Drug Testing in the Workplace

Hieu M. Phan, Pharm.D., Keith Yoshizuka, Pharm.D., M.B.A., J.D., Daryl J. Murry, Pharm.D., and Paul J. Perry, Ph.D.

Congress passed the Drug-Free Workplace Act in April 1988, which resulted in the Mandatory Guidelines for Federal Workplace Drug Testing Programs. The intent was to establish a substance-free work environment for all federal workers by requiring that all federal employees pass a urine drug test before employment. These guidelines specifically, and exclusively, focus on testing urine specimens for metabolites of marijuana, cocaine, phencyclidine, opiates (focusing on heroin metabolites), and amphetamines (including Ecstasy). Since then, there have been many scientific, technical, and legal challenges to the validity of urine drug testing. In response, the Substance Abuse and Mental Health Services Administration, a division operating under the executive branch of the United States Department of Health and Human Services, put forth, through many revisions, strict procedural guidelines and specimen validity-testing criteria to manage suspicious or adulterated samples during and after urine collection. This review focuses on the legal ramifications, the procedural process, and the sensitivity and specificity of the two urine drug tests used for workplace drug testing: immunoassay and gas chromatography–mass spectrometry. Moreover, we dissect the problematic issue of cross-sensitivity between illicit and prescription drugs, and how this affects the validity of future urine drug testing.

Key Words: workplace drug testing, urine drug testing, immunoassay screening, confirmation assay, specimen validity testing, forensic drug testing.
(Pharmacotherapy 2012;32(7):649–656)

OUTLINE

Drug abuse has become a national problem and is a large economic burden to employers through combined medical, criminal, and social effects.[1] As such, drug testing has become increasingly common in different workplace settings ranging from, but not limited to, athletics, criminal justice, and health care. Urine sampling is the gold standard because it is noninvasive and fast, and samples are easy to collect and test.[2] Currently, federal guidelines specify testing for only metabolites of illicit marijuana, cocaine, and opiates, as well as nonmetabolized phencyclidine (PCP) and amphetamines.[3] However, given the inherent nature of immunoassay testing, which uses antibodies to bind with the drug of interest or its metabolites, false-positive results are possible, due to cross-reactivity with metabolites of other prescription or over-the-counter drugs.[4] As such, the federal guidelines

require that all positive urine specimens be validated with a confirmatory test using gas chromatography–mass spectrometry (GC-MS) analytic instrumentation. The GC-MS testing is a more sensitive and specific analytic testing procedure than the initial immunoassay testing for the illicit drugs of interest.

Despite the specificity of the urine drug testing procedure, there continues to be litigation that challenges the validity of the test results. By examining the scientific testing principles of immunoassay and GC-MS, the goal of this review is to aid health care professionals in forming an evidence-based decision when faced with a dilemma such as a potential employee who tests positive on a urine drug test and claims assay cross-sensitivity with recently ingested prescription or over-the-counter drugs. Furthermore, court cases are included to illustrate the legality of mandated drug testing by employers.

Legal Issues

Despite the strict procedural processes set forth by the federal guidelines, there are many legal issues to consider when individuals undergo urine drug testing. The Drug-Free Workplace Act requires that all organizations that contract or receive money from the federal government maintain a drug-free workplace.[5] Furthermore, it requires that action be taken against employees who fail to comply with this prohibition in the workplace. However, for all other industries, private or public, the constitutional rights of individuals and governmental laws come to bear in the process of mandating a urine drug test sample from a potential, or current, employee.

According to the federal guidelines initially established in 1988, and later revised in 2004, the collection site must provide an area of privacy for donors to give urine unobserved.[6] Urine specimen collection may be directly observed only in response to a court order or in instances in which individuals have lost their civil rights, such as incarceration or probation. This presents a challenge to many employers to enforce an honest urine collection process. Augment this problem with an abundance of legally available detoxification kits on the market, both online and in stores, and one can see how a urine donor can easily be tempted to defraud the urine drug test. In response to this ever-growing problem, there is currently a reintroduced bill in Congress to prohibit the manufacturing, marketing, sale, and shipment of products that assist in defrauding the urine drug test.[7]

Although federal guidelines allow employers to drug test prospective employees, the Americans with Disabilities Act (ADA) requires that employers first make a conditional offer of employment before an employee is subjected to a urine drug test.[8] Furthermore, ADA law protects qualified individuals with a disability from being discriminated against on the basis of past drug-related problems, but the law does allow employers to require that the prospective employee enter a drug rehabilitation program as a condition of employment. If the employer suspects the prospective employee of returning to substance abuse, the employer may refuse to extend a job offer.

