Drugs of Abuse
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Occupational Pathology Services
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Why Implement a Drug Testing Program?

It is a legal obligation under the *Queensland Workplace Health and Safety Act 1995*, and equivalent Acts of other States and Territories (i.e. a common law duty) of all employers under their ‘Duty of Care’, to take reasonable action to provide a safe working environment to all employees and visitors to their workplace. In some industries, this has been interpreted as a requirement to establish a drug screening program. Employees too have a responsibility to ensure workplace practices are safe.

Drug and alcohol misuse is estimated to cost Australia billions of dollars annually. Recent data has demonstrated a fourfold increase in alcohol and illicit drug detection when testing is conducted on individuals involved in accidents and incidents in the workplace. Anecdotally, several of our clients have reported a reduction of 40% in worker time lost through illness and injury after introduction of a drug-free workplace policy enforced with regular testing.

Drug and alcohol testing is a method of identifying employees at risk of being impaired by drugs and alcohol. It can also be used as a deterrent as it creates a clear message that drug and alcohol abuse is unacceptable to the organisation.

Why Not Impairment Testing?

It is generally a computer-based test and assesses:

- Coordination
- Reaction time
- Perception
- Thinking skills against the worker’s previously-determined performance.

However, these tests are time consuming and do not differentiate from other ‘legal’ causes of impairment:

- Fatigue
- Poor sleep
- Medical conditions
- Stress originating outside the workplace
- Depression/anxiety/mental disorder.

There is currently no Australian Standard governing how impairment testing should be performed or interpreted.
Choice of Samples for Testing Purposes

There are several matrices (sample types) which are suitable in some circumstances for drug monitoring programs. All have their strengths and weaknesses and the choice of the particular matrix is best determined in consultation between employers, employees/unions, and WHS staff or consultants. If the industry has no previous experience with this testing, it is often advisable to contact an occupational health consultant or an accredited laboratory to obtain specific guidance regarding setting up and managing testing procedures. The mechanisms and interpretation of drug testing are not intuitive.

What matrices might be considered?

• Urine

Urine testing is by far the most widely used in industry and other medico-legal settings. Many laboratories are accredited and have years or decades of experience with collection and testing. The Standard AS/NZS 4308 dictates appropriate sample collection, handling and testing.

Urine drug testing typically detects drug use within the 3-4 days prior to sample collection. In most cases, the effect of the drug use will have abated by the time that the sample is collected. That is, urinary testing detects drug users, not subjects who are likely to be affected at the time.

• Oral Fluid (Saliva)

Considerable research has focused on the utility of saliva for the detection of recent drug use. The detection interval is generally 3 to 12 hours after last use. Contrary to statements that are frequently made, oral fluid findings do not relate directly to effect on performance. Because the detection interval is relatively short, a confirmed positive oral fluid drug screen is more likely in a subject who is affected by that drug but it is not absolutely indicative of impaired performance, nor is a negative screen indicative that performance cannot be affected by recent drug use.

With the recent release of a Standard (AS 4760) dictating appropriate collection, handling and testing of oral fluid and the accreditation of Australian laboratories to the Standard, this form of testing has gained significant credibility. However, this field is still relatively immature and experience is limited.

• Hair

Hair testing has emerged as an interesting and potentially powerful means of checking for past drug use. As a plethora of drugs are incorporated into
growing hair, this testing allows review of 6 or even 12 months prior to the time of sample collection (depending on the length of hair) and analysis of segments of the hair allow an assessment as to when over previous months drug use occurred.

However, this testing is largely limited to legal forms of drug monitoring in which it is important to determine whether a particular subject has used illicit or therapeutic substances in the recent or distant past.

It plays no role in occupational drug testing.

• Blood

Blood testing is the least used and recommended form of drug testing. The invasive nature of the collection, the need for skilled sample collectors, the risk of complications arising from collection and the relatively short detection interval ensure that this is unlikely to ever play a role in routine occupational testing.

• Breath Alcohol Testing

Breath testing is an effective and accurate way to screen for the presence of alcohol. Portable instruments provide a digital quantitative read out of alcohol concentration and experience has shown a strong correlation with blood alcohol concentrations.

The analysers are typically used for screening purposes but if disciplinary action is likely to be based on the result, an evidentiary standard analyser can and should be used unless confirmation is performed on blood collected promptly.

Alcohol testing is also performed routinely on urine and can be performed on blood if specifically requested.

In the interest of brevity, only urine and oral fluid testing will be further discussed. If further information on other forms of testing is required, this can be obtained by contacting the laboratory.

