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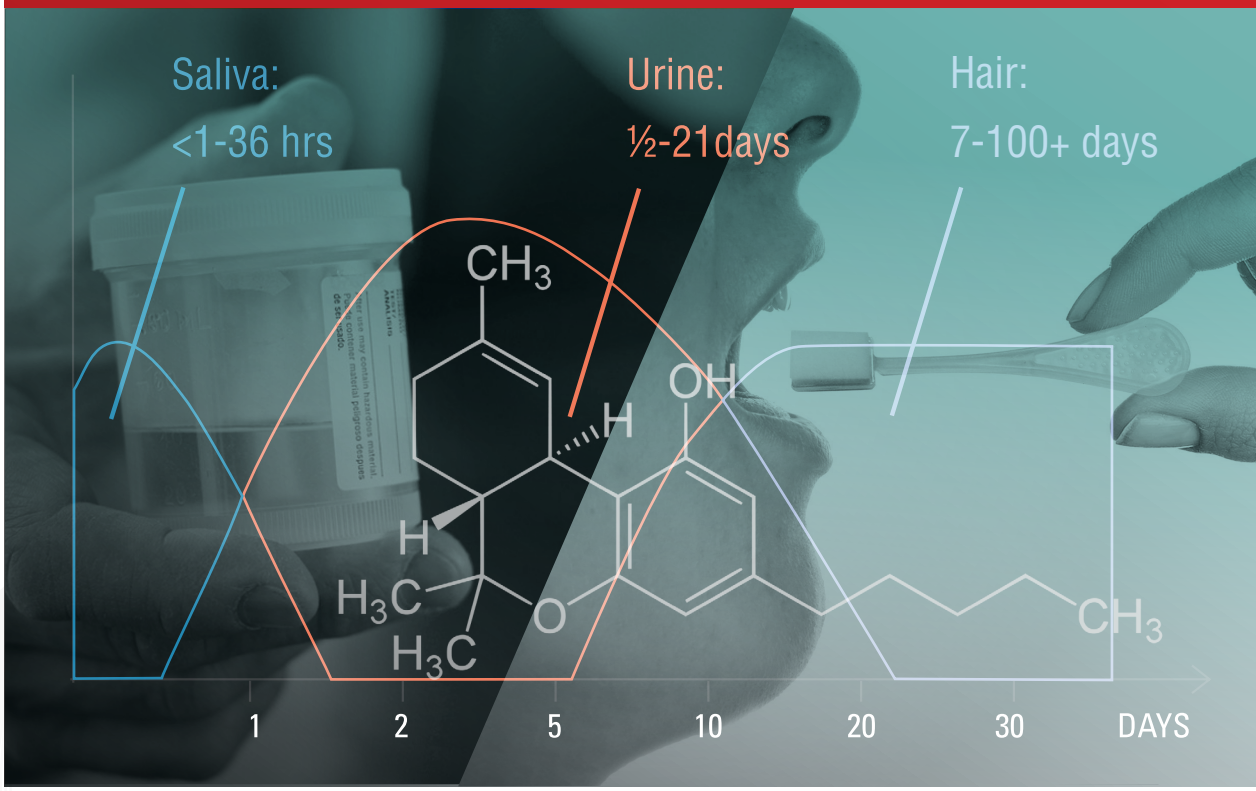


SELECTING A BIOSAMPLE FOR DRUG TESTING

ABSTRACT

Workplace drugs testing continues to grow across Australia with both Urine and Saliva testing procedures being utilised.

When deciding on which testing means should be adopted, each workplace must consider their specific circumstances and make a decision on what is best given their risk profile, employee demographic and desired outcomes.

INTRODUCTION

Saliva vs. Urine testing remains a contentious subject. But this is unnecessarily so.

Unless there are specific industry regulations and guidelines for one technique over the other, employers are free to evaluate the most appropriate testing procedure for their operational environment, risk management regimes, staff lifestyle implications and also their budgets.

This white paper seeks to inform and position drug detection specificities in order to assist in the selection between saliva (oral fluid) and urine drugs testing.