The United States Department of Transportation (DOT) allows for random drug testing for all employees in transportation safety–sensitive positions in areas such as aviation, trucking, railroads, mass transit, and pipelines.[9] Outside of DOT policies, the federal guidelines do not address random drug testing explicitly in that it might conflict with an individual's protection from unreasonable searches and seizures, protected by the Fourth Amendment of the U.S. Constitution. Therefore, it is up to each individual state and local government to develop legislation regarding the legality of employer's rights to perform random drug tests. Some states such as California allow for random drug testing by employers only in safety-sensitive occupations, whereas Rhode Island prohibits such tests altogether. More commonly, workers' unions negotiate explicit written policies regarding random drug testing with the employer.

Specimen Validity Testing

The simplicity of marketing on the Internet has resulted in urine drug test detoxification kits becoming readily available in the form of drinks, diuretics, and synthetic urines.[10] In

From the College of Pharmacy, Touro University–California, Vallejo, California (Drs. Phan, Yoshizuka, and Perry); and the College of Pharmacy, University of Iowa, Iowa City, Iowa (Dr. Murry).

For reprints, visit https://caesar.sheridan.com/reprints/redir.php?pub=10089&acro=PHAR. For questions or comments, contact Hieu M. Phan, Pharm.D., College of Pharmacy, Touro University–California, 1310 Club Drive Mare Island, Vallejo, CA 94592; e-mail: hieu.phan@tu.edu.

fact, by simply inputting "beat a drug test" into the Google search engine, one is able to retrieve approximately 2,370,000 hits in only 0.13 seconds. The street drug colloquialism "dilution is a solution" describes the primary mechanism by which most of these concoctions invalidate the urine drug test results. Another popular strategy is to use chemical compounds to adulterate the urine specimen, thereby mandating retesting.

A person does not have to travel far to obtain adulterants that will affect the outcome of a urine drug test immunoassay. When added in sufficient quantities, common household chemicals can drastically alter the pH of urine to produce false negatives in most immunoassay tests. The chemicals listed in Table 1 can easily invalidate and subvert the drug testing process if used properly. Table 2 illustrates how certain chemical adulterants can affect certain illicit drug classes and produce unreliable results.

To combat these adversarial efforts, while also ensuring the legal rights of individuals, the federal guidelines have set forth strict rules and procedures that govern the process of collecting, transporting, and testing urine specimens to ensure the privacy and the integrity of each sample. To prevent adulteration of the urine specimen, the donor is required to leave all personal belongings in a secure area away from the collection area, wash their hands, and then choose a collection kit before the collection process begins. After the collection process, the urine sample is then transferred to National Certified Testing Laboratories, using a standardized chain of custody procedure. To ensure adherence to the chain of custody, necessary documentation must be completed using the federal Custody and Control Form, a five-page carbonless form with each page intended for the parties involved: the laboratory, the medical review officer, the collector, the employer, and the donor.

Before proceeding with the initial immunoassay testing of the collected specimen, each urine sample is subjected to a specimen validity test to ensure its accuracy and legitimacy. Within 4 minutes of the urine collection, a trained collector tests the temperature of the sample to ensure that it is within the acceptable range of 90–100°F. If the specimen temperature is outside of this range, another sample will be collected, but under the direct supervision of the collector. Both samples are then sent to the laboratory for testing. Starting in 2004, the federal guidelines for the specimen validity test include testing for pH, creatinine concentration, specific gravity, and one or more oxidizing tests on every specimen. Table 3 lists the unacceptable ranges for specimen validity tests and reporting results. Using these newly created specimen validity test standards, approximately 6,800,000 federal urine specimens were tested through the National Certified Testing Laboratories from May 2004–April 2005. Of these, there were approximately 140,000 positive tests (2.1%) and 10,000 adulterated, substituted, or invalid tests (0.15%).[13] Unfortunately, there was an unknown number of false positives and false negatives reported in that study.

