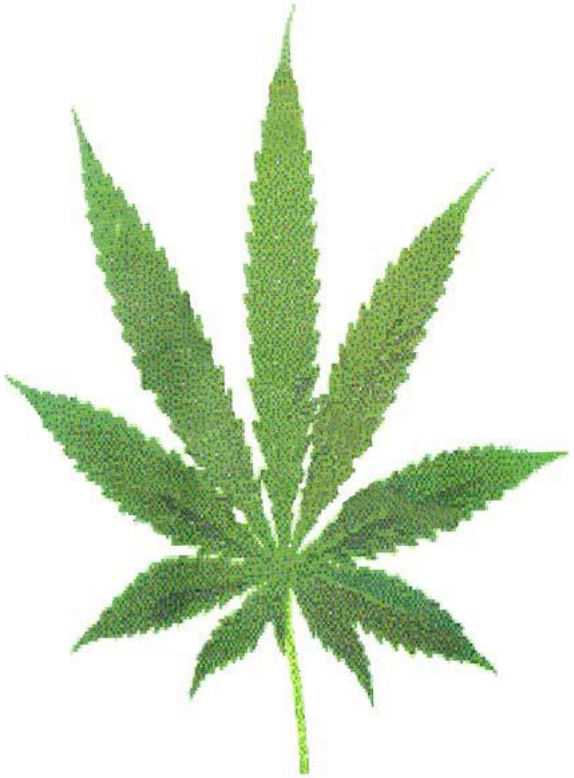
Pharmacokinetics of Marijuana and its impact to Canadian Impaired Driving laws



CARSP Presentation

Abe Verghis, P.Eng
Alcohol Countermeasure Systems (ACS)
June 20, 2017 Toronto, ON

ACS
life saving innovations

AGENDA

1. Introduction
   - Why legalize Cannabis
2. Pharmacokinetics of Cannabis
   - chemistry and composition
   - Metabolism of cannabinoids (absorption, metabolism, excretion)
   - Pharmacokinetics of Cannabinoids
3. Pilot Study
   - Introduction
   - Current DRE program & By the numbers
   - Public Safety objectives & results
   - Toronto Police results
   - Current Technology for Roadside detection
4. Bill C-46 (Changes to Impaired Driving Laws)
   - correlation between THC (and metabolite) content and driving impairment
   - technologies for roadside drug detection
   - Legislative approaches for dealing with drug impaired driving
5. Case Study

Why Legalize Cannabis

- 2015 Throne speech, Canada committed to legalizing, regulating and restricting access to marijuana
- Current prohibition laws are NOT working – Canadian youth continue to use Cannabis at some of the highest rates in the world
- Thousands of Canadians end up with criminal records for non-violent drug offences each year
- Organized crime reaps billions of dollars in profits from its sale
- Most Canadians no longer believe in Criminal sanctions for ‘simple” Cannabis possession

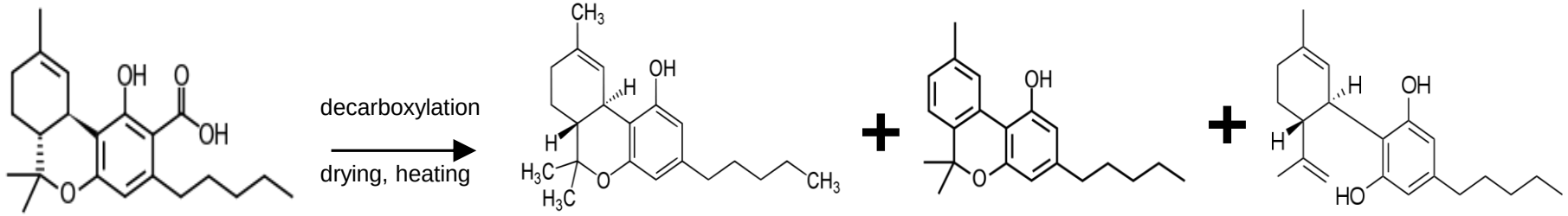
OTTAWA CITIZEN

An illegal pot shop on Bank Street recently had a sale on peanut butter cookies. The cannabis-laced sweets were $5, a third off the regular price of $15.

‘For this price, you can’t go wrong,” said a customer snapping up 10 of them, “Might as well stock up”.

OTTAWA CITIZEN

Marijuana – Chemistry and Composition



THC-Acid (living plant)
358.5 g/mol, **non-psychoactive**

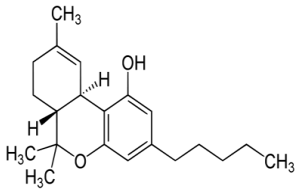
THC (Δ-9-tetrahydrocannabinol)
314.5 g/mol, **psychoactive**

CBN Cannabinol
310.4 g/mol
(~10% THC psychoactivity)

CBD Cannabidiol
314.4 g/mol **non-psychoactive**

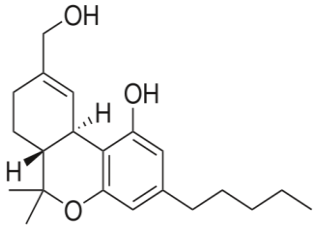
- **Marijuana**: dried flowers and leaves of the Cannabis plant
- **Contains** over 420 chemical compounds
- including over 60 belonging to chemical group of **cannabinoids** with psychoactive (mood changing) properties
- **Cannabinoids:** primarily concentrated in flowers (less concentrated in leaves and stems)
- **Amount and mixtures of cannabinoids** vary with species of the plant, growing practices, timing of the harvest
- **Most psychoactive** component of marijuana is **THC** (delta-9-tetrahydrocannabinol)
- **THC in living plant** occurs in non-psychoactive form **THC-A(cid)** or tetrahydrocannabinolic acid

Marijuana – Metabolism



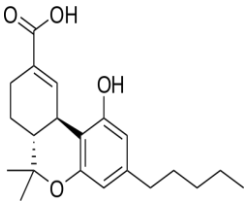
THC, **psychoactive**
314.5 g/mol

metabolism
Phase I oxidation



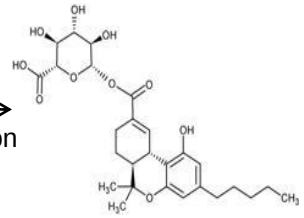
11-hydroxy THC
or 11-OH-THC psychoactive
330.5 g/mol,

metabolism
Phase I oxidation



11-nor-9-Carboxy-THC
or THC-COOH non-psychoactive
344.4 g/mol

metabolism
Phase II oxidation



11-norTHC-9-carboxylic acid glucuronide
or THC-COO-glu
520.6 g/mol, **non-psychoactive**

