From: Emily.Lawrence [personal information redacted]
Sent: May 30, 2020 6:36 PMConsultation (CNSC/CCSN)
To: PWU Feedback on RegDoc 2.2.4 v II
Subject: PWU_ Drug Testing_ PWU Submissions on RegDoc Version 3 May 30, 2020.PDF
Attachments:

Dear CNSC:

I act for the Power Workers' Union. I attach the PWU's submissions, and a report of an expert retained by the PWU and the Society.

Thank you.

Emily C. Lawrence

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SUBMISSIONS OF THE POWER WORKERS' UNION ON TO THE CANADIAN NUCLEAR SAFETY COMMISSION

REGARDING REGULATORY DOCUMENT 2.2.4, FITNESS FOR DUTY, VOLUME II: MANAGING ALCOHOL AND DRUG USE (Version 3) (March 2020)

May 30, 2020

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TABLE OF CONTENTS

OF THE SUBMISSIONS OF THE POWER WORKERS' UNION ON REGDOC 2.2.4 V. II (VERSION 3)

SUBMISSIONS OF THE POWER WORKERS' UNION ON REGDOC 2.2.4 V. II (VERSION 3)

EXECUTIVE SUMMARY

The Power Workers' Union ("PWU") is a trade union that represents over 15,000 workers employed in Ontario's electricity industry, most of whom are employed in the nuclear power industry. The PWU is actively involved in the development and maintenance of practices and policies within nuclear facilities to keep workers and the public safe. The PWU has made submissions to the Commission at every stage of the Commission's consideration of and implementation of alcohol and drug testing in nuclear facilities.

The PWU opposes the use of alcohol and drug testing in nuclear facilities, except testing that is consistent with the developed jurisprudence from arbitrators and the courts. Testing must balance the competing interests of an employer (and here, the Commission) to ensure a safe and productive work environment for employees and members of the public against an employee's constitutional, common law and statutorily-provided rights to privacy, dignity, equality, security of the person and security against unreasonable search and seizure, and to be free from discrimination. To appropriately balance these interests, testing of workers must be based on a reasonable suspicion of impairment or necessary to address an identified concern regarding the impairment of workers while at work.

The Commission's proposed adoption of oral fluid testing ("OFT") does not address the significant constitutional, human rights and privacy issues associated with drug and alcohol testing. OFT compels workers to provide bodily samples and is intrusive. OFT does not measure impairment; it only measures the presence of a drug in the body. The Commission's proposed cut-off levels measure the presence of a drug in the body for a longer period of time than the drug causes impairing effects. As a result, the Commission's testing regime is an attempt to control the off-duty conduct of workers, which is not justifiable, acceptable or appropriate role of a Canadian regulator.

The PWU also opposes the use of point-of-collection testing devices because they are not sufficiently reliable, and the Commission has not articulated the scope of their use nor a process for their use that ensures the worker's privacy rights.

PART I. INTRODUCTION

A. The PWU and its Past Submissions

1. The Power Workers' Union ("PWU") is a trade union that represents over 15,000 workers employed in Ontario's electricity industry, most of whom are employed in the nuclear power industry. Its members work throughout Ontario and make up a large majority of employees in the nuclear power industry, including at Ontario's nuclear power plants: Darlington Nuclear Generating Station, Pickering Nuclear Generating Station, and Bruce Power Generating Station ("PWU Employers"). PWU members form the majority of workers employed at Ontario's other electrical generating facilities, as well as transmission and local distribution companies.

2. As an external stakeholder who represents employees in nuclear facilities, the PWU has an important role to play in ensuring that Ontario's nuclear facilities are safe and secure through the development and implementation of effective policies to ensure fitness for duty ("FFD") of its employees.

3. In 2012, the PWU made lengthy submissions regarding the Commission's 2012 Discussion Paper for Public Consultation, DIS-12-03: *Fitness for Duty: Proposals for Strengthening Alcohol and Drug Policy, Programs and Testing* ("FFD Discussion Paper") and an accompanying Reference document: INFO-0831: *Recent Alcohol and Drug Workplace Policies in Canada: Considerations for the Nuclear Industry,* prepared by Barbara Butler and Associates Inc.

4. In 2016, the PWU made lengthy submissions regarding the Commission's draft Regulatory Document, 2.2.4 *Human Performance Management, Fitness for Duty* ("Draft Regulatory Document").These submissions set out the PWU's comments, concerns and feedback on the Draft Regulatory Document and in particular, the proposed requirement for alcohol and drug testing for certain employees in nuclear facilities, and appended two reports of experts, Professor Olaf Drummer and Professor Scott Macdonald.

5. In summary, the PWU's comments on the Draft Regulatory Document were three-fold:

    a. The PWU supported the "programmatic elements" for FFD including supportive employee assistance programs, and peer and supervisor behavioural observation. Licensees, their bargaining agents, managers and employees have been operating nuclear facilities safely for over 40 years, without evidence of safety issues arising from substance misuse, using these programs. They work, on a lawful and non-intrusive basis. The PWU supports the adoption of this set of general principles for successful and legal drug and alcohol policies, as long as they are flexible enough to permit nuclear facility licensees

to adopt policies and practices that are workplace-specific and comply with the legal duty to accommodate employees on a case-by-case basis under Human Rights legislation. Apart from such programs and the specific FFD assessments and tests mandated by the *Nuclear Security Regulations*, there is no need to mandate changes that intrude on the privacy rights of citizens employed in safety-sensitive positions at nuclear facilities.

b. The PWU opposed the Draft Regulatory Document's alcohol and testing requirements because they do not comply with human rights and privacy legislation, or the *Charter of Rights and Freedoms*. Most significantly, random alcohol and drug testing requirements do not strike the appropriate balance between safety concerns and the rights of employees, and is inconsistent with established Canadian jurisprudence.

c. The PWU also submitted that the Draft Regulatory Document contained insufficient guidance for the consequence of a positive alcohol or drug test, the circumstances under which substance abuse evaluations are required, or the appropriate collection of personal health and other information. The Commission must ensure that any changes to the regulatory regime are consistent with the licensees' duty to accommodate, comply with privacy legislation and ensure the highest level of protection of the privacy and respect for employees.

6. After the Commission announced that it would be publishing RegDoc 2.2.4, V. II in November 2017, which included alcohol and drug testing requirements, the PWU grieved the use of and implementation of workplace policies proposed by the PWU Employers, as did several other unions at nuclear sites across Canada. The PWU provided the CNSC with notice of these grievances in November 2017. RegDoc 2.2.4 V. II was published in January 2018 ("RegDoc Version 2").

7. The PWU is aware that the PWU Employers, who previously advised the Commission that a Commission-mandated FFD regime was not necessary, have since requested that the Commission revise RegDoc Version 2 to permit oral fluid testing.

8. The PWU continues to take the position that the alcohol and drug testing requirements set out in RegDoc Version 2 and maintained in version 3, released for public comment in March 2020 ("RegDoc Version 3"), are unnecessary for public safety and unlawful. The proposed adoption of oral fluid testing does not address the significant constitutional, human rights and privacy issues associated with drug and alcohol testing.

9. The PWU has provided these submissions in response to the Commission's direction that it will receive submissions only on the proposed revisions to

the RegDoc Version 3 (which relate primarily to the addition of oral fluid testing). None of the submissions of the PWU should be taken to agree with or accept the premise that the drug testing regime set out in any version of the RegDoc is appropriate or lawful.

PART II. THE PWU'S SUBMISSIONS ON THE ADDITION OF ORAL FLUID TESTING IN REGDOC VERSION 3

A. The Commission's Obligation to Balance Interests

10. In assessing the scope and propriety of alcohol and drug testing in the workplace, the Supreme Court of Canada has confirmed that the issue is one of balancing the competing interests of an employer (and here, the Commission) to ensure a safe and productive work environment for employees and members of the public against an employee's rights to equality, dignity and security of the person.[1] In past submissions, the PWU have described the employees' constitutional, common law and statutorily-provided rights to privacy, dignity, equality, security of the person and security against unreasonable search and seizure, and to be free from discrimination.

11. Compliance with the "Canadian model" from the jurisprudence on alcohol and drug testing, requires employers to have a reasonable basis for testing. Random testing, divorced from any employee-specific reasonable cause, has been upheld by adjudicators in very limited cases. In particular, arbitrators have permitted such programs *only* where there is compelling evidence of a widespread substance abuse problem in the workplace that cannot be addressed by less invasive measures.[2] In such circumstances, an employer may be able to meet the heavy onus to justify resorting to random alcohol testing if it has met the "threshold test of reasonable cause" to suspect widespread impairment in the workplace.

12. In short, in order to justify the adoption of any alcohol and drug testing as an appropriate balancing of interests, the Commission must demonstrate that (1) such testing addresses a legitimate safety issue present in nuclear sites; (2) that such testing provides accurate, relevant and significant information about employees and their ability to perform their duties, and (3) such testing actually results in a safer workplace using the least intrusive means possible.

13. The PWU submits that the Commission's RegDoc Version 3, like earlier versions, is not justifiable, appropriate or lawful. As set out in the PWU's prior submissions (on which the PWU continues to rely), the testing

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[1] *Communications, Energy and Paperworkers Union of Canada, Local 30 v. Irving Pulp & Paper, Ltd.*, [2013] 2 SCR 458, 2013 SCC 34 ("*Irving Pulp*"), at para 4, 50, 57.

[2] See for example, *Irving Pulp, ibid*.

requirements of the RegDoc (all versions) do not comply with constitutional, human rights or privacy protections of employees nor represent an appropriate balancing of interests. The testing requirements are not rationally connected to the objective of safety, and do not infringe as little as possible to achieve the safety objective.

14. There is no evidence of a safety issue arising from alcohol and drug use at nuclear sites. While the Commission's goal of safety and security in nuclear facilities is indisputable, the Commission has not explained why it has elected to adopt alcohol and drug testing, apart from a general reference to its mandate to protect public safety. The Commission has not explained why any testing is appropriate, given the robust practices and policies at nuclear sites that promote the prevention and early detection of substance abuse issues, while respecting the rights and privacy of employees,[3] or assessed any alternatives to assess impairment.

15. The use of oral fluid testing ("OFT"), in addition to other methods of testing, does not correct the Commission's ill-conceived decision to require licensees to implement testing. In particular:

    a. like other means of testing, OFT is highly intrusive and is an invasion of one's personal privacy and dignity;

    b. like other means of testing, OFT does not measure impairment; a positive test only confirms the presence of a drug in the body;

    c. the Commission has selected cut-off levels that will detect the presence of drugs for periods of time that exceed the period of likely impairment. The Commission has not tailored its proposed cut-off levels such that the detection window of the presence of a drug in the body will overlap entirely with expected periods of impairment, and thus could act as a proxy for impairment; and

    d. the RegDoc Version 3 permits licensees to adopt the use of point-of-collection ("POCT") device as a "screening tool." The RegDoc Version 3 is unclear as to the scope of permissible use of POCT. The Commission should not clarify that protocols for use of POCT screening devices must include their administration by trained personnel and conducted in a matter that protects the privacy of workers.

16. The PWU retained Professor Olaf Drummer jointly with the Society of United Professionals, to prepare an expert opinion regarding the use of OFT and the reliability of OFT testing. That report is attached as Appendix "A".

[3] See PWU Submissions on Draft Regulatory Document filed in March 2016.

B. Oral Fluid Testing is Highly Intrusive

17. The right to privacy, as protected by the *Charter of Rights and Freedoms* is an essential value of Canadian society and lies at the heart of liberty in the modern state.[4] This is particularly so for compelled searches of a person's body. As the Supreme Court of Canada has noted the "seizure of bodily samples is highly intrusive" and "the use of a person's body without his consent to obtain information about him invades an area of personal privacy essential to the maintenance of his human dignity."[5]

18. All forms of biomedical testing for alcohol and drugs are invasive. The collection of bodily fluids intrudes upon the bodily integrity and dignity of employees, regardless of the method of collection. In the *Irving Pulp* case, the Supreme Court of Canada affirmed that breathalyzer testing "effects a significant inroad" on privacy, involving coercion and restriction on movement[6] and that the compelled provision of bodily fluid for testing purposes (regarding of the form of testing) "effects a loss of liberty and personal autonomy. These are at the heart of the right to privacy."[7]

19. The PWU submits that like breathalyzer testing, OFT is the compelled provision of bodily fluids, even if the manner of testing may be perceived as less intrusive than urine or blood testing.[8] OFT also provides a much richer source of an individual's DNA than a breathalyzer sample.