Screening and Confirmatory Urine Drug Tests

Immunoassay Screening Tests

Once the urine specimen passes the specimen validity test, it is tested for illicit drugs. The primary screening test uses the immunoassay to detect the presence of illicit drugs or their metabolites. Developed in the 1950s, the immunoassay uses the binding between an antigen (drug or its metabolite) and its homologous antibody to identify if there are illicit substances in the urine sample. A known amount of the antigen—the drug or the drug's metabolite—

Table 1. Common Household Chemicals and Specimen Integrity Tests

	Specimen Integrity Test			
Household Chemical	pH	Creatinine Concentration	Temperature	Specific Gravity
Sodium chloride (salt)				X
Vinegar	X			
Sodium hypochlorite (bleach[a])	X			
Liquid soap	X			
Liquid drain cleaner	X			
Sodium bicarbonate	X			
Lemon juice	X			
Ascorbic acid (vitamin C)	X			

[a]Cloudy appearance of sample.
Adapted from reference11.

Table 2. Effect of Adulterants on Immunoassay Screening of Illicit Drugs

Adulterant	Drugs Affected	Comments
Sodium chloride	Amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, opiates, PCP	Produces false-negative results using EMIT
	Benzodiazepines	Produces slight decreases in response using FPIA
Hydrogen peroxide	Benzodiazepines	Produces decreased levels using EMIT
	Benzodiazepines	Produces false-positive results using FPIA
Liquid dishwashing detergent	Cannabinoids, PCP, benzodiazepines	Produces decreased levels using EMIT
Sodium bicarbonate	Opiates	Produces decreased levels using EMIT
Sodium hypochlorite	Cannabinoids, benzodiazepines	Produces false-negative results using EMIT
	Amphetamines, opiates, PCP	Produces false-negative results using FPIA
Denture-cleaning tablets	Benzoylecgonine, MDMA	Produces false-negative results using FPIA

PCP = phenylcyclidine; EMIT = enzyme-multiplied immunoassay technique; FPIA = fluorescence polarization immunoassay; MDMA = 3,4-methylenedioxymethamphetamine.
Adapted from reference 11.

Table 3. 2004 Federal Guideline Specimen Validity Test Criteria and Reporting[12]

Test	Unacceptable Ranges	Results
pH	< 3 or ≥ 11	Reported as adulterated
Nitrite concentration	$\geq$ 500 μg/ml	Reported as adulterated
Chromium concentration	$\geq$ 50 μg/ml	Reported as adulterated
Creatinine concentration	2 20 mg/dl	Reported as dilute
	$<$ 2 mg/dl	Reported as substituted
Specific gravity	$1.0010 < x < 1.0030$	Reported as dilute
	$1.0200 \leq x \leq 1.0010$	Reported as substituted
Oxidizing test	Presence of halogens (bleach, iodine, fluoride), glutaraldehyde, pyridine, surfactants	Reported as adulterated
Suspicious samples	Invalid or inconsistent ranges for the tests above	Reported as invalid

being tested is labeled by using enzymes and is then added to the urine specimen. Chemically, any drug present in the donor's urine will then compete with the enzyme-labeled antigen to bind with homologous antibodies to form antigen-antibody complexes. Because this is a competitive immunoassay, the amount of enzyme-labeled antigen-antibody complex is indirectly proportional to the amount of drug belonging to the donor. In contrast, in a noncompetitive immunoassay test, the amount of enzyme-labeled antigen-antibody complex is directly proportional to the amount of drug existing in the donor's urine. For more information on the principles of immunoassay testing, the reader is referred elsewhere.[14] In forensic urine drug testing, there are six primary types of immunoassays: radioimmunoassay, enzyme-linked immunosorbent assay (ELISA), enzyme-multiplied immunoassay technique (EMIT), cloned enzyme donor immunoassay (CEDIA), fluorescence polarization immunoassay (FPIA), and kinetic interaction of microparticles in solution (KIMS).

The results of an immunoassay test are qualitative. In other words, the test result is read as simply positive or negative. Table 4 presents the threshold concentrations and reporting requirements for the Substance Abuse and Mental Health Services Administration–certified laboratories. Despite the threshold values, the indiscriminate nature of these results make the immunoassay results sometimes ambiguous and problematic because they do not specifically indicate what legal or illegal substance(s) in the specimen triggered the positive test.

