WORKSHOP ON DRUG USE TESTING: FORENSIC SCIENCE AND LEGAL ISSUES

Yale H. Caplan,[1] *Ph.D.*

Drug Testing in Urine

REFERENCE: Caplan, Y. H., **"Drug Testing in Urine,"** *Journal of Forensic Sciences*, JFSCA, Vol. 34, No. 6, Nov. 1989, pp. 1417–1421.

ABSTRACT: Testing for drugs in the workplace has become commonplace as federal and private industry programs are developed. Effective use of laboratory results derived from testing urine specimens is a function of many factors including choice of specimen, testing modalities, specimen handling, and reporting. Since significant consequences can occur from positive test results, full understanding of the factors and the process is required.

KEYWORDS: toxicology, workshop, drug use testing, urine

To use the results derived from drug tests in urine properly, one must consider the complete process from specimen collection and transport through screening and confirmation analysis to final reporting and interpretation of the results.

Drug testing in urine has become commonplace throughout the United States. A recent survey showed that 30% of all Fortune 500 companies used some drug tests. Until several years ago, almost all tests for drugs were used by only three segments of society—the United States military, drug treatment programs, and corrections agencies. President Reagen's executive order mandating that all federal employees be tested initiated the current trend in drug testing. Many private companies are implementing programs as this arena undergoes rapid expansion. It has been estimated that 5 to 13% of the American work force has abused drugs, translating into a cost to employers of as much as $33 billion annually. Urine screening is not the panacea to solve the substance abuse problems in the workplace. When properly implemented, however, it can support a well thought-out and comprehensive program. Employees can be directed towards treatment rather than punitive actions, and in appropriate industries, safety can be enhanced.

Concern among the general public about the reliability of drug testing seems to center on the reported inaccuracy of the screening tests and particularly on the prevalence of false positive and false negative results and interferences. A variety of factors determines whether a laboratory is able to provide competent drug testing services. These include the laboratory's personnel and experience, the analytical methods used, and security and

[1]Chief toxicologist, Office of the Chief Medical Examiner, Baltimore, MD.

chain of possession procedures controlling the specimens. News media reports have often reported conclusions based on incomplete information. Drug tests can be done with a high degree of accuracy, and if one understands the factors and the process, the results of these tests can be effectively used.

The future of urine drug testing will focus not so much on the technology, which is already available, but on the acceptance and implementation of guidelines and the accreditation of laboratories and personnel involved in urine drug analysis. Such guidelines, covering the methods used from specimen collection through analysis and storage, have been recommended by the National Institute on Drug Abuse (NIDA). Two certification programs have been developed: the College of American Pathologists Forensic Urine Drug Testing Program and NIDA's National Laboratory Certification Program. Both have issued lists of approved laboratories. Urine drug testing should be considered a special application of analytical forensic toxicology.

General Considerations

Drug concentrations in biological fluids are affected by dose, route of administration, pattern of drug use, and the kinetics of the drug. Since most drugs are distributed to the site of action (usually the brain) by the blood, the measurement of a drug concentration in the blood or plasma provides the best information as to the potential effect on behavior. However, because of individual variations in the kinetics and responses to drugs, minimum plasma drug concentrations clearly associated with impairment have not been established for most drugs.

Drugs are chemically altered by the body, and breakdown products of this process or metabolites are produced. These metabolites may have drug actions of their own or may be inactive. There is a tendency for such metabolites to be excreted in significant quantities in the urine.

Drug concentrations in urine are highly variable and complicated by such factors as urine flow (volume) and pH. The evaluation of such specimens to predict time of drug use or impairment is not generally practical with single random specimens. This is due to the variations in urine drug concentration as well as the presence of inactive metabolites and is further complicated by the fact that most drug tests do not look for both a particular drug and its metabolites.

Why Use Urine to Test for Drugs of Abuse?

The advantages of using urine to test for drugs of abuse include the following. Urine is a readily available body waste product. Urine is easily collectable through noninvasive methods. Drugs are concentrated in urine. Urine is aqueous and easily manipulated for testing.

The disadvantages of using urine to test for drugs of abuse include the following. One cannot correlate concentration with physiological or behavioral effects. Positive tests can only indicate use at a time before collection. The sample concentration will vary. The analysis principally measures metabolites of drugs.

Screening and Confirmation

Because of the fact that the potential impact of the results of a urine test on an individual can be severe, only the most comprehensive and conclusive procedures should be used. Thus, an effective program incorporates both a screening and a confirmation procedure. The screening test should be sensitive and drug class selective, generally employing an immunoassay technique. These procedures will identify and eliminate negative specimens

and select presumptive positive specimens. A highly specific technique is then used for confirmation of the presumptive positive results. Gas chromatography coupled with mass spectrometry (GC/MS) is generally accepted; however, other techniques may be used.

Immunoassays

Immunoassays are based on the principle of competition between labeled and unlabeled antigen (drug) for binding sites on a specific antibody. Antibodies are protein substances with sites on their surfaces to which specific drugs or drug metabolites will bind. Three types of immunoassays are routinely employed for urine testing—the radioimmunoassay (RIA, Roche), the enzyme immunoassay technique (EMIT®, Syva), and the fluorescence polarization immunoassay (FPIA, Abbott/TDx). The difference between these methods is mainly in the indicator that is used. RIA uses a radioactive indicator, EMIT uses an enzyme, and FPIA uses fluorescence as the indicator. Since antibodies may cross-react with related drugs, and sometimes with unrelated compounds, confirmation of positive immunoassay results with an independent procedure based on a different chemical principle is essential for confirmation.