C. Oral Fluid Testing Measures the Presence of a Drug, Not Impairment

20. As noted in Professor Drummer's report attached as Appendix "A", the use of oral fluid to detect the presence of drugs has evolved substantially over the last fifteen years. OFT tests the amount of a drug in an individual's mouth/saliva, whereas urine testing tests predominantly for the metabolites of a drug that has been used.

21. Several cases have concluded that the inability of drug tests to measure current impairment is relevant in an assessment of whether a testing regime is reasonable and justified when balanced against the infringements on

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[4] *R v Dyment*, [1988] 2 SCR 417 at 427-28.

[5] *Ibid* at 431-32.

[6] Irving Pulp, *supra*, para 49.

[7] *Ibid*. para 50.

[8] To the extent that arbitrators or judges have concluded that OFT is minimally intrusive, the PWU submits that this analysis is inconsistent with the jurisprudence from the Supreme Court of Canada.

employees' rights. Where a drug test cannot accurately assess impairment, adjudicators have declined to uphold random testing.[9]

22. Despite the increased use of OFT in recent years, OFT testing does not, and cannot, accurately assess whether an individual is impaired by the drug being tested.

23. The Canadian Society of Forensic Sciences, Drugs and Driving Committee ("DDC"), is the expert advisory body to the Department of Justice with respect to issues of drug impaired driving laws. The DDC's report on oral fluid devices make this clear:

> Drug screening equipment does not measure drug impairment. Impairment is dependent upon the drug used, the dose, time since last use, route of administration, and is subject to inter-individual variability, among other factors.[10]

24. Both Dr. Huestis, the expert retained by the Commission, and Professor Drummer agree that OFT does not measure impairment of an individual by the drug:

    a. In her report to the Commission, Dr. Huestis stated: "Oral fluid drug concentrations document drug use but not impairment. Even blood drug concentrations are difficult to interpret, for instance the role tolerance plays in chronic frequent drug users. Urine drug concentrations also document drug use and may have slightly longer detection windows than oral fluid. Neither necessarily document impairment."[11]

    b. Professor Drummer noted in his report, "Importantly, neither the presence of a drug in oral fluid nor in urine can be used to determine whether impairment is present or not. Impairment, however defined, can only be assessed through some form of standardized field assessment protocol relevant to a worker's occupation by suitably trained personnel" and "Workplaces will usually require an ability to make rational informed decisions (cognitive performance) and have adequate limb-eye coordination

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[9] See for example, *Entrop v Imperial Oil Ltd,* 2000 CarswellOnt 2525, [2000] OJ No 2689 at para 99; *Greater Toronto Airports Authority v P.S.A.C., Local 0004*, [2007] LVI 3734-2, 90 CLAS 177 (Devlin) at para 28, among many others.

[10] Report on Drug Screening Equipment – Oral Fluid Canadian Society of Forensic Sciences, Drugs and Driving Committee (October, 2018) https://www.csfs.ca/wp-content/uploads/2018/10/Report-on-Drug-Screening-Equipment-%E2%80%93-Oral-Fluid.pdf ("DDC Report")

[11] *Oral Fluid Drug Testing Practices: Considerations for: Regulatory Document 2.2.4 Fitness for Duty Volume II Managing Alcohol and Drug Use. A report to the Canadian Nuclear Safety Commission prepared by: Dr. Marilyn A. Huestis* (March 2020), ("Huestis Report"), p. 47

> skills (psychomotor skills). Impairment or lack if [*sic*] impairment can only be assessed through a structured program conducted by a suitably trained person. The best parallel to compare against is in road safety and the use of standardized field sobriety tests (SFST) by Drug Recognition Experts (DRE); a program that is used in both Canada and the USA […] It is possible that a person, even after having passed a SFST a person could still have measurable concentrations of drugs in their oral fluid (and possibly also blood/urine)."[12]

25. Given the lack of evidence of safety issues in the nuclear sites, and the inability of OFT testing to assess impairment, the Commission cannot justify the imposition of OFT.

D. The Commission's Proposed Cut-Off Levels Will Not Measure Levels that Demonstrate On-the-Job Impairment

26. At its highest, OFT detects the presence of drugs in a window of detection that is shorter than the window of detection for urine testing. This is because the metabolites will usually be present in the urine for a longer period of time than drug analytes are present in oral fluid, and the concentrations of these metabolites will be often much higher than the parent drugs in oral fluid.

27. For both OFT and urine testing, the detection of drugs or drug metabolites that result in a positive test will depend on the drug, the dose(s) used and individual characteristics, and importantly, on the cut-offs that are applied to the analyses.

28. The term "cut-off", when it applies to analyses and reporting of such analyses, refers to concentrations below which a screening result is not analyzed further and confirmatory results are reported as negative. The use of cut-offs helps to regulate the collection, testing and reporting of positive results and ensures consistency for drug testing protocols at workplaces and in the laboratories. These cut-offs also act to limit, as far as practicable, interpretation of results that could arise from other sources of drug, such as contamination (of the worker) by a drug, or from other sources.

29. OFT is not equivalent to a breathalyzer device that tests alcohol. Over decades of research, there is now a cut-off point for a positive breathalyzer test that is widely accepted as demonstrating that an individual has a blood alcohol level that is impairing to most individuals most of the time. That consensus is essential to the acceptability of the alcohol breathalyser results as a measure of impairment.

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[12] Expert Report Relating To Drug Testing In Oral Fluid Prepared By Professor Olaf H. Drummer ("Drummer Report"), p. 3 and 13

30. In contrast, as evidenced by the reports of Professor Drummer and Dr. Huestis, there are no internationally-approved cut-off reporting limits established for the detection of drugs of abuse in oral fluid.[13] As noted above, no cut-off is accepted as demonstrating impairment. Among seven different agencies and jurisdictions compared by Dr. Huestis, the drug with the most variability in cut-off levels is cannabis.[14]

31. For OFT, the choice of the cut-off level(s) is relevant to the likely "detection window", being the window of time that an individual will test positive from the use of the drug. The variation among industries and countries in cut-off levels and associated detection windows represents the different policy choices and different purposes for undertaking testing:

    a. The cut-off level can be set sufficiently low, such that it captures a detection window of days or weeks, similar to the detection windows obtained through urine testing. A low cut-off level identifies and deters all drug usage, including off-duty usage; or

    b. The cut-off can be set sufficiently high to reflect a much shorter detection window. If the intent is to obtain a positive result only from those who are impaired when tested, the cut-off level should be set to identify a detection window which is equivalent to the period when a worker would be impaired.

32. For example, the screening cut-off for the U.S.-based SAMHSA is proposed at 4ng/mL; while the respective screening and confirmatory cut-offs for cannabis/THC in the standard used in Australia and New Zealand are 15 and 5ng/mL, respectively. As Professor Drummer notes, the higher cut-offs in Australia and New Zealand reduce the detection window for cannabis use and reduce the likelihood of a user testing positive when use of cannabis occurred several hours earlier.[15]

33. As noted by Professor Drummer, the proposed cut-offs in RegDoc Version 3 "represent low cut-offs, presumably in an attempt to prolong the detection time in oral fluid and hopefully have similar detection windows to urine."[16]

34. According to Professor Drummer, the use of the confirmation cut-off of 2ng/mL for cannabis, as set out in RegDoc Version 3, may give a detection window of up to about 24 hours, much longer than the period of 4-6 hours when impairment of recreational cannabis can be determined using standard assessments of sobriety.[17]

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[13] Drummer Report, p. 7; Huestis section 2,4.

[14] Notably, this variation is between U.S.-based and non-U.S. based entities and organizations.

[15] Drummer Report, p. 10.

[16] *Ibid,* p. 10.

[17] *Ibid*, P. 9.

35. Dr. Huestis provided a different opinion, without citation, regarding detection times for cannabis. She stated that at a confirmation cut-off at 2 ng/mL, the window of THC detection is 10 hours in occasional cannabis smokers and 24 hours in chronic frequent cannabis smokers, and that a 10 ng/mL cut-off provides a window of detection for occasional cannabis users of 2-3 hours and 10 hours in chronic users.[18] Dr. Huestis does not provide any opinion about the expected length of impairment by cannabis, nor does she assess whether there is a significant overlap between the detection windows at various cut-off levels and periods of likely impairment.

36. The DDC, in its report on which the Department of Justice relied to develop drug-impaired driving regulation in Canada, recommended the use of a 25ng/mL cut-off for oral fluid testing of drivers who are reasonably suspected to be impaired.[19] Dr. Huestis does not refer to this cut-off level in her comparison of workplace-based testing cut-offs.

37. The DDC noted that "[o]ne of the strongest factors that correlates with THC impairment is the time since last use. Occasional THC smoking causes impairment which begins almost immediately and generally resolves within 4 to 6 hours following last use. […] Individuals who test positive on drug screening equipment [at 25ng/mL] following THC use could do so for up to 4 hours. In general, a temporal association can be made between a positive drug screening equipment result for THC and impairment."[20] Dr. Huestis does not explain the discrepancy between the DDC Report's conclusion that the detection window at a cut-off of 25ng/mL is 4 hours and her uncited opinion that an occasional user will test positive for 2-3 hours at a cut-off of 10ng/mL.

38. Detection windows for cannabis use is variable among individuals and among drugs, and there is no consensus among experts like Professor Drummer, Dr. Huestis, and the DDC. The PWU submits that, to the extent that any random testing is appropriate (a premise the PWU rejects), the Commission is required to adopt the least restrictive OFT cut-offs that correlate with windows of impairment.

39. The Commission has not done so. It retained an expert who has not opined on the period of impairment by cannabis, nor assessed whether there is a significant overlap between the detection windows at various cut-off levels and periods of likely impairment. Dr. Huestis has recommended the U.S.-based cut-off levels and discounted cut-off levels used in Europe, Australia and by the Toronto Transit Commission, without any acknowledgement of the fact that the cut-off levels she recommends provide detection windows that exceed periods of impairment for cannabis.

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[18] Huestis Report, p. 32.

[19] DDC Report, p. 6.

[20] DCC Report, p. 6.

40. The overly low cut-off levels proposed by the Commission demonstrate a policy choice to deter drug use (including off-duty use of legalized drugs) by employees, not to address impairment while at work. The PWU notes that Dr. Huestis's report is peppered with examples that suggests that she holds a view that employees who engage in off-duty drug use (including cannabis which is legal for recreational use in Canada) should not hold safety-sensitive positions.[21]

41. Whether or not it is acceptable for regulators or employers to engage in deterrence of off-duty use of drugs or alcohol in the United States, a country afflicted with a constitutional right to bear arms and a history of a "war on drugs" culture, it has never been acceptable or lawful for Canadian employers or workplace regulators to invade and control the private lives of workers in that way.

42. As Professor Drummer recommends, the PWU submits that to the extent that any drug testing is appropriate (which the PWU disputes), to reflect the likely windows of impairment, the cut-off for cannabis should be 25ng/mL for screening as recommended by the DDC, or at a minimum 15ng/mL for screening used in Australia, and 5ng/mL for confirmation.

43. As noted in Professor Drummer's report, he also proposes the use of cocaine as a confirmatory analyte, along with benzoylecgonine, at 8ng/mL cut-offs and the removal of benzodiazepines from the list of substances subject to OFT given the inability to detect many members of this class reliably using immunoassay technology at worksites. Professor Drummer also notes a comprehensive testing regime could include other drugs, although the PWU notes that there is no evidence of use or misuse of these drugs in nuclear worksites and thus no reason or justification to expand the list of tested substances.

E. Use of Point-of-Collection Devices

44. The PWU has significant concerns about the inclusion of POCT devices in the RegDoc Version 3, for three reasons:

    a. POCT devices are not sufficiently reliable;

[21] See p. 32 of Dr. Huestis' opinion: "you do not want chronic frequent cannabis users in your safety-sensitive positions" without explanation, and p. 36: "I do not think it is appropriate for the CNSC to have individuals' using cocaine in their safety-sensitive positions" after stating that she recommends a lower cut-off, and noting that cocaine yields increased oral fluid concentrations and windows of drug detection. The PWU submits that Dr. Huestis' comments imply that she holds a moral view about the use of cannabis and cocaine generally, including off-duty use, which is not relevant to the assessment of a drug testing regime in Canada or appropriate cut-off levels.

b. The permissible use(s) of POCT devices is not well-articulated in the RegDoc; and

c. The RegDoc does not require trained individuals to administer POCT devices nor require licensees to adopt their use in a manner that protects the privacy and dignity of workers.