SUMMARY

THC → 11-OH-THC → THC-COOH → THC-COO-glu

psychoactive — **psychoactive** — **non-psychoactive** — **non-psychoactive**

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Physical

- Pronounced body sway
- Eyelid and body tremors
- Slow, deliberate speech
- Dilated pupils
- Watery, red eyes
- Increased Blood Pressure (new users)
- Increased pulse rate

Psychophysical

- Relaxed inhibitions
- Sharpened sense of humor
- Difficulty with concentration
- Disorientation
- Short-term memory problems
- Fatigue, lethargic
- Altered time and space perception

THC level in blood or saliva not indicative of what's in the brain

Marijuana – Psychoactive Symptoms & Route of Administration

Marijuana administration

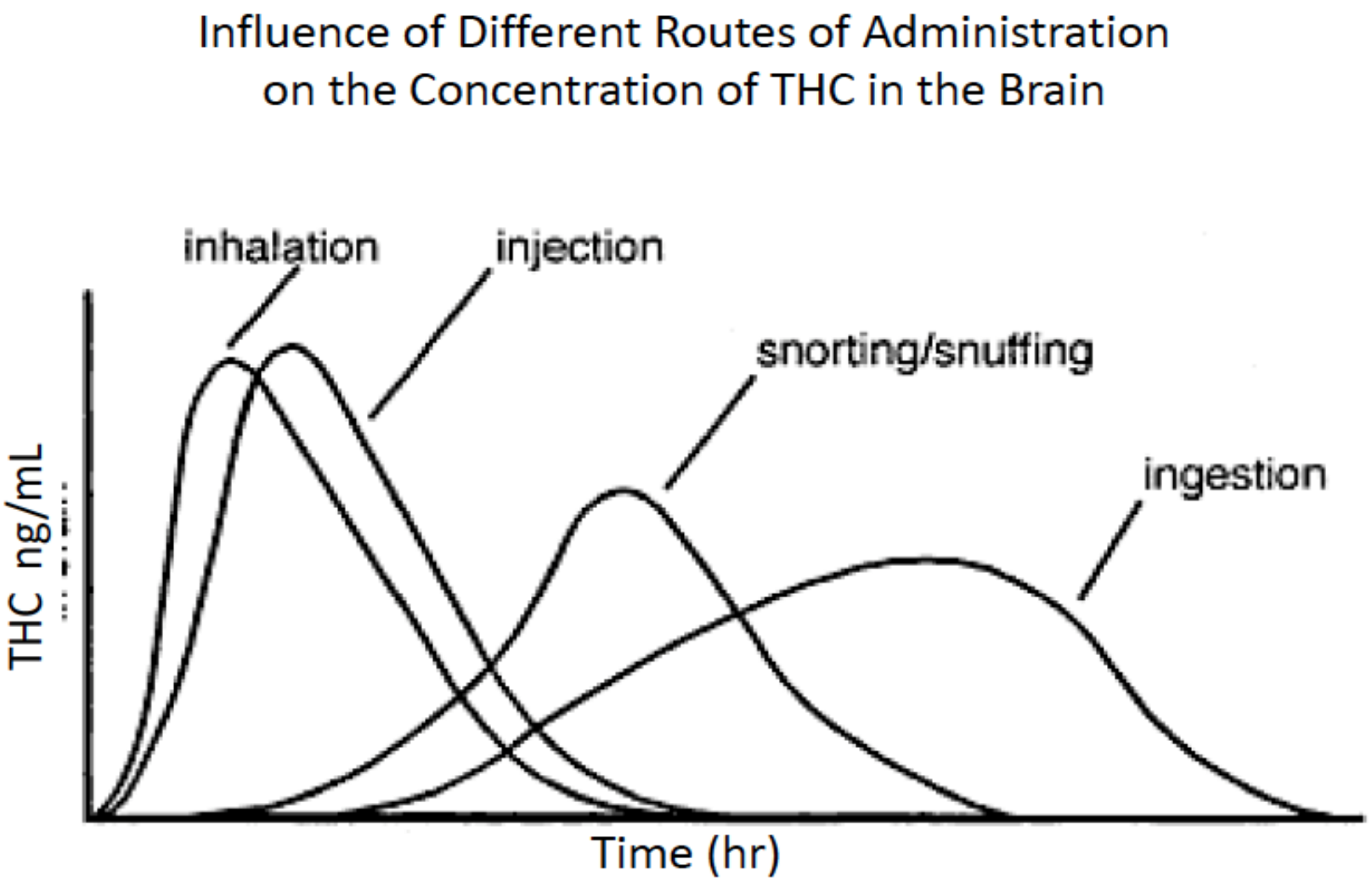
Smoking

Vaping

Ingestion

Most efficient drug delivery by smoking or vaping – affects CNS within seconds

Marijuana – Psychoactive Symptoms & Route of Administration



Properties of Cannabinoids

1. Fat Soluble
    - Delays elimination (water soluble chems are excreted)
    - Means relatively high concentration in brain (impairment)
    - Volume of Distribution = 10 L/kg
2. Highly protein bound = 97%

Kinetics

Absorption of THC	IV	100%
	Smoking	14 – 50%
	Edibles	6%
Blood conc. (1 joint)	Δ^9-THC	0 - 200 ng/mL
	11-OH THC	0 - 10 ng/mL
	THC-COOH free	0 - 50 ng/mL
	THC-COOH total	0 - 100 ng/mL
Vd (Vol. of Distrib.)	Acute dosing	9 L/kg
	Chronic dosing	11 L/kg
Half-life (distribution)	Δ^9-THC	< 1 hr
Half-life (distribution)	Δ^9-THC	1 – 4 days
	THC-COOH	2 - 5 days

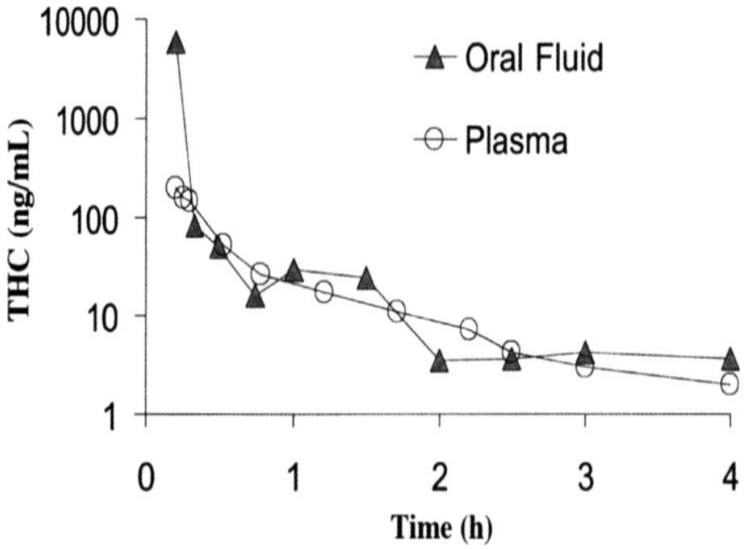
O. H. Drummer, *The Forensic Pharmacology of Drugs of Abuse,* Arnold, Oxford Univ. Press (2001), p. 187

