Opioid addiction is estimated to kill 130 people a day in the US.³ When considering the cost of health care, lost productivity, addiction treatment, and involvement in the criminal justice system, the entire economic burden of this crisis is estimated to be $78.5 billion per year.⁴

Key Opioid facts:
- Roughly 21% to 29% of patients prescribed opioids for chronic pain, misuse them.
- Between 8% and 12% of those that use opioids develop an opioid use disorder.
- An estimated 4% to 6% of those who misuse prescription opioids, transition to heroin.
- About 80% of people who use heroin, first misused prescription opioids.
- Opioid overdoses increased 30% from July 2016 through September 2017, in 52 areas, in 45 states.
- The Midwestern region saw opioid overdoses increase 70% from July 2016 through September 2017.⁵

The National Institute on Drug Abuse (NIDA) places blame for the drastic increase in opioid addiction squarely in the lap of pharmaceutical companies that assured the medical communities of no risk of addiction with these drugs. As a result of more widespread prescriptions across ages, races, and genders, the demographics of opioid addiction have changed dramatically in the US.⁶ The typical opioid addict of the 1960’s was a heroin addict on the corner, typically an unemployed, young, and male. Today,

---
³ https://www.drugabuse.gov/drugs-abuse/opioids/opioid-overdose-crisis
⁵ https://www.drugabuse.gov/drugs-abuse/opioids/opioid-overdose-crisis
the majority of addicts were initially introduced to opioids through the use of prescription drugs. This addict may be the other mom picking your kids up from football practice or your co-worker down the hall.\textsuperscript{7} There has been a shift away from young, non-white, minorities, to an older more suburban, predominantly white, and more women\textsuperscript{8}.

How opioids affect the body

Opioids bind to receptors on cells across the body, specifically, nerve cells. These interactions affect numerous neurological functions, including our ability to sense pain (analgesia), central depression, respiratory depression, euphoria, reduced gastrointestinal motility, sedation, and others (Levine 2013). Opioids stop pain by binding to receptors at the terminal nerved endings, impeding the release of a neurotransmitter. This results in blocking pain at that site (Levine 2013). In the brain, the drug binds to the mu opioid receptors to produce the sought after euphoric effects.\textsuperscript{9}

Prescription opioids are generally safe when take for a short period of time. However, regular use can result in dependence, addiction, an increase in use and possible overdose, and potential death.\textsuperscript{10} When used in combination with other drugs, missused, or when used in combinations with another opioid, these drugs can result in death most often due to respiratory depression.

Opioids have the potential to impair the mental and/or physical abilities of an individual to perform common tasks such as driving or conducting hazardous tasks (Levine 2013). Psychological effects seen with opioids include drowsiness, and depressed motor reflexes. Physiological effects include reduction in the ability to sense pain, dry mouth, respiratory depression, and low body temperature. These effects can be seen in

\textsuperscript{7} https://www.drugabuse.gov/publications/research-reports/relationship-between-prescription-drug-abuse-heroin-use/rx-opioids-heroin-have-similar-effects-different-risk-factors
\textsuperscript{8} https://www.drugabuse.gov/publications/research-reports/relationship-between-prescription-drug-abuse-heroin-use/rx-opioids-heroin-have-similar-effects-different-risk-factors
\textsuperscript{9} https://www.drugabuse.gov/publications/research-reports/relationship-between-prescription-drug-abuse-heroin-use/rx-opioids-heroin-have-similar-effects-different-risk-factors
\textsuperscript{10} https://www.drugabuse.gov/drugs-abuse/opioids/opioid-overdose-crisis
impaired driving skills, including slow driving, poor vehicle control, slowed reaction time, and difficulty following directions (Levine 2013).

**Opioids in combinations with other drugs**

Combining opioids with other drugs that act on the central nervous system, such as alcohol, antihistamines, barbiturates, benzodiazepines, or general anesthetics is dangerous. Mixing these drugs with opioids may result in death due to respiratory depression at lower doses of opioids than would typically be toxic or lethal.11 Opioids have an additive effect with respect to other central nervous system depressant drugs, such as alcohol.

