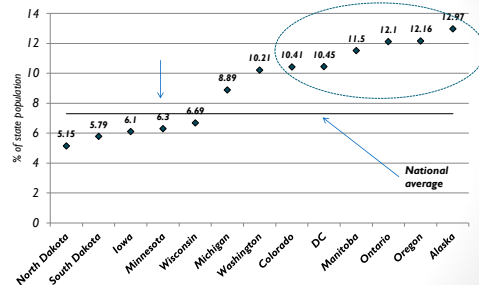---

Towards Zero Deaths
St. Cloud, MN

UTILITY OF ORAL FLUID IN DUID

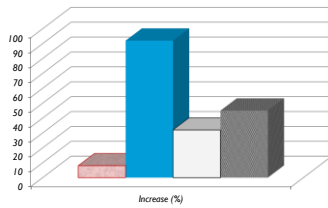*Christine Moore PhD DSc*

10/29/15
10.00 – 11.15am

RATES OF MARIJUANA USE

IMPACT OF MARIJUANA LEGALIZATION IN CO

➢ 2009 – present: Medical marijuana commercialization
➢ In 2014, retail marijuana businesses began operating

□ All traffic deaths (2010 - 2014)   ■ MJ related deaths (2010 - 2014)
□ MJ related deaths (2013 - 2014)   ■ Active THC Toxicology results (2013 - 2014)

PRESENTATION OVERVIEW

➢ 1. Impaired driving
  ➢ Drawbacks of blood collection
  ➢ Potential advantages of oral fluid
  ➢ Measuring the problem
➢ 2. Roadside testing devices
➢ 3. Frequently asked questions
➢ 4. Outcome when oral fluid testing has been implemented

STATES WHICH ALLOW DUID ORAL FLUID TESTING

- Alabama
- Arizona
- Colorado
- Georgia
- Indiana
- Kansas
- Louisiana
- Missouri
- New York
- North Carolina
- Ohio
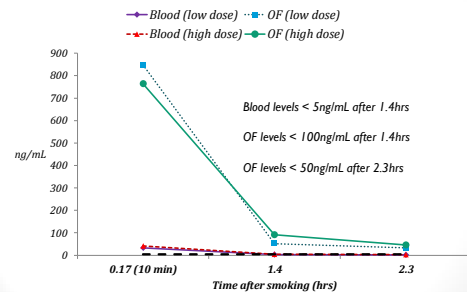- Oklahoma
- South Dakota
- Utah

DRAWBACKS OF BLOOD COLLECTION

➢ Blood:
  ➢ Considered the "gold standard" for DUID cases
  ➢ Majority of states use blood for DUID, although some still have urine
  ➢ Main drawback for marijuana detection in blood is the time between traffic stop and sample collection
  ➢ Medical personnel may be required to take the sample
  ➢ THC concentration decreases rapidly in the blood
    ➢ How rapidly ?

DRIVING SIMULATOR

- *National Advanced Driving Simulator (University of Iowa, IA)*
- *Current, occasional marijuana users*
- *THC doses:*
  - *Placebo with and without alcohol*
  - *Low dose with and without alcohol*
  - *High dose with and without alcohol*
- *Breath, oral fluid, blood collected at same time intervals*
- *Driving (0.8hrs)*
- *19 subjects completed study*

- *Hartman et al. Cannabis effects on driving lateral control with and without alcohol. Drug Alcohol Depend. 2015*

MEDIAN THC CONCENTRATIONS

Blood levels < 5ng/mL after 1.4hrs

OF levels < 100ng/mL after 1.4hrs

OF levels < 50ng/mL after 2.3hrs

ADVANTAGES OF ORAL FLUID

- *Oral fluid:*
  - *Drugs accumulate in saliva by diffusion from the blood, as well as oral cavity contamination*
  - *Easy, rapid collection*
  - *Non-invasive*
  - *Observed*
  - *No need for medical personnel to collect (sterile sample)*
  - *May provide information on recent drug intake*

MEASURING THE PROBLEM

- *2007: National Roadside Survey (Blood & oral fluid)*
- *2008, 2010, 2012: Canadian Roadside Survey, BC (Oral fluid)*
- *2010, 2012: California Roadside Survey (Oral fluid)*
- *2013: National Roadside Survey (Blood & oral fluid)*
- *2014: Canadian Roadside Survey, Ontario; (Oral fluid)*
- *2014: Washington State Initiative (Blood & oral fluid)*

WHY DO THIS RESEARCH ?