Left to right: Sample of collection kit elements: plastic urine container with temperature bar, transport tubes, tamper evident bags, security seals.
Urine and Oral Fluid

The Standards as they apply to collection and testing processes

Procedures for collection, handling, transport, on-site and laboratory initial screening, and definitive laboratory confirmation are defined in the respective Standards AS/NZS 4308 for urine and AS 4760 for oral fluid. QML Pathology is accredited to both.

Each Standard is divided into sections which cover each of the above processes. Unlike previous Standards, the current releases allow a company or laboratory to be accredited to individual sections without having to be accredited to the whole Standard. For instance, a laboratory may choose to be accredited for the definitive laboratory confirmation of findings without seeking accreditation for collection or on-site testing. Conversely, many industries are now seeking and achieving accreditation for collection and handling so as to provide a higher level of protection from claims of incorrect or inappropriate collection prior to referral for laboratory testing.

Experience shows that when action that was taken based on positive drug findings is challenged in court or in the industrial commission, the confirmed drug finding is rarely challenged. The basis for the challenge is typically incorrect collection, supervision, handling after collection or incomplete chain of custody documentation.

Collection and Handling

For both urine and oral fluid, the collection process is defined and includes photographic identification of the subject, unambiguous labelling of the sample, sealing of samples in such a fashion as to make any attempt at tampering evident and initiation of chain of custody documentation that will follow the sample through subsequent processes to ensure that the sample ultimately tested and reported upon is that which was received from the subject.

Clearly urine collection entails processes that may be seen as encroaching upon the individual’s privacy. The Standard requires the collector only to ensure that the subject’s coat or other heavy outer garments are removed, pockets emptied, that opportunity for tampering within the cubicle is minimised and that the sample integrity (temperature and creatinine) is tested immediately after collection.

With oral fluid collection these considerations generally do not arise. Privacy is less of a consideration and it is often argued that the sample is less subject to attempts at interference with findings. This contributes significantly to its rising popularity but it must be emphasised that despite the relatively limited history of this testing, it is already clear that tampering to avoid detection of recent drug use is happening.
Collection may take place either at a QML Pathology collection centre or a suitable facility on the worksite. The most appropriate site will depend on a number of factors (e.g., physical privacy, suitable facilities etc.) and is generally decided following consultation with the laboratory.

A Chain of Custody Form is initiated by both the collection supervisor and donor (employee). This is a legal document for recording the donor details, person supervising the collection, sample temperature, and personnel handling the sample at all critical stages of transport and testing, and other relevant information.

With urine testing, collection requires access to a toilet facility that provides suitable individual privacy. The employee is requested to provide a minimum of approximately 40 mL urine. The sample is passed directly into a fresh purpose-designed, unused plastic container to which a temperature strip is attached. This is handed directly to the person supervising the collection process who will note and record the temperature. The current Standard also requires creatinine to be tested or noted, and the result recorded.

With urine and oral fluid, the sample may be transferred to two or three plastic transport tubes, which are sealed in individual tamper-evident bags for transport to the laboratory. Conversely, the initial collection vessel may if suitable be sealed and transported.

A Drug Information Sheet may also be completed by the donor. This requests all recent prescribed and over-the-counter medications as well as illicit drugs taken during the past week. The information assists with the interpretation of any drug test findings.

The entire process to this point must be witnessed by the donor (employee).

Only one employee at a time should be processed by each collection supervisor to minimise errors and to maintain donor privacy.
Sample Tampering

Urine
There are numerous means by which a urine specimen might be interfered with in order to avoid a positive result. These include sample substitution (the substitution of ‘clean’ urine for that of the test subject) and sample tampering (e.g., by dilution or adulteration of the sample). Hence, procedures and tests are in place to either reduce the chances of interfering with samples or to detect the presence of an adulterant:

The QML Pathology Level 3 supervision protocol is designed to comply with the Standard and to minimise the possibility of inappropriate collection:

Level 3: Collector asks donor to remove coats etc., and empty pockets, but waits outside the cubicle while the donor passes the urine. Sources of water inside the cubicle will be ‘sealed off’ or coloured.

The temperature of the sample is noted and recorded within 4 minutes of passage. If it is outside of the normal physiological range of 33°C to 38°C, a repeat collection is requested. Urinary creatinine is tested on-site and the result recorded on the Chain of Custody Form.

If the initial testing is performed in the laboratory, a number of tests are routinely carried out to determine the likelihood of sample tampering (urine creatinine, testing for the addition of foreign interfering substances/adulterants).

Many products promoted as being able to ‘mask’ the presence of a particular prohibited substance in urine predominantly rely on the associated ingestion of copious quantities of fluid. This has the effect of diluting any urine sample, such that any substance in the urine is present in a decreased concentration. However, unusually dilute urine is identified via the laboratory measurement of creatinine.