SELECTING THE RIGHT BIOSAMPLE

There are many considerations as to which biofluids to analyse for Drugs of Abuse, here are some:

- **What drugs do you need to test for?** This is important because in some cases a single dose can be retained in the body for several weeks
- **What drug detection time do you seek?** Look for the detection time of the active drug component in a testing procedure – they vary and can have implications for both employee and employer.
- **Do drugs in biofluids and blood/plasma present for a drug test in the same way?** They differ, and some biofluids correlate with blood/plasma better.
- **What is the best way to collect a biosample?** Consider that: blood/plasma testing is invasive, urine requires same sex supervision but oral fluid is easy and relatively non-invasive.
- **How easy is it to adulterate or fake a sample?** It is worth considering that unless rigorous adulteration controls are run during testing, urine is relatively easy to adulterate. Oral fluid and blood/plasma are difficult to adulterate.
- **How quickly do you need test results?** Urine and oral fluid can be screened very quickly compared to blood – which requires a trained medic with lab access.
- **What analytical sensitivity of the testing equipment do you require?** It is important to be able to measure to ng/ml concentrations.

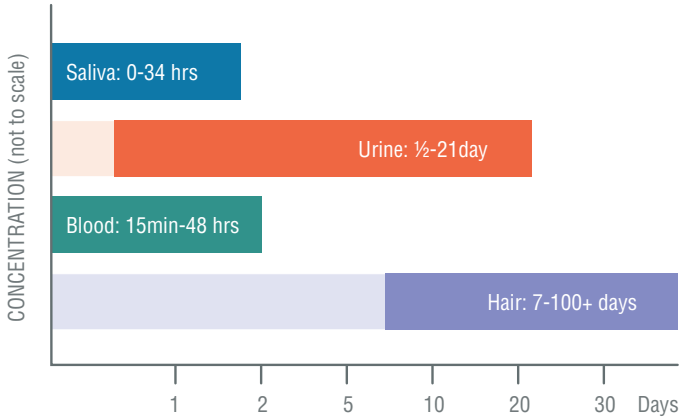
There are a number of factors that determine the detection time of a drug in a biological sample. In general, the detection time is longest in hair (7-100+ days), followed by urine (1-3 days), sweat (1-14 days), this body fluid is very useful for continuous monitoring of drugs, oral fluid (0-34 hrs) and blood.

In blood or plasma, most drugs of abuse can be detected at less than 20 minutes and at the low nanogram per millilitre level for 1 or 2 days.

Urine is the most widely used specimen for the detection of drugs. In chronic users, drugs of abuse can be detected in urine for approximately 1 week after last use, and in extreme cases even longer in cocaine and cannabis users [1].

Analysis of drugs in hair is complicated. The main routes of drug incorporation into hair are from the

General detection times of drugs in samples of Blood, Saliva, Urine and Hair



Detection times of drug parent types

DRUG TYPES	Blood/Plasma/Serum		Urine		Saliva		Hair	
	Measure	Detection Window	Measure	Detection Window	Measure	Detection Window	Measure	Detection Window
Amphetamines	Parent drug	15 min-48 hrs [3,13]	Parent drug	6-90 hrs [5]	Parent drug	12 min-50 hrs [9,13]	Parent drug	7-50+ days
Cannabis	Parent drug + THCCOOH	5 min-36 hrs [3]	THCCOOH	1-90 hrs [6,10] (22% positive at 1 hr)	Parent drug	0-34 hrs [10] (100% positive at 1 hr)	Parent drug	7-50+ days
Cocaine	Parent drug + Benzoylecgonine	15 min-8 hrs [3]	Benzoylecgonine	6-72 hrs [7]	Parent drug + Benzoylecgonine	20 min-24 hrs [11]	Parent drug + Benzoylecgonine	7-50+ days
Opiates	Morphine	15 min-20 hrs [4]	Morphine	6-34 hrs [10]	6-Acetyl Morphine	1-8 hrs [12]	Parent drug + Metabolites	7-50+

blood supply, sebum, sweat and from external contamination. Cocaine, heroin and its primary metabolite, 6-monoacetylmorphine, are less commonly detected in blood compared with their metabolites, but are the primary analytes found in hair [29].

Hair has different affinities and binding capacities for various drugs and the binding mechanisms may be unique for each drug.

It takes 7-10 days for hair to reach the surface of the scalp, hair grows on average at 1cm/mo (0.6 – 3.36cm/mo) so the earliest detection time is 7-10 days [30].

Drugs are very stable in hair, historical samples are several hundred years old.

Many conditions influence the detection time:

- the dose that was taken
- the preparation and route of administration
- acute versus chronic use
- choice of biofluid
- detection limit or cut-off of the analytical technique
- nature of the molecule or the metabolite sought
- the pH and concentration of the urine or oral fluid
- interindividual variation in metabolism [2].

In oral fluid the parent drug is the dominant species, whereas in urine, the drug metabolite tends to dominate [14].
Cannabis, particularly its active form, delta 9 tetrahydrocannabinol (THC), rapidly enters the bloodstream.