- *Increasing awareness that drugs, especially marijuana and impairing prescription drugs, are responsible for, or at least a factor in traffic accidents*
- *Improving forensic analysis of specimens and wider test panels*
- *What is the prevalence in driving population ?*
- *Societal need for information related to traffic problems*
- *Rehabilitation of drivers using illegal drugs*
- *Education of drivers using legal prescription drugs in the wrong way*

2007 AND 2014 NATIONAL ROADSIDE SURVEYS

- *Drivers randomly stopped at different locations in the USA primarily during night-time hours*
- *Not suspected of impaired driving*
- *Asked to consent to:*
  - *survey*
  - *breath alcohol test*
  - *oral fluid sample collection*
  - *blood sample collection*

SAMPLE COLLECTION

➢ *Blood: Gray-topped tube*
  ➢ *2007: 3,276 samples*

➢ *Oral fluid: Quantisal™ collection device:*
  ➢ *1 mL of oral fluid collected (+-10%)*
  ➢ *2007: 7,719 samples*

  PAIRED SAMPLES SENT SEPARATELY

All specimens sent to laboratory for testing – NOT ROADSIDE TESTS

2007 NATIONAL ROADSIDE SURVEY

➢ *16.3% of drivers positive for drugs (50% for THC)*

➢ *Paired positive samples (blood and oral fluid)*
  ➢ *75.7% were an exact drug match across all classes*
  ➢ *21.4% had at least one drug class match*

  ➢ *97.1% match for paired specimens*

  ➢ **"Oral fluid can be considered a reliable alternative to blood as a matrix for drug testing"** *Kelley-Baker et al. Traffic Inj. Prev. (2014); 15: 111-118*

CALIFORNIA SURVEY

Oral fluid:
➢ *2010 (900 drivers):*
➢ *14.4% of all drivers positive for drugs*
➢ *8.5% of all drivers positive for THC*

➢ *2012 (1300 drivers):*
➢ *14% positive for drugs*
➢ *7.4% positive for THC*

2012: DRUG POSITIVE BREAKDOWN

53%

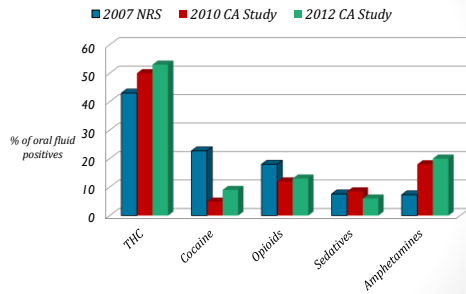- THC
- AMP/METH
- HYC/MOR
- COC/BZE
- BZD
- OXYC
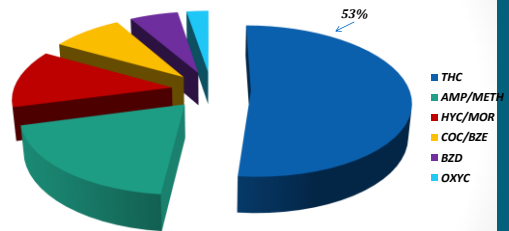
CALIFORNIA: 2007, 2010, 2012

➢ *Marijuana continues to be the drug of choice among drivers in California*
➢ *THC positive rates 7x higher than alcohol >0.08 (1%)*
➢ *Rates of THC use increased significantly from 2007 to 2010, but were fairly constant from 2010 to 2012*
➢ *Positive rates much higher in northern California*
➢ *Amphetamines were the second most prevalent drug class detected in oral fluid*
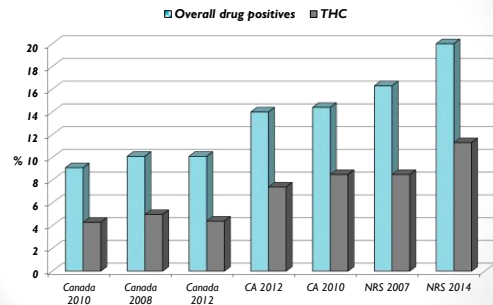
2014 COMPREHENSIVE DRUG TEST PANEL

➢ *Cocaine*
➢ *Marijuana*
➢ *Opiates*
➢ *Amphetamines*
➢ *Benzodiazepines (15)*
➢ *Tramadol*
➢ *Methadone*
➢ *Fluoxetine*
➢ *Sertraline*
➢ *Phencyclidine*
➢ *Barbiturates*
➢ *Antidepressants (16)*