Oral Fluid
The above considerations regarding privacy and potential for tampering apply less to the collection of oral fluid but with growing experience, we are aware of a number of methods that are being used to tamper with oral fluid findings. At the time of writing, no adulterant agents have been found to be effective.
The Testing Process

For both urine and oral fluid, drug testing is usually a two-step process – the screening test and the confirmatory test.

The screening step may be performed on-site at the workplace and provides a relatively quick and inexpensive process to establish whether a drug or drug class, is likely to be present in a given specimen. Immunoassay is the most common screening methodology employed. The results are expressed as 'non-negative' or 'negative'. The former term is equivalent to 'unconfirmed positive', an older term which is no longer encouraged.

Screening by Immunoassay

Essentially, the process involves using antibodies to detect the presence or absence of drugs in the sample. The specimen is compared to a calibrator (standard), which contains a known quantity of the drug being tested. Screening tests are relatively inexpensive and have a rapid turnaround time for results. However, the downside is that they are not designed to be definitive.

The two limitations of screening tests are specificity and cross-reactivity.

- Specificity refers to the extent to which the test can discriminate between different drugs of similar chemical structure. That is, screening tests can only identify classes of drugs and not the specific chemical component. For example, a positive screen for opiates does not distinguish whether the specific chemical component present is codeine or morphine, or both. Screening tests provide no information when attempting to identify the specific kinds of opiates, amphetamines and benzodiazepines present in the sample.

- Cross-reactivity occurs when the test is unable to distinguish between substances that are therapeutically unrelated but chemically similar. For example, the amphetamine assay will detect the over-the-counter sympathomimetic amine medications such as pseudoephedrine, as well as phenylethylamine (found in trace amounts in fermented products).

Therefore, as screening tests have less specificity and hence a higher potential for false positive results, it is essential that non-negative tests be viewed as presumptive, and that the sample be retested using a confirmatory assay.

Confirmation Testing

The confirmation test is a second test on the same sample, and is usually only performed if the screening test indicates the possible presence of a drug. It is a more sensitive and specific method for the detection of the desired substance and is not subject to the interferences associated with the immunoassay test. That is, the purpose of confirmation is to eliminate any false positive results that may have originated from the initial screen.
Gas chromatography/mass spectrometry (GCMS) and liquid chromatography/mass spectrometry (LCMS) are the methods of choice and are accepted by the courts as the ‘gold standard’. These identify a specific compound by its characteristic ‘fingerprint’, which is termed a ‘mass spectrum’. The method is specific and sensitive to very small quantities of the substance being tested. This testing is more time-consuming, more technically complex, requires sophisticated instrumentation, and is more expensive than screening tests.

**Cut-off Levels**

Each immunoassay screen and confirmation test has a corresponding ‘cut-off’ level, specified in the relevant Australian Standard. The ‘cut-off’ level is the administrative breakpoint above which the drug test is deemed ‘non-negative’ and below which the drug test is deemed ‘negative’. It is important to note that a ‘non-detected’ result only implies that no drug was detected at or above the corresponding cut-off level. The cut-off concentrations (levels) reflect an intention to minimise frankly erroneous findings (the risk of non-specific reactions is more likely at low levels) and to overlook ‘historical’ positive tests (i.e., findings reflecting drug exposure months before the present).

These cut-off levels are listed in Appendices A (urine) and B (oral fluid).

In addition to the above classes of drugs that have cut-off levels assigned by Standards Australia, the following classes may also be requested:

- Ethanol
- Phencyclidine
- Barbiturates
- Methadone and others.

There are a small number of abused substances that are not detectable in any routine laboratory testing regime. We avoid publishing these as a list may be seen as a guide to use of undetectable drugs. For further information, please contact the Central Laboratory on (07) 3121 4444.

**Why Test Urine For Creatinine?**

Creatinine is a muscle breakdown product, which is normally excreted in the urine at a relatively constant rate. Therefore, the urine creatinine level changes as the urine becomes more dilute (lower creatinine level) or more concentrated (higher creatinine level). Specifically, the urine will be more dilute following the ingestion of large amounts of water. A specimen is considered dilute when the creatinine level is less than 1.8 mmol/L. Similarly, dilute samples will have a lower concentration of drugs. For reference, the usual range for urinary creatinine is 5 - 15 mmol/L, but a higher or lower result is not regarded as abnormal; it simply indicates that the subject has consumed less or more water than the average.
Urine creatinine levels may also be used to assist in determining if a user has ceased using a drug with a prolonged clearance phase. For example, the THC level in the urine reflects marijuana use, but it will also fluctuate with the overall concentration of the urine. The urine THC/creatinine ratio should decrease over time when there is no new use of the drug.

**Interpretation of Results**

A sample reported confirmed positive contains the indicated drug and/or metabolite(s) at or above the cut-off level for that drug. A negative sample either contains no drug or contains a drug below the cut-off level.

