

The current status of drug testing in the U.S. workforce

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Drug testing has grown to an \$800 million business. This article provides a summary on the current status of drug testing with an emphasis on workplace urine testing and the future of drug testing.

Historical perspective

Drug screening was first initiated by the U.S. military to identify heroin users among returning Vietnam veterans. This program was extended in the early 1970s to screen soldiers reporting for active duty. In 1986, the U.S. government began full-scale efforts to advocate urine drug testing among federal employees to increase their productivity and reliability, to reduce absenteeism, and to increase safety in the workplace. In 1989, the U.S. Department of Transportation initiated drug testing of airline pilots, railroad workers, air traffic controllers, and other employees in safety-related positions after the engineer and the brakeman of a freight train that crashed and killed 16 passengers in Maryland tested positive for marijuana. In addition to the military and transportation markets mentioned above, drug testing has now been extended to other areas including preemployment screening for private industry (workplace market), testing of inmates and parolees (criminal justice market), toxicology screening in the emergency room (clinical market), monitoring of rehabilitating addicts (rehabilitation market), and testing of students participating in athletic activities (education and sports market).

In the U.S., the workplace niche is the largest market segment. Most workplace drug testing programs follow the guidelines established by the U.S. Department of Health and Human Services' Substance Abuse and Mental Health Services Administration (SAMHSA),¹ while the U.S. Department of Transportation (DOT)² establishes separate guidelines for programs under its jurisdiction.

Sample matrix used in drug testing

Currently four matrices are used in drug testing.³ The detection period and advantages and disadvantages

Table 1

Comparison of four specimen matrices used in drug testing

Matrix	Detection period	Advantages	Disadvantages
Urine	2 to 3 days	Extensive scientific literature available; legally and scientifically accepted; cutoff levels established; on-site screen test available for quick result	Susceptible to adulteration, dilution, substitution, and purging
Oral fluid	1 to 2 days	Easy sample collection under observed condition; not easily susceptible to adulteration; on-site screen test available for quick result	Cutoff levels still being developed
Hair	10 days to 3 months	Easy sample collection under observed condition; test for drug use for a long period of time	Inability to detect recent drug use; susceptible to adulteration; samples must be sent to laboratory for testing; poor sensitivity for marijuana use
Sweat	Up to 2 weeks	Noninvasive specimen collection; provides cumulative measure of drug exposure	Specimen collected has large volume variation from each collection period; risk of accidental removal and contamination during removal since sample must be sent to laboratory for testing

of each of the specimen matrices are briefly summarized in *Table 1*. Since urine is the predominant matrix, the rest of the article will concentrate on urine drug testing.

Drug testing process in the workplace

The workplace market segment consists of several components including employer, employee, collection site, express delivery service, the testing laboratory, medical review office (MRO), and third-party administrator (TPA).

When an employer requests a drug test from an employee, the employee is instructed to go to a collection site. There, the employee's urine is collected in a specially designed secure cup and sealed with a tamper-resistant tape. The cup is then sent by express delivery service to a testing laboratory where it will be tested for several drugs. The first step at the testing site is to split the urine into two aliquots. One aliquot is first screened for drugs using an analyzer that performs immunoassay as the initial screen. If the urine screens positive then another aliquot of the sample is used to confirm the findings by gas chromatography-mass spectroscopy (GC-MS) methodology. All test results are relayed to an MRO where a medical physician reviews the results. If the result of the screen is negative, the MRO informs the employer that the employee is clean and has no detectable drug in the urine. However, if the test result of the immunoassay and GC-MS are positive, the MRO contacts the employee and tries to determine if there is any legitimate reason for the employee to have a positive result such as a medical treatment or prescription. If it is determined that the positive result is truly due to drug use, the MRO then informs the employer of the positive result. Statistics show that about 5% of the urine samples tested in the U.S. turn out positive for drugs.⁴ The employer may contract the service of the various components by itself, or in most cases, it would retain the service of a TPA to oversee the entire process.

