

## Cannabis, Cannabinoids and Driving

What is the affect of cannabinoids on driving. The FDA has the best answer. It's apparent that the FDA does not believe that the mere presence of cannabinoids or their metabolites is a contraindication to driving or operating heavy equipment. In 1985 the federal government approved the sale of delta nine tetrahydrocannabinol THC (dranabinol – trade name Marinol). THC is the euphoric agent in cannabis. Marinol is delta 9 THC. THC is the euphoriant in cannabis. Cannabis contains an anti-euphoriant cannabidiols (CBDs). Therefore Marinol is more likely to cause dysphoria than cannabis, because of the presence of CBDs in cannabis.

According to extensive studies done by GW Pharmaceuticals of the UK, manufacturers of tincture of cannabis (Sativex), cannabis is much less euphoric than Marinol. This is because of the presence in marijuana of cannabinoids (CBDs). Marinol has no CBDs. Nevertheless the FDA clearly allows for the driving and operation of heavy equipment and engaging in any hazardous activity once "...it is established that they are able to tolerate the drug and to perform such tasks safely." This quote is from the FDA approval package insert for drabinol (Marinol) made by Unimed pharmaceutical Inc. A Solvay Pharmaceutical Inc. company.

### • **There is No Relationship between Blood Levels of Cannabinoids and Psychomotor Impairment**

The basic problem with trying to link the blood level of cannabinoids or their metabolites with level of impairment is that, unlike alcohol, cannabinoids' concentration in bodily fluids has no clear correlation to their activity in the brain. Urine tests of THC and/or metabolites are clearly useless for the obvious reason that they lag hours and days behind actual exposure. Blood concentrations are somewhat more useful in that they can at least help determine whether one has used marijuana recently. High levels of blood THC, ( $\leq 10$  ng/ml), are a good sign of having used marijuana in the last hour or two. The problems are that (1) blood levels are highly variable and (2) have no clear-cut relation to actual impairment, i.e., "being under the influence."

This was aptly illustrated in the most realistic study on marijuana and driving to date, HWJ Robbe's "Influence of Marijuana on Driving," (Institute for Human Psychopharmacology, Univ. of Limburg, Maastricht, 1994; sponsored by the U.S. National Highway Transportation Safety Administration). In this study, drivers were dosed with marijuana and observed while actually driving on the road in the Netherlands. Robbe looked at the blood THC of the subjects and found the following:

"Plasma Concentrations of the Drug: Though consumed dose differed little between subjects, THC and THC-COOH (e.g., metabolite) varied enormously. Thirty minutes after smoking 300 micrograms/kg, for example, THC ranged between 1.6 and 29.6 ng/ml..." "Drug Plasma Concentrations and Driving Performance": One of the program's objectives was to determine whether it is possible to predict driving

impairment by plasma concentrations of THC and/or its metabolite, THC-COOH. The answer is very clear: it is not. Plasma of drivers showing substantial impairment in these studies contained both high and low THC concentrations; and, drivers with high plasma concentrations showed substantial, but also no impairment, even some improvement..."

The authoritative Consensus Report of NIDA's Research Technology Branch ("Drug Concentrations and Driving Impairment (JAMA, Nov. 8, 1985 – Vol. 254 #18) said:

"What is known about correlations between driving impairment and drug concentration? – Except for ethanol, determinations of drug concentrations in body fluids are at present of limited value for establishing driving impairment..."

Although this report dates from 1985, its conclusions are still valid.

In a forensic review (Mason et al., 1985), the issue of marijuana's effect on driving was addressed, and it was indicated that isolated reports of adverse outcomes secondary to impairment by Cannabis as a sole inebriant were rare. The authors concluded that there was no suitable correlation between plasma or blood levels of THC and the degree of apparent impairment a human might exhibit.

The blood concentration of THC is meaningless as any predictor of psychomotor effect. Dr. Barry Beyerstein of Simon Fraser University said, "The relationship between THC (the psychoactive ingredient in marijuana) levels in blood and impairment of eye-hand coordination, reaction time and other components of driving skill is not a straightforward one. Also, individual differences of impairment among different users are so great that it would be very difficult to set a fair legal standard of impairment that would apply to everyone." This is the same conclusion which the U.S. Department of Transportation reached.

"A finding of 20 ug/L of THC in plasma (10 ug/L in blood) probably indicates that marijuana was smoked within the hour and with 10 uL plasma within two hours. THC concentrations greater than 50 ug/L indicate smoking within 20 minutes. Concentrations of THC-COOH, THC metabolite. It is unlikely that a range of plasma THC concentrations could be reliably equated with impaired performance.

Solowij (1998) states that blood plasma levels of THC of 10-15 ng/ml are suggestive of recent consumption but determining just how recent use was is not possible. A more precise measure is the ratio of THC to THC-COOH. If THC-COOH levels are greater than THC, use was probably more than 30 minutes ago but only in naive users.

#### • **Science, Cannabis and Driving**

As to cannabis having a clear adverse effect on driving, that also does not hold up to scientific scrutiny. Going back prior to the NIDA consensus report and the Robbe study, the Nixon Marijuana Commission concluded that there is no conclusive evidence that cannabis impairs driving. This was in part based on studies by Crancer et al. for the Washington State Highway Department, a similar study done at UCLA, and another at

Boston University. Crancer found that, "Simulated driving scores for subjects experiencing a normal social 'high' and the same subjects under control conditions are not significantly different. However, there are significantly more errors for alcohol-intoxicated than for control subjects."