There are several parameters, however, that a positive result cannot resolve:

- The amount of drug ingested
- The exact time of ingestion
- The route or mode of ingestion (i.e., oral, snorting, intravenous injection, smoking, etc.)
- The frequency of ingestion
- The purity of drug ingested
- Whether ingestion was deliberate, accidental; unknowing or legitimate
- Whether an individual was ‘under the influence’ at the time of sample collection.

Legitimate use: It must be recognised that some of the drugs for which we test have legitimate medical usage in this country. Codeine is a commonly prescribed drug. Cocaine is used as a topical anaesthetic in certain legitimate medical procedures.

Amphetamine and morphine (oral forms) have legitimate therapeutic applications and are available by prescription.

**Over the Counter Medications**

A large number of over the counter non-prescription medications may produce non-negative initial drug screens. For example, the following medications contain compounds (underlined) that will be detected by an immunoassay screen:

- ACTIFED: pseudoephedrine, triprolidine
- CODRAL, PANADEINE, MERSYNDOL: paracetamol, codeine
- ASPALGIN: aspirin, codeine
- PANADOL DAY & NIGHT: paracetamol, pseudoephedrine
- DEMAZIN: dextchlorpheniramine, pseudoephedrine
Confirmation by gas chromatography/mass spectrometry is therefore essential in assisting the differentiation of legitimate from illicit drugs. It should also be noted that the urinary or oral fluid presence of a drug does not necessarily relate to the degree of impairment of performance being demonstrated by an individual.
**Detection Times**
The table below was published in July 2003 by the National Institute on Drug Abuse (NIDA) and adapted to reflect local experience and conditions.

### Commonly Abused Drugs

<table>
<thead>
<tr>
<th>Substance</th>
<th>Proprietary or Street Names</th>
<th>Medical Uses</th>
<th>Route of Administration</th>
<th>Drug Detection Times in Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stimulants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphetamine</td>
<td>Biphetamine, Dexedrine; Black Beauties, Crosses, Hearts, Speed, Uppers</td>
<td>Attention deficit hyperactivity disorder (ADHD), narcolepsy</td>
<td>Injected, oral, smoked, sniffed</td>
<td>3-4 days</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Coke, Crack, Flake, Rock, Snow, Blow, Candy, Charlie</td>
<td>Local anaesthetic, vasoconstrictor</td>
<td>Injected, smoked, sniffed</td>
<td>3-4 days</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>Desoxyn: Crank, Crystal, Glass, Ice, Speed</td>
<td>No legal use in Australia</td>
<td>Injected, oral, smoked, sniffed</td>
<td>3-4 days</td>
</tr>
<tr>
<td>Nicotine</td>
<td>Habitrol patch, Nicorette gum, Nicotrol spray, Prostep patch: Cigars, Cigarettes, Smokeless tobacco, Snuff, Spit tobacco</td>
<td>Treatment for nicotine dependence</td>
<td>Smoked, sniffed, oral, transdermal</td>
<td>1-2 days</td>
</tr>
<tr>
<td><strong>Hallucinogens &amp; Other Compounds</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LSD</td>
<td>Acid, Microdot</td>
<td>None</td>
<td>Oral</td>
<td>Test not available</td>
</tr>
<tr>
<td>Amphetamine Variants</td>
<td>DOB, DOI, DOM, MDA, MDMA; Adam, Ecstacy, STP, XTC, X</td>
<td>None</td>
<td>Oral</td>
<td>1-2 days</td>
</tr>
<tr>
<td>Marijuana (Cannabis)</td>
<td>Blunt, Grass, Herb, Pot, Reefer, Dope, Skunk, Smoke, Weed</td>
<td>None</td>
<td>Oral, smoked</td>
<td>3-4 days if light user 3-4 weeks if heavy user</td>
</tr>
<tr>
<td>Substance</td>
<td>Proprietary or Street Names</td>
<td>Medical Uses</td>
<td>Route of Administration</td>
<td>Drug Detection Times in Urine</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------</td>
<td>--------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td><strong>Opioids &amp; Morphine Derivatives</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>Tylenol w/codeine, Robitussin A-C, Panadeine, Mersyndol, Nurofen Plus, Fiorinal w/codeine</td>
<td>Analgesic, antitussive</td>
<td>Injected, oral</td>
<td>3-4 days</td>
</tr>
<tr>
<td>Heroin</td>
<td>Diacetylmorphine; Horse, Smack</td>
<td>None</td>
<td>Injected, smoked, sniffed</td>
<td>3-4 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>Physeptone Biodone forte</td>
<td>Analgesic, treatment for opiate dependence</td>
<td>Injected, oral</td>
<td>1 day - 1 week</td>
</tr>
<tr>
<td>Morphine</td>
<td>Kapanol, MS Contin</td>
<td>Analgesic</td>
<td>Injected, oral, smoked</td>
<td>3-4 days</td>
</tr>
<tr>
<td><strong>Depressants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Amytal, Seconal, Phenobarbitone; Barbs</td>
<td>Anaesthetic, anticonvulsant, hypnotic, sedative</td>
<td>Injected, oral</td>
<td>2-10 days</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Ativan, Librium, Valium, Serepax, Temaze, Xanax, Roofies, Sleeping pills</td>
<td>Antianxiety, anticonvulsant, hypnotic, sedative</td>
<td>Injected, oral</td>
<td>1-6 weeks</td>
</tr>
</tbody>
</table>