➢ *Zolpidem*
➢ *Carisoprodol*
➢ *Methylphenidate*
➢ *Oxycodone /Oxymorphone*
➢ *Meperidine*
➢ *Propoxyphene*
➢ *Dextromethorphan*
➢ *Ketamine*
➢ **Diphenhydramine**
➢ **Chlorpheniramine**
➢ **Doxylamine**
➢ **Fentanyl**
➢ **Buprenorphine**

IS IT NECESSARY ?
>90% OF POSITIVES

■ 2007 NRS ■ 2010 CA Study ■ 2012 CA Study

% of oral fluid positives

THC, Cocaine, Opioids, Sedatives, Amphetamines

ORAL FLUID ANALYSIS:
NORTH AMERICAN RESULTS

■ Overall drug positives ■ THC

%

Canada 2010, Canada 2008, Canada 2012, CA 2012, CA 2010, NRS 2007, NRS 2014

CONCLUSIONS FROM ROADSIDE SURVEYS

➢ Oral fluid is a viable, reliable alternative to blood for DUID
➢ Drug prevalence among drivers (voluntary setting) has been established
➢ Drug positives for both medications and illegal drugs in US drivers have increased since 2007
  ➢ 16.3% to 20%
➢ THC is most prevalent drug detected in all recent surveys
➢ 5 drug classes accounted for > 90% of positive results
  ➢ THC
  ➢ Cocaine
  ➢ Opioids (including oxycodone)
  ➢ Sedatives (predominantly benzodiazepines)
  ➢ Amphetamines

2. ROADSIDE ORAL FLUID TESTS

➢ What about roadside testing and collection ?

➢ Several countries already using roadside oral fluid testing
➢ Australia were first to implement analysis
  ➢ THC & Methamphetamine
➢ Belgium
➢ Spain
➢ UK introduced roadside tests this year (2015)
  ➢ THC and cocaine at roadside
  ➢ If positive, blood sample collected and analyzed for other drugs at the laboratory

REQUIREMENTS FOR QUALITY DRUG TESTING

➢ **Scientifically accepted, reliable, defensible process**
  ➢ Appropriate collection of valid sample(s)
  ➢ Established chain-of-custody
  ➢ Accurate test results
  ➢ Preservation of results
  ➢ Minimal false negatives
  ➢ Protection of donor, collector, other stakeholders

HOW CAN WE IMPROVE CURRENT TESTING ?

➢ Collect specimens which reflect active drug in the driver
➢ Collect specimens closer to the time of incident/traffic violation – "roadside testing"
➢ Ensure results can empower law enforcement to retain driver if BrAC is negative

➢ **So, closer look at oral fluid rapid tests (sometimes called Point-of-care POC tests)**

MANY RAPID TEST CHOICES……..

OrAlert

iScreen

Ora-Check

OralCube

SalivaConfirm (replaces Oraline)

Oral AQ7

Oratect (FDA approved)

MORE CHOICES……..

Oral fluid cassette

Oral View–8

Rapid Detect SDS

6 panel saliva drug test

Stat Swab

Rapid STAT

Drug Check Saliva Scan

BUT, THINGS ARE NOT ALWAYS AS THEY SEEM..

CALIFORNIA OFFICE OF TRAFFIC SAFETY INITIATIVE

> 2013: California initiated a roadside testing research project

> Which of the many oral fluid test devices were chosen for the CA project, and why ?

> Easy, rapid collection at time of traffic incident
> Fast results (all devices run within 10 minutes)

> **Instrumented testing device preferred**
> **Printed or stored test result**

> Outcome must assist law enforcement in decision making regarding the driver's competence

CA-OTS INITIATIVE

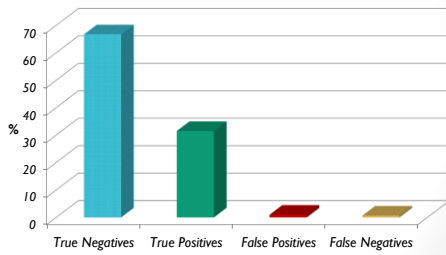> Alere DDS2 and Draeger Drug Test 5000 chosen

