On-site drug testing

O. H. DRUMMER

Victorian Institute of Forensic Medicine and Department of Forensic Medicine, Monash University, Southbank, Australia

ABSTRACT

Drug testing outside the laboratory environment has become widespread and provides presumptive results within minutes of collection of the specimen. This has become particularly useful for testing of urine and oral fluid. Applications include workplaces where drug use has safety implications, drivers of vehicles at the roadside and situations where drug impairment is suspected. The present article explores the relative advantages of this form of testing for the specimens that can be collected and discusses issues such as cut-offs, the need for laboratory confirmation and safeguards to ensure legal defensibility.

Keywords: on-site drug testing; cut-offs; initial tests; confirmatory tests; quality management

Introduction

In recent years drug testing has undergone a technological revolution. Drug testing has become more sensitive and more flexible. New confirmation techniques have also become available for laboratory-based testing. In addition, the number of kits for initial testing (often called "initial screening"*) has increased and these are now widely used. In particular, kits are now designed for on-site drug detection without the need for sophisticated laboratory screening equipment and are able to provide a presumptive (unconfirmed) drug result within minutes. However, such devices do have their limitations, which should be recognized before a decision is made to replace laboratory-based screening with on-site testing (also known as "point-of-care" testing).

The present article outlines the roles and applications of on-site testing for drugs of abuse and describes the relative advantages and disadvantages of this form of testing compared with laboratory testing. The focus is on testing for drugs controlled under the international drug control conventions. The article does not cover clinical applications of on-site drug testing for therapeutic substances, but includes a review of the specimens that can be used with this application.

*The process of testing a specimen for the presence of drug or metabolite using non-specific class tests.

Applications

On-site testing spans a range of applications that are similar to laboratory-based testing. Primarily it provides a rapid presumptive drug result at the site where drug use is not desired. This may be a workplace where testing is conducted on a random basis or following an incident or it may be at the roadside and involve the driver of a motor vehicle. Other applications include testing of inmates of prisons and other correctional institutions and monitoring by drug courts of efforts of former drug abusers to abstain from abusing drugs.

One of the most frequently conducted on-site drug tests is for alcohol (ethanol). Breath tests are commonplace throughout the world and, depending on the device used, are considered a reliable indication of the presence of alcohol in the body.

A result that can be obtained in this way for abused drugs can assist the employer, medical practitioner or other authority in deciding if drug use may have adversely affected a person or indicate that the person is a drug abuser. It must be stressed that the on-site test result may not be confirmed by subsequent laboratory analysis and is by definition an unconfirmed positive. While this does not occur too often, users of on-site testing should ensure that they have performed a thorough risk analysis on the application of this form of testing, as opposed to laboratory-based testing, which may take a day or more to produce a result.

Specimens

The specimens primarily used for on-site testing are oral fluid (saliva) and urine. The relative advantages of these types of specimen are listed in table 1. They have also been described elsewhere [1-3].

Table 1. Relative advantages and disadvantages of on-site specimens

Urine	*Oral fluid*
Large volume (up to 50 ml)	Limited volume (up to 1 ml); sometimes not collectable in a reasonable time frame
Privacy issues for collection; requires a toilet	Few (if any) privacy issues
Significant potential for adulteration or substitution	Low potential for adulteration and substitution, although can be affected by pH changes, food debris and rinsing with fluids
Metabolites predominately detected	Parent drugs predominately detected
Drug data reflect only past use	Drug data usually reflect recent use

Urine has been the specimen taken most frequently for on-site drug analysis. Its main application is detection of past use of abused drugs. For most drugs, this means that a result reflects use, or abstinence, for 1-3 days, although in the case of cannabis, excretion of cannabinoids can occur for a period ranging from many days to weeks after last use, depending on the amount and frequency of exposure. Table 2 summarizes the approximate detection times for commonly abused drugs in urine and oral fluid.

Table 2. Approximate detection times of selected drugs in urine and oral fluid

	Detection time (days)[b]	
Drug[a]	*Urine*	*Oral fluid*
Amphetamine	1-3	1
Methamphetamine	1-3	1
MDMA[c]	1-3	1
Cocaine	1-2	<1
Morphine	1-3	<1
Cannabis	3-4	<1
Diazepam	7-21	1-3

[a]Data refers to the main type found in the respective specimen.
[b]Detection times will vary depending on amount used and duration of exposure.
[c]Methylenedioxymethamphetamine, commonly known as Ecstasy.