The above time frames are general estimates and are influenced by any or all of the following:

- Amount of drug ingested
- Frequency of drug usage
- Fluid intake
- Positive cut-off level of initial screen
- Individual metabolism rates
- pH of urine
- Mode of ingestion.

The higher the dose of drug taken and the greater the frequency of use, the more likely it is to be detected. Although drugs are excreted over varying lengths of time, some may accumulate in the body with continued use.
Drug Classes - A Brief Overview

Benzodiazepines

Classified as central nervous system depressants, benzodiazepines are prescribed therapeutically to produce sedation, induce sleep, manage anxiety, relieve muscle spasms and to prevent seizures. As many as 2000 have been synthesised and are relatively free of dangerous acute toxic overdose effects. They include drugs such as diazepam (Valium), oxazepam (Serapax) and clonazepam (Rivotril).

Flunitrazepam, which produces diazepam-like effects, had become increasingly popular among young people as a drug of abuse and was referred to as one of the ‘date-rape drugs’. The common trade name, Rohypnol, has been withdrawn from the market but the drug remains available with prescription under other trade names.

This class of drugs is minimally secreted into oral fluid. This consideration, as well as their being frequently used on prescription, has led to their omission from the oral fluid detection panel.

Cannabinoids

Marijuana, from the hemp plant Cannabis sativa, is reported to contain at least 61 compounds collectively known as cannabinoids, of which ∆⁹-tetrahydrocannabinol (THC) is the primary psychoactive compound. Cannabinoids are ingested primarily for their euphoric and relaxation effects. The initial immunoassay drug screen is sensitive to many of the cannabinoids, while the confirmation test looks for only one characteristic metabolite; 11-nor-∆⁹-tetrahydrocannabinol-9-carboxylic acid (THC-COOH).

THC is quickly absorbed into the systemic circulation from inhaled smoke. The detection time frame of cannabinoids may vary considerably depending upon a number of influences. One of these influences is the lipophilic property of cannabinoids. This means that cannabinoids are, to a certain extent, deposited in the body's fatty tissues and gradually released over time. Thus, chronic users may continue to excrete cannabinoids in the urine in detectable quantities for as long as six weeks after cessation of drug use. Conversely, cannabinoids may be cleared only after two days, using a 50 µg/L cut-off, from the urine of a naive user who smokes one marijuana cigarette. Consequently, it is difficult to draw conclusions concerning an individual's marijuana usage based on a single random urinalysis.

Passive Inhalation

A frequent excuse to explain a THC positive in urine is passive inhalation. This is a term used to describe the inhalation of atmospheric or room air in a closed space, by an individual present where marijuana is being smoked by others. These situations may include an automobile, rock concert or party.
Scientific studies performed to establish the validity of passive inhalation causing a positive THC urine test conclude that it is an unlikely excuse (even under unrealistic contrived conditions) when the 50 µg/L screen level is used. Cannabis too is minimally secreted into oral fluid but due to its resinous nature it coats teeth, gums etc., after use and dilutes off over several hours. Vigorous mouth cleansing (e.g., toothbrush, hand towel) will substantially shorten the detection interval after use.

**Sympathomimetic Amines (Amphetamines)**

Amphetamines and amphetamine derivatives are classified as sympathomimetic amines with central nervous system (CNS) stimulant activities. The term sympathomimetic amines (SMAs) generally refers to several compounds that are related chemically and pharmacologically to naturally occurring epinephrine and norepinephrine, and are chemically of the phenylethylamine class of drugs.

The amphetamines (amphetamine, methamphetamine, phentermine, and the structurally related designer drugs, e.g., Ecstasy) are CNS stimulants that increase wakefulness and suppress appetite, at the same time causing a sense of increased energy, self-confidence, well-being and euphoria.

The rate of metabolism and excretion is dependent on the urinary pH: Acidic urine increases (e.g., amphetamine: up to 78% / 24 h, 68% unchanged), alkaline urine decreases the excretion (45% / 24 h, 2% unchanged).