DDS2

Drug Test 5000

Printed or retained results
Published field studies
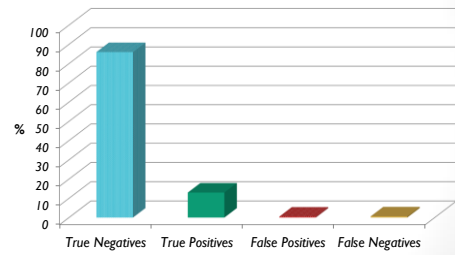*Law enforcement / DRE involvement*

CALIFORNIA INITIATIVE

58 Counties in California

Sacramento

My House

Bakersfield

Los Angeles

Fullerton

COMBINED DATA:
DDS2 .V. QUANTISAL™ (N = 126)
FULLERTON AND SACRAMENTO PD

DRUG TEST 5000 .V. QUANTISAL™ (N = 235)
LA & KERN COUNTY PD

CONCLUSIONS FROM ROADSIDE TESTS

➢ Two instrumented systems for drug detection in oral fluid were tested under realistic conditions in California Police Departments during 2014

➢ Overall device performance was excellent when compared to either oral fluid confirmation or blood as the "gold standard"

➢ Less than 1% false results on both devices

3. FREQUENTLY ASKED QUESTIONS..

➢ 1. WHAT CONCENTRATION OF THC IN ORAL FLUID IS EQUIVALENT TO THC IN BLOOD ?

➢ 2. WHAT CONCENTRATION OF THC IN ORAL FLUID CORRELATES WITH IMPAIRMENT ?

➢ 3. IS PASSIVE EXPOSURE TO THC AN ISSUE ?

FREQUENTLY ASKED QUESTIONS..

➢ 1. WHAT CUT-OFF CONCENTRATION FOR THC IN ORAL FLUID IS EQUIVALENT TO THC IN BLOOD ?

➢ 2. WHAT CONCENTRATION OF THC IN ORAL FLUID CORRELATES WITH IMPAIRMENT ?

➢ 3. IS PASSIVE EXPOSURE TO THC AN ISSUE ?

EQUIVALENT CUT-OFFS

Drug	Cut-off in blood (ng/mL)	Cut-off in OF (ng/mL) 95%CI	Correlation R^2	n
Alprazolam	10	2.8 (1.8 – 4.2)	0.998	106
AMP	20	290 (84 – 680)	0.993	86
Clonazepam	10	1.2 (0.2 – 2)	0.962	57
Cocaine	10	190 (26 – 350)	0.932	112
Codeine	10	83 (50 – 130)	0.999	92
Diazepam	50	1.1 (0.3 – 3.6)	0.930	94
METH	20	630 (120 – 1800)	0.993	55
Morphine	10	100 (37 – 180)	0.902	76
Nordiazepam	50	2.2 (1.2 – 4.5)	0.997	130
THC	1	44 (27 – 90)	0.991	182
Tramadol	50	490 (85 – 1500)	0.966	51

36

Gjerde et al. Estimation of equivalent cutoff thresholds in blood and oral fluid for drug prevalence studies. J. Anal. Toxicol. 2014; 38(2): 92 – 98 (Table II)
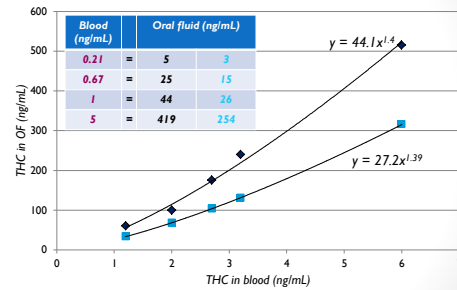
EQUIVALENT CUT-OFFS

> Calculated from DRUID project results

Drug	Blood (ng/mL)	Oral fluid (ng/mL)	Conversion (y = blood cutoff; x=OF cutoff)
Alprazolam	3	1.1	$y = 0.35x$
Cocaine	60	1230	$y = 20.5x$
Diazepam	57	2.2	$y = 0.0392x$
Methamphetamine	45	930	$y = 20.7x$
Morphine	9	86	$y = 9.5x$
THC	**1.3**	**39**	$y = 27.2x^{1.39}$

Bogstrand & Gjerde. Which drugs are associated with the highest risk for being arrested for driving under the influence? A case-control study. Forens. Sci. Int. 2014; 240: 21-28

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1. GJERDE ET AL. FIGURE 1. THC
2. BOGSTRAND & GJERDE – ADDED GRAPH

Blood (ng/mL)		Oral fluid (ng/mL)
0.21	= 5	3
0.67	= 25	15
1	= 44	26
5	= 419	254

$y = 44.1x^{1.4}$

$y = 27.2x^{1.39}$

FREQUENTLY ASKED QUESTIONS..