With the improvement in the accuracy of on-site test devices (notably the lateral flow test devices), an increasing number of collection sites are running the tests themselves instead of sending the samples to the laboratory for analysis. In this new scenario, the employee goes to the collection site where the urine is collected and tested by the collection site staff using an on-site test device. The results are known within minutes. If the results are negative, the employee is notified that he/she is cleared and can go to work. Since about 95% of employees test negative, most employees can be cleared quickly. The positive samples are sent to the laboratory by express delivery service for confirmatory testing. The result of that testing goes through the MRO route before the employer is informed.

There are several significant implications of this new trend. This trend comes about only because on-site devices have become more reliable, enabling them to be widely accepted by both the scientific and regulatory communities. This new scenario simplifies the testing process and saves time. In the older process, turnaround time was at least 24 hours whereas the current turnaround time is down to about a half an hour. Economically, the employer realizes substantial savings by eliminating the costs associated with ex-

Table 2

Cutoff concentrations (ng/mL) of common drugs of abuse		
Drug	Cutoff concentration for screen test	Cutoff concentration for GC-MS confirmation test
THC-COOH	50	15
BE	300	150
PCP	25	25
AMP	1000	500
MET	1000	500
MOR	2000	Codeine 2000, morphine 2000, and 6-acetylmorphine 10
MTD	300	300
BAR	300	300
BZO	300	300
TCA	1000	
MDMA	500	

press delivery, laboratory testing, and MRO service for 95% of the testing. Consequently, these entities are losing large portions of their current business. However, the business for collection site and on-site test device manufacturers is increasing.

What drugs are being tested

Most of the testing follows the SAMHSA guidelines, which mandates testing for five drugs including marijuana (THC), cocaine (COC), morphine (MOR), amphetamine (AMP), and phencyclidine (PCP). Additional drugs commonly tested include methamphetamine (MET), methadone (MTD), barbiturates (BAR), benzodiazepines (BZO), tricyclic antidepressants (TCA), and methylenedioxymethamphetamine (MDMA or ecstasy).

Most of the testing utilizes urine as the sample matrix. However, for certain drugs the parent drugs may not exist or only exist in minute amounts in the urine. Therefore, drug testing for THC and cocaine actually detects their respective metabolites named THC carboxylic acid (THC-COOH) and benzyecognonine (BE), respectively. Moreover, some of the cutoff concentrations for the confirmatory GC-MS processes are lower than the cutoff concentrations of the screening immunoassays. This is because GC-MS detects the actual drug or drug metabolite whereas immunoassays also detect cross-reactivity due to structurally closed metabolites. *Table 2* shows the cutoff concentrations of the 11 most common drugs.

Drug screen technologies

In the 1960s and 1970s, the screening method of choice was thin-layer chromatography (TLC), which is inexpensive, quick, and permits the simultaneous detection of many substances. However, TLC is not specific and not adaptable to mass screening. In the 1970s

radioimmunoassay (RIA) and enzyme multiplied immunoassay technique (EMIT) began to appear, leading to automation and lower costs. EMIT and other nonradioactive immunoassays soon were adapted to large analyzers capable of running thousands of samples per day. Currently, simple on-site tests are beginning to replace large automated machines.

The most common form of on-site test uses the lateral flow immunoassay format in which an immobilized drug competes with the drugs in the samples for limited antibody binding sites. Such a test device contains a nitrocellulose membrane strip onto which drug conjugates are precoated at specific regions known as the test regions. One end of the membrane is in contact with an absorbent pad, while the other end is in contact with a colored antibody-colloidal gold conjugate coated pad, which in turn is in contact with a sample pad. In the test procedure, urine specimen is added to the sample pad and allowed to migrate across the antibody-colloidal gold pad and the membrane by capillary action. The absorbent pad acts as a sink to help the movement of the liquid. If any drug is present in the urine sample, it binds with the colored antibody conjugate to form a complex. This complex is then prevented from binding to the immobilized drug in the test region. Therefore, the absence of a color band at a specific test region indicates a positive result for that particular test. If no drug is present in urine, the colored antibody conjugate will flow up to the test region and bind to the immobilized drug forming a visible red line. Therefore, the presence of a color band at a specific test region indicates a negative result for that particular drug. A band with a different antigen/antibody reaction is added to the membrane strip at the control region to indicate that the test performed properly. This control line always appears regardless of the presence of drug. Because of its simplicity, speed, and accuracy, lateral flow immunoassay has been gaining popularity and SAMHSA is allowing on-site drug screening.