Immunoassay tests produce results with high sensitivity that can be defined as the probability that a test indicates a person has used illegal substances when in fact they have. Sensitivity is how likely a test can detect someone who has been using illegal substances with relatively few false negatives. Despite high sensitivity, the major concern with interpretation of immunoassay results is the relative lack of specificity, which means that the immunoassay can produce relatively higher rates of false positives. Specificity is defined as the probability that a non–substance abuser tests negative. That is to say, how reliable is a test when it tells you that a person has not used any illegal drug. Contributing to the less than favorable specificity level is the cross-reactivity between certain narcotic and

Table 4. Threshold Concentrations and Reporting Requirements for Substance Abuse and Mental Health Services Administration–Certified Laboratories.[15]

Drug Class	Immunoassay Screening (ng/ml)	GC-MS Confirmation (ng/ml)
Amphetamines	1000	Amphetamine: 500 Methamphetamine[a]: 500
Cannabinoids	50	THC-COOH: 15
Cocaine metabolites	300	Benzoylecgonine: 150
Opiates	2000	Morphine[b]: 2000 Codeine: 2000 6-Monoacetylmorphine: 10
PCP	25	PCP: 25

GC-MS = gas chromatography–mass spectrometry; PCP = phencyclidine; THC-COOH = 9-carboxy-Δ^9tetrahydrocannabinol.
[a]Must contain amphetamine concentration $\geq$ 200 ng/ml.
[b]If morphine concentration exceeds 2000 ng/ml, test for 6-monoacetylmorphine.

Table 5. Cross-Reacting Drugs in Immunoassay Testing[16]

Illicit Drug	Common Cross-Reacting Drugs
Amphetamines	Amantadine, bupropion, chloroquine, chlorpromazine, desipramine, ephedrine, fenfluramine, labetalol, mexiletine, procainamide, phentermine, phenylephrine, propranolol, pseudoephedrine, quinacrine, ranitidine, selegiline, trazodone
Benzodiazepines	Oxaprozin, sertraline
Barbiturates	Phenytoin
Marijuana	Dronabinol, efavirenz, pantoprazole, esomeprazole, omeprazole, lansoprazole
Cocaine	None known
Opiates	Fluoroquinolones, papaverine, poppy seeds, rifampin
PCP	Diphenhydramine, dextromethorphan

PCP = phencyclidine.

illicit drugs and legal prescriptions or over-the-counter drugs.[16] Table 5 lists common cross-reacting drugs for amphetamines, benzodiazepines, barbiturates, marijuana, cocaine, opiates, and PCP. As a result of either chemical properties or metabolites, many drugs can cause false-positive results on immunoassay. Codeine, a legal drug, is a prototypical example of the problem. Codeine and heroin, an illicit street drug, are both metabolized to morphine. As a result, patients with a significant cough who are prescribed codeine as an antitussive can unwittingly test positive for opiates and be suspected of being a heroin user due to the presence of morphine in the urine sample.[2] Fortunately, misidentification due to analyte cross-reactivity can be corrected by a confirmatory GC-MS test. Federal guidelines mandate that any positive immunoassay urine drug test be confirmed with a GC-MS test.[17]

Gas Chromatography–Mass Spectrometry Confirmatory Test

The GC-MS test is a powerful and reliable scientific method that is used to identify and quantify chemical components in a sample such as urine or blood. Gas chromatography separates the different chemical components in a sample, whereas mass spectrometry produces a characteristic series of ions that may be used to identify and quantify each component. The combination of chromatography and highly specific detection greatly reduces the chances of false-positive results, and when considered in combination with an immunoassay constitutes proof to a legal standard of certainty. As Table 4 illustrates, GC-MS is at least as sensitive and more specific than immunoassay testing, and the results of the confirmatory GC-MS test are legally indisputable. Revisiting the codeine scenario from earlier, the GC-MS would easily differentiate the difference between a heroin abuser and an antitussive codeine user through the low-level detection of 6-monoacetylmorphine. What the immunoassay test lacks in specificity, GC-MS testing compensates by undeniably confirming the existence and accuracy of the identified substance within each positive urine specimen.

Accuracy of the Test Results

Theoretically, it can be argued that there does not exist an infallible scientific test, including

the immunoassay and GC-MS. Therefore, how can employers be confident in the results of these tests when employees with positive urine drug tests argue that their results are false positives due to drug cross-reactivity? As an example, an employee with an immunoassay result positive for amphetamine may claim that the result stemmed from ingesting pseudoephedrine within the preceding 48 hours. To invalidate this employee's claim, the employer needs to look no further than examining the accuracy and sensitivity data sections of the product information sheet available for all U.S. Food and Drug Administration (FDA)-approved immunoassay tests.

