# **Marijuana and Impairment**

#### By Richard Bayer, MD

Does cannabis alone, inhaled eight or more hours before activities such as driving a vehicle or working with machinery, cause significant mental or motor impairment that might increase risk to self or others? This is the question that Oregon legislators should have considered during the session just ended.

Instead, the Republican-controlled House passed a bill that would allow employers to fire — without evidence of impairment— workers who register with the Oregon Medical Marijuana Program and who use marijuana as medicine. Fortunately, the house bill failed in a Democrat-controlled Senate committee after heated testimony, but this may be a temporary reprieve as this legislation will probably be introduced again in the next round.

#### The scientific evidence

Cannabis has been used to relieve pain for centuries throughout the world, including the US, prior to the enactment of the Cannabis Tax Act of 1937.<sup>1</sup> Cannabinoids are a category of substances with cannabis-like properties and include the natural cannabis plant, synthetic cannabinoids, and internal (endogenous) hormones that mimic cannabis.

Case reports of the benefit of smoked cannabis to relieve pain are published.2 The major psychoactive cannabinoid, THC, is as effective as codeine for relieving pain. Researchers wrote, "This trial has demonstrated an analgesic [antipain] effect of THC in patients with cancer pain."3 Experiments with monkeys and rats show unequivocal science for the analgesic effect of cannabinoids in laboratory animals.4 Endogenous cannabinoids are important in pain control.<sup>5</sup> GW Pharmaceuticals has performed randomized double-blind placebo-controlled trials showing Sativex, a cannabis extract administered under the tongue, markedly improves pain and muscle spasm.6 Canada recently approved Sativex for treating pain with applications pending in the US and other countries.<sup>7</sup> The International Association for Cannabis as Medicine (IACM) lists dozens of clinical studies including studies on pain.<sup>8</sup> Perhaps the best summary is from the prestigious Institute of Medicine, "In conclusion, the available evidence from animal and human studies indicates that cannabinoids can have a substantial analgesic effect."9

The Oregon Medical Marijuana Act passed in 1998 states, "The people of the state of Oregon hereby find that: (1) Patients and doctors have found marijuana to be an effective treatment for suffercal marijuana treated like medical morphine, medical synthetic THC, or Food and Drug Administration-approved medicines.

An inhaled medicine typically works faster but the effects usually do not last as long as a medicine taken by mouth that must be absorbed by the digestive tract.

The psychoactive effects of both synthetic THC (Marinol) and herbal marijuana are due primarily to THC.<sup>11</sup> The timing issues about how a drug behaves in the body are called pharmacokinetics and are mostly dependent on the method of administering the drug. For example, an inhaled medicine typically works faster but the effects usually do not last as long as a medicine taken by mouth that must be absorbed by the digestive tract. Inhaling cannabis through smoking or vaporizing cannabis bypasses the digestive tract.

In "A Primer of Drug Action," pharmacologist Robert Julian, MD, PhD, states, "absorption of inhaled drugs is rapid and complete. The onset of behavioral effects of THC in smoked marijuana occurs almost immediately after smoking begins and corresponds with the rapid attainment of peak concentrations in plasma. Unless more is smoked, the effects seldom last longer than three to four hours."<sup>12</sup>

In "Clinical Pharmacokinetics of Cannabinoids" Franjo Grotenhermen, MD, wrote, "Pulmonary [lung] assimilation of inhaled THC causes a maximum plasma concentration within minutes, while psychotropic effects [the "high"] start within seconds to a few minutes, reach a maximum after 15 to 30 minutes, and taper off within two or three hours."

Grotenhermen states, "The peak psychotropic effects ('high') after intravenous and inhaled THC application were noted after 20-30 minutes and decreased to low-levels after three hours and to baseline after four hours (Hollister et al 1981, Lindgren et al 1981, Chiang and Barnet 1984)... Hence about one to four hours after smoking there is a good correlation between plasma level and effects (Chiang and Barnett 1984). There was also a good correlation between THC plasma levels and other effects in this phase, with heart rate (Cocchetto et al 1981) and with psychomotor impairment (Barnett et al 1985)." In summary, this

## Washburn v. Columbia Forest Products



The Oregon Supreme Court has agreed to review Washburn v. Columbia Forest Products, Inc., a case that will clarify how much protection the Oregon Medical Marijuana Act (OMMA) affords workers.