45. Dr. Huestis does not recommend POCT over laboratory testing in her report. She noted that successful development of a POCT device that performs acceptably for all drug classes "is a challenge".[22] She also stated that "perhaps the greatest current limitation for oral fluid testing is the small number of controlled drug administration studies available to inform interpretation of oral fluid tests."[23] The Commission has not explained why it has elected to include POCT devices in the RegDoc Version 3, given Dr. Huestis' view that laboratory testing is superior to POCT.

46. In terms of the reliability of POCT devices, the PWU submits that the reliability of POCT devices have not been sufficiently studied to justify their use. Professor Drummer noted that one study found that the ability of the Draeger POCT device to detect a true negative (specificity) for THC was just under 50%.[24] Given Dr. Huestis' recommendation, the limited study of POCT devices, and the mediocre results in terms of reliability, the Commission should not permit their use.

47. The PWU submits that the Commission has not adequately considered how licensees would use POCT devices. The RegDoc Version 3, section 6.2.3 states that "Licensees may choose to utilize point of collection testing (POCT) as a screening tool or to assess the risk of having a worker return to safety-sensitive or safety-critical duties, pending the medical review officer's report on the urine- or oral-fluid-based laboratory test." It also states that POCT devices shall not be used in pre-placement or follow-up testing circumstances.

48. Section 6.2.3 does not clearly explain the scope of the use of POCT devices. The circumstances in which POCT devices may be used as a "screening tool" are not set out, nor is the term "screening tool" defined. In addition, the RegDoc does not clarify the circumstances in which a worker returning to duties may be subject to POCT, if such devices cannot be used in follow-up testing. To the extent that the RegDoc is intended to permit licensees to use POCT as a screening tool for testing only of workers with diagnosed substance use disorders and who have negotiated a random testing regime as part of their return to work, the RegDoc should be clarified to express this limited use.

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[22] Huestis Report, p. 50.

[23] *Ibid.*

[24] Drummer Report, p. 14.

49. The oral fluid screening cut-off levels set out in Table B5 relate to cut-off values to be used for immunoassay screening and do not reference the use of POCT devices. To the extent that the Commission intended to permit licensees to adopt POCT collection in addition or in lieu of laboratory screening for reasonable cause testing, post-incident testing, and/or random testing, the PWU opposes this use.

50. The results of reasonable cause, post-incident, and random testing can have significant consequences for a worker. As set above and in past submissions, the Commission's alcohol and drug testing regime, as a whole, does not comply with constitutional, human rights or privacy protections of employees nor represent an appropriate balancing of interests. As the Commission is determined to impose an unlawful testing regime, the Commission should, at a minimum, clarify that licensees' protocols for the use of POCT devices must include the administration of testing using POCT devices:

    a. will be conducted only by trained individuals; and

    b. will be conducted in a manner that safeguards the privacy and dignity of workers.

PART III. CONCLUSION

51. Nuclear generating facilities have been operated safely in Ontario for over 40 years without the mandating by any regulator of a specific means of ensuring that employees at these facilities are fit for duty, let alone the mandating of a drug or alcohol testing regime.

52. The PWU maintains its position that the Commission's drug testing regime is unnecessary and unlawful. The Commission's drug testing regime does not meet its stated objective of detecting and avoiding workplace impairment. The proposed OFT testing is based on a report that does not provide a clear connection between testing and length of impairment, and does not give due regard to relevant cut-off levels in other non-U.S. jurisdictions. OFT does not provide accurate evidence of impairment. The cut-off levels selected will capture past drug use, not current impairment, and are therefore not justifiable or appropriate. If the Commission elects to include OFT, it should increase the cut-off levels to reflect only detection windows that correlate with periods of likely impairment. The PWU further submits that the Commission has not carefully considered the use of POCT devices, and that the use of such devices should, at a minimum, be undertaken by trained individuals in a privacy-protective manner.

53. The PWU thanks the Commission for the opportunity to make submissions.

ALL OF WHICH IS RESPECTFULLY SUBMITTED,

POWER WORKERS' UNION

May 30, 2020

EXPERT REPORT RELATING TO DRUG TESTING IN ORAL FLUID

This expert report has been commissioned for the Power Workers' Union and Society of United Professionals on the Canadian Nuclear Security Commission RegDoc 2.2.4 Vol II.

prepared by

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AUSTRALIA

May 21, 2020

Table of Contents

Executive Summary

Oral fluid, together with urine are useful biological fluids that can be used to detect for the presence of drugs of abuse. However, oral fluid is not strictly interchangeable with urine for drug testing, with each fluid having advantages and disadvantages.

Key advantages of oral fluid over urine for the detection of drugs include: a) the collection process is less intrusive than the collection of urine and can occur relatively quickly without the need for toilet facilities; b) oral fluid is less likely to be subject to adulteration or substitution; c) the drugs present in oral fluid are the parent drugs that may be causing impairment, whereas urine mostly consists of drug metabolites that are usually inactive; and d) the presence of drugs in oral fluid can more closely represent the period that a drug is causing a pharmacological effect. However, due to the difficulty in collecting a known amount of oral fluid, an exact concentration of drug cannot usually be determined.

While, both oral fluid and urine can give positive results to the use of drugs, the production of these fluids is subject to very different biological processes and the target analytes are also mostly different leading to different detection windows for drugs. These detection windows are therefore also dependent on the selection of appropriate cut-off reporting limits.

There are no internationally approved cut-off reporting limits established for the detection of drugs of abuse in oral fluid, although a number of organizations and jurisdictions have defined cut-offs relevant to their activities. However, cut-off limits for cocaine, opiates and amphetamines in REGDOC-2.2.4 are not too dissimilar to those used in other jurisdictions, but for other drugs there are significant variations from one jurisdiction to another.

Importantly, the choice of cut-off can determine whether the likely detection window is either sufficiently long to approximately mirror that usually obtained for urine, or more closely represents a period when a worker is likely to be impaired. This is especially relevant for cannabis. The current choice of a 2 ng/mL confirmation cut-off for THC in REGDOC-2.2.4 would enable detection for about 24 hours even though acute impairment may only be detectable using standardized field assessment protocols for a few hours. The use of a higher cut-off, such as 15 ng/mL for screening and 5 ng/mL for confirmation will reduce the detection window to a period that is more likely to represent a period for detectable acute impairment. In contrast, the cut-offs suggested in REGDOC-2.2.4 for benzodiazepines are speculative and are more likely to just detect use of some of these drugs in this class for a short period and for a lesser time than their impairment from misuse of the drug. A number of other recommendations have been made in relation to cut-off limits that are designed to improve the ability to use oral fluid for drug detection, should oral fluid drug testing be used in this workplace.

The two recommended oral fluid collection and detection devices for on-site testing (SoToxaTM with Abbott SotoxaTM Test Cartridge and the Draeger DDT5000) have been available for some years and show reasonable performance for amphetamines, some opiates and cocaine, but as with all such devices, will be less able to detect cannabis and benzodiazepines. However, some of the current published cut-offs for these devices do not align with those proposed in REGDOC-2.2.4.

Importantly, neither the presence of a drug in oral fluid nor in urine can be used to determine whether impairment is present or not. Impairment, however defined, can only be assessed through some form of standardized field assessment protocol relevant to a worker's occupation by suitably trained personnel.

Recommendations

These recommendations are designed to improve the ability to use oral fluid for drug detection, should oral fluid drug testing be used in the workplace.

Recommendation 1: Since cannabis has a legal use in Canada and can be prescribed for defined medical uses consideration should be given to increase the screening and confirmation cut-off limits in oral fluid to avoid detecting THC for past use when acute impairment will no longer be evident.

Recommendation 2: Include cocaine as a confirmatory analyte, together with benzoylecgonine; with both cut-offs at 8 ng/mL.

Recommendation 3: Depending on their use in Canada considerations should be given to include MDMA, MDA and at least MDEA as confirmatory drugs; with cut-offs at the same concentration as methamphetamine and amphetamine.

Recommendation 4: If methadone is to be included as a target drug then it is advisable to include methadone as an analyte: at a confirmatory cut-off of 20 ng/mL.

Recommendation 5: Consideration should be given to include fentanyl and other designer fentanyls to detect abuse of this class of opioids.

Recommendation 6: It is not advised to include benzodiazepines for routine on-site drug screening in oral fluid given the inability to detect many members of this class reliably using immunoassay technology at worksites.

1. Introduction

The use of oral fluid to detect the presence of drugs, particularly drugs of abuse, has evolved substantially over the last 15 years, together with urine and to a lesser degree hair. This expert report provides an overview of the collection and testing processes that can occur at a worksite, and critiques how well this specimen compares with urine, and, in particular, whether oral fluid drug concentrations can be used to determine the ability of an employee to work safely.

Saliva, or oral fluid, as it is more commonly known is excreted primarily by the parotid, submaxillary and sublingual glands and also by other smaller glands such as buccal, labial, and palatal glands. The fluids secreted by these glands differ considerably from each other and their composition is affected by time of day, food, age, gender, state of health, and by drugs. Saliva is made of the usual electrolytes as well as mucus and amylase and has a protein content of less than 5 % of that of plasma.

Drugs enter the oral fluid by a partitioning process from blood that circulates within these glands and the mouth, with the amount of drug present in the oral fluid dependent on the physiochemical properties of the drug (pKa[1]), pH of the fluids and degree of protein binding. For drugs that are smoked, or where there is contact time of the drug in the mouth, there will be local absorption into the internal tissues surrounding the oral cavity. This route of absorption is particularly significant for smoked cannabis, but also other drugs that are smoked, such as methamphetamine and cocaine.

2. The Collection Process and Issues Associated with the Collection

The collection process for oral fluid is an important element and, depending on the technique used, can affect the drug concentration. Spitting (expectoration) provides neat oral fluid, but this gives a relatively viscous fluid and its collection can involve some potential occupational health and safety issues. Because spit may also be contaminated with food and other debris from the mouth, it may not provide a fluid of uniform composition.

The volumes of oral fluid collected are generally small, often 1-mL or less; however, this is usually diluted with a proprietary diluent (2 to 3 volumes of a buffer solution) as part of the collection process.

Typically, an absorbent pad/foam is used to collect the oral fluid, and this is squeezed or mixed into a diluent to extract the oral fluid and provide a relatively non-viscous fluid appropriate for analyses. In persons with normal amounts of oral fluid the collection time is typically 1 to 3 minutes. Most devices now have a color indicator to show if sufficient oral fluid has been collected, however this will only provide an approximate guide as to how much fluid was collected. This also means that the precise volume of oral fluid collected is not known (unless it is weighed); hence, measuring concentrations accurately is not usually possible. The use of an absorbent collector that contains agents to promote salivation, e.g. citric acid, can alter the pH pf oral fluids affecting the amount of drug present in these fluids.

Some subjects will not be able to provide sufficient oral fluid on demand either due to their physiology operating at that point in time (anxiety, or some disease that may be present), or because drugs consumed by them have reduced oral fluid secretions. A number of prescribed drugs can reduce secretions but also amphetamines and cannabis will do the same and will

[1] See glossary of terms and abbreviations at end of document

either require a longer collection time or require the collector to use an alternative fluid, such as blood or urine.

Contamination of the oral cavity by recently ingested food (or even drug) will temporarily, affect the concentration of drug in these secretions. Cannabis is the best example: its presence in oral fluid is mostly a result of oral contamination. Rinsing the mouth before a collection (to avoid a positive test) will temporarily reduce a drug concentration in collected oral fluid; however, the concentration should be restored in about 10-15 minutes.

Users of smoked cannabis will show high oral fluid concentrations for at least a few hours after last use, even if relatively small amounts are actually absorbed in the body, however this is usually when the most of the pharmacological effects of cannabis occur and measurable impairment is likely.

3. The Testing Process

Each of the available collection devices have advantages and disadvantages, but the speed of collection and ease of use largely determine their acceptability. Some collectors have been shown (at least in the past) to absorb drug irreversibly; that is, the drug does not leech out into a buffer post-collection to allow drugs to be analyzed. Because concentrations of drugs are generally low in oral fluid, poor recoveries or instability limit the detectability of drug. It is therefore essential that collection devices also be tested for drug recovery and drug stability before they are used[2].