To illustrate this point, consider the CEDIA product information for the amphetamine and Ecstasy assay manufactured by Microgenics (Fremont, CA). Their data indicate 100% sensitivity and 93% specificity for amphetamine and Ecstasy concentrations greater than 1000 ng/ml among 249 test samples.[18] However, when confirmed with GC-MS at cutoff concentrations of 500 ng/ml, the test concordance rates for GC-MS versus CEDIA are 95% for positive tests and 94% for negative tests. As shown in Table 6, the CEDIA is still extremely reliable in differentiating between amphetamines and other chemically unrelated structures. Conversely, Table 7 presents a series of chemically related phenylethylamine compounds for which one would logically expect cross-reactivity to be a potentially viable issue at the mandated immunoassay cutoff concentrations of 1000 ng/ml. Furthermore, Table 7 shows that the cross-reactivity rate for the case illustrative drug, pseudoephedrine, is merely 0.9% using the Microgenics CEDIA for amphetamine and Ecstasy when tested on samples with a pseudoephedrine level of 160,000 ng/ml. To put this into context, the mean calculated urine pseudoephedrine concentration in pseudoephedrine fatal overdoses is reported to be 105,000 ng/ml.[19] Therefore, one might conclude with a reasonable degree of certainty that in order for the employee to generate a false-positive result on the CEDIA, due to cross-reactivity, a potentially fatal dose of pseudoephedrine compounds would have to have been ingested. Based on this, an employer can confidently make the correct decision to deny employment based on only the CEDIA urine drug test results. However, it should be noted that the system still has built in a fail-safe GC-MS confirmatory procedure.

Table 6. Compounds with No Cross-Reactivity in the Cloned Enzyme Donor Immunoassay for Amphetamine and Ecstasy[18]

Compound	Concentration (ng/ml)
Acetaminophen	1,000,000
Aspirin	1,000,000
Cimetidine	500,000
Codeine	1,000,000
Diazepam	1,000,000
Fluoxetine	1,000,000
Ibuprofen	1,000,000
Levothyroxine	100,000
Methadone	1,000,000
Ranitidine	250,000
Secobarbital	1,000,000
Verapamil	1,000,000

Compared with CEDIA, the ELISA (MP Biomedicals, Burlingame, CA) shows similar high sensitivity and high specificity for amphetamines. The product information for ELISA indicates a concordance rate between the ELISA and GC-MS as 91% each for the true positive and true negative tests. As shown in Table 8, the product information indicates that pseudoephedrine as well as 10 other phenylethylamine compounds shows no cross-reactivity rates at a cutoff concentration of 100,000 ng/ml. To reiterate, the reported mean calculated urine pseudoephedrine concentration in fatal overdoses is 105,000 ng/ml. This means that, using ELISA, even someone using pseudoephedrine should still have a negligible chance of testing positive for amphetamines on an immunoassay urine drug test.

The only shortcoming of these tests does not stem from accuracy, but rather from the short detection time available for the illicit drugs. The detection window is influenced by how fast a drug is metabolized and excreted from the body after the consumption of the drug. Table 9 shows that depending on the dose, route of administration, metabolism, and pharmacokinetics, detection time for workplace drugs of abuse can range from days to weeks. Most drugs are detectable only within several days, whereas more lipid-soluble drugs such as marijuana, diazepam, or PCP may be detectable in the urine for weeks.[2, 21] Chronicity of use may also increase the duration of time the drug can be detected in the urine.

Court Case Scenarios

The process of drug testing and the punitive consequences associated with positive results are

Table 7. Compounds with Cross-Reactivity in the Cloned Enzyme Donor Immunoassay for Amphetamine and Ecstasy[18]

Compound	Concentration (ng/ml)	Cross-Reactivity (%)	Mean Fatal Urine Concentration (ng/ml)[19]
Phentermine	25,000	3.3	50,000
Phenylpropanolamine	500,000	0.3	Not reported
Pseudoephedrine	160,000	0.9	105,000
Ephedrine	250,000	0.5	262,000

Table 8. Compounds with No Cross-Reactivity in the Enzyme-Linked Immunosorbent Assay at Concentrations up to 100,000 ng/ml[20]

Caffeine
Ephedrine
Ecgonine
Ecgonine methyl ester
Epinephrine
Isoproterenol
Ketamine
Methylphenidate
Phenethylamine-α
Phenylpropanolamine
Pseudoephedrine

met with many challenges because they are often intertwined with constitutional and legal rights of individuals. There is often conflict between labor laws and the infringement of personal privacy rights. Consequently, many individuals pursue legal action against their former employers citing violation of their constitutional rights or other federal protection laws.