Edible Cannabis products:

1. Dose and absorption are difficult to control
2. Typical edible product contains more than one dose
3. Increase the risk of consumption by children
4. High dose ingestions can induce severe respiratory insufficiency in children

Marijuana – Pharmacokinetics of cannabinoids – smoking – blood/saliva ratio

Controlled laboratory conditions:



Simultaneous measurement of THC in oral fluid and plasma by GC-MS analysis (cutoff concentrations = 0.5 ng/mL) in a human subject over 4 h following smoking of a single cannabis cigarette (3.55%), Huestis & Cone, J. Analytical Toxicology, Vol. 28, September 2004

- Good correlation between THC content in blood and oral fluid in clinical, controlled setting due to transmucosal absorption of THC into blood
- Very high initial THC concentration in oral fluid caused by contamination of oral fluid during smoking and dissipated within ~30 min after smoking
- THC-COOH concentration in saliva ~1000 x lower than THC from THC metabolism

Marijuana – Correlation between THC content and driving impairment

Alcohol impairment – good correlation between BAC and impairment, BAC can be back-extrapolated, simple metabolism

THC impairment - no simple and direct correlation between THC concentration in blood and impairment

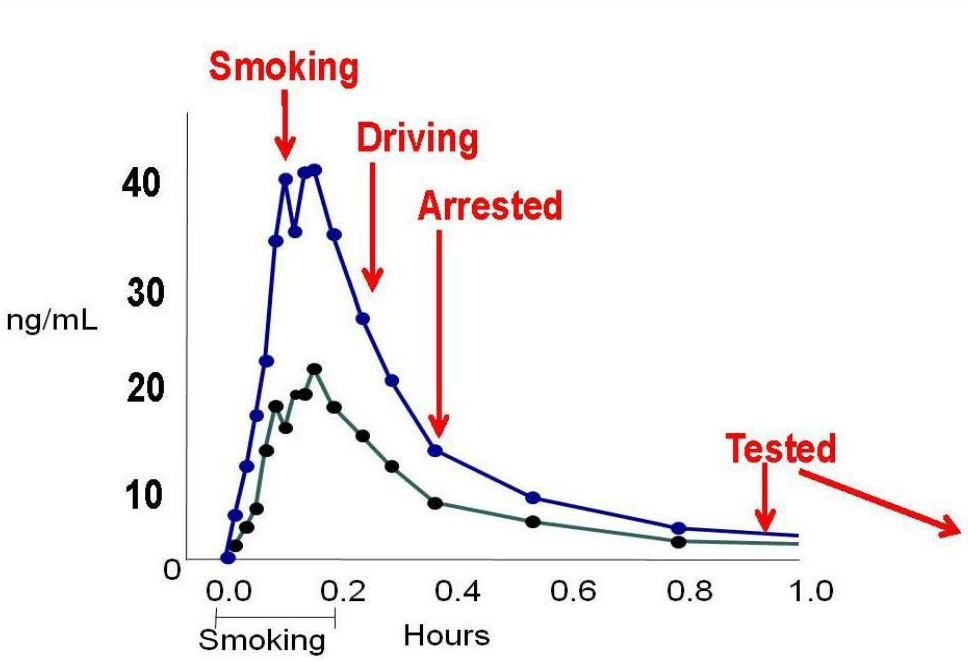
Lack of correlation between THC concentration and impairment due to:

- THC lipid solubility and thus its retention
- various individual metabolic profile
- administration frequency (chronic vs. casual users)
- driving experience
- health, age and other physiological factors
- THC concentration cannot be back-extrapolated due to unknown intake time, inter-subject variability in metabolic rate
- little evidence of relation between crash risk and THC concentration

Marijuana – Correlation between THC content and driving impairment

- Blood test always significant delayed (up to 1-2 hours) since sampling performed in medical facility
- Oral fluid test for evidential purpose collected at the time of roadside check is fast and convenient methodology for potential prosecution

- Challenges:
  - sample storage and transportation
  - sufficient number of certified / qualified labs



Marijuana – Correlation between THC content and driving impairment

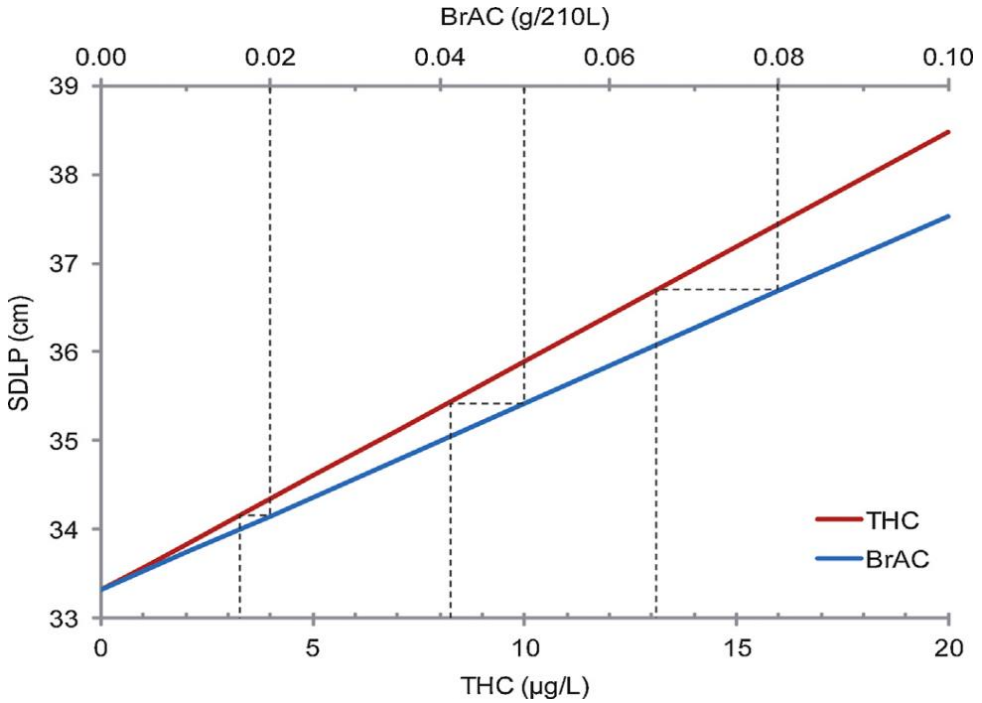
Effect of Cannabis on driving:

- Decision-making
- Divided attention
- Visual search
- Focus, concentration
- Reaction time
- Road tracking, vehicle control (e.g. SDLP)

SDLP – clinically controlled studies with simulator - marijuana vs. alcohol:

SDLP for alcohol vs. cannabis:
• BAC=50 equivalent to 8.2 ng/mL THC
• BAC=80 equivalent to 13.1 mg/mL THC

Hartman et al., Drug & Alcohol Dependence, 154(2015)25-37



Effect of drugs on driving performance – methodologies:

- Epidemiological studies: drug incidence in fatal and non-fatal accidents, causal drugs effects, culpability & responsibility analyses
- Performance impairment studies: effect of drugs on cognitive and/or psychomotor tasks
- Driving simulator and open road driving studies: effects of drugs in situations closely resembling real driving

Marijuana – Correlation between THC content and driving impairment

Fundamental Challenges:

- THC presence vs. impairment – no correlation
- Establishing per se THC limit similarly as for alcohol and proof of impairment has no scientific basis
- Delays between roadside screening test and confirmatory blood testing may miss the impaired drivers due to fast THC decay below cut-off level, particularly for casual users
- Habitual users have elevated THC level and likely above typical per se levels and being charged even though may not be impaired
- Necessity of science-based performance and driving ability measures

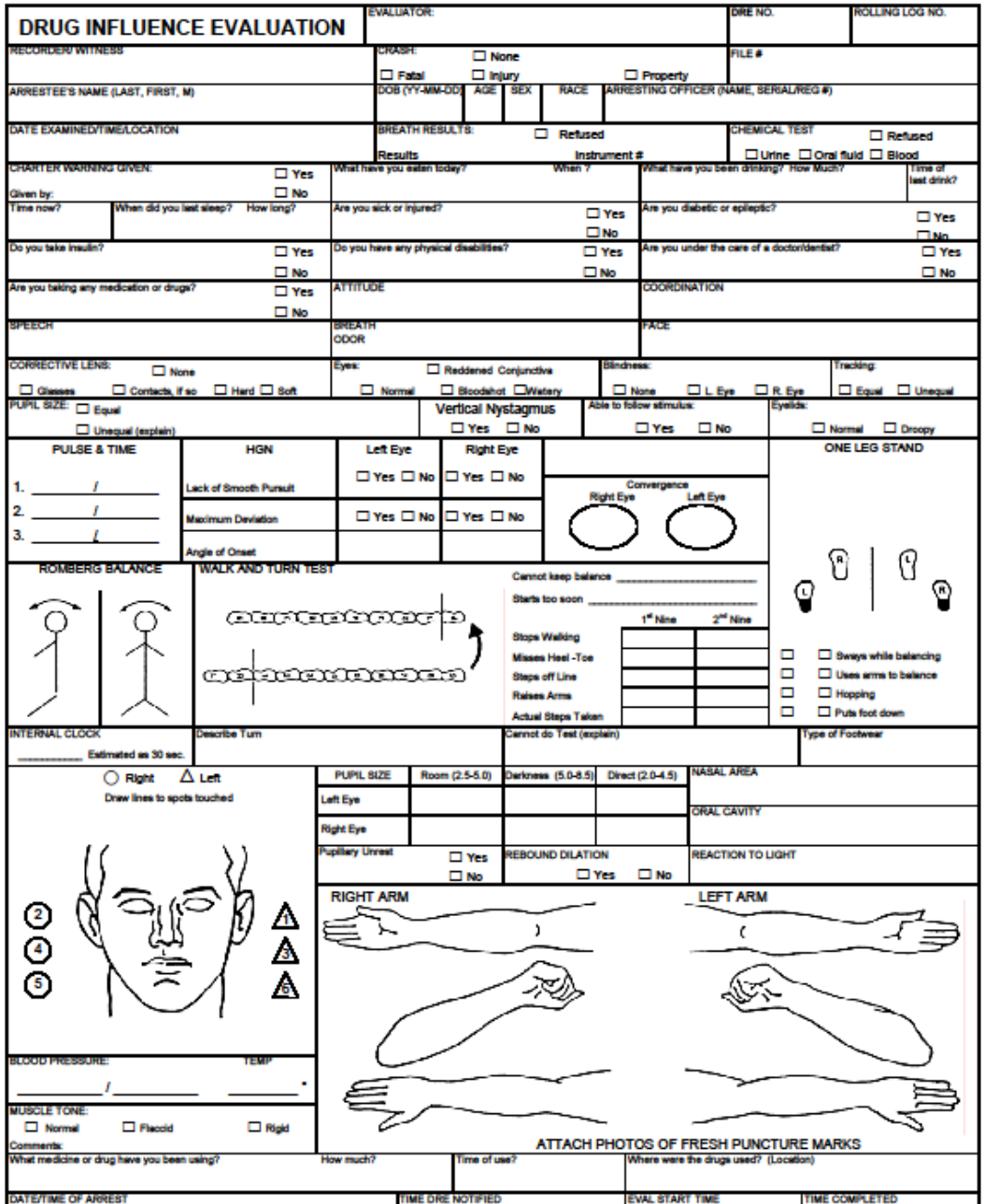
Pilot Study – Public Safety Canada & CCMTA

Pilot Study – DRE Overview

Current DRE program

- The DRE program was developed by LAPD in the early 1970's, administered by IACP
- Bill C-2 was adopted into the Criminal Code of Canada on July 02, 2008 which allows Law Enforcement to conduct SFST and DRE tests
- DRE program is being used throughout Canada and US, with over 7,300 active, 600 are in Canada
- Currently no established per-se limits for drugs
- Currently no instrument capable of detecting drug effect

Pilot Study – DRE exam



DRUG INFLUENCE EVALUATION

EVALUATOR: | DRE NO. | ROLLING LOG NO.

RECORDER/ WITNESS | CRASH: ☐ None ☐ Fatal ☐ Injury ☐ Property | FILE #

ARRESTEE'S NAME (LAST, FIRST, M) | DOB (YY-MM-DD) | AGE | SEX | RACE | ARRESTING OFFICER (NAME, SERIAL/REG #)

DATE EXAMINED/TIME/LOCATION | BREATH RESULTS: ☐ Refused Results Instrument # | CHEMICAL TEST ☐ Refused ☐ Urine ☐ Oral fluid ☐ Blood

CHARTER WARNING GIVEN: ☐ Yes ☐ No Given by: | What have you eaten today? When ? | What have you been drinking? How Much? | Time of last drink?