Once a specimen of oral fluid is obtained and diluted with the buffer it can be either analyzed at the point of collection (POCT) using a screening device, or sent to a certified laboratory for testing. When a screening test is performed on-site the screening device will provide a preliminary indication of whether the specimen is positive to the targeted drugs, or not. If a preliminary positive result is found then the oral fluid collection is sent to a certified laboratory for a confirmatory analysis. Only when a drug is confirmed by a mass spectrometric method above the reporting cut-off is the specimen called a positive. Alternatively, the original collection can be sent direct to a certified laboratory which will conduct its own screening test, and, if necessary, conduct confirmatory analyses[3].

This process is fundamentally similar to a urine test. Collected urine can be tested with a screening device on-site (POCT), and if positive sent to certified laboratory for confirmatory analyses if the test result is a presumptive positive, or the urine is sent to a laboratory for the screening test, and, if necessary, conduct confirmatory analyses.

The main difference between the two types of specimens, is that urine contains predominately metabolites, and these metabolites usually will be present in the urine for a longer period of time than oral fluid, and the concentrations of these metabolites will be often much higher than the parent drugs in oral fluid. However, the detection window will depend not only on the drug, the dose(s) used and individual characteristics, but also the cut-offs that are applied to the analyses, particularly the screening cut-off (this will be discussed later).

While both specimens can be used to determine if a person (worker) is using non-prescribed drugs there are a number of other important differences that exist between use of oral fluid and urine. One of main advantages in the use of oral fluid is that it is relatively non-invasive. Oral fluid requires a mouth swab with almost no ability for the worker to adulterate the specimen. In contrast, urine collections require strict and much more complex collection

[2] This aspect is usually evaluated by regulatory agencies before a device is approved for use.
3 The Australian and New Zealand Standard AS/NZS 4760:2019 provides guidance on the collection of oral fluid for drugs of abuse testing, on-site screening and laboratory confirmation.

protocols to prevent adulteration or substitution and the need to provide appropriate toileting facilities.

For oral fluid collections it is important that food has not been recently consumed, as any food debris in the mouth will affect the collection process. Usually 10 min after the last meal should be a sufficient delay.

Screening tests[4] use immunoassay technology in which tagged antigens compete with antibodies raised to recognize a drug or drug class. These will usually only give a positive or negative reading to a particular drug or drug class at or above the screening cut-off. Any positive readings are presumptive and require confirmation. The ability and reliability to detect a drug above the cut-off will depend on the device used, the specimen collected and substances present in the specimen that will immunoreact with the test kit. Mostly it is the presence of the drug that triggers a response, but sometimes specimen quality, or the presence of other substances including drug metabolites will also influence the response. Hence, there will always be some cases that falsely trigger a positive response (false positives) and some cases that may be positive (above the confirmatory cut-off for the target analyte) but did not trigger a response (false negatives). Companies producing these devices and testing kits will try to minimize the incidence of false negatives and false positives, but unless a formal confirmation test is conducted a result cannot be called. In principle, this is no different to use of test kits for POCT urine testing, except of course different test kits are used.

Devices and test kits that have gone through a formal evaluation process will have performance criteria assessed and will need to meet detectability requirements at the established cut-offs, amongst other criteria. If cut-offs are different to that designed by the manufacturer it may be possible for the manufacturer to develop batches suitable for the regulatory agency, providing it is technically feasible[5].

Since drugs are usually present in lower concentrations than for urine, immunoassay test kits have not been as reliable, particularly for those drugs that are present at lower concentrations. THC[6] and the benzodiazepines are noteworthy examples of drugs that are technically more difficult to detect in oral fluid, compared to urine.

4. The Cut-off Reporting Limits

The term cut-off, when it applies to analyses and reporting of such analyses, refers to concentrations below which a screening result is not analyzed further and confirmatory results are reported as negative. The use of cut-offs helps to regulate the collection, testing and reporting of positive results and ensure consistency for drug testing protocols at workplaces and in the laboratories. These cut-offs also act to limit, as far as practicable, interpretation of results that could arise from other sources of drug, such as contamination (of the worker) by a drug, or from other sources, and also to provide guidance to laboratories and device manufacturers as to what concentrations of a particular drug are required to be detected.

While cut-off limits are used in both oral fluid and urine testing there is no overall international consensus cut-off concentration for all relevant drugs. Professor Huestis in her report documented the seven different cut-off limits as they apply to various organizations. The drug with the most variability is cannabis. The screening cut-off established by the

[4] Also termed first test or presumptive test.
[5] This has occurred for Australia that have different cut-offs for some drugs.
[6] An abbreviation for Δ9-tetrahydrocannabinol, the most active substance in cannabis and the usual analyte detected in oral fluid.

European Workplace Drug Testing Society (EWDTS), the Toronto Transit Commission (TTC) and the Australian and New Zealand Standard for drug testing in oral fluid (AS/NZS 4760:2019) are 10, 10 and 15 ng/mL, respectively, while four other organizations, including a proposal by SAMHSA[7], recommend 4 ng/mL. Confirmation cut-offs are also different and range from 2 to 10 ng/mL.

Cocaine cut-offs are also not harmonized and differ significantly. Screening cut-offs range from 15 to 50 ng/mL, while confirmatory cut-offs range from 8 to 50 ng/mL.

There are also differences for the other drugs and also what drug or drug group is listed in oral fluid drug testing.

Similarly, cut-offs in urine also differ from one regulatory body/organization to another with the most significant difference being detection of opiates. The screening and confirmatory cut-offs for opiates (essentially morphine and codeine in urine) for the CNCS (REGDOC-2.2.4) and SAMHSA is 2000 ng/mL, whereas most other bodies around the world use a much lower cut-off at 300 ng/mL.

These differences highlight the variability around the world for what is essentially the same type of testing to identify and hopefully also deter drug use by workers in safety critical workplaces. It also illustrates that there may not be one "optimum" cut-off.

When an immunoassay is used for screening, either as POCT at the workplace or in a certified laboratory, much higher concentrations can be realistically detected than what is possible in a laboratory using a mass spectrometric method. For example, it is very easy to detect concentrations of THC, methamphetamine (and other amphetamines), cocaine, opiates, opioids and even benzodiazepines well below those detectable using immunoassay testing kits. This would require sending the collected oral fluid to a certified laboratory for testing and forego POCT. While this is not necessarily recommended by me, it does illustrate that depending on the methodology specimens can give widely different results.

Screening cut-offs are often higher than confirmatory cut-offs, particularly for cannabis. The reason for this is that immunoassay screening technology will invariably also detect related substances, namely metabolites, which will assist in giving a positive reading. When a confirmation test is performed then specific analytes are targeted requiring lower cut-offs such that false positive immunoassay screening results are minimized.

5. The Detection Windows

This will vary from one drug to another, and of course on the dose(s) used and route of administration, amongst other factors involved in the physiology involved in the production of these fluids, the ability of drugs to enter these fluids and the collection process.

A feature advocated by many unions in Australia, is the use of cut-offs to shorten the detection window for oral fluid than when urine is used, and therefore it would be less likely for a worker to test positive when they had used the drug well before a shift (e.g. a day or three before) and when they are no longer unable to work safely (i.e. not impaired)[8]. This contrasts with urine testing that is largely conducted to detect use in the past 1-3 days[9].

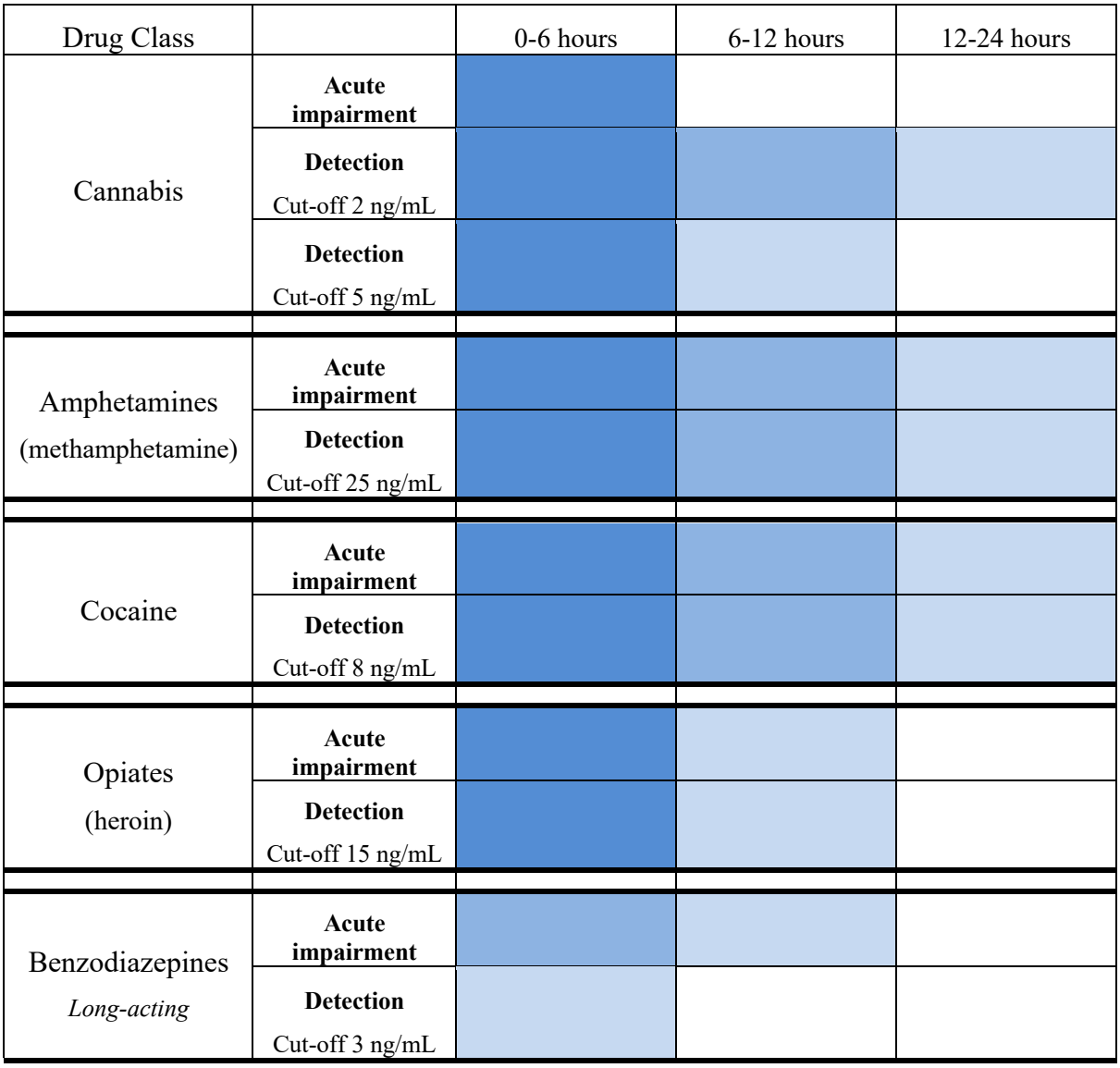
[7] US Substance Abuse Mental Health Services (SAMSHA).

8 This argument has been subject to a number of Australian Industrial Relations Commission hearings (now the Fair Work Commission) over the last several years.

9 This detection window is dependent on at least dose(s) and urinary excretion, but this window of up to three days applies for most illicit drugs and can even be a few weeks for heavy cannabis users.

Approximate windows for likely acute impairment and analytical detection windows for the main classes of drugs are shown below using confirmation cut-offs as listed in REGDOC-2.2.4 (**Figure 1**). The heavier shading illustrates the likelihood of being impaired and having a positive result for an oral fluid collection. The time periods are chosen to simplify the visualization and will vary from person to person, and with dose.

Figure 1. *Diagram illustrating approximate likely periods of acute impairment and detection windows using listed analytical cut-off limits from common recreational doses for the main classes of drug.*



Note: These are very approximate windows and are only meant to illustrate the difference in possible detection times for the main drug groups and likely impairment following a common recreational dose of drug. The actual windows will vary from person to person and will also depend on dose(s) and a variety of other factors outlined in this document.