To illustrate the sensitive nature of the federal ADA laws, the case of *Bates v Dura Auto Systems* deserves consideration.[23] The plaintiffs were seven former employees of Dura Auto Systems who challenged the company's drug testing policy under the ADA. Dura, who manufactured glass window units for cars, trucks, and buses, grew concerned about the increased workplace accident rates at the facility where the plaintiffs were formerly employed. To improve safety, Dura implemented a new drug policy that prohibited employees from using legal prescription drugs that would adversely affect safety, job performance, or company property. Subsequently, Dura worked with an independent drug testing company to screen for 12 substances that were considered dangerous in the workplace. These substances were found mainly in prescription drugs that were potential central nervous system depressants, such as alprazolam, hydrocodone, and oxycodone.

In this case, the U.S. Court of Appeals ruled in favor of Dura Auto Systems, citing that the plaintiff could not assert claims under the ADA (42 U.S.C.S. § 12112(b)(6)), since none of the seven individuals were disabled. Although nondisabled individuals may bring claims under some ADA rules and regulations, the section of 42 U.S.C.S. § 12112(b)(6) is intended only—by Congress—for "individuals with disabilities," and not a broader class of individuals who are just "employees."

Random drug testing is a highly contentious and sensitive issue, and employers who mandate unannounced testing continually face legal challenges. There are numerous legal cases that consider this controversial practice. A case that illustrates this issue is *Kreig v Seybold*.[24] The plaintiff, a former city employee of Marion, Indiana, challenged the city's random drug testing policy, claiming that it violated his Fourth Amendment rights after he was terminated for refusing to take the test. The city held the position that the plaintiff's job was a "safety sensitive" position and that the public's safety was at risk. The job involved operation of large vehicles and equipment such as snow plows. As such, an individual involved in such job activities who was intoxicated with a central nervous system depressant would put the public at significant

Table 9. Detection Time of Drugs of Abuse and Their Metabolites in Urine[21, 22]

Compound	Cutoff Level (ng/ml)	Detection Time in Urine
Amphetamine	1000	Up to 5 days
THC-COOH level after smoking 1 marijuana cigarette	50	2–4 days[a]
Benzoylecgonine level after cocaine 20 mg i.v.	300	Up to 1.5 days
Benzoylecgonine level after "street doses" of cocaine[b]	300	2–3 days; up to 1 wk at higher doses
Morphine level after low-dose (3 12 mg) heroin[b]	300	1–1.5 days

THC-COOH = 9-carboxy-Δ^9tetrahydrocannabinol.
[a]Detection time may be longer for extraordinarily high doses in chronic users.
[b]Administered by different routes.

risk of injury if these machines were operated under the influence of alcohol or drugs.

The U.S. Court of Appeals found in favor of the city in agreement with the Supreme Court's decision about random drug testing. The Supreme Court has deemed random drug testing to be constitutionally permissible when it "serves special government needs," or involves a "safety sensitive" position (as alluded to above).

Conclusion

To ensure a drug-free workplace, all federal employees are required to pass a urine drug test before employment. Urine drug screening is a quick and noninvasive method used to test for drug abuse. The primary limitation of urine sampling is that the majority of drug metabolites may remain detectable in the urine for only several days. More problematic is that the urine specimen may be manipulated or adulterated, resulting in an invalid specimen. That notwithstanding, given a valid urine specimen, the detection methodology using an initial immunoassay screening test and a confirmatory GC-MS test is legally foolproof given the high sensitivity and high specificity of these combined tests, thereby rendering excuses such as recent pseudoephedrine or codeine ingestion as illegitimate explanations for a positive urine drug test result.