Time now? | When did you last sleep? How long? | Are you sick or injured? ☐ Yes ☐ No | Are you diabetic or epileptic? ☐ Yes ☐ No

Do you take insulin? ☐ Yes ☐ No | Do you have any physical disabilities? ☐ Yes ☐ No | Are you under the care of a doctor/dentist? ☐ Yes ☐ No

Are you taking any medication or drugs? ☐ Yes ☐ No | ATTITUDE | COORDINATION

SPEECH | BREATH ODOR | FACE

CORRECTIVE LENS: ☐ None ☐ Glasses ☐ Contacts, if so ☐ Hard ☐ Soft | Eyes: ☐ Normal ☐ Reddened Conjunctiva ☐ Bloodshot ☐ Watery | Blindness: ☐ None ☐ L. Eye ☐ R. Eye | Tracking: ☐ Equal ☐ Unequal

PUPIL SIZE: ☐ Equal ☐ Unequal (explain) | Vertical Nystagmus ☐ Yes ☐ No | Able to follow stimulus: ☐ Yes ☐ No | Eyelids: ☐ Normal ☐ Droopy

PULSE & TIME
1. ____ /____
2. ____ /____
3. ____ /____

HGN | Left Eye | Right Eye
Lack of Smooth Pursuit ☐ Yes ☐ No | ☐ Yes ☐ No
Maximum Deviation ☐ Yes ☐ No | ☐ Yes ☐ No
Angle of Onset

Convergence: Right Eye | Left Eye

ONE LEG STAND
☐ ☐ Sways while balancing
☐ ☐ Uses arms to balance
☐ ☐ Hopping
☐ ☐ Puts foot down

ROMBERG BALANCE

WALK AND TURN TEST
Cannot keep balance ____
Starts too soon ____

	1st Nine	2nd Nine
Stops Walking		
Misses Heel -Toe		
Steps off Line		
Raises Arms		
Actual Steps Taken		

INTERNAL CLOCK ____ Estimated as 30 sec. | Describe Turn | Cannot do Test (explain) | Type of Footwear

○ Right △ Left
Draw lines to spots touched

PUPIL SIZE	Room (2.5-5.0)	Darkness (5.0-8.5)	Direct (2.0-4.5)
Left Eye			
Right Eye			

NASAL AREA | ORAL CAVITY

Pupillary Unrest ☐ Yes ☐ No | REBOUND DILATION ☐ Yes ☐ No | REACTION TO LIGHT

RIGHT ARM | LEFT ARM

ATTACH PHOTOS OF FRESH PUNCTURE MARKS

BLOOD PRESSURE: ____/____ | TEMP ____°

MUSCLE TONE: ☐ Normal ☐ Flaccid ☐ Rigid
Comments:

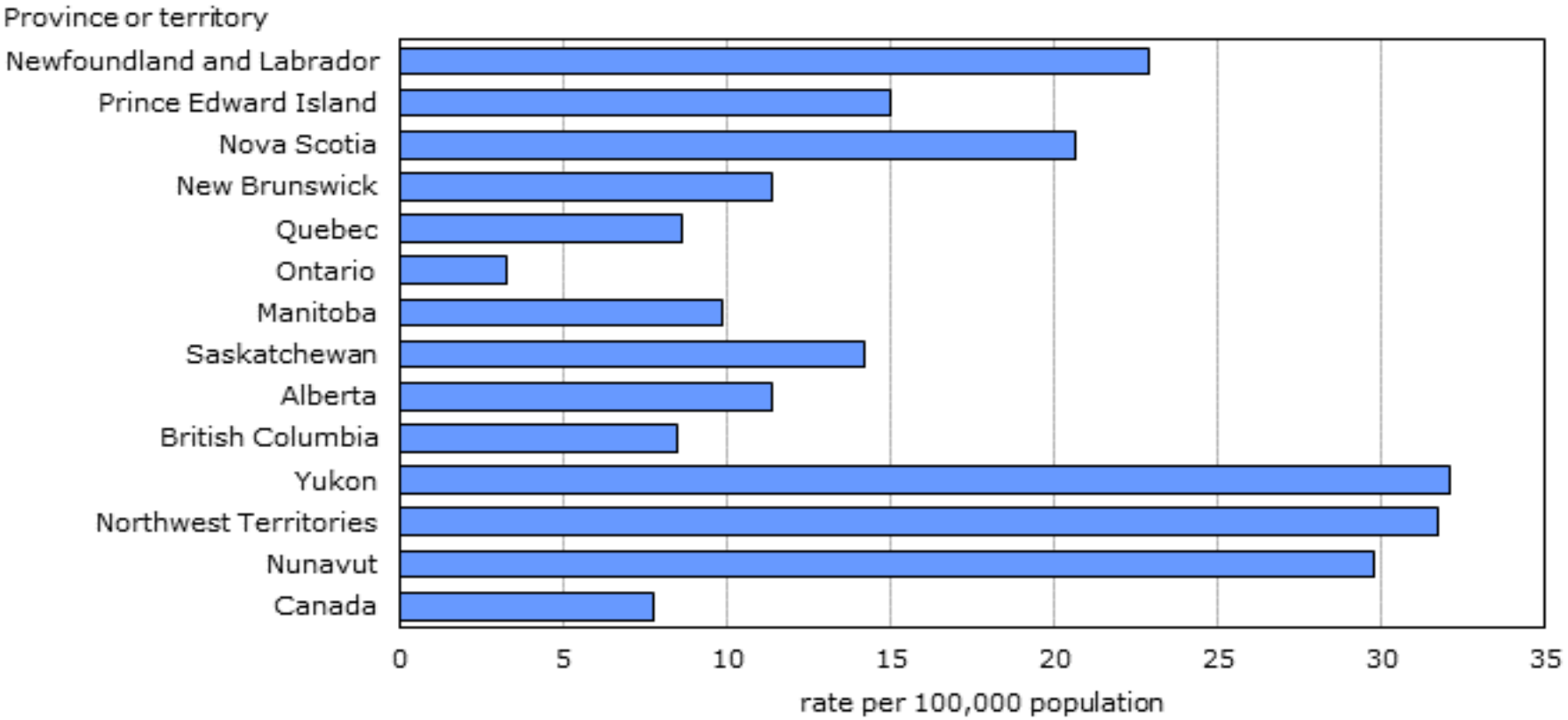
What medicine or drug have you been using? | How much? | Time of use? | Where were the drugs used? (Location)

DATE/TIME OF ARREST | TIME DRE NOTIFIED | EVAL START TIME | TIME COMPLETED

ACS

Pilot Study – by the #s

Chart 1.3
Rate of police-reported drug-impaired driving incidents, by province or territory, 2015



Note: The different ways in which police services deal with traffic violations can impact police-reported statistics. Counts are based on the most serious offence in the incident. One incident can involve more than one traffic violation under the *Criminal Code*. Populations are based on July 1st estimates from Statistics Canada, Demography Division.
Source: Statistics Canada, Canadian Centre for Justice Statistics, Uniform Crime Reporting Survey.