Robert Washburn was hired by Columbia in 1996 to work in a Klamath Falls mill that produced plywood. Washburn got a card through the state medical marijuana program in 1999 after a doctor approved its use for painrelated insomnia. Washburn never showed signs of impairment on the job, but was fired in 2001 after his urine

## Impairment from smoked cannabis or marijuana resolves within four hours.

peer-reviewed scientific article informs us that the impairment resolves when plasma THC levels return to low-levels at three hours and baseline around four hours after smoking marijuana.<sup>13</sup>

Since THC acts identically whether synthetic or herbal, we should look at the warnings section of the US Food and Drug Administration (FDA)-approved dro-nabinol (synthetic THC marketed as Marinol): "WARNINGS: 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 perform such task safely."<sup>14</sup> This is sound advice.

In the above studies, impairment from smoked cannabis or marijuana resolves within four hours. Since synthetic THC and herbal THC are identical once inside the body, there is no scientific rationale for discrimination against those who prefer medical THC from an herbal rather than a synthetic source. The Marinol package insert warnings should be heeded regardless of whether a person uses synthetic FDA-approved THC (as in Marinol) or herbal THC (as in marijuana or cannabis). When a clinician monitors drug therapy, s/he educates a patient through a careful explanation of the procedure (method of use and expected results), alternative therapies, and risks involved in using or not using the medicine. There are many medicines --prescription or non-prescription- that cause drowsiness or impairment. These include medicine for blood pressure, diabetes, arthritis, respiratory infection, allergies, mood stabilization, and pain. Physicians and patients use good communication to lessen risks of adverse drug reactions.

tested positive for marijuana metabolites.

Washburn sued for reinstatement and back pay. A Multnomah County Circuit Court judge ruled against him, citing a clause in OMMA saying the act shall not be construed to require "an employer to accommodate use of medical marijuana in the workplace."

Washburn appealed, arguing that he didn't use marijuana at the mill ("in" his workplace) but only at home, before going to bed. In January of this year the Court of Appeals ruled for Washburn. Columbia Forest Products then asked the state supreme court to review the ruling. They will hear arguments November 7.

The prospect of Washburn prevailing inspired an employers' consortium to try to undermine OMMA by a bill, HB2693, confirming their "right" to fire workers who use marijuana whether on or off the job. It passed the Republican-controlled House this summer, then failed in a Democrat-controlled Senate committee. "This may be a temporary reprieve," says Bayer, who expects the employers to reintroduce the measure.

This article is based on Bayer's July 10 testimony to the Senate committee opposing HB2693.

It is important to avoid impairment when driving, operating machinery, or engaging in any hazardous activity whether in the workplace or not. Monitoring by family, friends, peers, and coworkers for anyone's impairment can improve safety. One reason that direct observation of impairment is important is that impairment can be caused by



ing caused by debilitating medical conditions, and therefore, marijuana should be treated like other medicines."<sup>10</sup> This means Oregonians voted to make medi-

• Richard "Rick" Bayer, MD is boardcertified in internal medicine and a Fellow in the American College of Physicians. He was a chief petitioner of the Oregon Medical Marijuana Act in 1998, and has appeared as an expert witness in Oregon state courts. He can be contacted through his website, www.omma1998.org

• The Safety posters were made in the 1930s by artists employed by the federal Works Progress Administration. Urine testing is a demeaning substitute for regulations and programs that protect workers.



#### poor no no work uparts

health problems not related to prescription medicines. Things like non-prescription over-the-counter medicines, acute influenza, or a family emergency resulting in lost sleep can cause impairment. This means good communication between employees and employer can lessen risk of impairment at work.