**Opioid testing**

Opioids and their metabolites can be detected in blood or urine samples. A typical urine toxicology test is performed using an immunoassay. An immunoassay is like a pregnancy test, it uses engineered antibodies that are bound to a color reagent that bind to the drug or its metabolite(s). Immunoassays are the most commonly used and affordable technique for rapid screening. Typical cut-off values (the level above which the test is positive and below which the test is interpreted as negative), are relatively high, which may lead to a ‘false negative’. There is also a question of antibody specificity and the possibility for cross-reactivity with other substances that could result in a ‘false positive’. Some compounds that can cause cross reactivity in an immunoassay include poppy seeds, rifampin, chlorpromazine, and dextromethorphan. Samples that test positive during an immunoassay screen should be confirmed by gas chromatography/mass spectrophotometry (GC/MS) or liquid chromatography mass

---

spectrophotometry LC/MS/MS. These testing techniques are very specific, measures the exact chemical, and provides a quantitative measurement at very low levels.

Opioid use can be detected for up to 4 days after use. As such, determining exact time and dose of opioid cannot be determined with only urine samples.

**Summary**

Most experts suggest that the opioid epidemic has not peaked yet in the US and the demographics of the typical addict have changed dramatically from the stereotype. Opioid addiction may afflict anyone, regardless of economic status or race. Testing for this drug in blood or urine should be verified and quantitated using GC/MS methodology in order to ensure there is not a false positive.

**Supportive literature**


Cannabidiol (CBD)

By Carla J. Kinslow, Ph.D.

Cannabidiol (CBD) is one of over 100 cannabinoids found in the cannabis plant and is thought to primarily contribute its anti-anxiety and anti-inflammatory properties, yet no psychotic effects (Russo, 2011). As such, CBD-containing products are attractive to consumers who are trying to treat such conditions without the side-effects of the psychoactive component of cannabis and this market is growing. Concentrations of CBD present in the cannabis plant are highly variable and depend on the plant genetics, growing conditions, climate and light (Bruni et al., 2018). For all strains of cannabis plants, the highest concentration of CBD is found in the sticky, resinous secretions from the female inflorescence (Pavlovic et al., 2018). Commonly, preparations of CBD from the plant begin with crushing or grinding the inflorescence, but freezing methods are also used. Once crushed or frozen, CBD is isolated from the other resinous materials via solvent extraction. Extraction solvents for this compound vary, including ethanol and isopropyl alcohol, petroleum-ether, naphtha, or butane (Hazekamp, 2018). There is no standardized method of extraction and the choice of method can have an impact on taste, color, and viscosity of the final product (Hazekamp, 2018). Once extracted, CBD can be then added to edible oils such as sunflower, hemp, or olive oil to make it palatable for the consumer (Hazekamp, 2018).

Application, absorption and therapeutic effects of CBD

There are dozens of CBD producers in the market place and a quick internet search with the keyword “CBD” indicates consumer options that include numerous forms, including edible oils, lotions, and vaping products. Thus, there are several routes of exposure to this drug based on the product used, including oral, dermal or inhalation. The route that the drug enters the body plays a major role in the how, when and where effects may be observed. Each route has a unique profile of absorption into the body.
For example, CBD is a lipid-soluble compound, which makes dermal absorption an efficient route of entering the body (Bruni et al., 2018).

Once inside the body, CBD binds to cellular receptors on cells to illicit cellular responses and it is thought that CBD may interact with, or affect the binding, of THC (Bruni et al, 2018). It is well established that there is highly complex relationship of synergism, as well as inhibition, with the cannabinoids and other compounds such as terpenes present in cannabis that collectively result in observed, but not well characterized, medical benefits. This interplay may also help explain some of the very diverse and individual effects of CBD, including those related to its analgesic, anti-inflammatory, anti-anxiety and anti-psychotic activity (Bruni et al., 2018).

**Pain and inflammation**

CBD’s proposed benefit for pain relief is well documented in the anecdotal literature; however, due to the high variability in product quality, individual responses, and the lack of a fully characterized human endocannabinoid system, the mechanism of this medical benefit remains largely illusive.