For example, the acute impairment for a common smoked dose of cannabis is up to about 4-6 hours, but using a low confirmation cut-off of 2 ng/mL (as listed in REGDOC-2.2.4) this may give a detection window of up to about 24 hours, much longer than the period when acute impairment can be determined using standard assessments of sobriety. If a higher cut-off is

chosen, such as 5 ng/mL, the detection window more closely represents the likely impairment window. The lighter shadings represent a decreasingly lower likelihood of detection.

For both the amphetamine class (largely methamphetamine) and cocaine the impairment period and detection windows are similar, whereas for the benzodiazepines, such as alprazolam and diazepam, the reverse situation that could occur for cannabis is likely. These drugs have much lower concentrations in oral fluid and will be difficult to detect for any significant period, however likely impairment from significant[10] doses will last for much longer that what could be detected analytically.

Clearly these windows will also be different for different members of each of the drug classes, i.e. different amphetamines, opioids and benzodiazepines. For example, the hypnotics, such as oxazepam, temazepam and zolpidem that have a shorter half-life will have shorter duration of action and a correspondingly shorter detection period.

See section 11 for more details of individual drugs in "Drug Case Studies".

6. Commentary on the Proposed Cut-offs

The cut-offs listed for the targeted drugs in oral fluid as listed in REGDOC-2.2.4 Appendices B.5 (screening) and B.6 (confirmation) mostly reflect those proposed by SAMSHA although there a number of differences and disparities. Notably the proposed cut-offs in REGDOC-2.2.4 represent low cut-offs, presumably in an attempt to prolong the detection time in oral fluid and hopefully have similar detection windows to urine.

Establishing reporting thresholds such as cut-offs to enable optimum detectability of drug use will never be perfect. In some jurisdictions, such as Australia and New Zealand higher cut-offs in oral fluid were deliberately chosen to limit detectability of drugs to hours rather than days that usually applies to urine testing. The reason for this is to limit detectability to times when impairment may be present, rather than detect past use when measurable impairment is not likely.

For cannabis the proposed screening cut-off is 5 ng/mL and the confirmation cut-off is 2 ng/mL. The screening cut-off for SAMHSA is proposed at 4 ng/mL. The respective screening and confirmatory cut-offs for cannabis/THC in the AS/NZ 4760:2019 are 15 and 5 ng/mL, respectively. The higher cut-offs in AS/NZ 4760:2019 will reduce the detection window for cannabis use and will reduce the risk of a user having a positive test when use of cannabis occurred several hours earlier.

Recommendation 1: Since cannabis has a legal use in Canada and can be prescribed for defined medical uses consideration should be given to increase the screening and confirmation cut-off limits in oral fluid to avoid detecting THC for past use when acute impairment will no longer be evident.

For cocaine a slightly higher screening cut-off is proposed (20 ng/mL) compared to SAMHSA (15 ng/mL), however the confirmation cut-off is 8 ng/mL for benzoylecgonine. However, cocaine is not listed as a confirmatory analyte. Cocaine should be included if oral testing were to proceed, since this is the major analyte in this specimen following use of cocaine.

[10] Significant in this context means doses that are usually well above those normally prescribed. Low or common therapeutic doses are unlikely to cause observable impairment unless in combination with other impairing drugs.

Recommendation 2: Include cocaine as a confirmatory analyte, together with benzoylecgonine; with both cut-offs at 8 ng/mL.

The cut-off for amphetamines (screening and confirmation) is not controversial and there is good concordance with other published cut-off limits, however MDMA (Ecstasy) is not included, nor are other important amphetamines, such as MDEA and MDA[11]. MDMA is a commonly used drug, particularly in nightclubs, parties and other gatherings and is included in most (if not all) of the methamphetamine/amphetamine screening test kits and is easy to confirm using standard mass spectrometric methods.

Recommendation 3: Include MDMA, MDA and at least MDEA as confirmatory drugs; with cut-offs at the same concentration as methamphetamine and amphetamine.

The opiates are a more complex class of drugs. Opiates normally only refers only to morphine and codeine. Heroin is metabolized rapidly to 6-acetylmorphine (6AM)[12] and then to morphine. Codeine is also partly metabolized to morphine, and is usually present in smaller amounts to codeine in urine except in the tail end of excretion when it may have a higher concentration than codeine, although the concentrations are usually below 2000 ng/mL (hence the reason for the higher urine cut-off in the SAMHSA guidelines). The proposed cut-offs in REGDOC-2.2.4 are the same as that proposed by SAMSHA (screening at 30 ng/mL, and confirmation for morphine and codeine at 15 ng/mL). These are somewhat lower than the AS/NZS 4760:2019 standard (50/25) but this may not make too much difference in the detectability of these drugs. The usual target analyte for heroin is 6-AM, and again the proposed cut-off limits are the same as those proposed by SAMSHA but significantly lower than that in AS/NZS 4760:2019 (10 ng/mL). REGDOC-2.2.4 also includes hydromorphone, hydrocodone, oxymorphone and oxycodone[13] at the same screening and confirmation cut-offs as for morphine/codeine. It is not controversial that these cut-off limits are same.

Methadone, a commonly prescribed opioid for pain relief and to treat heroin addiction will not be detected by the "opiate" class detection using immunoassays and is in part metabolized to EDDP. It is most often seen in persons prescribed this drug, rather than a recreational drug, but this will depend on local drug using habits and illicit availability. The proposed screening and confirmation cut-off limits for this drug refer only to this metabolite, when it should also include (or only include) methadone. Methadone is the main analyte in the oral fluid of persons using methadone. The reasons for the cut-off limits in REGDOC-2.2.4 is not clear since it differs from EWDTS which has a screening and confirmation cut-offs of 50 and 20 ng/mL, respectively. AS/NZS 4760:2019 does not include methadone since it is not regarded as a significant drug of abuse in these jurisdictions.

Recommendation 4: If methadone is to be included as a target drug then it is advisable to include methadone as an analyte: at a confirmatory cut-off of 20 ng/mL.

[11] These amphetamines are commonly included in drugs of abuse drug testing regimens, although it is not clear to this author their use in Canada. MDMA (often know as Ecstasy) is 3,4-methylenedioxymethamphetamine, MDEA is 3,4-methylenedioxyethylamphetamine, and MDA is 3,4-methylenedioxyamphetamine (which is also a metabolite of both of these potent impairing amphetamines).

[12] Also known as 6-monoacetylmorphine or 6-MAM.

[13] Oxycodone is metabolized in part to oxymorphone, and hydrocodone is metabolized in part to oxymorphone.

Another opioid of significance that is not included is fentanyl. This has been subject to abuse in recent times including a number of designer fentanyls [1, 2], many of which have caused sudden death.

Recommendation 5: Consideration should be given to include fentanyl and designer fentanyls to detect abuse of this class of opioids.

The benzodiazepines are included as a class screening test in REGDOC-2.2.4 at a cut-off of 10 ng/mL and confirmation at 3 ng/mL. However, it does not list individual benzodiazepines. Given that there are several benzodiazepines used legally in Canada and have significantly different potencies (and expected concentrations) it is probable that by including these as they stand will miss many users of this class of drugs. Of course, this is a class of drugs that are legally available by prescription in Canada, although they can be misused and abused; but when they are used recreationally, they are often in conjunction with other (illicit) drugs. Due to their physiochemical properties the concentration of benzodiazepines in oral fluid are very low and much lower than their concentrations in blood and appear to be about 1/20th of the concentration in serum. There are very few controlled administration studies for these drugs to provide any guidance over a useful cut-off limit, let alone the time frame of detection for any one of these benzodiazepines. For further information see section 11 on benzodiazepines.

Recommendation 6: It is not advised to include benzodiazepines for routine on-site drug screening in oral fluid given the inability to detect many members of this class reliably using immunoassay technology at worksites.

7. Comparisons between Oral fluid and Other Biological Fluid Concentrations

The appearance and disappearance of drugs (and drug metabolites) in tissues clearly varies with time and is mostly dependent on the pharmacokinetic properties of the drug but also which specimen is being tested. Drugs will appear rapidly in oral fluid even if local deposition in the tissues of the oral cavity has not occurred with drug-containing smoke/vapors. The time course of drugs in oral fluid generally parallels that of blood, although the concentrations in oral fluid can be quite different to those in blood.

It is not possible to determine with any useful accuracy a blood concentration from an oral fluid concentration of a drug. Even without local deposition of drugs in the oral cavity there are other factors that influence the respective concentrations in these fluids.

One important factor for drugs of abuse is that repeated use causes the body to adapt to the drug, which invariably lessens the drug effects and will require higher doses to be used to achieve the same desired effect than what was achieved when first used. This is called tolerance, or neuroadaptation. Tolerance to the effects of the drugs and various individual pharmacokinetic differences are major factors that reduce any correlation between dose, blood concentration and effect.

As a general rule, blood concentrations of drugs of abuse only show a poor correlation with the pharmacological effects of the drug, including one or more signs of impairment that can be measured using a standardized field (sobriety) assessment test.

Urine is a collection of waste products in excreted water. Ingested drugs are usually predominately metabolized to (mostly) inactive products, whereas oral fluid contains mostly the parent (ingested/inhaled) drug. The concentration of these metabolites in urine also will

depend on the degree of hydration, kidney function and frequency of voiding. The net effect of this is that concentrations in urine will bear no relation to those in blood.

8. Can Impairment be Determined from Oral Fluid Concentrations?

The simple answer is no; there is no effective relationship between an oral fluid concentration and impairment.

The same answer applies to urine; there is no relationship between a urine concentration and impairment.

In the REGDOC-2.2.4 a requirement for the employer is to "prohibit reporting to work or remaining at work under the influence of alcohol, cannabis, cannabis-derived products, or illicit drugs". Each occupation requires a different set of skills and training. The workplace would need to establish what features in a worker establishes that s/he is under the influence of a substance.

Impairment to a drug is a difficult behavior to determine. In the acute phase of active drug use; usually in the hours after use, impairment and behavioral differences can be quite obvious even to an untrained eye. This may be a situation involving consumption of too much alcohol or shortly after a binge session with methamphetamine, cocaine or cannabis. It is much more difficult to establish impairment from the recreational use of drugs beyond this acute phase even when drug concentrations are easily measurable in blood, oral fluid or urine.

Apparent impairment, or behavior that might be different to normal, can also be caused by illness. Therefore, it is vital that a proper assessment of being fit-for-work includes an assessment of any current illness. It is also important that the features, behaviors, skills required to be assessed as fit-for-duty in an occupation need to be clearly outlined. Workplaces will usually require an ability to make rational informed decisions (cognitive performance) and have adequate limb-eye coordination skills (psychomotor skills). Impairment or lack if impairment can only be assessed through a structured program conducted by a suitably trained person. The best parallel to compare against is in road safety and the use of standardized field sobriety tests (SFST) by Drug Recognition Experts (DRE); a program that is used in both Canada and the USA.

It is possible that a person, even after having passed a SFST a person could still have measurable concentrations of drugs in their oral fluid (and possibly also blood/urine). Conversely, while less likely, a person can fail a SFST and not have a measurable drug in their submitted specimen.

9. Assessment of Oral Fluid Detection Devices

There are a number of studies published that show the performance of the two devices approved for use in Canada.

The SoToxaTM, an Abbott SotoxaTM Test Cartridge appears to be essentially the same as the Alere DDS2 device before Alere was taken over by the Abbott group. There is no recent performance data to support this that I have been able to obtain in the public domain, however the Alere DDS2 device has been available for some years and has been widely used in workplace drug testing. Cut-offs for THC, amphetamines and cocaine are 25, 50 and 30 ng/mL, respectively. The cut-off for opiates (morphine) is 40 ng/mL, while for benzodiazepines using temazepam as calibrator is 20 ng/mL. Notably, the cut-off for cannabinoids is much higher than that proposed in REGDOC-2.2.4.

A pilot study using the Alere DDS2 with Quantisal collector occurred in Wisconsin in which 104 drivers suspected of being under the influence of alcohol or drugs gave 29 positive readings of which 28 were confirmed by a blood confirmation (almost all were THC) [3]. Another study using this screening device tested 50 drivers in California [4]. Valid results were obtained in 76% of cases; however, there were only six positive results: five for THC and one for methamphetamine.