Various forms of lateral flow on-site test

The advance of lateral flow immunoassay technology has allowed the simultaneous testing of multiple drugs on a single test device. This new approach has simplified testing and decreased the cost of running a drug test, thus contributing to the increasing popularity of such devices.

In general, there are essentially four different formats of lateral flow on-site devices. The dipstick is a bare test strip containing the sample pad, conjugate pad, membrane, and the absorbent pad. It can test for one or more drugs. To run the test, the sample pad is

dipped into the urine and results can be obtained in approx. 5 min. Because of its low manufacturing cost, it is usually the lowest-priced device.

The second format, called the cassette, is the most popular at the present time. In this version, the test strip is placed in a plastic housing, which exposes the membrane and sample pad. A small disposable pipet is used to transfer the urine sample onto the sample pad. Multiple drugs can be determined simultaneously; several manufacturers have designed two- or three-strip format cassettes to accommodate more drugs.

In the dipcard format, several test strips are bundled together with their sample pads exposed. The nitrocellulose membrane section of the strips are either opened or covered in transparent plastic. Many dipcards also come with a cap. To run the test, the sample pad side of the dipcard is dipped into the sample collection cup for a short period of time (approx. 1–5 min); the dipcard is then removed and capped to prevent the dripping of the urine sample. The advantage of a dipcard is that it is easy to run.

The most sophisticated format of an on-site device is the cup. A drug test cup incorporates three functions: 1) urine sample collection, 2) drug testing device, and 3) transportation device for confirmation. The challenge of a cup design is to bring the collected sample fluid to the lateral flow drug test device in a convenient manner without causing the cup to leak. Essentially, there are two cup designs. One design separates the test device from the other two functions of the cup using a derivative of the dipcard design, and the other more advanced design incorporates the test device as part of the cup. In the first design the test device is dipped into the cup and then removed before recapping the cup for transport. In the second design the test device is built into the cup and the sample is introduced to the strip by tilting the cup so that urine can flow to the strip via a small capillary channel. Another modification of this second design places a nonremovable dipcard inside a cup and, as the cup collects urine, the sample is immediately introduced to the strips. The newest design has the strips embedded on the cap and the urine samples are introduced to the test strips either by a mechanical scoop or by hydraulics.

Because of the engineering and production costs, cups are always higher priced. However, the advantages of a hands-free operation may outweigh its cost.

Issue of adulterant

One of the inherent concerns of employers who use drug testing is the validity of the urine sample. Illicit drug users have attempted to defeat drug tests by adding foreign substances (adulterants) to the urine to

invalidate the test results. Such adulterants act either by interfering with the immunoassay procedures or by converting the target drugs to other compounds. It is estimated that approx. one million adulterant products were purchased in 2001.

Currently, most laboratories performing drug screens test for adulterants routinely. Two U.S. companies have successfully developed on-site adulterant test strips using urinalysis technology. To determine contamination, samples are evaluated against several parameters. These parameters include testing for creatinine and specific gravity conditions; testing for nitrite and glutaraldehyde; checking pH for the addition of basic or acidic adulterants; and testing for oxidizing substances such as bleach and pyridinium chlorochromate.⁴

Adulteration testing is gaining importance because some of the new generations of adulterants are quite effective. Indeed, recent data⁵ show that a few of these adulterants are not detectable after 5–6 hours. In this instance, rapid testing to check for adulterants could effectively be done by the use of an on-site adulterant dipstick device.

Future trend

It appears that saliva-based testing is gaining importance due to the challenges of adulteration and monitoring murine-based testing. However, because of the low concentrations of drugs present in oral fluids and the complexity of the matrix, development of oral fluid drug testing has been slow. The first generation of oral fluid testing has an analytical sensitivity down to 5–50 ng/mL; the next generation of screen with sensitivity down to less than one ng/mL will enable such tests to be used in situations comparable to urine and expand the usefulness of the technology to other markets.

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