Although this system is not well characterized, animal studies provide some insight into this mechanism. For example, a study by Pagano et al., 2016 evaluated the effect of orally administered pure CBD oil and CBD oil in a “botanical extract” on intestinal inflammation in mice. The researchers found that the pure CBD oil had no effect, yet the “botanical extract” with high CBD oil reduced the extent of inflammatory damage to the mouse colon (Pagano et al., 2016). In a separate study by Philpott et al. (2017), the researchers found that pure CBD oil treatment clearly reduced osteoarthritis (OA)-associated joint pain in male rats with end-stage OA. Positive endpoints included increased weight bearing, reduction in acute inflammation and protection against late joint inflammation and pain, and were also neuroprotective (Philpott et al., 2017). Taken together, these studies indicate that the beneficial effects of CBD may be disease-and/or organ-specific and may depend on a synergistic mechanism of action between other compounds in the medication.
Other applications

Interestingly, CBD oil has been shown to have potential applications in other areas of scientific research. For example, pure CBD oil (i.e., oil without other possible synergistic partners such as terpenes) has been shown to substantially inhibit methicillin-resistant *Staphylococcus aureus* (MRSA) (Russo, 2011). This research indicates a possible role of cannabinoids in antibacterial applications in the future.

The pharmaceutical industry has also moved forward in the evaluation of cannabinoids. Epidiolex is a highly purified and concentrated liquid formulation of CBD that was the first ever cannabis extract to be approved by the US Food and Drug Administration (USFDA)\(^\text{12}\). It is specifically used for the treatment of two very rare forms of childhood epilepsy, Lennox-Gastaut and Dravet syndromes\(^\text{13}\). This medication is taken by mouth twice daily, starting at a lower dose at first and then gradually increased weekly. Studies have shown that taking Epidiolex along with other seizure medications results in fewer seizures compared to the placebo group.\(^\text{14}\) Importantly, studies evaluating the medical benefits of Epidiolex should not be applied to other, less pure products, specifically whole cannabis. As discussed above and in the following sections, non-FDA approved products do not go through the same stringent safety or quality control standards as Epidiolex and may harbor additional pharmacologically active compounds such as terpenes or other cannabinoids, including THC.

Product Consistency and Safety

As of 2018 and with the exception of Epidiolex, there were no specific guidance that could help the consumer use this product. Specifically, there is no standardized guidance from FDA regarding dosage, route of administration, maximum recommended daily dose, shelf life, and stability (Pavlovic et al., 2018). The purity of the CBD oil may

\(^{12}\) https://www.fda.gov/Drugs/InformationOnDrugs/ucm613357.htm
\(^{13}\) https://www.fda.gov/Drugs/InformationOnDrugs/ucm613357.htm
\(^{14}\) https://www.fda.gov/Drugs/InformationOnDrugs/ucm613357.htm
also vary among products, and labeled “CBD oil” may contain additional medically active compounds, including THC and terpenes (Pavlovic ne et al., 2018).

As discussed above, isolation of CBD oil from the cannabis plant is a multi-step process and can include introducing solvent extraction methods that may result in residual solvent contamination in final product. In an effort to avoid this possible quality issue, researchers have now bio-engineered cannabinoid genes into yeast (Luo et al., 2019). This is a significant step forward in product quality and standardization.

Although the safety of CBD and its oils have not been fully evaluated, the information to date does not indicate that consumption of the drug CBD poses a high degree of toxicity or adverse effects. Importantly, the safety of long-term treatment and the emergence of any possible chronic adverse effects after acute use have not been evaluated to date. Side effects of acute use of pure CBD oil are inconsistent across a population and within studies, but have been reported to include tiredness, diarrhea, and changes of appetite/weight (Iffland et al., 2017).

Summary

In general, CBD oil has been shown to have medical benefits in very specific patients with seizures; however the average consumer should understand the limitations to how the medical and scientific community understands this drug.

References

2. Natascia Bruni, Carlo Della Pepa, Simonetta Oliaro-Bosso, Enrica Pessione, Daniela Gastaldi, Franco Dosio. Cannabinoid Delivery Systems for Pain and
Inflammation Treatment. Molecules. 2018 Oct; 23(10): 2478. Published online 2018 Sep 27.


4. Philpott, K et al. Attenuation of early phase inflammation by cannabidiol prevents pain and nerve damage in rat osteoarthritis. Pain. 2017 Dec; 158(12): 2442–2451. Published online 2017 Sep 1


Department of Transportation (DOT) Drug testing – what it does and does NOT show

By Carla J. Kinslow, Ph.D.