Urine output and subsequently drug concentration is subject to considerable variation. Of most importance is the degree of hydration and overall kidney function of a person. Persons who are mildly or substantially dehydrated will have much more concentrated urine than persons who are much more hydrated. This will be reflected in the concentration of the drug in the urine at any part of the excretion profile of a substance. People who load themselves with large amounts of water (>1,000 millilitres (ml)) shortly before a urine test for drugs can reduce the concentration of drug to below the cut-off* levels applied for detection of drugs in urine. The measurement of urinary creatinine and/or specific gravity (SG) can be used to monitor for this possibility. For example, creatinine concentrations of less than 200 milligrams (mg) suggest diluted urine, as does a low SG (less than 1.0030). For this reason it is usual to conduct validity tests on urine to ensure that no adulteration has occurred. Such validity tests can also include colour of urine, pH of urine and tests for substances added to urine to potentially affect the drug screening process, including oxidizing agents such as glutaraldehyde, chromium, nitrite and halogens. Most of these factors can now be screened for on-site using multifunctional test strips.

*A cut-off is a threshold concentration above which drug presence is reported.

Sometimes pathological changes will contribute to unusual drug concentrations in urine. All results should therefore be reviewed by a medical officer or other suitably qualified person before a result leads to an action against a person.

Oral fluid (saliva) is excreted primarily by three glands, the parotid, the submaxillary and the sublingual, and also by other smaller glands. Oral fluid has a low protein content (5 per cent of plasma) and can vary in flow rate from zero to several ml/minute (min) depending on various factors, including emotional state and hunger. A review on the physiology of oral fluid is available [4].

Oral fluid can be collected less invasively than urine, in that privacy issues are not involved. The subject can either take a specimen him/herself or allow a collector to take the fluid without regard to privacy issues. The collection of oral fluid can occur through use of an absorbent sponge or wad placed in the mouth for a short time, usually one or several minutes, depending on the amount of fluid in the oral cavity. In some cases a simple "swipe" on the surface of the tongue or inside the cheek can provide an adequate sample for on-site analysis. Since the specimen can be viewed by a second person while it is collected, issues such as potential adulteration are less of an issue than for urine, although it is still possible that the oral cavity can be treated with some substance prior to collection in order to affect the amount or composition of the oral fluid itself.

It may happen that oral fluid cannot be collected within a few minutes because of a dry mouth. People can experience a dry mouth if they are dehydrated or nervous. Alternatively, drugs such as cannabis and the amphetamines can also cause a dry mouth.

Cut-off and threshold concentrations

Cut-off concentrations are applied to immunoassay initial testing methods. For example, a positive result for cannabinoids (i.e. >50 ng/ml cut-off) in urine will require confirmation by gas chromatography/mass spectrometry (GC/MS). Any result below this cut-off is reported as "not detected". A "not detected" result implies only that no drug was detected at or above the cut-off value chosen. The choice of a lower cut-off value or the use of a more sensitive assay that has a lower threshold concentration may subsequently detect the presence of drug.

Any programme designed to detect drugs will need to take into account the concentrations of drugs that can be detected with reasonable reliability. On-site devices are no different from laboratory-based initial tests in that the detectability of drugs in a particular specimen will vary from drug to drug and also between commercial products. This is further compounded by the lack of international harmonization of cut-offs [5]. For example, the initial screening cut-offs for opiates may vary from 300 ng/ml (Australia, Europe) to 2,000 ng/ml (United States of America). The choice of a higher cut-off for opiates (i.e. 2,000 ng/ml) has the advantage of reducing the detection of codeine users that are ordinarily not an interest group as distinct from persons using heroin. For heroin users, 6-acetylmorphine can be monitored in urine as a specific marker for heroin use.