The Draeger DDT5000 has also been available for some years and also has been widely used. Cut-offs for THC, methamphetamine and cocaine are 5, 35 and 20 ng/mL, respectively. The cut-off for opiates (morphine) is 20 ng/mL, while for benzodiazepines using diazepam as calibrator is 15 ng/mL. Several publications have provided data on its performance. The device was used on oral fluid collected from drivers suspected of being under the influence of drugs in both German [5] and USA [6] studies. Positive oral fluid specimens were confirmed through a blood specimen. The sensitivity for THC, opiates, methamphetamine were 80% or better, while for cocaine it was 76%. However, the ability to detect a true negative (specificity) for THC was just under 50%. The device has also been used successfully to assess its ability to detect cocaine and THC in volunteers that have taken the drug [7, 8].

The two devices have been compared with each other in a study involving consumption of oral cannabis (as a brownie). Both devices performed similarly and were able to detect THC in oral fluid for at least a few hours post consumption [9]. They both use lateral flow immunoassays as the basis for technology and have an electronic read-out for presumptive drug results from the collected oral fluid.

It is possible that both devices have already, or may be able to adjust their cut-offs as technology improves and/or demand for altered cut-offs occur. If cut-offs cannot be altered, then the actual detectability of drugs for these devices will not align with the proposed cut-offs in REGDOC-2.2.4.

10. Drug Case Studies

Cannabis:

Cannabis is the most used of the common drugs of abuse. It is usually smoked (joints, spliffs, bongs) but can be consumed orally by the consumption of baked cookies. This is no doubt cannabis can impair a range of cognitive functions and psychomotor skills during the acute stage of intoxication, although the extent of any deficits depends very much on the quantity taken and any developed tolerance that has developed with repeated use. Substantial and repeated use can lead to anxiety disturbances, marked agitation and even psychoses. These can last for several hours, together with impairment of memory and attention, however occasional low dose use, that might occur in some recreational settings may not show any substantial deficits [10].

Neurocognitive performance was assessed in volunteers during acute THC intoxication in occasional and heavy users. The researchers showed that THC significantly impaired performance of occasional cannabis users on critical tracking, divided attention and the stop signal task for a few hours [11]. Similar findings have been seen in another study suggesting some tolerance develops to psychomotor impairment in frequent users [12]. However, there is no simple relationship between a blood concentration of THC and impairment: indeed, a measure of the persistence of adverse effects of the drug does not necessarily correlate with blood concentration of THC and will often persist during the decline in blood concentrations [13]. However, the measurable effects of low to modest doses of acute cannabis use seem to persist for about 4-6 hours [14].

As discussed earlier it is present in oral fluid; often in high concentrations largely due to local deposition from smoking. The average oral fluid to blood concentration ratio varies considerably depending on time since last use, but can easily exceed 10 fold.

Cocaine

Cocaine is a strong stimulant and is most commonly consumed by nasal insufflation (snorting), but can also be used by other routes. It is rapidly metabolized to the inactive benzoylecgonine (BE or BZE; main target analyte in urine) and to ecgonine methyl ester (EME).

Low dose cocaine use leads to a sense of euphoria and an increased awareness and energy but will also be associated with increased anxiety and nervousness. The effects will usually wear off after a few hours, however binge use can lead to profound negative behavioural changes. Long term use can lead to permanent cognitive deficits (learning, memory, reaction time and cognitive flexibility) although this has recently been disputed as lacking sufficient evidence [15, 16]. Tolerance and dependence will occur with repeated use.

The oral fluid concentration ratio for amphetamines to blood are high, due to their basic properties, and can exceed 10-fold. Local deposition from smoking will give higher oral fluid concentrations for a period of time.

Methamphetamine

This strong stimulant is also widely used and can be readily manufactured in clandestine laboratories. It can be smoked (as Ice), injected, taken orally or even snorted. Amphetamine is a minor metabolite of methamphetamine: approximately 10% of the dose is found in urine.

Similarly to cocaine, use leads to a sense of euphoria and an increased awareness and energy but will also be associated with increased anxiety and nervousness. Long term use will lead to negative behavioural changes and psychotic tendencies such as paranoid behaviours [17]. As for cocaine, tolerance and dependence will occur with repeated use.

As for cocaine, oral fluid concentration ratios to blood are high, and can exceed 10-fold. Local deposition from smoking will give higher oral fluid concentrations for a period of time.

Opiates and Opioids

This large class of drugs comprise both the opiates morphine and codeine as well as those chemically derived from morphine, such as the widely abused oxycodone and hydrocodone, as well as the synthetic narcotic analgesic drugs with properties similar to morphine, namely methadone, fentanyl etc. Heroin is chemically derived from morphine by acetylation which when absorbed into humans is rapidly converted (hydrolyzed) to the metabolite 6-acetylmorphine and is then further metabolized back to morphine.

A number of designer fentanyl drugs exist, that are often classified as novel psychoactive drugs (NPS), but only some of which are detected by fentanyl-based immunoassays.

No one immunoassay kit can recognize all members of this class of drug, hence the need to have separate immunoassays for opiates, 6-acetylmorphine and the wider opioid family. This is also further complicated by their widely differing potencies and relevant concentrations

expected in biological fluids. However, laboratory-based mass spectrometric methods can easily identify these opiates/opioids.

Their duration of action as well as their detection windows in oral fluid will depend on the drug, the route of administration. Some are used orally, while others can be injected, and others can be absorbed sub-lingually (under the tongue) and some (e.g. fentanyl) are absorbed through the skin by the use of patches as well as sub-lingually.

Heroin, for example, even when injected, will be detected for a short time in oral fluid, although it is unclear for how long, and of course will be dependent on dose.

Codeine detection in oral fluid has been subject to a controlled administration study which has shown a detection window of about 7 hours using 60 and 120 mg oral doses, although the cut-off was slightly higher (40 ng/mL) than that proposed by the RegDoc [18]. The average oral fluid to blood concentration ratio was about 4.

Oxycodone, when given as 20 mg sustained-release tablets orally to volunteers, has given a detection window of about half-a-day using a 15 ng/mL confirmation cut-off [19]. The average oral fluid to blood concentration ratio was about 5.

Hydrocodone is readily detected in oral fluid following oral administration. A controlled dose of 20 mg to volunteers gave a detection window of about half day using a 15 ng/mL confirmation cut-off. The main metabolite detected was norhydrocodone at about 40% of the concentration of hydrocodone. No hydromorphone was detected in oral fluid [20]. The average oral fluid to blood concentration ratio was about 3. This substance is also a minor metabolite of codeine [21], although oral fluid concentrations are unknown following use of codeine.

Methadone is also readily detected in oral fluid, however there is little EDDP metabolite present with only 10 patients positive to the metabolite of 60 patients receiving methadone treatment. The oral fluid to blood concentration ratio is near unity [22]. Therefore, it is essential that if methadone is included in RegDoc, that the parent drug be measured in oral fluid, not EDDP. EDDP can also be included but since the proportion to that of methadone is low it will not be detected in every person using methadone.

Benzodiazepines

There are some controlled administration studies with benzodiazepines using sensitive techniques that provide some idea of the expected oral fluid concentrations following use of some of these benzodiazepines. Importantly, the oral fluid concentration is only a fraction to that of blood. The data for some of these benzodiazepines are summarized below, however for the most part they have given very low oral fluid concentrations, often near or below the recommended cut-offs in RegDoc, although it is likely that those persons abusing these drugs will have higher concentrations than those detected in most of the published studies.

A recent study in volunteers that were given 5 mg oral diazepam have shown that the average maximum diazepam concentration in oral fluid was under 4 ng/mL which occurred at 1 h post-dose. While the drug was detectable in oral fluid for 2 weeks the concentrations were very low and beyond the ability of immunoassay screening techniques to be detected. The main metabolite, nordiazepam, was detected, but invariably under 1 ng/mL [23]. Similar low concentrations were detected in volunteers given 10 mg [24].

In patients admitted to a ward for detoxification, who prior to admission consumed diazepam, had oral concentrations ranging up to 25 ng/mL (LOD 1.3 ng/mL). Nordiazepam was also detected in this cohort in concentrations up to 45 ng/mL [25]. In other patients that had previously consumed alprazolam had oral concentrations ranging up to 22 ng/mL (LOD 1

ng/mL); while those who had consumed clonazepam and the metabolite, 7-aminoclonazepam, had concentrations ranging up to 35 ng/mL and 10 ng/mL, respectively [25].

A volunteer study involving the commonly used alprazolam (0.5 mg) gave maximum oral fluid concentrations well below the confirmation cut-off of 3 ng/mL (Cmax approximately 1 ng/mL) [24].

A controlled administration of 25 mg oxazepam to ten volunteers only gave mean peak oral fluid concentrations of 2.5 ng/mL which is under the proposed cut-offs [26]. A study involving administration of 15 and 30 mg oxazepam to volunteers gave higher concentrations, with Cmax at 13 and 24 ng/mL, respectively [27].

A single dose of the potent hypnotic flunitrazepam to 4 volunteers gave oral fluid concentrations below 4 ng/mL [28].

A single oral dose of 7.5 mg zopiclone (a related hypnotic) gave peak oral fluid concentrations above 3 ng/mL, but only for a relatively short period [26].

This information indicates the wide range of concentrations seen in oral fluid and the variability from one benzodiazepine to another suggesting that confirmation tests should have individual cut-offs rather than a generic one. It also means that persons using low doses of benzodiazepines, particularly the more potent benzodiazepines, may not produce a positive result in oral fluid, or a result may only be possible for a short period of time post use of these drugs.

11. Materials Provided and Instructions

Materials Provided

- Report on Drug Screening Equipment – Oral Fluid (October 2018) by the Canadian Society of Forensic Sciences Drugs and Driving Committee;
- Report by Professor Marilyn Huestis (March 2020) on Oral Fluid Drug Testing Practices;
- Regulatory Document from Canada's Nuclear Safety Commission (CNSC) on Human Performance Management on Fitness for Duty, Volume II: Managing Alcohol and Drug Use, version 3 - REGDOC-2.2.4 (March 2020).

These documents contain details of:

- Drug Screening Equipment – Oral Fluid Standards and Evaluation Procedures (November 1, 2017); Amendment to Standards and Evaluation Procedures (April 2018);
- Amendment to Standards and Evaluation Procedures (July 2018);
- For the Report on Drug Per Se Limits (September 1, 2017);
- Recommendations for a Drug Screening Equipment Program – Oral Fluid (March 27, 2018); and
- Scientific paper by Beirness and Smith (2017) on "An assessment of oral fluid drug screening devices" published in the Canadian Society of Forensic Science Journal, 50(2), pp 55-63.

Client Instructions

The technical process of establishing the presence of drugs in oral fluid, both in laboratory and by point of collection testing (including any limitations, if any, arise from these processes (for example, metabolites vs parent drugs, false negatives or false positives, etc, and what is the correlation, if any, between the presence of drugs in oral fluid and in blood or in urine?

1. Are there generally accepted international standards thresholds for positive results for drug or drug metabolites in oral fluid? If so, are the threshold set out in Appendices B5 and B6 of the RegDoc consistent with those thresholds?
2. What are the retrospective detection windows in which drugs may be detected in oral fluid? Please refer to the list of drugs to be tested at Appendices B5 and B6 the RegDoc and address each of these drugs at the listed cut-off levels, and include any factors that may affect the presence or absence of drugs in oral fluid.
3. What is the relationship between a positive oral fluid test and impairment with respect to the drugs listed in Appendices B5 and B6 of the RegDoc at the listed cut-off levels?
4. What are the limitations, if any, on using oral fluid testing to establish that the subject was impaired at the time the sample was taken?
5. What, if anything, does the quantity of a presence of a drug or drug metabolites in oral fluid demonstrate in terms of the subject's impairment?

6. Do point of collection devices provide accurate and reliable results of screening past drug use? What are the limitations, if any, in using point of collection devices? Note that in Canada, the following devices have been approved for point of collection testing in the criminal context:

    a. The Dräger DrugTest® 5000 STK-CA (collection kit) when used with the Dräger DrugTest® 5000 (reader).

    b. The SoToxaTM, an Abbott SotoxaTM Test Cartridge and an Abbott SoToxa Oral Fluid Collection Device, when used together.