Urine drug testing to monitor therapy is not routinely used in clinical medicine. It is helpful in toxicology or poisoning cases when a doctor is uncertain what drugs are in the body. Urine tests are also used in medical-legal settings. The standard urine test for "marijuana" does not test for the "parent drug," THC, but tests for an inactive non-psychoactive metabolite or breakdown product of THC.

continued on next page

### **Impairment** from previous page

Inactive breakdown products in a standard "urine marijuana test" can remain positive for weeks to months after consuming cannabis, even when there is no impairment.

Inactive breakdown products in a standard "urine marijuana test" can remain positive for weeks to months after consuming cannabis, even when there is no impairment. The US Department of Transportation commented about urine drug testing that, "while a positive urine test is solid proof of drug use within the last few days, it cannot be used by itself to prove behavioral impairment during a focal event." 15 In other words, urine drug testing does not prove impairment, mer's work adds, "While drivers with low it only proves recent use.

#### **Flight-simulator studies**

Between 1976 and 1991, there were at least four flight-simulator studies published according to a Library of Medicine search. One showed impairment for at least two hours that resolved by four to six hours.<sup>16</sup>Three others by a different research team showed conflicting results. Two of those three show some impairment at 24 hours,17,18 while one of the three studies showed abnormal flight simulator results only at four hours but none at eight or 24 hours.<sup>19</sup> Another unpublished study by the same group failed to find impairment, bringing the total studies to five.

These mixed results create confusion. Since blood levels of THC are near baseline four hours after smoking cannabis and impairment beyond four hours cannot be consistently demonstrated, the researchers actually call this flight simulator result a "hangover effect" rather than intoxication. According to Dr. Leirer, the purported hangover effect is "very marginal" and is only detected in tests of "very complex human/machine performance." Comparable subtle effects are reported at very low blood-alcohol levels of 0.025%, which is well below the .04% level allowed in commercial motor vehicle drivers.20

Possibly because of confusion surrounding flight simulator data, other researchers study actual motor vehicle accidents. In 2002, authors Gregory Chesher and Marie Longo concluded, "At the present time, the evidence to suggest an involvement of cannabis in road crashes is scientifically unproven." <sup>21</sup> However as they note, some of this may be because of evolving science. As mentioned above, testing for inactive urine (like patients) can have levels as high as

metabolites does not test for impairment. Recent studies continue to show that "no increased risk for road trauma was found for drivers exposed to cannabis."  $^{\rm 22}$ 

But there is also an effort to base impairment on measuring the "parent drug" responsible for impairment, namely THC. Dr. Olaf Drummer, measured THC levels in fatal crashes in Australia and noticed an association between high THC levels and risk of traffic fatality even in the absence of other drugs.<sup>23</sup> Based on forensic evidence, he determines whether a driver is "culpable" or responsible for the fatal accident and correlates it to blood THC levels. Drummer and colleagues conclude, "Recent use of cannabis may increase crash risk, whereas past use of cannabis does not."24

Grotenhermen's review of Drumconcentrations [of THC] in their blood had a lower probability of causing a traffic accident than drug free drivers, higher THC concentrations were associated with a considerably higher culpability ratio.'

It remains unclear how to define the gray area about what is "recent" and what is "past" use of cannabis, even if one supports using parent-drug blood THC levels as a marker for impairment. This is because the THC level below which there is no impairment, varies dramatically among individuals. Plus, the actual numbers of persons who have only THC in the blood and are involved in accidents is low and studies still lack adequate statistical significance to draw scientifically firm conclusions.