44% of methamphetamine is excreted unchanged, 6-20% as amphetamine and 10% as 4-hydroxymethamphetamine. It is generally detected as the parent drug in oral fluid for 6-8 hours after use.

**Ecstasy (MDMA), MDA, MDEA**

The most prominent members of this group of methylenedioxy-amphetamines known as designer drugs are:

- MDA (methylenedioxyamphetamine)
- MDMA (3,4-methylenedioxymethamphetamine) or commonly referred to as Ecstasy
- MDEA (methylenedioxyethylamphetamine).

The effects of these drugs are similar to those of amphetamine and methamphetamine.

**Cocaine**

Cocaine is a powerfully addictive drug of abuse. The major routes of administration of cocaine are sniffing or snorting, injecting, and smoking (including free-base and crack cocaine). ‘Crack’ is the street name given to cocaine that has been processed from cocaine hydrochloride to a free base for smoking.
Cocaine is a strong central nervous system stimulant. Physical effects of cocaine use include constricted peripheral blood vessels, dilated pupils, and increased temperature, heart rate, and blood pressure. The duration of cocaine’s immediate euphoric effects which include hyperstimulation, reduced fatigue, and mental clarity, depends on the route of administration.

The main metabolites are benzoylecgonine and ecgonine methylester, resulting from enzymatic (pseudocholinesterase) or spontaneous hydrolysis. Anhydroecgonine methylester is a specific marker of ‘crack’ consumption. Cocaethylene is detected after simultaneous use of cocaine and alcohol.

Cocaine too is generally detected as the parent drug in oral fluid for 6-8 hours after use.

**Opiates**

The naturally occurring opiates such as codeine and morphine, are derived from the unripe pods of the opium poppy (*Papaver somniferum*). Codeine and morphine, used in prescriptive drugs, are analgesics (pain reducers), which act on the central nervous system and can depress the respiratory system. They are also precursors for the notable semi-synthetic drugs; heroin, hydrocodone, hydromorphone, oxycodone.

**Codeine** is excreted in urine as free and conjugated codeine (approx. 80%), and free and conjugated morphine (approx. 15%). After codeine administration the urinary codeine/morphine ratio is generally greater than 1.0 within the first 24 hours, but will fall often below 1.0 between 24 – 30 hours. As codeine may be eliminated faster than morphine, some urine samples may show only the presence of morphine after 36 – 48 hours.

**Morphine** is excreted in urine mainly as conjugated morphine (60 – 80%). Depending on the dose, morphine may be detected in urine up to 72 hours after last administration of either morphine, codeine or heroin.

**Heroin** (diacetylmorphine, diamorphine) is rapidly metabolised to 6-monoacetylmorphine (6-MAM), which is further degraded and excreted in urine principally as conjugated morphine. It is considered that 6-MAM and morphine, account for most of the narcotic activity of heroin. Because 6-MAM is a metabolite unique to heroin, its presence may be regarded as evidence of recent heroin use. However, the absence of 6-MAM does not exclude the use of heroin.

Elimination half-life:

- 3 - 20 min (diacetylmorphine)
- 9 - 40 min (6-monoacetylmorphine)
- 1 - 7 hours (morphine).
Again, heroin, morphine and codeine are generally detected as the parent drug in oral fluid for 6-8 hours after use, however, it is possible that heroin users may show only morphine in oral fluid toward the end of this detection window.

**The Effect of Poppy Seeds**

The scientific literature has clearly shown that ingestion of poppy seeds, contained in curries and bakery products such as bagels, can produce measurable urine concentrations of morphine and codeine for periods of up to 36 hours. Poppy seeds are coated with the plant liquor of the opium poppy, which contains morphine and some codeine. Washing and heating the poppy seeds does not remove all of the opiate coating.

Generally, high levels of codeine above the morphine level, indicates codeine ingestion. However, elimination of morphine following codeine use, long after the codeine was taken, may reveal only morphine. Nevertheless, interpretation of urinary opiate results can be complex.

It would not be unusual for ingestion of a single bagel containing poppy seeds to produce a urine opiate level of approximately 300 ug/L within three to four hours. A negative urine opiate would be expected within 12 – 24 hours. Also, the amount of opiates present in poppy seeds varies with the origin of the seeds.

Although thebaine is a natural constituent (and hence a marker) of poppy seeds, the concentration is variable and such that it is below the limit of detection of many analytical systems.

An in-house trial has recently demonstrated that poppy seed positives can be seen in oral fluid for up to 4 hours after ingestion.
Our Credentials - Corporate Information

QML Pathology has offered a drug screen service for over 18 years and has continually kept abreast of current requirements and trends.