> 1. WHAT CONCENTRATION OF THC IN ORAL FLUID IS EQUIVALENT TO THC IN BLOOD?

> 2. WHAT CONCENTRATION OF THC IN ORAL FLUID CORRELATES WITH IMPAIRMENT?

> 3. IS PASSIVE EXPOSURE TO THC AN ISSUE?

SHORT-TERM EFFECTS OF CANNABIS

- Euphoria, relaxation
- Increased appetite
- Impaired short-term memory
- **Distorted perception**
- **Difficulty thinking and problem solving**
- **Loss of motor coordination**
- **Loss of cognitive skills**

- **Not helpful for safe driving………….**
- **Numerous publications: THC + alcohol extremely dangerous for driving situations**

THC CONCENTRATION IN SALIVA AND SIGNS OF IMPAIRMENT

> **Fierro et al. The relationship between observed signs of impairment and THC concentration in oral fluid. Drug Alcohol Depend 2014; 144: 231- 238**

> Spanish researchers investigated whether the judgment of a police officer regarding signs of impairment was related to the concentration of THC in oral fluid
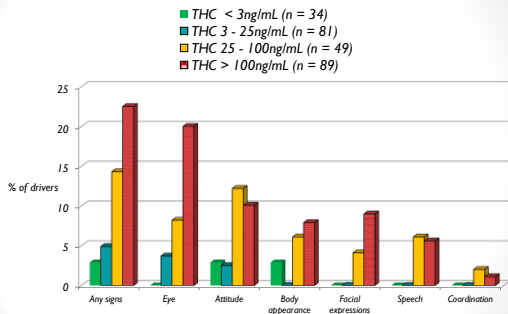
> 2632 drivers were investigated;
> > **253 were positive in oral fluid for THC only**

> Recorded 31 signs of impairment in 6 categories

2014: FIERRO ET AL.

> **1. Eye signs:** Red eyes; Brusque movement; Nystagmus; Pupil dilation or constriction; Slow pupil reaction

> **2. Attitude:** Nervous; Euphoric; Provocative; Tearful; Sleepy; Scratching; No comprehension

> **3. Body appearance:** Trembling; Perspiration; Restlessness; Superficial breathing

> **4. Facial expressions:** Blinking; Red nose; Sniffing; Swallowing; Cannabis smell

> **5. Speech:** Talkative; Difficulty speaking; Low tone

> **6. Co-ordination:** Staggering; No co-ordinated movements; Legs trembling

RESULTS

Legend:
- THC < 3ng/mL (n = 34)
- THC 3 - 25ng/mL (n = 81)
- THC 25 - 100ng/mL (n = 49)
- THC > 100ng/mL (n = 89)

% of drivers

Categories: Any signs, Eye, Attitude, Body appearance, Facial expressions, Speech, Coordination

SPANISH STUDY

➤ A relationship was found between THC concentration in OF and some observed signs of impairment
➤ Eye signs were noticeable at OF THC >3ng/ml
➤ OF THC >25ng/ml was related to behavior, facial expression, and speech signs of impairment
➤ Alcohol and THC contributed to impairment independently and, when taken simultaneously, effects were comparable to the sum of the effects when consumed separately

FREQUENTLY ASKED QUESTIONS..

➤ 1. WHAT CONCENTRATION OF THC IN ORAL FLUID IS EQUIVALENT TO THC IN BLOOD ?

➤ 2. WHAT CONCENTRATION OF THC IN ORAL FLUID CORRELATES WITH IMPAIRMENT ?

➤ 3. IS PASSIVE EXPOSURE TO MARIJUANA AN ISSUE ?