This assessment is affirmed by the FDA approved package insert language for Marinol that driving and operating heavy equipment after use of synthetic  $\Delta 9$  THC is permissible. The package insert states that patients receiving treatment with Marinol should be specifically warned not to drive, operate machinery, or engage in any hazardous activity until it is established that they are able to tolerate the drug and to perform such tasks safely.

According to research by British scientists, a moderate amount of cannabis may actually improve driving performance. A group of 20 drivers aged 21-40 participated in a driving simulator test. Ten of them smoked the equivalent of about half a cannabis cigarette. Subjects under cannabis scored superior than the sober subjects in most of the tasks, including reaction time and number of collisions. Simon Smith Wright, director of the laboratory where the studies were conducted, said "The results of our test clearly show that a small or moderate amount of cannabis is actually quite beneficial to someone's driving performance."

A story published in January 2004 in Britain's Evening News characterized the results this way:

"A group of 20 volunteers participated in the study, which tested respondents' performance on a video game that simulated driving. Half of the drivers played the game after smoking the equivalent of half a marijuana cigarette. The results showed that for those who had smoked...cannabis, 80 percent demonstrated superior reaction times; 60 percent finished a lap faster; 70 percent experienced a lower number of collisions; 60 percent reached a higher level in the game."

### **National Highway Safety Study 1993**

According to the National Highway Traffic Safety Administration study titled "Marijuana and Actual Driving performance" (published November 1993), "THC's adverse effects on driving performance appear relatively small" and "Evidence from the present and previous studies strongly suggests that alcohol encourages risky driving, whereas THC encourages greater caution."

According to this study, it is not possible to conclude anything about a driver's impairment on the basis of his/her plasma concentrations of THC and THC-COOH determined in a single sample.

A 1993 study of cannabis and driving (Robbe & O'Hanlon, 1993) which was sponsored by the U.S. National Highway Safety Traffic Administration included a review of the literature. The authors' comments in summary of their literature review and of their own results include the following:

The foremost impression one gains from reviewing the literature is that no clear relationship has ever been demonstrated between marijuana smoking and either seriously impaired driving performance or the risk of accident involvement. The epidemiological evidence, as limited as it is, shows that the combination of THC and alcohol is over-represented in injured and dead drivers, and moreso in those who actually caused the accidents to occur. Yet there is little if any evidence to indicate that drivers who have used marijuana alone are any more likely to cause serious accidents than drug-free drivers.

The U.S. Transportation study results were more than confirmed by a 1998 Australian study of 2500 injured drivers which found that drivers who use marijuana are less likely to cause road accidents than drunk drivers or even drug-free drivers. This goes even further than the Australian Government Report (1996) "There is no controlled epidemiological evidence that cannabis users are at increased risk of being involved in motor vehicle or other accidents."

A study from Tilburg, The Netherlands reported in May 2004, "Researchers at the St. Elisabeth Hospital in the Netherlands estimated the association between drug use and motor vehicle accidents by conducting a prospective observational case-controlled study. Cases were drivers involved in road crashes requiring hospitalization. Controls were drivers recruited at random while driving on public roads.

Authors found that driver's risk for road trauma significantly increased with the use of benzodiazepines and alcohol. Increased risks, although not statistically significant, were also assessed for drivers using amphetamines, cocaine, or opiates. The authors concluded that,

**"No increased risk for road trauma was found for drivers exposed to cannabis."**

- **Second Hand Cannabis Smoke**

The possible dangers of second-hand smoke is a dubious proposition. This is largely because there does not appear to be any significant cancer risk from even first-hand cannabis smoking. A study by Kaiser Permanente of 66,000 patient charts comparing cancer rates in cannabis smokers to non-cannabis smokers found no difference in cancer rate between the two groups. Dr. Donald Tashkin of UCLA, whose work is often erroneously cited to support the canard that cannabis smoke is a worse irritant to the bronchial tree than tobacco smoke, actually found the opposite. In comparing the irritation to the bronchial tree of research monkeys by 29 components of tobacco smoke to similar components in cannabis smoke, tobacco was more irritating in 28 instances. The one exception was where the tobacco smoke he found that was five times component caused almost 0 irritation and almost zero for cannabis smoke. Tashkin himself has said on more than one occasion that he does not know of a single case of cancer caused by smoking cannabis.

- **FDA Administrative Law Judge – The Last Word**

In 1988 action was initiated through the FDA to reclassify marijuana to Schedule 2, potentially making it available for prescription to patients. The FDA Administrative Law Judge, Francis Young, reviewed a tremendous amount of testimony from patients,

scientists, and politicians in rendering his ruling. He stated, “By any measure of rational analysis marijuana can be safely used within a supervised routine of medical care.”

When it comes to cannabis safety, we have (1) the findings of the FDA by Administrative Law Judge Young, (2) the FDA's approval of Marinol (synthetic  $\Delta 9$  THC), (3) Marinol (drabinol) is far more dysphoric than cannabis, but driving is permissible. This finding on the dysphoria with Marinol is per GW Pharmaceuticals (GW is the manufacturer of Sativex - tincture of cannabis - which was approved for sale by Health Canada two or three weeks ago and will soon be distributed by Bayer). This is because the cannabidiols (CBDs) in cannabis counter the euphoric impact of THC. Marinol is all THC. One of the best supports for the safety of cannabis is the fact that Marinol is used by tens of thousands, and with the approval of the FDA.