Most of us have had a pre-employment drug screening at some time in our lives, so we understand what drug testing entails. But…have you ever asked yourself, “What does it not entail?” “What will they find?” “What will they not find?” “Should I have eaten that poppy seed muffin this morning?”

Testing rules for the Department of Transportation (DOT) are described under the Code of Federal Regulations (CFR): TITLE 49: TRANSPORTATION: PART 40 - PROCEDURES FOR TRANSPORTATION WORKPLACE DRUG AND ALCOHOL TESTING PROGRAMS. This evaluation only includes testing urine for five drugs or drug classes: marijuana metabolites, cocaine metabolites, amphetamines, opiate metabolites, phencyclidine (PCP). Importantly, this test is required to only identify these compounds in urine and only at certain cut-off level. It does not indicated if a person has low levels of the drug or its metabolites, unless a confirmatory test is conducted on a positive screen. So, the first thing the screening test does not indicate is if a person has any evidence of these drugs in their system. This is due to the limitations of the screening methodology and with the biological media -urine.

The urine screening methodology is based on using engineered antibodies to seek out and bind to drug metabolites in the urine sample. This method is quick, technically easy to perform, comes in a commercial kit, and provides information that is easily read and understood. It's the most commonly used technique in all settings, such as OSHA, pre-employment and pre-surgical settings. The scientific limitations of this technique are based on the specificity of the antibody for the specific molecule and the concentration of the drug in the urine. If the antibody used in the kit cannot bind strongly enough to the drug or metabolite, the test may result in a ‘false negative’. Additionally, if the antibody makes a mistake (poor specificity) and binds to the wrong molecule, there could be a ‘false positive’. This is termed cross-reactivity. Compounds that have the

potential to cross react in an immunoassay for DOT urine testing include some very common over the counter drugs or prescription drugs or foods, such as, poppy seeds, rifampin, ephedrine (Sudafed), and nonsteroidal anti-inflammatory drugs (NSAIDS such as ibuprofen).16

Urine screens only detect the drug or its metabolites after they have passed through the body. Thus, if one is posed with the question of, “When did he/she take the drug?” That exact answer cannot be provided based solely on the urine drug screen results and additional information and/or literature would be needed to address that question. Furthermore, acute impairing effects of a drug is typically seen while the drug is binding to and/or affected the cells of the body and the presence of the drug in the urine cannot be correlated with an exact time of possible impairment. For all of these drugs, the rate of drug absorption, metabolism, and elimination is highly variable and some of these drugs can be detected in urine for several days to weeks after past last use. With that being said, there is some forensic value in these tests. They can be used to determine past use and past exposure, and to ask the question of chronic exposure. Chronic exposure to several of these drugs has the potential to cause long-term decrements in executive functions, motor skills, and decision making (Levine 2013). These tests can also be used in conjunction with other medical information to help understand the potential for impairment or approximate time of last use on an individual basis.

**Confirmatory testing**

Because of the limitations described above, the DOT requires that all positive testing results be evaluated through a confirmatory testing method. Samples that test positive during an immunoassay screen should be verified by liquid chromatography, gas chromatography/mass spectrophotometry (LC/GC/MS). This is very specific, measures the exact chemical, and provides a quantitative measurement at very low

---

levels. This testing takes substantial technical skill above that of the immunoassay, requires a specific laboratory, and comes at a substantial cost.

**Confirmatory cutoff values vary for each drug or metabolite:**

<table>
<thead>
<tr>
<th>§ 40.87 What are the cutoff concentrations for drug tests?</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) As a laboratory, you must use the cutoff concentrations displayed in the following table for initial and confirmatory drug tests. All cutoff concentrations are expressed in nanograms per milliliter (ng/mL). The table follows:</td>
</tr>
<tr>
<td>Initial test analyte</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Marijuana metabolites</td>
</tr>
<tr>
<td>Cocaine metabolites</td>
</tr>
<tr>
<td>Opiate metabolites</td>
</tr>
<tr>
<td>Codeine/Morphine&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>6-Acetylmorphine</td>
</tr>
<tr>
<td>Phencyclidine</td>
</tr>
<tr>
<td>Amphetamines&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>AMP/MAMP&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>MDMA&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>MDA&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>MDEA&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>1</sup>Delta-9-tetrahydrocannabinol-9-carboxylic acid (THCA).
<sup>2</sup>Morphine is the target analyte for codeine/morphine testing.
<sup>3</sup>Either a single initial test kit or multiple initial test kits may be used provided the single test kit detects each target analyte independently at the specified cutoff.
<sup>4</sup>Methamphetamine is the target analyte for amphetamine/methamphetamine testing.
<sup>5</sup>To be reported positive for methamphetamine, a specimen must also contain amphetamine at a concentration equal to or greater than 100 ng/mL.
<sup>6</sup>Methylenedioxymethamphetamine (MDMA).
<sup>7</sup>Methylenedioxycyclohexylamphetamine (MDEA).