PASSIVE EXPOSURE

➤ Could occur with any drug, but marijuana is most problematic
➤ Medical use of marijuana is legal in many states
➤ Recreational use of marijuana is currently legal in CO & WA states
➤ Recently approved for recreational use in OR, AK and DC
➤ Other states have upcoming ballot measures

KEEPING THE WORLD HIGH 1985 - 2010

PASSIVE EXPOSURE

➤ Recent publication:

➤ Cone E. et al. Nonsmoker exposure to secondhand cannabis smoke: III. Oral fluid and blood drug concentrations and corresponding subjective effects. J. Anal. Toxicol. 2015; doi: 10.1093/jat/bkv070
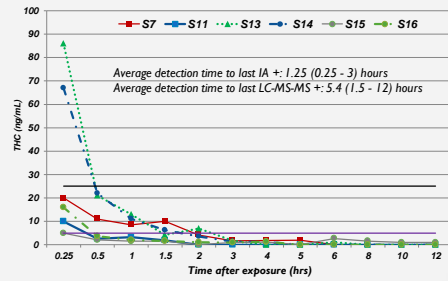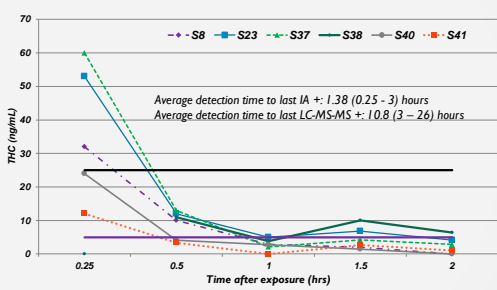
2015 JOHNS HOPKINS UNIVERSITY

➢ Six experienced cannabis users smoked cigarettes "ad libitum"
  ➢ 5.3% THC cigarettes in Session 1
  ➢ 11.3% THC cigarettes in Sessions 2 and 3
  ➢ Session 3 was carried out in a ventilated room
➢ Six non-smokers seated alternately with smokers for 1 hour
➢ Oral fluid and whole blood samples collected before starting the sessions and at multiple time points afterward
➢ Non-smokers:
  ➢ 0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 10, 12, 22, 26, 30 and 34 hours after exposure
➢ Smokers:
  ➢ 0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8 hours after smoking
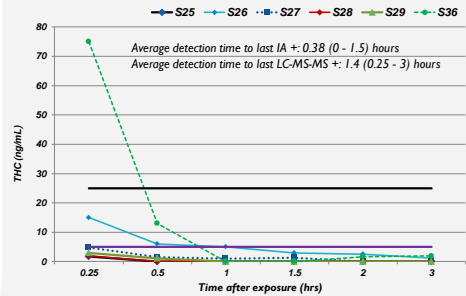

SESSION #1
NON-SMOKERS: THC IN ORAL FLUID

Average detection time to last IA +: 1.25 (0.25 - 3) hours
Average detection time to last LC-MS-MS +: 5.4 (1.5 - 12) hours

---

SESSION #2: NON-SMOKERS: THC IN ORAL FLUID
(0.25 MIN: 1 OUTLIER, 307NG/ML)

Average detection time to last IA +: 1.38 (0.25 - 3) hours
Average detection time to last LC-MS-MS +: 10.8 (3 – 26) hours

---

SESSION #3 (VENTILATED ROOM)
NON-SMOKERS: THC IN ORAL FLUID

Average detection time to last IA +: 0.38 (0 - 1.5) hours
Average detection time to last LC-MS-MS +: 1.4 (0.25 - 3) hours

---

AVERAGE (RANGE) THC CONCENTRATION (CMAX)

	THC in oral fluid (ng/mL)		
	Session 1	Session 2	Session 3 (ventilated)
Non-smokers	34 (4 – 86)	81.5 (12 – 308*) *60	16.9 (1.7 – 75)
Smokers	969.5 (102 – 3512)	721 (369 – 1358)	1089 (168 – 3207)

	THC in blood (ng/mL)		
	Session 1	Session 2	Session 3 (ventilated)
Non-smokers	1.4 (0.6 – 1.8)	3.1 (1.2 – 5.6)	0.5 (0 – 0.9)
Smokers	18.8 (12 - 36)	20.5 (7.8 - 48)	20.9 (9.4 - 37)

AVERAGE THC CONCENTRATION (N = 6)

Concentrations: x10
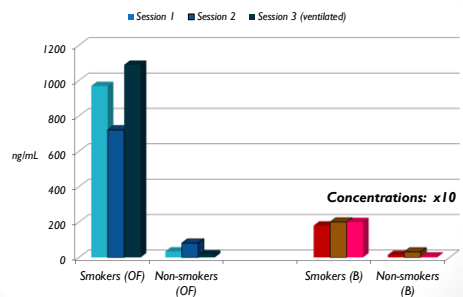
CONCLUSIONS – CONE ET AL.