Drug Screen Services Offered by QML Pathology

The drugs of abuse occupational screening and confirmation service offered by QML Pathology includes supply of the following options, allowing us to customise the drug testing program to specific requirements:

- Chain of Custody Forms coupled with strict conformation to chain of custody procedures
- Tamper-evident urine collection kits
- Specific pre-printed QML Pathology request forms
- On-site screening test kits
- On-site urine collection
- Staff training in collection procedures
- Specimen collection arrangements to suit individual client needs
- Adherence to Australian Standard AS/NZS 4308 and AS 4760
- Testing for adulterants
- Confirmation of positive results by legally defensible state-of-the-art technique (GCMS and LCMS)
- A Chemical Pathologist available for consultation, and where necessary for an additional fee, as an expert witness in cases of litigation
- Range of pricing and billing options
- Results available via post, electronic dispatch, facsimile to the nominated Medical Practitioner and/or Occupational Health and Safety Officer.

Corporate Accreditations

QML Pathology is formally accredited by NATA for drugs of abuse testing in accordance with AS/NZS 4308 and AS 4760 guidelines.

In addition, QML Pathology has ISO/IEC 17025 accreditation and participates in all Australian-based drug testing quality assurance programs:

- AUSTOX Urine Toxicology Proficiency Program
- RCPA-AACB Urine Toxicology Program
- TOXI-LAB Proficiency Testing Program.
Personnel Accreditations
The Director of Biochemistry/Toxicology (Dr C Appleton) and our other Chemical Pathologist (Dr J Chang) are medically qualified doctors (MBBS) who have obtained further specialist qualifications in Chemical Pathology (FRCPA). Scientific staff are tertiary qualified.

Confidentiality
All QML Pathology employees are required to sign a confidentiality agreement acknowledging the sensitive and confidential nature with which they may come into contact during their work. Policies and procedures relating to confidentiality are strictly enforced.

Further Information

Australia

Australian Drug Information Network (ADIN)
ADIN provides a central point of access to quality Internet-based alcohol and drug information provided by prominent organisations in Australia.

http://www.adin.com.au

DRUG-ARM (Drug Awareness, Rehabilitation and Management)
DRUG-ARM is a non-government, non-profit organisation committed to the promotion of a healthy lifestyle without the use of unnecessary drugs.

http://www.drugarm.com.au

International

National Institute on Drug Abuse (NIDA)
A part of the U.S. National Institutes of Health, Department of Health and Human Services. The Institute is organised into divisions and offices, each of which plays an important role in programs of drug abuse research.

http://www.nida.nih.gov

Substance Abuse and Mental Health Administration (SAMHSA)
An Agency of the U.S. Department of Health and Human Services charged with improving the quality and availability of prevention, treatment, and rehabilitative services in order to reduce illness, death, disability, and cost to society resulting from substance abuse and mental illnesses.

http://www.samhsa.gov

There are numerous Internet sites claiming to offer advice and products to assist in avoiding detection of drugs of abuse. The information provided is often inaccurate and may bear no relevance to Australian testing standards.
### APPENDIX A: Urine Cut-off Values

#### AS/NZS 4308:2008 Initial Test Cut-off Concentrations

<table>
<thead>
<tr>
<th>Substance</th>
<th>Cut-off Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis metabolites</td>
<td>50 µg/L</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>200 µg/L</td>
</tr>
<tr>
<td>Cocaine metabolites</td>
<td>300 µg/L</td>
</tr>
<tr>
<td>Opiates</td>
<td>300 µg/L</td>
</tr>
<tr>
<td>Amphetamine type substances</td>
<td>300 µg/L</td>
</tr>
</tbody>
</table>

