

Chapter 43

Forensic Drug Testing

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43.1 Introduction

Review of this chapter will assist counsel in understanding the tests, in communicating with their own experts, and also in cross-examining opposing experts.

In order for a scientist, toxicologist, pharmacologist, pharmacist, or pathologist to correlate drug action or effects with the drug found in the body, the concentration found in the body must be sufficient to cause the adverse reaction or be beyond the expected therapeutic dose. In addition, the type of specimen collected must be one that will properly reflect the drug concentration in the body at the time of the incident/death. For these reasons, the interpretation of the drug's reaction for the purposes of determination of cause and effect can be problematic. The method of sample analysis and a review of the laboratory data are of key importance. Test results have the potential for error, and may need to be critiqued by a qualified expert.

The analysis of a biological specimen can take several steps. The first step, which is sometimes bypassed, is the presumptive or screening test, which enables the analyst to identify a class of drugs that may be present in a biological specimen. This step is followed by the extraction of the drug or unknown substance from the biological matrix, followed

by an analysis on a scientific instrument capable of quantifying the amount of specific drug in the specimen.

43.2 The Screening Test

Laboratory analysis of a subject's urine or blood sample is often performed in two stages. The first analysis is performed using immunoassay technology and is often called a "screening" or "presumptive" test. Most commercially available immunoassay kits are screening tests for the common drugs of abuse (cocaine, methamphetamine, marijuana, phencyclidine, morphine), although some kits are available for testing other types of drugs such as the benzodiazepines and the phenothiazines. When possible, most laboratories avail themselves of the commercial screening tests since they are generally quick and inexpensive.

Presumptive drug screening is simple to perform, but difficult to interpret. Most immunoassays are called "presumptive tests," since a positive reaction is an indication that a drug or drug class is present, yet the method does not rise to the required level of certainty. Confirmation by a second test is required. The main reason why presumptive tests are not used forensically is because there is considerable cross-reactivity with drugs other than the target drug.

Lack of specificity is a common problem with immunoassay tests. For example, an immunoassay test for "opiates" will flag positive for codeine, naloxone, morphine, heroin, hydrocodone, and hydromorphone. Thus a presumptive "positive" opiates result may mean that an individual has taken Tylenol with codeine, Vicodin for pain relief, or heroin. In addition, depending on the kit used and the manufacturer of the kit, still other drugs that are not considered an "opiate" may cross-react. Moreover, sometimes the analysis will give a random "false positive," flagging a sample positive when there is no target drug present at all.

There are a variety of different types of immunoassay techniques on the market. Some immunoassay techniques are more specific to the target drug than others. However, all immunoassay techniques utilize an antibody-antigen relationship to identify a drug class in a sample. An antigen is a

foreign substance, such as a drug, that has been introduced into a host body. This antigen will cause an immune response in the host's body, which, in turn, will prompt the host's B- lymphocytes and plasma cells to create an antibody protein. This antibody will then be able to identify and bind to any similar antigen that is introduced into the host.

Commercial immunoassay kits contain a substrate with an antibody to a specific class of drugs, and also the target drug that is "labeled" with a tracer. In radioimmunoassay kits, the label is radioactive iodine or carbon. In fluorescence immunoassays, the label is a fluorochrome. In enzyme immunoassays, the label is a lysozyme or other enzyme. One of the most popular enzyme immunoassay kits is the enzyme multiplied immunoassay test (EMIT) developed by Syva Corporation.

The EMIT utilizes a technique known as "competitive binding." The drug (antigen) labeled with the enzyme competes with any drug found in the subject's sample for a limited supply of antibodies. When the labeled drug in the kit is bound with the antibody, the enzyme activity is inhibited. When a sample has a measurable amount of the target drug, antibodies will not bind to some of the labeled drug and the enzyme will be active and can give a measure of the target drug concentration in the tested sample.

More target drug in the subject's sample means that there are fewer antibodies available to bind to the kit's enzyme-labeled antigen. By measuring the magnitude of enzymatic change on a substrate, the amount of drug present in the subject's sample can be determined. For example, a subject's sample with no target drug will enable most of the kit's enzyme-labeled drug to be bound to the antibodies and will result in an inhibition of the enzyme's activity. When the enzyme activity is inhibited, the substrate in the kit, NAD, cannot be oxidized into NADH. The result is a small absorbance change at 340 nm, measured spectrometrically. Conversely, a large amount of drug in a subject's sample will leave few antibodies to react with the kit's enzyme-labeled drug, and many enzymes will be able to convert NAD to NADH, and result in a large absorbency change. The amount of NAD produced and measured is inversely proportional to the amount of target drug in the sample.