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Glossary of Scientific Terms and Abbreviations Used

Amphetamine:	A metabolite of methamphetamine, but also can refer to a class of drugs with chemical structures and properties similar to amphetamine;
Benzodiazepine:	A large class of related drugs with anxiolytic and/or sleep-inducing properties, that include alprazolam, bromazepam, diazepam, flurazepam, oxazepam, temazepam;
Cmax:	Maximum concentration (a useful pharmacokinetic parameter measured in dosing studies);
Cut-off:	a concentration in which a positive result below this value is not reported as negative;
DRE:	Drug Recognition and Evaluation;
EDDP:	A major methadone metabolite, chemically 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine;
EWDTS:	European Workplace Drug Testing Society;
h:	hour(s);
Half-life:	time taken for blood concentration to halve after absorption has completed;
Hypnotics:	Drugs that induce sleep;
Immunoreactivity:	Ability of an antibody-based kit to detect a related substance;
Impairment:	A term used to define an inability to work safely due to decrements in one or more measurable skills;
LOD:	Limit of detection;
MDA:	3,4-Methylenedioxyamphetamine;
MDMA:	3,4-Methylenedioxymethamphetamine;
mg/L:	Milligrams of drug per liter of fluid; also sometimes written as μg/mL but numerically the same concentration;
Metabolite:	A substance produced by the body from a parent drug; often to hasten excretion of the drug;
Methamphetamine:	Sometimes known as methylamphetamine; a strong illegal stimulant;
NPS:	Novel psychoactive drugs;
Opiate:	Drugs related to morphine; includes codeine;
Opioid:	A large class of synthetic narcotic analgesic drugs with stimulant effects on the opioid-receptor and with actions similar to opiates;
Oral fluid:	A term used to refer to a number of secretions into the oral cavity from various glands;
Pharmacokinetics:	A term used to describe the time changes in the concentration of substances (drugs and metabolites) in biological samples against time;
pH:	A measure of the acidity (<7) or alkalinity (>7) of an aqueous solution;

pKa:	negative logarithm of the acid dissociation constant – a measure of the acid strength of a substance;
SAMHSA:	Substance Abuse and Mental Health Services (USA).
SFST:	Standardized Field Sobriety Test;
THC:	Most active substance associated with cannabis (marijuana), chemically Δ^9-tetrahydrocannabinol;
Tolerance:	The neuroadaptation of the body to become less sensitive to effects of drugs.

CURRICULUM VITAE
Professor Olaf H. Drummer AO

Current Position

Professor (Forensic Medical Science), Department of Forensic Medicine, Monash University, and Forensic Toxicology Consultant Specialist, Victorian Institute of Forensic Medicine (part-time).

Qualifications and Fellowships

- Doctor Honoris Causa (University of Antwerp) March 23, 2016 (Dr. h. c.).
- Fellow of Faculty of Science of The Royal College of Pathologists of Australasia (RCPA) (2010-)
- Honorary Fellow, The Royal College of Pathologists of Australasia (RCPA) (2009-),
- Fellow of the Australasian College of Biomedical Scientists (2006-).
- Ph.D. (Medicine) (Melb) 1981
- Chartered chemist (Royal Australian Chemistry Institute, RACI, 1974-)
- B.App.Sci. (Chemistry) (RMIT) 1974

Awards and Honours

- Officer (AO) in the general division of the Order of Australia honour, January 26, 2019.
- Alan Curry Award from the International Association of Forensic Toxicologists (TIAFT) for distinguished contributions to the field of forensic toxicology and to TIAFT (2016).
- Awarded Honorary doctorate in forensic pharmacology (Doctor Honoris Causa) from University of Antwerp – March 2016.
- Jean Servais Stas award and life membership from the German Society of Toxicology and Forensic Chemistry (GTFCh) (2013).
- Excellence in Higher Degree supervision, School of Public Health and Preventive Medicine, Monash University (2013).
- Irving Sunshine award from the International Association of Therapeutic Drug Monitoring and Clinical Toxicology for Excellence in Clinical Toxicology (2005).
- Australian Drug Foundation award for Excellence in Alcohol and Drug Research (2000).

Memberships and Roles in Professional Societies

- Member of Order of Australia Association (January 26, 2019)
- Honorary Fellow of the Faculty of Forensic and Legal Medicine of the Royal College of Medicine (UK) (2019-)
- Inaugural President, Forensic and Clinical Toxicology Association (FACTA) (2010-2016)
- The International Association of Forensic Toxicologists (TIAFT) (President 2008-11, Treasurer 1998-2005)
- Founding member of Australian Academy of Forensic Sciences – Victorian Chapter (AAFS)
- Royal Australian Chemical Institute (certified practising chemist CChem since 1974)
- Life Member German Society of Toxicological and Forensic Chemistry (GTFCh)
- Honorary member of the Italian Forensic Toxicology society (GIFT)
- Member Australian & New Zealand Forensic Science Society (ANZFSS)
- Member Australasian Society of Clinical &Experimental Pharmacologists and Toxicologists (ASCEPT) 1981-2015
- Member International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) to 2014.

Key International Activities and Board Memberships

- Editorial Board for Data-in-Brief Publications (Elsevier) (2018-).
- Honorary visiting professor at the Shanghai Institute of Forensic Science 2013-.
- Co-author (with Dr Steven Karch) of Karch's Pathology of Drug Abuse (5th Edition) CRC press 2015.
- Co-editor and Author, eBook on "Forensic Drug Analysis" Future Science publishers, 2013.
- Editor (Toxicology) – Forensic Science International 2003 –
- Editorial Advisory Board, Journal of Forensic Science and Medicine – 2015-
- Advisory Board Member, Forensic Toxicology 2009 -
- Advisory Board for the Journal Drug Testing and Analysis 2009-
- Editorial Advisory Board, Encyclopaedia of Forensic Sciences, 2nd Edition (2010)
- President, The International Association of Forensic Toxicologists, 2008-11 and board member of the International Association of Forensic Toxicologists (TIAFT) 1999-2014.
- Section Editor for toxicology and drugs, Encyclopaedia of Forensic Science (Wiley).

- Editorial Boards of Journal of Analytical Toxicology, Forensic Science Medicine & Pathology. Drug Testing & Analysis, Bioanalysis.
- Editorial Board for The Pharmaceutical Press (London) for a second edition of Clarke's Isolation and Identification of Drugs (2000-) for three encyclopaedias on Forensic Science (Wiley and Elsevier).
- Referee for several journals in forensic science and medicine.
- Plenary and keynote speaker in many national and international conferences.
- Past Chair – Drugs of Abuse and Clinical toxicology committee – International Association of Therapeutic Drug Monitoring and Clinical Toxicology – 2005-2013.
- Chair – Organising Committee for the conference for the International Association of Forensic Toxicologists (TIAFT), November 16-20, Melbourne 2003.
- Member of Consultative committee for the United Nations Drug Control Program (UNDCP), and editor of the booklet on the Analysis of Benzodiazepines and Barbiturates held in Hong Kong, November 1995 and member of Consultative committee, rapporteur and editor of the booklet on the analysis of hallucinogens and on the use of alternative specimens in toxicology testing, held in Barcelona, December 1997.

Research Interests

- Opioids in sudden death,
- Novel psychoactive drugs,
- Causation in death by drugs,
- Post-mortem drug metabolism and artefacts,
- Involvement of drugs in driving,
- Drug awareness and harm reduction in public health.

Research Funding

20 funded research projects (CIA and/or associate investigator) over working career totalling $2.5M from several funding bodies including National Health & Medical Research Council (NH&MRC), National Heart Foundation (NHF), National Institute of Forensic Science (NIFS), AustRoads, VicRoads, Victorian Drug Law Enforcement Fund (VDLEF) on mechanism of drug effects and epidemiology of drugs in sudden death; involvement of drugs in sudden death and injury and designer drugs in Victorian drivers.

Previous Positions

- Deputy Director (Academic Programs), Victorian Institute of Forensic Medicine, 2014-2017 (retired)
- Head, Department of Forensic Medicine, Monash University, 2010-2017 (retired)
- Head (Forensic & Scientific Services), Victorian Institute of Forensic Medicine, 1989-2014.
- Associate Professor, Department of Forensic Medicine, Monash University 1995-2001.
- National Health & Medical Research Council Research Fellow (Melbourne University 1986-89). Leader of research team examining the metabolism and biochemical pharmacology of drugs used in cardiovascular medicine. In charge of Mass Spectrometry and manager of drug analysis laboratory (Austin hospital and Clinical Pharmacology Unit of the Dept of Medicine, Melbourne University), 1980-1989.
- National Health & Medical Research Council Research Officer (Melbourne University 1980-85). Leader of research team examining the metabolism and biochemical pharmacology of drugs used in cardiovascular medicine. In charge of Mass Spectrometry and Drug Analysis Laboratory.
- NH&MRC Research Officer (Melbourne University 1975-76). Member of research team examining the detection, metabolism and biochemical pharmacology of drugs used in cardiovascular medicine.
- Sessional Scientist (Drugs) (Royal Children's Hospital) (1973-80). Responsible for the design, validation and conduct of routine drug analyses in the Biochemistry Section of the Hospital.
- Technical Officer (RMIT) (MLT Biochemistry) (1973-74). Scientist responsible for designing and coordinating laboratory experiments in Clinical Biochemistry II.

Patent

Co-inventor of the international patent (WO/1997/013744) 3-AMINO-PROPOXYPHENYL DERIVATIVES (I) published in 1997. No. WO/1997/013744. Publication Date: 17/04/1997, Australia.

Publications (see list)

Over 300 peer reviewed papers in the forensic and scientific literature, books and book chapters and other contributions, and over 200 papers presented at national and international meetings.

- 13,008 citations and Hirsch Index 58 (Google Scholar, 427 articles);
- 8360 citations with Hirsch Index 48 (Scopus; 280 publications);
- Research Gate Score 45.06 (Hirsch Index 50, 9252 citations, 311 articles).

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Canadian Society of Forensic Science
La Société canadienne des sciences judiciaires

Report on Drug Screening Equipment – Oral Fluid

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October, 2018

Introduction

This document provides general information about oral fluid drug screening. This discussion is specific to three target compounds: tetrahydrocannabinol (THC), cocaine and methamphetamine and to the Drugs and Driving Committee's (DDC) standards and evaluation procedures for drug-screening equipment – oral fluid[1] [drug screening equipment] which are formulated for the purposes of investigations under the Criminal Code of Canada. This document discusses drug screening equipment in general, without reference to any specific product or manufacturer. The information in this document is based upon a review of the relevant scientific literature.[2]

The technological basis for drug screening equipment – oral fluid

Currently, drug screening equipment employs immunoassay-based technology to identify target compounds in oral fluid. Immunoassay-based analyses are commonly used both in clinical and forensic settings as they are rapid, robust, amenable to use in portable/roadside/single use technologies, and commonly use a small sample volume. The general population may be familiar with the use of immunoassay technology in home pregnancy tests.

Immunoassay involves the ability of a specific antibody to bind to a target compound of interest, resulting in a measurable effect (e.g., colour change). The utility of a particular immunoassay is dependent upon the ability of that antibody both to bind the target compound of interest and to not bind other compounds.

Immunoassay-based analyses are commonly used as preliminary analyses, providing presumptive results. To confirm the presumptive results, more specific methods of analysis are performed. Whereas immunoassays are reliant upon a single marker for identification of a target compound (antibody binding), more specific methods of analysis commonly rely upon multiple means of identification for increased confidence (e.g., mass spectra). For Criminal Code investigations, drug screening equipment is recommended for use as a preliminary means of identification of specific target compounds (THC, cocaine, and/or methamphetamine).

The DDC's standards are designed so as to both maximize the specificity (identification of true negatives[3]) and the sensitivity (identification of true positives[4]) of drug screening equipment. In addition, by:

- setting suitable cut-off concentrations for the target compounds;
- specifying that the target compounds must be the drugs themselves, as opposed to other related compounds or metabolites; and

[1] https://www.csfs.ca/

[2] It should be noted that there are limited studies which examine the use of these drugs in "real life"/recreational situations due to inherent ethical considerations.

[3] True negatives are oral fluid samples for which the target compound is either not present or present below the oral fluid cut-off concentration.

[4] True positives are oral fluid samples for which the target compound is present at or above the oral fluid cut-off concentration.