Pilot Study – Public Safety & CCMTA

December 2016 – March 2017

- Current roadside screening devices – a good indication of recent cannabis use
- Two different “oral fluid” screening systems – Type models only
- Toronto, Vancouver, Halifax, Gatineau, North Battleford & Yellowknife RCMP, OPP – 53 officers trained
- 1141 Oral fluid samples collected
- Anonymous samples collected by driver & passenger volunteers

Aim of the study:

- **Determine operational effectiveness within all Canadian environments (analysis time)**
- **Establishing Canadian standards for Oral Fluid (OF) devices similar to alcohol screening & evidential tests**

Pilot Study – Objectives

Climate

- Conduct testing with OF devices in both temperature extremes
- Conduct testing in wet climates
- Validity and stability of test results

Pilot Study – Objectives

Training guidelines

- A core module on the science related to per se limits, oral fluid and the functionality of the device
- A module on ‘drugs that impair”
- Instruction on the device use by the manufacturer
- An officer safety component
- Hands-on training using the device and the swab

Pilot Study – Objectives

Standard operating procedures

- A dual approach for the use of the printer
- Additonal measures to keep devices and swabs at operating temperatures in areas with extreme temperature conditions
- A safety component for officers in the collection of oral fluid
- The use of SFST or DRE in the event of a device failure or malfunction

Pilot Study – Objectives

Device Standards

- A high reliability in extreme temperatures
- Capacity to analyze samples in 8 minutes or less
- Capacity to backup and store analysis results
- Capacity to capture and/or report various types of data (e.g. oficer name, location, date/time, etc.)

Pilot Study – Drug Impaired Driving

Next Steps

- Public Safety Canada will work with provinces and territories to identify law enforcement needs related to tools, training and technology to detect and deter drug-impaired driving
- Partnerships with police to develop training and device operating procedure
- Develop plan forward to complete screening of devices for use in Canada
- Public Awareness and data collection

Pilot Study – Public Safety & CCMTA

Results – Toronto Police

Ease of Testing Procedure	**Very Easy**	**152**	**73%**
	Easy	**24**	**12%**
	Neither	**22**	**11%**
	Difficult	**8**	**4%**
	Very Difficult	**1**	**0%**
Most difficult part of procedure	**No difficulties**	**146**	**70%**
	Obtaining the sample	**31**	**15%**
	Printing the analysis	**16**	**8%**
	Using the device	**5**	**2%**
	Other	**3**	**1%**
Device Malfunction	**Yes**	**26**	**13%**
	No	**181**	**87%**

Pilot Study – Public Safety & CCMTA

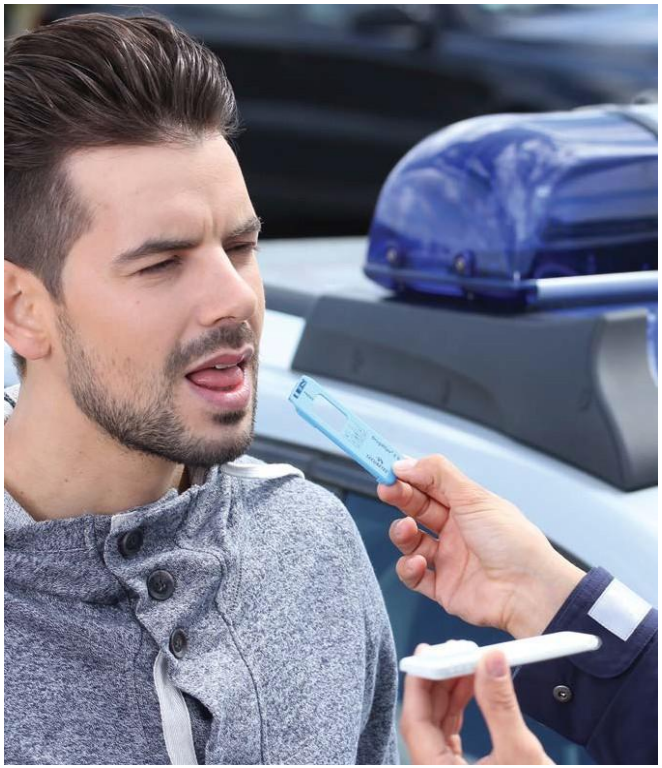
Results – Toronto Police

- 187 drivers were tested along with 18 passengers
- 9 people had tested positive for a drug (4%)
  - Cannabis in 3 instances
  - Cocaine in 4 instances
  - Methamphetamines / Amphetamines 4 instances
  - Benzodiazepines in 2 instances

Pilot Study – Current technologies for roadside drug detection

Roadside drug screening vs. evidential analysis

- Good correlation in the concentration of THC in oral fluid and blood
- Positive test - strong indication of marijuana use over the last ~4 hours



- State-of art drug screening devices based on classical immunoassay capable to detect THC with high sensitivity / accuracy /specificity in 5 minutes and low detection limit 5 ng/mL
- Methodology adopted successfully in Australia, Europe, Scandinavia and UK for mandatory roadside drug & alcohol screening
- High deterrence effect in view of growing worldwide trend in marijuana legalization