- Extreme exposure to marijuana results in THC deposition in oral fluid
- After only 1 hour of exposure some individuals showed significant concentrations of THC in oral fluid
- Only one non-smoker was positive by THC immunoassay (4ng/mL) 3 hours after exposure
- Most non-smokers tested positively for less than 3 hours
- In the ventilated room the number of positive tests was much lower
- From the paper:
- **"Extreme exposure of non-smokers could lead to positive drug tests and drug-induced behavioral changes not unlike those produced by active cannabis smoking"**
- **"It seems likely that exposure under less extreme conditions, such as casual encounters with cannabis smoke and in situations where an individual was not aware of smoke exposure, would be very unlikely to result in positive tests and behavioral changes"**

4. OUTCOME: ORAL FLUID TESTING IMPLEMENTATION

- In the USA, no jurisdiction is routinely carrying out oral fluid testing for DUID
- Several pilot studies have been completed, in progress or planning stages
  - Guidelines for implementing a pilot project available from SOFT DUID oral fluid subcommittee
- What are results from areas where oral fluid roadside testing has been implemented ?
- Belgium:
  - Van der Linden et al. **Roadside drug testing: comparison of two legal approaches in Belgium.** Forensic Sci Int. 2015;249:148-55.

2009 NEW LEGISLATION

Fast, limited field sobriety test; oral fluid roadside screening; lower laboratory cut-off for plasma confirmation

1999	2009
Driver stopped	Driver stopped
Drug recognition test battery	Checklist for external signs of recent drug use
If impairment indicated, **urine** onsite screening test	If indication of use, **oral fluid** onsite screening test
If positive, blood sample taken	If positive, blood sample taken
Laboratory confirmation	Laboratory confirmation (lower cut-offs)

CUT-OFFS FOR ROADSIDE TESTS

	1999	2009
Drug	Dipro-Druglab® Urine (ng/mL)	Securetec Drug-Wipe-5® Oral fluid (ng/mL)
Amphetamine	1000	50
Methamphetamine - MDMA	1000	25
Cocaine (BZE)	300	25
Opiates (Morphine)	300	10
Cannabis	50	25

CUT-OFFS: LABORATORY CONFIRMATIONS

	1999 Plasma (ng/mL)	2009 Plasma (ng/mL)	2009 Oral fluid (ng/mL)
Amphetamine	50	25	25
MDMA	50	25	25
Cocaine	50	25	10
Benzoylecgonine	50	25	10
Morphine	20	10	5
6-acetylmorphine	NA	NA	5
THC	2	1	10

DECREASE IN FALSE POSITIVE RESULTS

- Prefer to avoid false positives because a screen positive results in an automatic 12 hour driving ban even if confirmation is negative
- Comparison of the two approaches demonstrated the percentage of false positives decreased from 17% to 8%
- For cannabinoids, increase in **true positives** is significant because oral fluid detection window is more similar to blood than to urine

- **Conclusion (from paper):**
- **"The number of drivers where none of the positively screened target drugs could be confirmed above the legal cut-off value has dropped significantly and our data suggests that more recent drug use is being detected. This trend is undoubtedly demonstrated for cannabis, which is the most widely used illicit drug in Belgium."**

Summary

- Oral fluid is a valid, appropriate specimen for drug analysis in DUID
- Extent of problem assessed by roadside surveys
- Oral fluid analysis provides similar information to blood regarding recent drug intake
- Oral fluid collection can occur more quickly than blood sampling following a traffic stop (saving time and money)
- Some rapid oral fluid test instruments have improved significantly and reliable, instrumented devices are available
- Some have been tested in extreme temperature conditions
- Suitable for remote locations
- All rapid test positive results must be confirmed with a second specimen laboratory test (preferably Quantisal oral fluid or blood)

Final Analysis

- 1. Impaired driving
  - Oral fluid is a valid specimen for drug analysis
  - Extent of problem assessed by roadside surveys

- 2. Roadside testing devices
  - Vastly improved over recent years
  - Reliable instrumented devices are commercially available

- 3. Frequently asked questions: On-going research
  - More publications on correlation of blood and oral fluid in DUID cases
  - More interest in drug concentrations as they relate to impairment
  - More passive exposure studies

- 4. Outcome of oral fluid testing implementation
  - Countries that have implemented oral fluid roadside testing starting to publish their experiences and data
  - Belgium: Fewer false positives, more true positives reported

Thank you for the invitation and hospitality...

Christine Moore
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cmoore@immunalysis.com