Very little THC or its metabolites are transported from blood to saliva and THC measured in oral fluid is mainly due to contamination of the oral mucosa [15].

The detection of cannabinoids in urine is indicative of prior cannabis exposure. The long excretion half-life of the metabolite THCCOOH in the body, especially in chronic cannabis users, makes it difficult to predict the timing of past drug use.

Oral Fluid testing of drugs exhibit a better correlation with blood concentrations than urine which implies that oral fluid may better reflect the impairment window [16].

Adulteration of oral fluid is difficult as its collection can be observed without infringing privacy this is not true for urine collection [21].

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Where evidence of prior exposure to drugs of abuse is sought then urine should be chosen.

Hair is much better at exhibiting long term exposure to drugs. However, if evidence of recent use of drugs is required then either blood or oral fluid are the preferred specimens.

Oral fluid has the advantage that it can be obtained non-invasively.

Amphetamines: The effects of the drugs generally last around 2-4 hours and has a half-life of 6-12 hours for elimination from blood.
MET and AMP appear rapidly in plasma and oral fluid after administration and are detected for roughly the same length of time.

DRUG TYPES

AMPHETAMINE TYPE DRUGS

Drugs that are chemically related to phenylethylamine are collectively referred to as amphetamine type drugs.

These drugs include Amphetamine (AMP), Methamphetamine (MET), 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) and 3,4-methylenedioxyamphetamine (MDA).

Acute doses lead to enhanced stimulation of the central nervous system and induce euphoria, alertness, reduced appetite, and a sense of increased energy and power.

Cardiac responses include increased blood pressure and arrhythmias. Other responses include anxiety, paranoia, hallucinations and psychotic behaviour.

The effects of the drugs generally last around 2-4 hours and has a half-life of 6-12 hours for elimination from blood.

A significant part of these drugs is excreted unchanged in urine, especially if the urine is acidic. In urine it is important to measure the pH as lower pH values will give higher AMP results. AMP undergoes aromatic hydroxylation to para hydroxyamphetamine and oxidative deamination to benzoic acid [17].

A major metabolite of MET is AMP. Urinary samples can be positive for amphetamine for up to 5 days after intake of the drug [18].

The average ratio of oral fluid to blood concentration for amphetamines is relatively high ranging from 2 for AMP to 7 for MET [22].

MET and AMP appear rapidly in plasma and oral fluid after administration and are detected for roughly the same length of time.

Orally administered MDMA reaches maximal blood and oral fluid concentrations in approximately 1.5 hours.

BARBITURATES

There are at least 12 different barbiturates which are used medically worldwide, common barbiturates include secobarbital, pentobarbital and phenobarbital.

After smoking one marijuana cigarette, THCCOOH in urine is detectable (using a screening cut-off of 50 ng/mL) for 2-4 days. More frequent use will be detectable for almost 1 month and in exceptional cases, 3 months [18].

Barbiturates are central nervous system depressants. They are used therapeutically as sedatives, hypnotics, and anticonvulsants.
They are almost always taken orally as capsules or tablets. Their effects resemble those of alcohol intoxication.

They are extensively metabolised to a number of different metabolites. Peak concentrations of barbiturate post oral administration are found at 1 hour on both oral fluid and serum [24], and are detected in urine at 2 hours [26]. Only a small amount (less than 5%) of most Barbiturates are excreted unaltered in the urine.