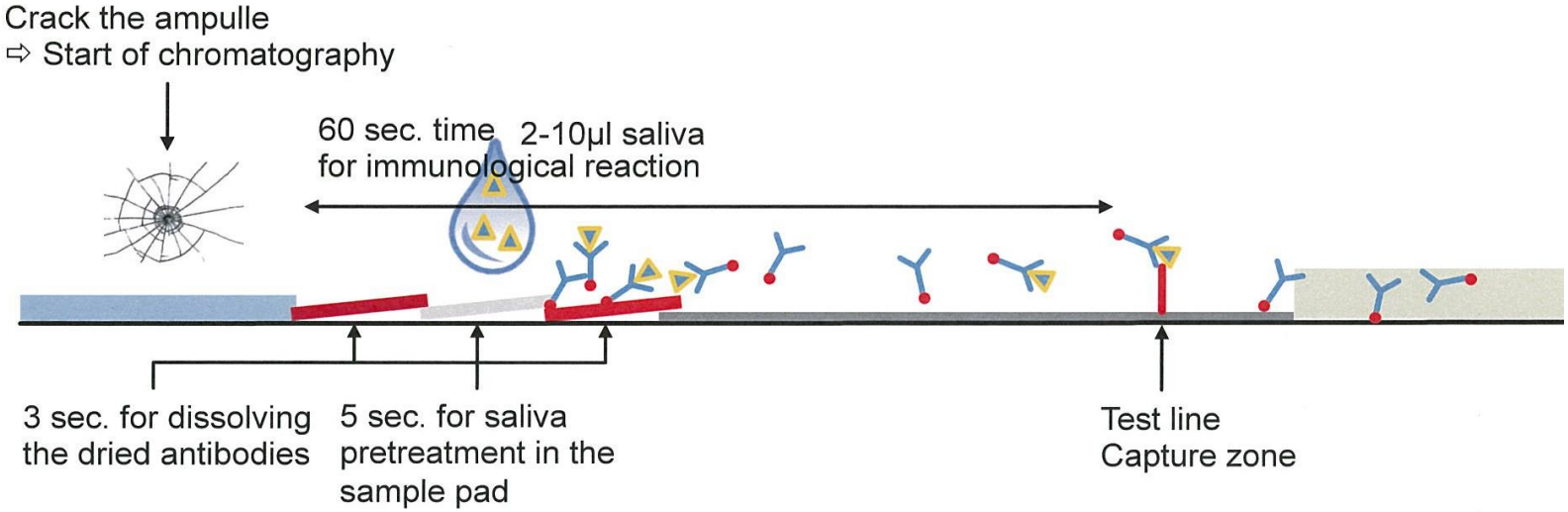
Pilot Study – Current technologies for roadside drug detection

(DrugWipe® 5S)

- 95 - 97% in sensitivity, specificity & accuracy
- 5 ng/mL detection limit for THC
- 5 minute testing time for THC

Screening by lateral flow immunoassay:

- Saliva collection followed by lateral flow immunoassay technique
- Extraction with buffer and deposition on cellulose test strip containing antibodies
- Sample fluid moves by capillary action to colorimetric marker conjugated with antibodies
- Color change measured visually or colorimetrically



- Fast, noninvasive, saliva multiple sampling
- Good indication of recent use (2 to 4 hours)
- Good correlation of THC concentration with blood
- Primary THC deposition in oral mucosa followed by transmucosal absorption into blood

Bill C-46 Strengthening Impaired Driving Laws

Bill C-46 – Strengthening Impaired Driving Laws

1. **Introduced on April 13th, 2017 and has currently undergone the Second Reading within Parliament (May 31)**
2. **Main goal: <u>Presenting evidence of impairment</u>** regardless of the results of roadside drug screening test
    - No devices can measure drug impairment at roadside
3. **Challenges of current approaches:**
    - chronic users including medical marijuana users may have residual but measurable THC in the body without showing obvious signs of impairment
    - occasional & "first time" users (adolescents) may show impairment with little dose not measurable by roadside screening devices
    - bias related to "evidential" blood analysis due to delay in sample collection – current procedure

Bill C-46 – Strengthening Impaired Driving Laws

Proposed Legislation - Highlights

- Demand for an oral fluid sample at roadside (similar to breath sample)
- “Qualified Technicians” would be able to draw blood - Phlebotomy
- Law Enforcement will be able to provide “direct” opinion evidence without the use of “expert witness”
- Number of laws to strengthen alcohol-impaired driving

Legal Drug Limits – set by regulation

- 2 – 5 ng/ml THC **in blood** results in a summary conviction ($1,000 fine)
- > 5 ng/ml THC **in blood** results in indictment or summary conviction (Hybrid offence - $1,000 fine, followed by 30 days jail)
- > 2.5 ng/ml THC + 50 mg/dL alcohol results in drugs-with-alcohol offence

Bill C-46 – Strengthening Impaired Driving Laws

STRENGTHENING IMPAIRED DRIVING LAWS

On April 13th, 2017, the Government of Canada introduced legislation that would strengthen impaired driving laws and help ensure the public is better protected from both alcohol and drug-impaired driving. This legislation would also help to better deter and detect drug-impaired driving.

ADDRESSING DRUG-IMPAIRED DRIVING

Impaired driving is the leading criminal cause of death and injury in Canada, and drug-impaired driving is increasing. As the Government of Canada moves towards legalizing and strictly regulating cannabis, there is a need to strengthen our impaired driving laws to better address drug-impaired driving.

CURRENT LAWS

The *Criminal Code* currently prohibits driving while impaired by any drug. Police officers are currently able to conduct standardized field sobriety tests (SFST) if they suspect a driver has a drug in their body.

In addition, blood tests must currently be overseen by a doctor, which is time consuming and often requires transportation to a hospital.

PENALTIES

Current penalties for drug-impaired driving range from **$1,000 fine on a first offence to 120 days of imprisonment on a third or subsequent offence**. Drug-impaired driving that results in death could result in life imprisonment.

PROPOSED LEGISLATION

MAKING TESTING AND PROSECUTION EASIER

The new legislation would allow for the following:

- Police would be able to demand an oral fluid sample at the roadside if they suspect a driver has a drug in their body. This would be similar to the current method of testing for alcohol at the roadside with an approved screening device.
- Qualified technicians would be able to take blood samples from a driver without a doctor's oversight, allowing for testing sooner after a person is pulled over. Accurate and timely testing that reflects the degree of impairment is important for successful prosecutions, because it allows the police to capture evidence of impairment relatively closely to the time that the person is pulled over and relieves a burden on the healthcare system.
- Police officers would be able to provide opinion evidence in court as to whether they believe a driver was impaired by a drug at the time of testing, without the need for an expert witness in each trial. This will mean that cases are prosecuted more efficiently and more successfully.

LEGAL DRUG LIMITS

Under the new legislation, legal limits for drugs would be set by regulation.

For THC, the proposed levels would be:

- 2 nanograms (ng) but less than 5ng per 1 millilitre (ml) of blood for the summary conviction offence
- 5 ng or more per 1 ml of blood for the drug-only hybrid offence
- 2.5 ng or more per 1 ml of blood combined with 50 mg or more of alcohol per 100 ml of blood for the drugs-with-alcohol offence

Levels for some other impairing drugs would be set at detectable levels. This includes LSD, 6-MAM (a metabolite of heroin), Ketamine, Phencyclidine (PCP), and Psilocybin/Psilocin (magic mushrooms). Scientific advice indicates that these drugs are incompatible with safe driving at any level.