- examining cross-reactivity results so that the potential for "false positives" caused by related compounds and metabolites is minimized;

the standards are designed to:

- maximize the likelihood at the time that an individual tests positive on drug screening equipment, they have those target compound(s) in their blood at or above any *per se*[5] levels; and
- minimize the likelihood of individuals testing negative on drug screening equipment who have these target compounds present in their blood at or above any *per se* levels.

Oral fluid

Oral fluid is commonly referred to as saliva, but is actually a mixture of saliva and other materials that may be present in the mouth. Advantages of oral fluid as a sample for roadside drug screening include the ease of collection, low health and safety risks, and minimal privacy issues associated with its collection. However, there are challenges that need to be considered and addressed with use of oral fluid as a sample for drug-impaired driving investigations.

Certain drugs, including THC, cocaine and methamphetamine, may decrease saliva production and make it difficult for individuals to provide sufficient oral fluid required for analysis. To address this challenge, manufacturers commonly minimize sample volumes required. DDC standards require drug screening equipment collect sufficient oral fluid for analysis within 4 minutes of the start of collection.

Drugs generally become detectable in oral fluid shortly after administration. They can be present as a result of drug excretion and partitioning into the oral fluid from the body as well as from residual drug deposits in the oral cavity. For example, following injection there may be a lag period of minutes between administration and detection in oral fluid due to the time needed for drug distribution throughout the body and excretion into oral fluid. In contrast, oral fluid may be positive immediately following smoking due to residual drug deposits.

Due to their specific chemical and pharmacokinetic properties, cocaine and methamphetamine are relatively well-excreted into oral fluid from the body in contrast to THC, which is weakly distributed into the oral fluid.

There is a risk that oral fluid may be contaminated by a drug as a result of passive exposure. However, the oral fluid cut-off for THC in the DDC's standards is higher than those concentrations reported from scientific studies of passive exposure, virtually negating the possibility of individuals testing positive on drug screening equipment by this means. While there is a paucity of research on passive exposure to cocaine and methamphetamine, given the typical means of consumption, patterns of use, and basic

[5] http://www.gazette.gc.ca/rp-pr/p2/2018/2018-07-11/html/sor-dors148-eng.html

scientific principles, the potential for passive exposure and resultant contamination of oral fluid is unlikely.

As positive drug screening results generally occur as a result of consumption[6] (whether from excretion and/or residual drug deposits), and with cut-off concentrations selected so as to virtually negate the possibility of passive drug exposure, positive oral fluid results on drug screening equipment can be considered as a preliminary indication of the presence of that drug in the body.

Relationship between drugs in oral fluid and in blood

There is not a direct correlation between drug concentrations in oral fluid and in blood. The oral fluid:blood ratio for a particular drug can vary both between individuals, and over time for a given individual following drug administration. There are numerous factors which affect both drug excretion into the oral fluid and overall oral fluid concentrations. There are also numerous factors that affect drug concentrations in the blood. These factors are separate from each other. For example, decreasing the acidity (increasing the pH) of the oral fluid will decrease the concentration of methamphetamine in the oral fluid, but will not affect its concentration in the blood. In addition, the presence and magnitude of residual methamphetamine deposits in the oral cavity can further complicate any attempt to correlate oral fluid and blood concentrations.

Cocaine and methamphetamine distribute well into both blood and oral fluid. While oral fluid concentrations of these drugs do not correlate directly with blood concentrations, in general the presence of cocaine and methamphetamine in the oral fluid indicates their presence in blood.

THC does not distribute well into either blood or oral fluid, and concentrations in both of these fluids can vary greatly dependent upon dose, route of administration and patterns of use. In general the presence of THC in the oral fluid indicates its presence in blood. It is more difficult to make this association for individuals immediately following oral THC consumption, prior to significant absorption into the body. The time frame for detection of THC in oral fluid varies, but may be much shorter than in blood. This is particularly applicable to frequent high-dose THC smokers who may have positive blood concentrations for several days since last use.

How long after drug use will an individual test positive on drug screening equipment?[7]

The time period for which an individual will test positive on drug screening equipment is dependent upon a number of factors: the drug in question, the time since last drug use, the drug dose and route of administration, the cut-off concentration of drug screening equipment, and the drug consumption history of the individual.

[6] Consumption includes all possible routes of drug administration, including oral ingestion, smoking, and intravenous use.

[7] Based on relevant scientific literature and the cut-offs required by the DDC standards for drug screening equipment.

The oral fluid cut-off concentration for cocaine required by the DDC's standards is 50 ng/mL. Cocaine is well excreted into oral fluid. Nevertheless, after cocaine use some individuals may not have oral fluid concentrations exceeding the cut-off; this is most likely after single low dose oral ingestion which is not a common route of administration for recreational cocaine use. While the time period for which individuals may test positive with the above-noted cut-off will vary, recreational users[8] would generally test negative on drug screening equipment within 4 to 6 hours after last use. Frequent high-dose cocaine users would be expected to test positive on drug screening equipment for the longest period of time, which could be a day since last use.

The oral fluid cut-off concentration for methamphetamine required by the DDC's standards is 50 ng/mL. Methamphetamine is well excreted into oral fluid. Nevertheless, after methamphetamine use some individuals may not have oral fluid concentrations exceeding the cut-off; this is most likely after single low dose oral ingestion. However, individuals in this population who do test positive, could do so for up to 4 to 6 hours since last use. While the time period for which individuals may test positive with the above-noted cut-off will vary, recreational users would generally test negative on drug screening equipment within 24 to 48 hours after last use. Frequent high-dose methamphetamine users would generally test positive on drug screening equipment for the longest period of time after last use, which could be 3 to 4 days.

The oral fluid cut-off concentration for THC required by the DDC's standards is 25 ng/mL. THC does not excrete well into oral fluid. However, as THC is commonly consumed via smoking or oral ingestion of edibles, individuals may have oral fluid concentrations exceeding the cut-off for short periods of time due to residual deposits in the oral cavity. In contrast, oral ingestion of THC-containing capsules would be less likely to result in residual deposits and oral fluid concentrations that exceed the cut-off. THC smokers (ranging from occasional smokers to frequent high-dose smokers) would generally test negative within 4 hours after smoking. Similarly, the available literature indicates that oral THC users would also generally test negative on drug screening equipment within 4 hours after ingestion. Thus, positive results on approved drug screening equipment can indicate recent THC use.

The relationship between a positive result on drug screening equipment and impairment[9]

Drug screening equipment does not measure drug impairment. Impairment is dependent upon the drug used, the dose, time since last use, route of administration, and is subject to inter-individual variability, among other factors. Nevertheless, depending on the drug involved, and the specifics of its use, a temporal association between a positive drug screening equipment result and impairment can be made.

Impairment from cocaine use is most pronounced within the first 1 to 2 hours following a single dose. Frequent high-dose cocaine use[10] prolongs the impairment and produces a subsequent crash phase[11],

[8] Individuals who occasionally use drugs primarily for the euphoric/high effects.
[9] Based on relevant scientific literature and the cut-offs required by the DDC standards for drug screening equipment.
[10] Includes "binge" use and common patterns of crack cocaine use
[11] A dysphoric phase commonly characterized by agitation, irritability, anxiety, depression, craving, and paranoia.

during which impairment is also present. Recreational cocaine users would generally test negative on drug screening equipment within 4 to 6 hours after last use; impairment would be expected to extend beyond this period. Thus, a temporal association between a positive drug screening equipment result for cocaine and impairment may be made for this population. Frequent high-dose cocaine users could test positive on drug screening equipment for a day since last use; impairment from this pattern of use would be expected to extend beyond this period. Thus, a temporal association between a positive drug screening equipment result for cocaine and impairment may be made for this population.

Methamphetamine has wide variations in the patterns of use, and resultant variability in its detection time periods in oral fluid. It has been suggested that low dose methamphetamine may improve performance; however, the dose and pattern of use are not typical of recreational methamphetamine use, and do not apply to drug abuse situations. Individuals who test positive on drug screening equipment following a single low dose oral ingestion could do so for up to 4 to 6 hours. As such, it is difficult to associate a positive result for methamphetamine on drug screening equipment with impairment for this population.

Impairment following recreational methamphetamine use extends beyond the initial euphoria or "high". With increased dose and frequency of use, a user becomes more likely to experience a subsequent "crash" phase, during which impairment persists. Recreational methamphetamine users would generally test negative on drug screening equipment within 24 to 48 hours after last use, while frequent high-dose methamphetamine users would generally test negative within 3 to 4 days. Despite an extended impairment period for these populations, individuals may test positive for methamphetamine on drug screening equipment beyond the time period for which impairment would be expected. Thus, it is difficult to make a temporal association between a positive drug screening equipment result for methamphetamine and impairment.

One of the strongest factors that correlates with THC impairment is the time since last use. Occasional THC smoking causes impairment which begins almost immediately and generally resolves within 4 to 6 hours following last use. THC enters the body more slowly following oral consumption, delaying the onset of action and extending the impairment period. In addition to acute impairment, frequent high-dose THC users may experience extended periods of performance deficits.

Individuals who test positive on drug screening equipment following THC use could do so for up to 4 hours. In general, a temporal association can be made between a positive drug screening equipment result for THC and impairment. It is more difficult to make this association for individuals who test positive on drug screening equipment immediately following oral THC consumption.

Potential for "false positive" results on drug screening equipment

Theoretically, false positive results are possible in any single analysis. Specific to drug screening equipment, false positive results fall into two general categories, but do not necessarily represent an instrument error or malfunction:

1. A positive result when that drug is either present below the cut-off concentration, or not present, in the oral fluid of the individual.
2. A positive result that is not confirmed in a subsequent blood sample (blood result is either negative or below *per se* levels).

While there is the theoretical possibility of the first category inherent in immunoassay-based technology, the specific DDC standards and evaluation procedures minimize the potential for this situation in drug screening equipment.

The second category could occur in a variety of theoretical and/or potential situations:

- Drug contamination of oral fluid or oral fluid collection systems in the absence of drug consumption. As previously noted, oral fluid cut-offs for THC in the DDC's standards are higher than those concentrations reported from scientific studies of passive exposure, virtually negating the possibility of individuals testing positive on drug screening equipment by this means. The potential for this situation is also minimized by sample collection procedures that avoid the risk of environmental contamination.

- Drug presence in oral fluid beyond the period for which it is present in the blood of that individual. The specific drug cut-off concentrations required by DDC standards minimize the potential for this situation to occur.

- Decreasing blood concentrations in the body during the period between oral fluid testing and blood collection from the individual. The likelihood of this situation increases with increasing delay between oral fluid testing and blood collection, for drugs which are rapidly eliminated or removed from blood, and for drugs which were present in blood at concentrations at or near their analytical limits of detection at the time of oral fluid testing. THC and cocaine are particularly susceptible to this situation.

- Drug degradation or loss from the blood sample between the time of collection and the time of analysis. Cocaine is particularly susceptible to this situation. The potential for this is minimized by reducing the delay between collection and analysis and by use of standard forensic laboratory practices.

- Oral cavity contamination following recent THC ingestion. Blood concentrations could be either negative or below *per se* levels due to the delay in THC absorption into the blood following oral ingestion, and typically low blood concentrations which result from oral consumption.

Potential for "false negative" results on drug screening equipment

Theoretically, false negative results are possible in any single analysis. Specific to drug screening equipment, false negative results fall into two general categories, but do not necessarily represent an instrument error or malfunction:

1. A negative result when that drug is present above its cut-off concentration in the oral fluid of the individual.

2. A negative result despite that drug's presence in the individual's blood at or above a *per se* level.

While there is the theoretical possibility of the first category inherent in immunoassay-based technology, the specific DDC standards and evaluation procedures minimize the potential for this situation in drug screening equipment.

The second category is a possibility, dependent upon the drug in question and the specifics of its use. This is reflective of the lack of direct correlation between drug concentrations in oral fluid and blood, as previously outlined.

Conclusions:

Drug screening equipment is a useful addition to the tools available for law enforcement in Criminal Code drug-impaired driving investigations, but should not be expected to address all situations. Confirmatory analyses of positive results are recommended given the nature of immunoassay-based technology. Given the complex and diverse nature of impairing drugs, a single tool cannot be expected to provide all information necessary to an impaired driving investigation. However, it can provide additional relevant information to law enforcement.

Representative peer-reviewed scientific literature

This is a list of representative articles which may be helpful to further educate readers on the topic. It is not an exhaustive list of the scientific literature available on this topic or which was considered by this committee in formulating its opinions.

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