**Drugs that are not detecting with the DOT urine drug screen**

There are several over the counter and prescription medications that have the potential for impairing a driver that are not on this screen. Prior to January 1, 2018, synthetic opioids such as oxycodone, hydrocodone, buprenorphine, or methadone were not included. These medications have same potential for conferring impairing effects as
non-synthetic opioids. After January 1, 2018, they included hydrocodone, hydromorphone, oxycodone, and oxymorphone to the screen.

Opioids have the potential to impair the mental and/or physical abilities of an individual to perform common tasks such as driving or conducting hazardous tasks (Levine 2013). Psychological effects seen with opioids include drowsiness, and depressed reflexes. Physiological effects include reduction in the ability to sense pain, dry mouth, respiratory depression, and low body temperature. These effects can be seen in impaired driving skills, including slow driving, poor vehicle control, slowed reaction time, and difficulty following directions (Levine 2013).

The DOT testing does not test for benzodiazepines. These drugs are commonly prescribed to individuals for treatment of mental disorders, including depression. Notably, in 2009, a panel of experts agreed that:

“Individuals who take benzodiazepines for any length of time should not be allowed to drive until the drug has been cleared from their system (i.e., within seven half-lives of the drug and any active metabolites). Chronic users of benzodiazepines (i.e., regular use for more than a month) should also wait an additional week after the drug has cleared from their system before resuming driving to ensure that the drug has been completely eliminated. It is also suggested that FMCSA provide information regarding the half-life and seven half-lives of benzodiazepines and active metabolites to medical examiners for use at the time of examination.”

Seven half-lives of benzodiazepines is highly variable, depending on the medication. For example, seven half-lives of Triazolam (Halcion) is as few as 14 hours and alprazolam (Xanax) can be as few as 42 hours, but Diazepam (Valium) can be as

---

17 https://www.transportation.gov/odapc/DOT_5_Panel_Notice_2018
18 Commercial names for these include: OxyContin®, Percodan®, Percocet®, Vicodin®, Lortab®, Norco®, Dilaudid®, Exalgo®
19 https://www.transportation.gov/odapc/DOT_5_Panel_Notice_2018
long as 1400 hours (58 days)\textsuperscript{22}. Other drugs used to treat mental disorders that are not benzodiazepines and not on the DOT test, but can cause similar impairing affects include Zaleplon (Sonata), Zolpidem (Ambien) and Eszopeclone (Lunesta)\textsuperscript{23}.

Notably, urine taken for DOT testing cannot be used for additional testing. Nor can the result of another test be considered for DOT testing.

**Summary**

DOT drug testing has several limitations which should be considered on an individual basis when evaluating a positive sample. Application of these testing results to questions beyond those related to DOT should be considered with these limitations in mind.

**Supportive literature**

- \url{https://www.transportation.gov/sites/dot.dev/files/docs/PART40_2012.pdf}

\textsuperscript{22} \url{https://www.fmcsa.dot.gov/sites/fmcsa.dot.gov/files/docs/Medical-Expert-Panel-Psychiatric-Psychiatric-MEP-Panel-Opin.pdf}

\textsuperscript{23} \url{https://www.fmcsa.dot.gov/sites/fmcsa.dot.gov/files/docs/Medical-Expert-Panel-Psychiatric-Psychiatric-MEP-Panel-Opin.pdf}
Law Enforcement Drug Recognition Experts

By Jim Jarrow

A Drug Recognition Expert, known as a “DRE”, is a law enforcement certification issued by the International Association of Chiefs of Police, with funding provided by the National Highway Traffic Safety Administration. More and more law enforcement agencies now have DRE officers. A DRE evaluation is typically done post arrest, where the officer is attempting to determine if impairment is drug related. Attorneys and transportation industry professionals should know what a DRE entails, to understand information on a vehicle driver should DRE examination be conducted on any driver involved in an accident.