CANNABINOIDS

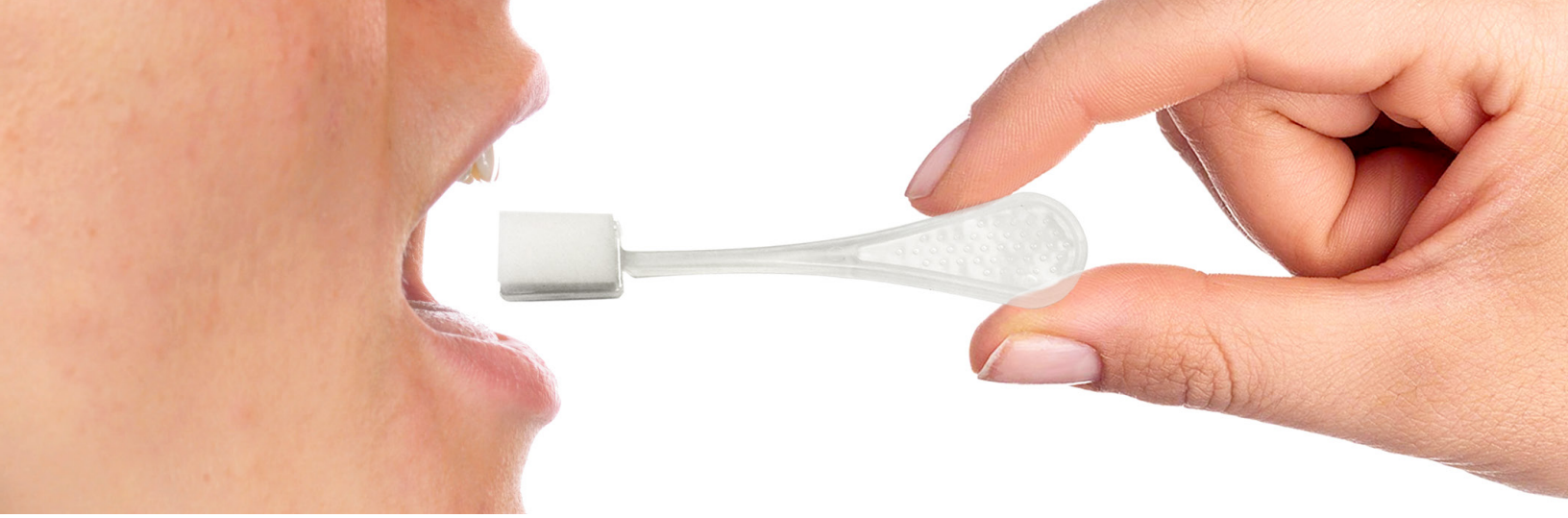
The cannabis plant, Cannabis sativa, contains over 60 cannabinoids, the most psychoactive compound of this group is delta 9 tetrahydrocannabinol (THC).

When smoked or orally administered, it produces euphoric effects. Users have impaired short-term memory and slowed learning. They may also experience transient episodes of confusion and anxiety. Long term relatively heavy use may be associated with behavioural disorders.

THC decomposes when exposed to air, heat or light: exposure to acid can oxidise the compound to cannabinol (CBN) a much less potent cannabinoid.

When smoked, THC is rapidly absorbed from the lungs into the bloodstream, from which it rapidly distributes into tissue.

A maximum plasma THC concentration occurs within minutes of smoking. THC is rapidly metabolized by hepatic enzymes to
11-hydroxy-delta 9 – tetrahydrocannabinol (11-OH-THC) also 11-nor-9-carboxy-delta 9-tetrahydrocannabinol (THC-COOH). THC elimination is biphasic, the concentration in blood or oral fluid rapidly decreases within the first 1-2 hours post smoking and then declines more slowly. In chronic smokers it may be detected for several days.



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BENZODIAZEPINES

There are around 50 different drugs in this class and the common ones are diazepam, temazepam, alprazolam, lorazepam and clonazepam.

These drugs can cause sedation, muscle relaxation, impaired memory and cognition and loss of inhibition.

The half-life of these drugs varies widely depending on the particular drug, between 1 and 36 hours [19]. They are extensively metabolized by liver enzymes and are excreted in urine often as the glucuronide conjugate.

There appears to be some variability between different donors in the plasma/oral fluid ratio.

COCAINE

Cocaine is abused as the hydrochloride salt which can be snorted.

> *Cocaine: Initially, it brings about extreme energy and restlessness while gradually resulting in tremors, over-sensitivity and spasms.*
> *..Its metabolites appear rapidly in oral fluid following all routes of administration.*

Crack cocaine is a form of cocaine which has not been acid neutralized.

It is a potent central nervous system stimulant and a local anaesthetic. Initially, it brings about extreme energy and restlessness while gradually resulting in tremors, over-sensitivity and spasms. In large amounts, cocaine causes fever, unresponsiveness, and difficulty in breathing and unconsciousness.

Cocaine is often self-administered by nasal inhalation, intravenous injection and free-base smoking.

Cocaine has a short half-life in blood (0.5-1.5hr) and is rapidly metabolised to the inactive metabolite benzoylecgonine, which has a much longer half-life (5-8 hours). Benzoylecgonine represents the major cocaine complexes in urine.

In oral fluid cocaine and its metabolite has a similar half-life as in blood.

Cocaine and its metabolites appear rapidly in oral fluid following all routes of administration.

Immunoassays to detect cocaine in urine and oral fluid are targeted against the metabolite benzoylecgonine and use a cut-off of 300 or 40ng/ml.

An intravenous dose of 20 mg cocaine can be detected for 1.5 days. Street doses (administered via different routes) are detectable up to 1 week, and

extremely high doses up to 3 weeks in urine [18].