Gas Chromatography/Mass Spectrometry

Chromatography describes the method of analysis in which the various components in a biological specimen can be separated by a partitioning process. Once separation has been accomplished, a detection method distinguishes the components for identification and measurement. The combination of gas chromatography with mass spectrometry (GC/MS) provides the most specific analytical tool currently used for confirmation.

A molecular identification can be produced by the mass spectrometer. The MS instrument can be operated in a variety of modes, the choice of which dictates how the drugs are detected and the minimum concentration of drug that will constitute a positive identification. The method used for extraction and preparation of the drug(s) from the urine vary and must be considered. If appropriate methods are used by well-trained analysts in accordance with properly established criteria and protocols, a GC/MS analysis can insure conclusive identification for a suspected drug.

Sensitivity, False Positives, and False Negatives

The ability of an assay to detect low concentrations of drugs has an inherent limit. The concentration of drug in a urine sample below which the assay can no longer be considered reliable is the sensitivity limit or detection limit. This is generally the lowest concentration that can be differentiated from zero with 95% confidence. Manufacturers of commercial urine screening systems set cutoff limits for their assays well above the sensitivity limits of the assay to minimize the possibility of a sample that is negative giving a positive result.

A false positive is the report of a drug that is not present. Any sample that contains the drug of interest at a concentration equal to or greater than the designated cutoff concentration is reported positive. Any sample that is less than the cutoff concentration is reported negative. The confirmatory procedure must be at least as sensitive or preferably more sensitive than the screening procedure. If confirmatory procedures are not sufficiently sensitive, the screened positive may not be confirmed and the result would be an unconfirmed positive. The distinction between an unconfirmed positive and a true false positive is sometimes confusing. A sample determined positive by the screening method and negative by a confirmation method could be caused by a situation where a false result occurred in the initial analysis and the drug was in fact not present, or

alternatively, the drug might be present but was not detected in the second assay because of the differences in the sensitivity of the two assays.

Depending on the laboratory and the techniques used, cutoff concentrations may differ. It is for this reason that negative screening reports should contain a statement with reference to established cutoff concentrations. Urine specimens testing negative generally do not require a confirmatory test. A false negative is the failure to report a drug or metabolite that is present above the threshold or cutoff concentrations. Performing duplicate analyses on specimens testing negative may prevent some false negatives. Testing procedures should be designed to prevent false positives unequivocally while allowing greater tolerance for false negatives.

Laboratory Results

Organizations requesting testing should have a clear understanding as to why the drug testing has been ordered. Urine drug analysis may be used for preemployment, probable cause, or random testing purposes. There should also be a definite preestablished policy on how the test results will be used. The drug test results may lead to the denial of employment, job termination, discharge from military service, a jail sentence, or counseling, among others. The use of the test result may have a significant impact on an individual's career and on a company's legal liability. Therefore, considerable care must be exercised when drawing conclusions from the laboratory's report.

The end user of the results of a urine drug analysis must develop a general understanding of the laboratory method used to perform the analysis and have some understanding about the drugs. Such information will facilitate the correct interpretation of laboratory results, particularly when taken in conjunction with a particular set of circumstances, if applicable.

There are a number of questions that might arise in response to a positive test result. Is the subject using the drug chronically or intermittently? Is the drug being taken under a physician's order? Was the subject under the influence of the drug when the sample was collected? A number of other questions may be asked when a test result is negative. Was the subject really taking the drug, but either not in sufficiently large quantities or with high enough frequency of use be detected? Was the urine collected too long after use? Was the urine diluted or otherwise tampered with? The results of urine drug testing should be thought of as qualitative. Impairment cannot be diagnosed or presumed from a single urine test result. Additionally, the time since intake or the dose cannot effectively be determined.

The identification and reporting of metabolites may be confusing to clinicians and others reviewing toxicology reports. For example, heroin (diacetylmorphine) is rapidly metabolized to morphine, therefore, the presence of morphine in urine may be associated with heroin abuse. However, codeine is also metabolized to morphine and may be present in significant concentrations in the urine of an individual on an approved codeine medication. Thus, the presence of morphine under such circumstances does not necessarily indicate abuse or imply heroin use.

There is a significant difference between reporting a false positive urine acetone to a patient's physician and a false positive urine phencyclidine to a person's employer. A physician does not base a diagnosis on a single laboratory test, but rather on a comprehensive examination of the patient which includes the individual's medical history. The recipient of the urine drug analysis report is often a nonmedical individual who may not be able to interpret the report. The testing process occurs in a context devoid the individual's history. The laboratory report constitutes the only evidence available. The analysis for drugs of abuse in urine is not simple and the interpretation of such results should be left to those who have the necessary training and experience. In forensic urine drug

testing, one must consider the ramifications of a misinterpreted report, leaving no room for speculation.

Current and Future Status

The Workshop, Drug Use Testing: Forensic Science and Legal Issues explored the current issues and potential trends and problems as we proceed to test the masses of America in the interest of an enhanced workplace and efficient economy. Highlights of the workshop are presented in the papers that follow. Technical considerations include the appropriate use of mass spectrometry in confirmatory testing and the use of hair for the detection of drug abuse. The latter provides another noninvasive technique; however, its scientific acceptance awaits field trials in the hands of a variety of investigators and extensive comparison with other techniques. Drug testing also faces legal hurdles encompassing the proper introduction of and challenge to such tests both individually and collectively. A variety of court cases will dictate drug testing's future; however, the trend is here to stay. Finally, drug testing in the United States will be correlated with that of Canada, our neighbor, where demands for drug testing legislation have become an issue in response to efforts in the United States.

Address requests for reprints or additional information to
Yale H. Caplan, Ph.D.
Office of the Chief Medical Examiner
111 Penn St.
Baltimore, MD 21201