Those concerned about legislation suggest that since no culpability appears to exist below blood levels of 10 nanograms per milliliter (ng/ml), that any proposed cutoffs be above 10 ng/ml of THC.26 A study using coordination testing showed inevitable failure on field sobriety testing if blood THC levels were 25-30 ng/ml but many failed testing at 90 and 150 minutes after smoking even though plasma concentrations were rather low

The researchers had the foresight to conclude that "establishing a clear relation between THC plasma concentrations and clinical impairment will be much more difficult than for alcohol."27 This is primarily because alcohol and THC are chemically different and are metabolized differently inside the body. With passage of medical marijuana laws, we need additional research to show if there is a correlation between clinical impairment and blood THC levels. Daily cannabis users

6 to 10 ng/ml without clini

## YOUR GOGGLES



from smoking marijuana and no scientific evidence of any increased risk of motor vehicle accidents beyond four hours after smoking marijuana. As a medical cannabis expert, I do not condone any medical marijuana use of cannabis at work. But, private employeremployee agreements to abstain within four to eight hours prior to work seem a reasonable type of compromise. This still preserves safety, and would be consistent with medical treatment plans using other medicines that may impair.

Registration in the Oregon Medical Marijuana Program should never be sole cause for termination of employment. Medical use of marijuana within Oregon law should be treated like medical Marinol, medical morphine, and other medications both in and out of the workplace. It is discriminatory to fire an unimpaired worker whose only cause for firing is registration with the Oregon Department of Human Services Oregon Medical Marijuana Program.

#### **References:**

1 Tod Mikuriya, MD. Editor of Marijuana: Medical Papers 1839 - 1972. Medi-comp Press 1973. www.mikuriya.com/mmp.html

2 B Zimmerman PhD, R Bayer MD, & N Crumpacker MD: Is Marijuana the Right Medicine For You? A Factual Guide to Medical Uses of Marijuana: Chapter 10. Keats Publishing 1998.

3 R Noyes, F Brunk, D Avery, & A Canter: "The analgesic properties of delta-9-tetrahydrocannabinol and codeine". Clinical Pharmacology and Therapeutics: vol. 18, pg. 84, 1975. www.omma1998.org/Noyes-THC v Codeine for pain CPT 1975.pdf

4 Deadwyler, Vivian, Meng, Walker, Simone, & Hargreaves. Marijuana & Analgesia. Press Conference October 26, 1997 at the 27th Annual Meeting of the Society for Neuroscience in New Orleans. LA. USA. www.omma1998.org/

analgesia\_mj.htm

nabis Therapeutics. Volume 3. Number 1. Pp 3 -51. 2003 Haworth Press

14 Marinol( brand of dronabinol (THC) manufacturer's package insert from Unimed Pharmaceuticals Inc. www.marinol.com

15 US Department of Transportation National Highway Traffic Safety Administration. State of Knowledge of Drug-Impaired Driving. September 2003. DOT HS 809 642.

www.nhtsa.dot.gov/people/injury/research/ StateofKnwlegeDrugs/StateofKnwlegeDrugs/

16 Janowsky, Meacham, Blaine, Schoor, Bozzetti. "Simulated flying performance after marihuana intoxication." Aviation Space and Environmental Medicine. Feb 1976. 47(2): 124-8

17 Yesavage, Leirer, Denari, Hollister. "Carry Over Effects of Marijuana Intoxication on Aircraft Pilot Performance: A Preliminary Report. American Journal of Psychiatry. 142: 1325, 1985.

18 Leirer, Yesavage, Morrow. "Marijuana Carry-Over Effects of Marijuana Intoxication on Aircraft Pilot Performance". Aviation Space and Environmental Medicine. March 1991. 62:221-7

19 Leirer, Yesavage, Morrow. "Marijuana, Aging, and Task Difficulty Effects on Pilot Performance". Aviation Space and Environmental Medicine. Dec 1989. 60:1145-52

20 Gieringer, D. "Evidence for 24-hour pot hangover". California NORML newsletter. August 1991

21 Chesher G. and Longo M. "Cannabis and Alcohol in Motor Vehicle Accidents". Chapter 28: page 322 from Cannabis and Cannabinoids: Pharmacology, Toxicology, and Therapeutic Potential. Edited by Grotenhermen and Russo. 2002 Haworth Press

22 Movig, Mathijssen, Nagel, van Egmond, de Gier, Luefkens, Egberts. "Psychoactive substance use and the risk of motor vehicle accidents". Accident Analysis and Prevention. 36: 631, 2004.