The questions the DRE officer seeks to answer are: 1) Is the person impaired by something other than alcohol; 2) If impaired, is the impairment related to drugs or a medical condition; and 3) If drugs, what category or categories are involved.

Current certification involves nine days of classroom instruction with written testing, field training work evaluating individuals who are non-alcohol impaired individuals where the officer’s opinion of the category of drug has to match toxicology results, and a comprehensive written exam with an interview by a board of instructors. This results in a two year certification which requires recertification.

A DRE officer may be called when an agency believes they have a suspected impaired driver. Typically the DRE officer is contacted after the initiating officer has made a decision to take the person into custody. It is used not only in motor vehicle accidents, but in other applications such as drug issues at schools, probation or parole offenders,
family or child in need of care situations, or any issue where an officer non-alcohol impairment may be an issue in a case.

The subject is typically Mirandized, and if the subject agrees to the evaluation, the following process is followed:

12 STEP PROCEDURE

1. BREATH ALCOHOL SCREENING TEST
2. INTERVIEW OF ARRESTING OFFICER
3. PRELIMINARY EXAMINATION
   A. FIRST PULSE
4. EYE EXAMS (EQUAL TRACKING/EQUAL PUPIL SIZE)
   A. HORIZONTAL GAZE NYSTAGUS
      — SMOOTH PURSUIT
      — MAXIMUM DEVIATION
      — ANGLE OF ONSET
   B. VERTICAL GAZE NYSTAGMUS
   C. NON-CONVERGENCE
5. DIVIDED ATTENTION TESTS
   A. ROMBERG
      — BODY SWAY
      — 30 SECOND INTERNAL CLOCK
   B. WALK AND TURN
      — 9 STEPS / 9 STEPS
   C. ONE LEG STAND (30 SEC. EACH LEG)
      — LEFT LEG THEN RIGHT LEG
   D. FINGER TO NOSE
      — LEFT/RIGHT/LEFT/RIGHT/RIGHT/LEFT
6. VITAL SIGNS AND SECOND PULSE
7. DARK ROOM CHECKS OF PUPIL SIZE (WAIT 90 SECONDS); NASAL & ORAL CAVITY EXAM
8. CHECK FOR MUSCLE TONE
9. CHECK FOR INJECTION MARKS AND THIRD PULSE
10. INTERROGATION, STATEMENTS AND OTHER OBSERVATION
11. OPINION OF EVALUATOR
12. TOXICOLOGICAL EXAMINATION

The subject has the right to refuse the evaluation, which begs the question of why would anyone ever agree to the evaluation? It is possible that a person fails field sobriety
tests, but has not taken any drugs, and the evaluation can help exonerate the subject. A recent real life example is police were called to a traffic accident behind a drug rehabilitation center. One of the residents was involved in a motor vehicle accident, failed field sobriety tests, had a possible drug indicator of foaming at the mouth, and showed zero alcohol on a pre-breath test (commonly referred to as a “PBT”). A DRE was called, evaluated the subject, and ruled out a drug issue. The subject was then unarrested.

The evaluation is a twelve step process. If the person is over .08%, typically would not do the evaluation because the blood alcohol is already at a level where the subject can be prosecuted. Also, when the alcohol is at or above a legal limit, it becomes difficult to differentiate signs and symptoms between alcohol and drugs. So the classic case is where a person is exhibiting indications of impairment but has a low or negative breath alcohol content.

The DRE gives an opinion, which ultimately leads to one of three findings: no impairment, impairment related to a medical issue, or impairment within one of seven drug categories. The DRE uses a matrix in performing the evaluation.
DREs are recognized by courts as a legitimate field of expertise.

Documents filled out during the DRE exam, may include the officer taking handwritten notes, and a Drug Influence Evaluation form, that is used internationally. An example of this form is attached at the end of the Toxicology Update materials. The DRE officer would also typically do a narrative report.