OPIATES

Opiate refers to any drug that is derived from the opium poppy, including the natural products, morphine and codeine, and the semi-synthetic Opioid refers to any drug that reacts with the opioid receptor.

Opioid analgesics comprise a large group of substances which control pain by depressing the central nervous system.

Large doses of morphine can produce higher tolerance levels, physiological dependency in users, and may lead to substance abuse.

Morphine, the principal natural opiate, is the structural building block for many of the semi-synthetic opioids including heroin, oxycodone, oxymorphone, hydrocodone, hydromorphone and levorphanol. The majority of morphine is excreted in urine unmetabolized or as morphine-3-glucoronide. Codeine is metabolised to morphine in the liver.

Urine immunoassays for heroin are calibrated with morphine but important cross-reactivity occurs and positive results must be confirmed by GC-MS to determine which opioid group is present.

Opiates Detection Windows:
- *Morphine in Urine = 6-34hrs[10]*
- *6-Acetyl Morphine in Oral Fluid = 1-8hrs[12]*

Experimental data for total morphine using a cut-off of 300 ng/mL suggest a detection time of 1 to 1.5 days for relatively low doses of heroin (3-12 mg) administered via IV, IN or IM route.

Urine tests can detect codeine for up to 48 hours, morphine for 48-72 hours and Hydrocodone for up to 3 days.

Oral fluid tests can detect opiates within 5-10 minutes of use and for up to 24-36 hours later.

Blood tests can detect morphine for up to 6-8 hours, codeine for up to 12 hours and hydrocodone up to 24 hours.

Methadone, although a synthetic opioid, is structurally unrelated to the natural opioids.

The elimination half-life of methadone is 15-55hr, it is mainly metabolised in the liver but also in the intestines.

Patients taking methadone excrete both the parent drug and the major metabolite 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP) in urine.

In oral fluid the parent drug gives the highest concentration although both EDDP and methadol can be detected [28].

A 20ng/ml methadone oral fluid cut-off was recommended from the DRUID project for a positive result in drivers [27].

Heroin rapidly metabolises to 6-acetylmorphine and morphine. Immunoassays for heroin are calibrated with morphine but important cross-reactivity occurs and positive results must be confirmed by GC-MS.

Experimental data for total morphine using a cut-

off of 300 ng/mL suggest a detection time of 1 to 1.5 days for relatively low doses of heroin (3-12 mg) administered via IV, IN or IM route.

DECISION MAKING

For safety officers, managers and operators having a comprehensive drug and alcohol policy that fits the operational environment, risk regimes, budgets and staff lifestyle impacts is critical in determining which test procedures are appropriate.

Alcolizer Technology is a world-leader in Alcohol and Other Drugs (AOD) testing solutions and can assist in AOD policy development as well as decision-making around drugs testing procedures.

You can contact Alcolizer to discuss your specific business needs by telephone within Australia on **1300 789 908** or email contact@alcolizer.com

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ABOUT ALCOLIZER TECHNOLOGY

Alcolizer Technology is a world-leader in the provision of Alcohol and Other Drugs (AOD) testing solutions.

Headquartered in Perth with nationwide offices and certified AOD technicians and across Australia, Alcolizer is also bolstered by an established global network of distributors and Certified calibration service providers.

For 30 years Alcolizer is one of the world's leading manufacturers of alcohol breath testing and more recently, sophisticated drug testing equipment.

Alcolizer provides the complete end-to-end solution – from tailored drug and alcohol testing programs to equipment supply, education, support and expert advice.

Alcolizer is the largest provider of alcohol detection equipment to law enforcement in Australia.
Law enforcement agencies, industry and personal users trust Alcolizer to keep themselves and their employees safe.

ABOUT THE AUTHOR

Murdo Black has worked in medical diagnostics for over 30 years and is the Chief Scientist for Alcolizer Technology. Murdo resides in Dundee, United Kingdom and develops market-leading technologies at Alcolizer Technology UK.

His first degree was in Biochemistry followed by a Masters in Instrumental Methods and a PhD in Toxicology from Strathclyde University. He also has an MBA from Warwick. His diagnostic career started at MediSense where during 9 years he was in charge of next generation glucose sensors.

He moved to Hypoguard as R&D Director andled a department of 35 scientists developing electrochemical biosensors. Prior to his role with Alcolizer he was Technical Director of OxTox Ltd and prior to that, R&D Director at Axis-Shield where he launched over 16 Immunoassay products. He has in excess of 15 patents in handheld electrochemical biosensors and membrane technology.