23 Drummer, Gerostamoulos, Batziris, Chu, Caplehorn, Robertson, Swann, "The incidence of drugs in drivers killed in Australian road traffic crashes". Forensic Science International. 2003. 134:154-162

24Ramaekers, Berghaus, van Larr, Drummer. "Dose related risk of motor vehicle crashes after cannabis use," Drug Alcohol Depend, Feb 7, 2004. 73(2): 109-119

25 Grotenhermen, F. International Association for Cannabis as Medicine (IACM) Bulletin of Feb 15, 2004. www.acmed.org/english/nav/homebulletin.htm

26 Armentano, P. DUID Legislation: What It Means, Who's Behind It, and Strategies to Prevent It. Senior Policy Analyst. NORML Foundation. 2004 Winter Legal Conference www.norml.org/pdf\_files/ NORML You Are Going Directly To Jail.pdf

27 Reeve, Grant, Robertson, Gillespie, Hollister. "Plasma concentration of delta-9-tetrahydrocannabinol and impaired motor function". Drug Alcohol Depend. April 1983.11(2): 167.

28 Skop, Richter, Potsch. "Serum Cannabinoid levels 24 to 48 hours after cannabis smoking". Arch Kriminol (German). Sept-Oct 2003. 212 (3-4): 83-95.

29 Chesher, Gregory and Marie Longo: "Cannabis and Alcohol in Motor Vehicle Accidents. Chapter 28. Page 318 from Cannabis and Cannabinoids: Toxicology, Pharmacology, and Therapeutic Potential. Edited by Franjo Grotenhermen and Ethan Russo. 2002 Haworth Press

30 Grotenhermen, Franjo, Gero Leson, Günter Berghaus, Olaf Drummer, Hans-Peter Krüger, Marie Longo, Herbert Moskowitz, Bud Perrine, Jan Ramaekers, Alison Smiley, Rob Tunbridge. Developing Per Se Laws for Driving Under the Influence of Cannabis (DUIC): Presented at the 17th International Conference on Alcohol, Drugs, and Traffic Safety (ICADTS): August 10th, 2004, Glasgow, Scotland



24 or more hours of abstinence.28,29 While the science evolves, most experts think it remains premature to make firm conclusions about the proper cutoff levels using blood THC for "Driving Under the Influence" suspicion.30 Proper clinical discussion of medical marijuana therapy and necessary clinical observation for impairment remain the primary methods of monitoring for possible adverse reactions at this time.

In summary, there is no consistent scientific evidence showing any impairment beyond four hours

5 Walker, Huang, Strangman, Tsou, & Sanudocal impairment even after Pena: "Pain modulation by release of the endogenous cannabinoid anandamide". Proceeding of the National Academy of Sciences: October 12, 1999. 6 GW Pharmaceuticals Research and Development on pain: www.gwpharm.com/ research\_pain.asp

7 GW Pharmaceuticals Press Release: www.gwpharm.com/

8 International Association for Cannabis as Medicine: www.acmed.org/english/nav/homescience.htm

9 J.Jov, S Watson, J Benson, Editors of Marijuana and Medicine: Assessing the Science Base. Institute of Medicine. 1999. Page 145 of hardback edition. www.nap.edu/catalog/6376.html

10 ORS 475.300 - ORS 475.346 www.dhs.state.or.us/publichealth/mm/ 475a.cfm#300

11 Wachtel, ElSohly, Ross, Ambre, de Wit. "Comparison of subjective effects of Delta(9)-tetrahydrocannabinol and marijuana in humans". Psychopharmacology (Berlin). June 2002. 161(4): 331.

12 Julian PhD MD, Robert. A Primer of Drug Action (8th edition, Freeman 1998) page 329.

13 Grotenhermen MD, Franjo. "Clinical Pharmacokinetics of Cannabinoids". Journal of Can-