Depending on the drug category at issue, the preferred time frame for a DRE evaluation is within three hours of the accident or traffic stop. In some states, the standard for some chemical testing to be prima facie evidence is within three hours of a stop, and because some drug symptoms begin to dissipate between four and six hours.
To Test or Not to Test, That is the Question

A common but not always so easy a question to answer that arises is whether or not a driver should be tested following a motor vehicle accident. This involves following the DOT guidelines, and a consideration of other factors that may affect jury deliberations and your verdict. The guiding regulation is 382.303, which states:

§382.303 Post-accident testing.

(a) As soon as practicable following an occurrence involving a commercial motor vehicle operating on a public road in commerce, each employer shall test for alcohol for each of its surviving drivers:

(1) Who was performing safety-sensitive functions with respect to the vehicle, if the accident involved the loss of human life; or

(2) Who receives a citation within 8 hours of the occurrence under State or local law for a moving traffic violation arising from the accident, if the accident involved:

(i) Bodily injury to any person who, as a result of the injury, immediately receives medical treatment away from the scene of the accident; or

(ii) One or more motor vehicles incurring disabling damage as a result of the accident, requiring the motor vehicle to be transported away from the scene by a tow truck or other motor vehicle.

(b) As soon as practicable following an occurrence involving a commercial motor vehicle operating on a public road in commerce, each employer shall test for controlled substances for each of its surviving drivers:

(1) Who was performing safety-sensitive functions with respect to the vehicle, if the accident involved the loss of human life; or

(2) Who receives a citation within thirty-two hours of the occurrence under State or local law for a moving traffic violation arising from the accident, if the accident involved:

(i) Bodily injury to any person who, as a result of the injury, immediately receives medical treatment away from the scene of the accident; or

(ii) One or more motor vehicles incurring disabling damage as a result of the accident, requiring the motor vehicle to be transported away from the scene by a tow truck or other motor vehicle.

(c) The following table notes when a post-accident test is required to be conducted by paragraphs (a)(1), (a)(2), (b)(1), and (b)(2) of this section:
TABLE FOR §382.303(A) AND (B)

<table>
<thead>
<tr>
<th>Type of accident involved</th>
<th>Citation issued to the CMV driver</th>
<th>Test must be performed by employer</th>
</tr>
</thead>
<tbody>
<tr>
<td>i. Human fatality</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>ii. Bodily injury with immediate medical treatment away from the scene</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>iii. Disabling damage to any motor vehicle requiring tow away</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td>NO</td>
<td>NO</td>
</tr>
</tbody>
</table>

(d)(1) Alcohol tests. If a test required by this section is not administered within two hours following the accident, the employer shall prepare and maintain on file a record stating the reasons the test was not promptly administered. If a test required by this section is not administered within eight hours following the accident, the employer shall cease attempts to administer an alcohol test and shall prepare and maintain the same record. Records shall be submitted to the FMCSA upon request.

(2) Controlled substance tests. If a test required by this section is not administered within 32 hours following the accident, the employer shall cease attempts to administer a controlled substances test, and prepare and maintain on file a record stating the reasons the test was not promptly administered. Records shall be submitted to the FMCSA upon request.

(e) A driver who is subject to post-accident testing shall remain readily available for such testing or may be deemed by the employer to have refused to submit to testing. Nothing in this section shall be construed to require the delay of necessary medical attention for injured people following an accident or to prohibit a driver from leaving the scene of an accident for the period necessary to obtain assistance in responding to the accident, or to obtain necessary emergency medical care.

(f) An employer shall provide drivers with necessary post-accident information, procedures and instructions, prior to the driver operating a commercial motor vehicle, so that drivers will be able to comply with the requirements of this section.

(g)(1) The results of a breath or blood test for the use of alcohol, conducted by Federal, State, or local officials having independent authority for the test, shall be considered to meet the requirements of this section, provided such tests conform to the applicable Federal, State or local alcohol testing requirements, and that the results of the tests are obtained by the employer.

(2) The results of a urine test for the use of controlled substances, conducted by Federal, State, or local officials having independent authority for the test, shall be considered to meet the
requirements of this section, provided such tests conform to the applicable Federal, State or local controlled substances testing requirements, and that the results of the tests are obtained by the employer.