References

1. **Center for Substance Abuse Prevention, Substance Abuse and Mental Health Services Administration.** Worksite health care costs/claims. Available from http://store.samhsa.gov/shin/content/SMA07-4298/SMA07-4298.pdf. Accessed May 3, 2012.
2. **Moeller KE, Lee KC, Kissack JC.** Urine drug screening: practical guide for clinicians. Mayo Clin Proc 2008;83(1):66–76.
3. **Center for Substance Abuse Prevention, Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services.** Mandatory guidelines for federal workplace drug testing programs. Available from http://workplace.samhsa.gov/DrugTesting/pdf/HHS%20Mandatory%20Guidelines%20(Effective%20November%201,%202004).pdf. Accessed December 5, 2011.
4. **Brahm NC, Yeager LL, Fox MD, et al.** Commonly prescribed medications and potential false-positive urine drug screens. Am J Health-Syst Pharm 2010;67:1344–50.
5. Mandatory guidelines for federal workplace drug testing programs. Fed Regist 1989;54(19):4946.
6. **Center for Substance Abuse Prevention, Substance Abuse and Mental Health Services Administration.** Urine specimen collection handbook for federal workplace programs. Available from http://workplace.samhsa.gov/DrugTesting/pdf/Specimen_Collection_Handbook.pdf. Accessed November 7, 2011.
7. **Drug Testing Integrity Act of 2011.** U.S. House of Representatives. Available from http://www.house.gov/list/press/oh02_schmidt/reintroducedrugleg.html. Accessed November 7, 2011.
8. **American with Disabilities Act.** Questions and answers. Available from http://www.ada.gov/pubs/adastatute08.htm. Accessed November 14, 2011.
9. **United States Department of Transportation.** Title 49 Part 40: Procedures for transportation workplace drug and alcohol testing programs. Available from http://www.dot.gov/odapc/documents/PART40.pdf. Accessed November 14, 2011.
10. **Tunnel K.** Pissing on demand: workplace drug testing and the rise of the detox industry. New York, NY: New York Univ Press, 2004: 65.
11. **Dasgupta A.** A health educator's guide to understanding drug abuse testing. Dugbury, MA: Jones & Barlett Publishers, 2009.
12. **Center for Substance Abuse Prevention, Substance Abuse and Mental Health Services.** Specimen validity testing. Available from http://workplace.samhsa.gov/DrugTesting/pdf/Specimen%20Validity%20Testing%20-%20February%202005.pdf. Accessed December 5, 2011.
13. **Center for Substance Abuse Prevention, Substance Abuse and Mental Health Services Administration.** Subversion of drug testing programs. Available from http://workplace.samhsa.gov/DrugTesting/pdf/CongresHearingDrgTestingPrgms.pdf. Accessed December 5, 2011.
14. **Levin B.** Principles of forensic toxicology. 2nd ed. Washington, DC: AACC Press, 2003.
15. Mandatory guidelines for federal workplace drug testing programs. Fed Regist 2004;69(71):19659.
16. **Drug Test Systems.** Cross reaction table – drug check. Available from http://www.drugtestsystems.com/cross_reaction_table.php. Accessed November 7, 2011.
17. Mandatory guidelines for federal workplace drug testing programs. Fed Regist 2004;69(71):19654.
18. **Microgenics Corp.** CEDIA amphetamine/Ecstasy assay product information. Fremont, CA: 2011.
19. **Randall BC.** Disposition of toxic drugs and chemicals in man. 8th ed. Foster City, CA: Biomedical Publications, 2011: 1458.
20. **MP Biomedicals LLC.** DOA (ELISA) panel test product information. Burlingame, CA: 2010.
21. **Douglas DL, Caplan YH, Heit HA.** Urine drug testing in clinical practice: dispelling the myths & designing strategies. Cal Acad of Fam Phys 2006;3:1–28. Available from http://www.familydocs.org/files/UDTMonograph_for_web.pdf. Accessed November 7, 2011.
22. **Vandevenne M, Vandenbussche H, Verstraete A.** Detection time of drugs of abuse in urine. Acta Clin Belg 2000;55(6):323–33.
23. Bates v. Auto. Sys., Inc. 625 F.3d 283 (2010). Available from http://hr.cch.com/EMPNews/bates.pdf.
24. Kreig v. Seybold, 481 F.3d 512 (2007). Available from http://www.kentlaw.iit.edu/Documents/Academic%20Programs/7CR/v3-1/lobelle.pdf.