Government of Canada / Gouvernement du Canada

Canada

Bill C-46 – Strengthening Impaired Driving Laws

Bill C-46 Proposal

Steps:

1. Observed driving behavior: speeding, unable to maintain lane position, ran red light or stop sign, unsafe lane change, going to slow, collision – obvious initial observation
2. Physical indicators: green tongue, dilated pupils, red eyes – obvious initial observation
3. Standard Field Sobriety Test (SFST) – 2 to 5 cues
4. Drug screening test by existing oral fluid drug screening devices
5. Confirmatory / evidential analysis - collection body fluid (blood) – lab analysis

Marijuana – Conclusions

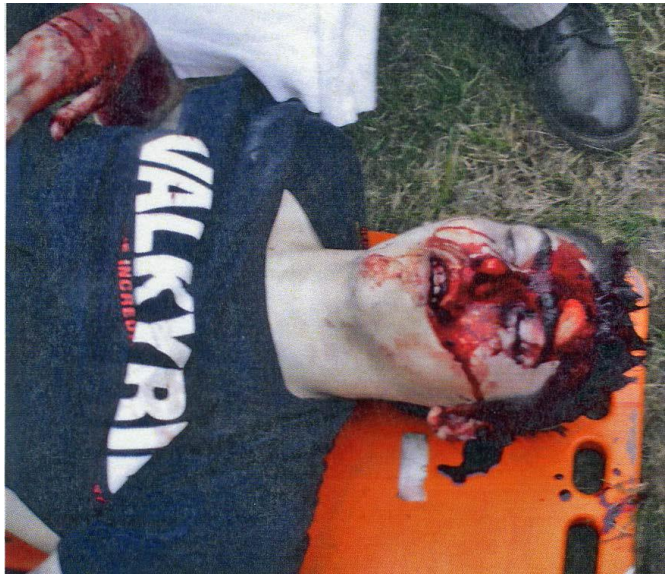
Cannabis Impaired Driving Injuries & Deaths Mount

SF, 16 yr old driver's ed

Failed to stop at intersection

His blood on ceiling inside

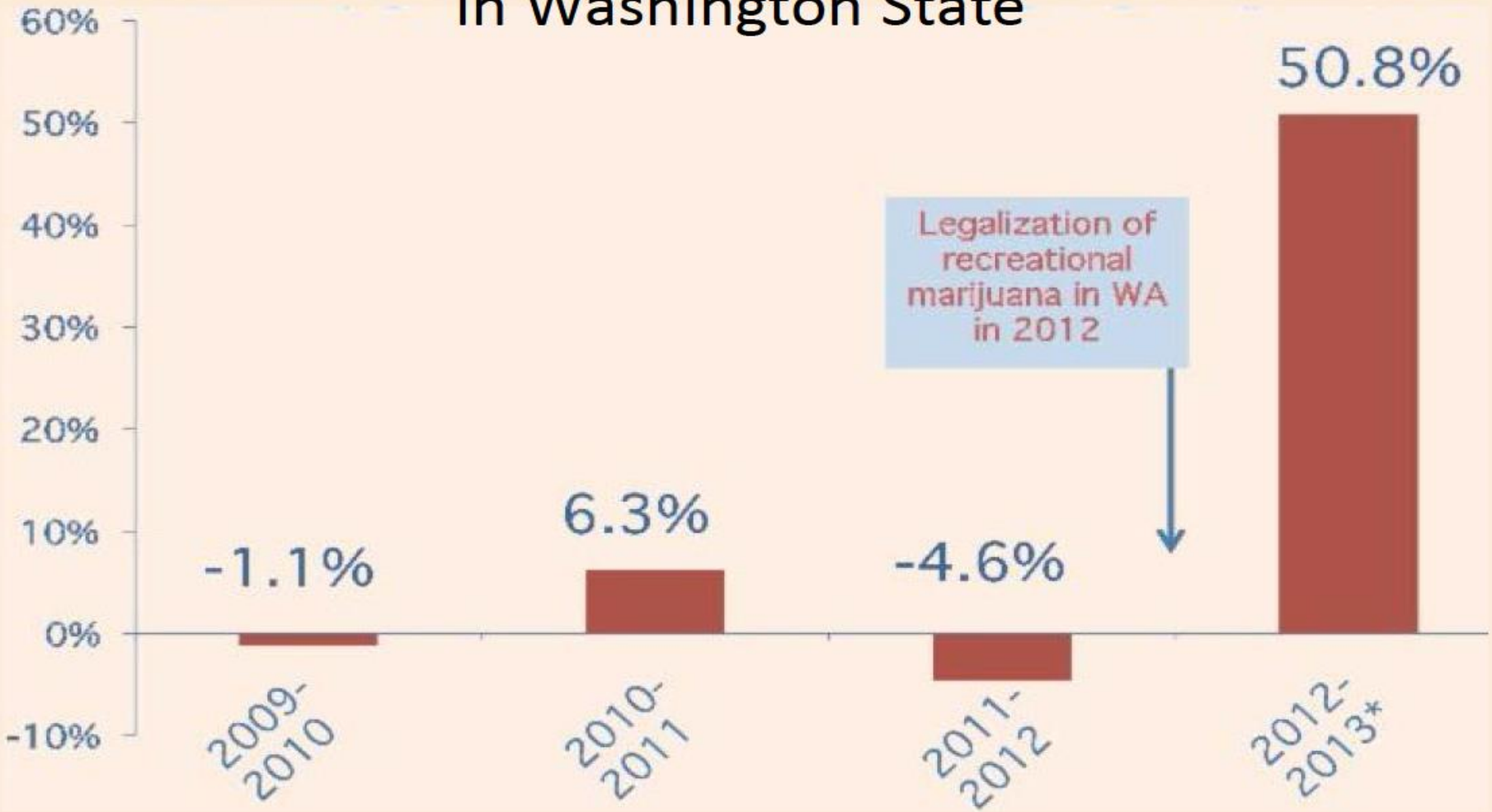
Steering wheel with air bag deployed



SF 16 yo white male MVC w THC

Toxicology	Specimen	Result
Ethanol	Blood	Not Detected
Δ-9 THC-COOH	Urine	>200 ng/mL
Δ-9 THC-COOH	Blood	**Not Detected**
11-OH THC	Blood	51 ng/mL
Δ-9 THC	**Blood**	**10 ng/mL**

Percent Change in Driver's Testing Positive for THC in Washington State



Source: Fiona Cooper, Ph.D., Washington State Toxicologist

Thank you!

Q & A

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