(h) Exception. This section does not apply to:

1. An occurrence involving only boarding or alighting from a stationary motor vehicle; or

2. An occurrence involving only the loading or unloading of cargo; or

3. An occurrence in the course of the operation of a passenger car or a multipurpose passenger vehicle (as defined in §571.3 of this title) by an employer unless the motor vehicle is transporting passengers for hire or hazardous materials of a type and quantity that require the motor vehicle to be marked or placarded in accordance with §177.823 of this title

The panel will present some thoughts, observations on these issues.
### DRUG INFLUENCE EVALUATION

<table>
<thead>
<tr>
<th><strong>Evaluator</strong></th>
<th><strong>DRE #</strong></th>
<th><strong>Rolling Log #</strong></th>
<th><strong>Case #</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Recorder/Witness</td>
<td>Crash: □ Fatal □ Injury □ Property</td>
<td>Arresting Officer (Name, ID#):</td>
<td></td>
</tr>
<tr>
<td>Arrestee’s Name (Last, First, Middle)</td>
<td>Date of Birth</td>
<td>Sex</td>
<td>Race</td>
</tr>
<tr>
<td>Arresting Officer Agency:</td>
<td>Date Examined / Time / Location</td>
<td>Breath Results: Test Refused □ Instrument #: Chemical Test: Urine □ Blood □ Test or tests refused □</td>
<td></td>
</tr>
<tr>
<td>Miranda Warning Given</td>
<td>Yes □ No</td>
<td>What have you eaten today? When?</td>
<td>What have you been drinking? How much?</td>
</tr>
<tr>
<td>Given By:</td>
<td>Time now/ Actual</td>
<td>When did you last sleep? How long</td>
<td>Are you sick or injured?</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you take insulin?</td>
<td>Yes □ No</td>
<td>Are you under the care of a doctor or dentist?</td>
<td>Yes □ No</td>
</tr>
<tr>
<td>Do you have any physical defects?</td>
<td>Yes □ No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are you taking any medication or drugs?</td>
<td>Yes □ No</td>
<td>Attitude:</td>
<td>Coordination:</td>
</tr>
<tr>
<td>Speech:</td>
<td>Breath Odor:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corrective Lenses: □ None □ Hard □ Soft □ Contacts, if so</td>
<td>Eyes: □ Normal □ Bloodshot □ Watery</td>
<td>Blindness: □ None □ Left □ Right □ Equal □ Unequal</td>
<td>Tracking: □ Equal □ Unequal</td>
</tr>
<tr>
<td>Glasses</td>
<td>Vertical Nystagmus □ Yes □ No</td>
<td>Able to follow stimulus □ Yes □ No</td>
<td>Eyelids □ Normal □ Droopy</td>
</tr>
<tr>
<td>Pupil Size: □ Equal □ Unequal (explain)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse and time</td>
<td>HGN</td>
<td>Left Eye</td>
<td>Right Eye</td>
</tr>
<tr>
<td>1.</td>
<td>Lack of Smooth Pursuit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Maximum Deviation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Angle of Onset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Modified Romberg Balance</td>
<td>Walk and Turn Test</td>
<td>Cannot keep balance</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Starts too soon</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal clock</td>
<td>Describe turn</td>
<td>Cannot do test (explain)</td>
<td>Type of footwear:</td>
</tr>
<tr>
<td>estimated as 30 seconds</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finger to Nose</td>
<td>PUPIL SIZE</td>
<td>Room Light (2.5 – 5.0)</td>
<td>Darkness (5.0 – 8.5)</td>
</tr>
<tr>
<td>(Draw lines to spots touched)</td>
<td>Left Eye</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Right Eye</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Temperature</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle tone: □ Normal □ Flaccid □ Rigid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comments:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>What drugs or medications have you been using?</td>
<td>How much?</td>
<td>Time of use?</td>
<td>Where were the drugs used? (Location)</td>
</tr>
<tr>
<td>Date / Time of arrest:</td>
<td>Time DRE was notified:</td>
<td>Evaluation start time:</td>
<td>Evaluation completion time:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Officer’s Signature:</td>
<td>DRE #</td>
<td>Reviewed/approved by / date:</td>
<td></td>
</tr>
<tr>
<td>Opinion of Evaluator: □ No Impairment □ Alcohol □ Medinal □ CNS Stimulant □ Dissociative Anesthetic □ Inhalant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Rev 01/15