For class tests* not all members of the family will have similar detection limits for all drugs within the class. For example, for amphetamines, opiates and benzodiazepines classes, the sensitivities of the initial test will be different for the various drugs. These can vary considerably, so it is important that the selection of on-site testing device best reflects the needs of the testing authority. For example, in countries in Western Europe amphetamine is much more common than methamphetamine, whereas in Australia, the United States and countries in South-East Asia methamphetamine is much more frequent. A monoclonal test kit for amphetamine will not detect methamphetamine and vice versa. Consequently, the appropriate immunoassay needs to be selected to target a specific type of amphetamine.

Confirmatory or final testing

Whatever type of initial screening test is conducted, the specimen must be subject to confirmatory testing** in a properly certified laboratory. This should occur as soon as feasible after the initial test, using techniques that have been appropriately validated on the specimen (or specimens) of interest. The preferred technique should involve mass spectrometry (MS), since this is far more specific and sensitive than most other techniques and is universally accepted as the most reliable and specific technique for final testing.

MS can be linked to a gas chromatograph (GC-MS), a liquid chromatograph (LC-MS) or even to a capillary electrophoresis instrument (CE-MS). Some laboratories will be able to use tandem mass spectrometry (MS-MS) or high-resolution MS such as time-of-flight MS (TOF-MS). Whatever the technique, it is important that the detection limits or cut-offs applied to confirmation testing are the same, or preferably lower, than the initial testing threshold concentration. This avoids not being able to confirm an initial on-site positive because of insufficient sensitivity. Most drugs are metabolized and metabolites will often cross-react with antibodies used in most on-site testing devices, thus giving a higher apparent concentration of the drug than is actually present in the specimen, since one substance is being targeted in the final testing. For example, in urine cannabinoids (all cannabis metabolites) are often screened with a cut-off of 50 ng/ml, but the metabolite carboxy-tetrahydrocannabinol (THC-COOH) is confirmed with a cut-off of 15 ng/ml.

Quality considerations

Laboratories performing any form of drug testing are expected to conduct their procedures using standardized and validated methods by appropriately trained staff. The laboratory staff and the analysts should also take part in proficiency testing programmes to ensure that satisfactory results are produced. Moreover,

*Tests that detect more than one member of a class of drugs (amphetamines, opiates etc.).

**Final testing that determines unequivocally the presence of a drug or drug metabolite.

in many parts of the world, laboratories require accreditation or another form of certification to ensure that all aspects of the testing meet current scientific and quality system standards. For example, in many parts of the world the International Organization for Standardization ISO 17025 quality standard is applied. Specific technical standards are also applied in different parts of the world.

This means that laboratories testing batches of specimens should also employ blank samples, samples with known concentrations (calibrators) and quality controls to ensure that the results of each batch of specimens meet appropriate laboratory performance criteria. Only results from those batches where performance criteria are satisfactorily met should be accepted. All other results are rejected and the analysis repeated.

These principles of good laboratory practice should also be considered in on-site testing. In practice this may be more difficult, given that in on-site testing, the environmental conditions and location are much less controlled than in a laboratory. Nevertheless, it is imperative that the collection and testing process is as controlled as reasonably feasible and the staff performing the collection of specimens and the testing are properly trained; otherwise it is likely that initial on-site results will be less reliable, and that may produce a higher rate of false negatives* and false positives.**

Furthermore, it is recommended that on-site testing facilities incorporate a checking process for each batch of cases, or once daily, with known blank (drug-free) and drug-positive (control specimens or solutions) cases. Periodic testing of externally submitted proficiency material is also highly recommended. All of these quality steps provide an assurance to the client and any authority that the on-site testing is reliable and has been properly conducted.

Cost considerations

Depending on the nature of an on-site testing programme, it can lead to reduced costs compared with laboratory-based initial testing. Cost savings may be associated with reduced transportation costs of specimens for initial testing at laboratories. Larger savings are associated with the ability to act on a result at the time of collection rather than waiting for a laboratory test result. The risk of drug users at a workplace causing an accident can be significant and in the case of post-accident testing can lead to improved care management practices. There is often little difference in unit cost per initial test between laboratory and on-site device costs, but there can be significant differences depending on the local arrangements and the type of kit used [6].

*Specimens containing a drug above the cut-off that is not detected as being drug-positive.

**Positive initial test results that are not confirmed by subsequent testing.

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