#### AS/NZS 4308:2008 Confirmatory Test Cut-off Concentrations

<table>
<thead>
<tr>
<th>Substance</th>
<th>Cut-off Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis metabolite</td>
<td></td>
</tr>
<tr>
<td>11-nor-(9)-tetrahydrocannabinol-9-carboxylic acid (THC-COOH)</td>
<td>15 µg/L</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td></td>
</tr>
<tr>
<td>Nordiazepam</td>
<td>200 µg/L</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>200 µg/L</td>
</tr>
<tr>
<td>Temazepam</td>
<td>200 µg/L</td>
</tr>
<tr>
<td>Diazepam</td>
<td>200 µg/L</td>
</tr>
<tr>
<td>α-hydroxy-alprazolam</td>
<td>100 µg/L</td>
</tr>
<tr>
<td>7-amino-clonazepam</td>
<td>100 µg/L</td>
</tr>
<tr>
<td>7-amino-flunitrazepam</td>
<td>100 µg/L</td>
</tr>
<tr>
<td>7-amino-nitrazepam</td>
<td>100 µg/L</td>
</tr>
<tr>
<td>Cocaine metabolites</td>
<td></td>
</tr>
<tr>
<td>Benzoylecgonine</td>
<td>150 µg/L</td>
</tr>
<tr>
<td>Ecgonine methyl ester</td>
<td>150 µg/L</td>
</tr>
<tr>
<td>Opiate metabolites</td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>300 µg/L</td>
</tr>
<tr>
<td>Codeine</td>
<td>300 µg/L</td>
</tr>
<tr>
<td>6-monoacetylmorphine</td>
<td>10 µg/L</td>
</tr>
<tr>
<td>Sympathomimetic amines</td>
<td></td>
</tr>
<tr>
<td>Amphetamine</td>
<td>150 µg/L</td>
</tr>
<tr>
<td>Methylamphetamine</td>
<td>150 µg/L</td>
</tr>
<tr>
<td>Methylenedioxyamphetamine (MDMA)</td>
<td>150 µg/L</td>
</tr>
<tr>
<td>Methylenedioxymethamphetamine</td>
<td>150 µg/L</td>
</tr>
<tr>
<td>Phentermine*</td>
<td>500 µg/L</td>
</tr>
<tr>
<td>Ephedrine*</td>
<td>500 µg/L</td>
</tr>
<tr>
<td>Pseudoephedrine*</td>
<td>500 µg/L</td>
</tr>
<tr>
<td>Benzylpiperazine*</td>
<td>500 µg/L</td>
</tr>
</tbody>
</table>

*These drugs are optional in the confirmation testing.
#APPENDIX B: Oral Fluid Cut-off Values

<table>
<thead>
<tr>
<th></th>
<th>Initial Immunoassay Test Target Concentrations</th>
<th>Confirmatory Target Concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AS 4760-2006</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opiates</td>
<td>50 ng/mL</td>
<td>Morphine</td>
</tr>
<tr>
<td>Amphetamine-type stimulants</td>
<td>50 ng/mL</td>
<td>Codeine</td>
</tr>
<tr>
<td>Δ⁹-tetrahydrocannabinol (THC)</td>
<td>25 ng/mL</td>
<td>6-Acetyl morphine</td>
</tr>
<tr>
<td>Cocaine and metabolites</td>
<td>50 ng/mL</td>
<td>Amphetamine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methylamphetamine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methylenedioxymethylamphetamine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methylenedioxyamphetamine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Δ⁹-tetrahydrocannabinol (THC)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cocaine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Benzoylecgonine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ecgonine methyl ester</td>
</tr>
</tbody>
</table>


APPENDIX C: Assay Methodology

Immunoassay
Essentially, the process involves using antibodies to detect the presence or absence of targeted compounds, such as drugs. However, antibodies used in immunoassays often cannot recognise subtle differences in chemical structure between the targeted drugs (and their metabolites) and analogous compounds. Analytical specificity is therefore a major challenge for drug testing. Pharmaceuticals and other substances with structures similar to those of the target drugs are often detected by immunoassays, even though they are not members of the drug group of interest.

Owing to the inherent limitations of immunoassay screening, particularly in the area of specificity, it is recommended all positive urine drug tests be confirmed by a more definitive and legally defensible procedure, such as Gas Chromatography/Mass Spectrometry (GCMS). This confirmation test is intended to determine whether the drug or drugs in question are present in the sample and were responsible for the initial test result, or whether that result is traceable to an interfering drug or metabolite. Confirmation analysis must involve retesting a sample that was presumptively positive on the initial test, not collecting and testing a new sample from the donor.

Gas Chromatography/Mass Spectrometry (GCMS)
GCMS is a two-step process, where GC separates the sample into its constituent parts, while MS provides the exact molecular identification of the compounds. Compounds are separated by GC and are then introduced, one at a time, into a mass spectrometer. As the sample constituents enter the MS they are bombarded by electrons, which cause the compound to break up into molecular fragments. The fragmentation pattern is reproducible and characteristic, and is considered the ‘molecular-fingerprint’ of a specific compound. GCMS is considered to be the most definitive method for confirming the presence of a drug in the urine and is approximately 100 to 1,000 times more sensitive than Thin Layer Chromatography (TLC).

Thin Layer Chromatography (TLC)
TLC testing is based on the differences in the migration rate of various substances through a porous supporting medium. The degree of migration and the colour are characteristic of certain drugs. TLC can demonstrate the presence of a drug, but this procedure can only at best, semi-quantitatively estimate the quantity of drug present.

QML Pathology utilises a commercial TLC system, TOXILAB®, which is a standardized thin layer chromatography system for broad spectrum and specific analyte screening. There are over 700 drugs and their metabolites documented in the TOXILAB® System.
This Information Booklet has been prepared and published by QML Pathology for the information of referring Doctors and corporate clients. Although every reasonable effort has been made to ensure that it is free from error or omission, readers are advised that it is not a substitute for detailed professional advice.