In the past, thin-layer chromatography (TLC) was occasionally used as a confirmation test. However, with the advent of more specific instruments, such as the GC-MS, TLC is now generally used as a screening test. TLC is a simple procedure that enables the chemist to determine the number and possible identity of each compound present in a mixture. This instrument allows a mixture of two or more substances in a specimen (such as urine or a pharmaceutical pill dis-

solved in a volatile solvent) to distribute between a stationary phase and a mobile phase. The stationary phase is a thin layer of adsorbent (silica gel or alumina) coated on a glass, metal, or plastic plate.

The mobile phase is a solvent, into which one edge of the plate is placed. A small amount of the mixture to be analyzed is spotted on the stationary phase, near the bottom of the TLC plate. The plate is then placed in a solvent in a developing chamber so that only the very bottom of the plate is in the liquid. The chamber is capped, and the solvent, by way of capillary action, is allowed to rise up the layer of silica on the plate. For each one of the mixture's components, as the solvent moves through the spot that was applied, equilibrium is established between the molecules that have adsorbed on the solid and the molecules in solution.

Since the components in the applied mixture differ in solubility in the mobile phase and in the strength of their adsorption to the stationary phase, each component will move up the plate at a unique rate, based on its partitioning between the mobile liquid phase and the stationary phase. Highly polar organic molecules interact fairly strongly with the polar adsorbents and will tend to adsorb onto the particles of the adsorbent. In contrast, weakly polar molecules are allowed to move more freely.¹ Thus, weakly polar molecules will move through the adsorbent more rapidly than the polar species, and will be seen higher up the plate than the polar molecules. In this manner, the components of a specimen are separated and may be identified by comparison to known compounds.

When the solvent front reaches the other edge of the stationary phase, the plate is removed from the solvent reservoir and dried. When the plate is examined, the original sample will have resolved into a row of spots running up the plate, with each spot containing one of the components of the original mixture

Some substances are colored, which allows a simple visual comparison of the amount of movement up the plate the compound traveled. Generally, however, the spots are difficult to detect, and must be visualized with an ultraviolet lamp or with staining agents. When the dried plate is placed in a chamber with iodine vapor, the iodine vapor oxidizes the substances in the various spots, making them visible to the eye. Ninhydrin (0.2-percent solution), is effective for visualizing amino acid spots.² When sprayed on the plate, amino acids display a purple coloration. In addition, visualization can be achieved through the use of an ultraviolet lamp. In this method, the adsorbent is impregnated with a fluor (zinc sulfide), which enables the plate to fluoresce everywhere except where an organic compound is present on the plate.

The amount of movement up the plate is determined by and compared against a known standard. This “retention factor,” or R_f , is defined as the distance traveled by the compound divided by the distance traveled by the solvent. If the two substances have the same R_f value, they may be the same compound. If they have different R_f values, they are definitely different compounds. Since the amount of movement up the plate also is dependent on the solvent system used, the type of adsorbent, the thickness of the adsorbent, and the amount of material spotted, R_f values will change from system to system. For this reason, a known standard must be run on the same plate as the unknown specimen (so that their relative R_f values may be compared).

There are a variety of different TLC separation techniques. TLC can be automated using forced solvent flow in a vacuum-capable chamber. The ability to program the solvent delivery makes it convenient to do multiple developments in which the solvent flows for a short period of time. This method enables a higher resolution than in a single run.³ A two-dimensional TLC process can also be applied. After running a sample in one solvent, the TLC plate is removed, dried, rotated by ninety degrees, and run in another solvent. After this process, any of the spots from the first run that contain mixtures can now be separated.

Although TLC seems like a simple procedure, there are some potential difficulties. For example, a sample that has been too heavily applied will visualize as a streak, rather than a spot. A sample possessing a strongly acidic or basic group (such as an amine) may visualize as a smear or an upward crescent. The plate solvent front may run crookedly, which makes it harder to measure R_f values accurately. Sometimes no compound can be seen on the plate because an inadequate sample was applied; or, due to heavy sample application, components with similar R_f values may not be resolved and may appear to be one large spot.

A legal action cannot be scientifically supported solely by a screening test, since a positive result may be due to a different substance or a random error. The laboratory must perform a “confirmation” test on an instrument—such as a gas chromatograph or mass spectrometer (GC-MS)—capable of differentiating between the many drugs in a drug class and quantifying the amount of drug present in the specimen. However, a biological specimen must first be properly prepared before it can be analyzed on a GC/MS instrument.

43.3 Extraction of the Drug from the Biological Matrix

Preparation of the sample for analysis requires that the biological sample be “extracted” from the biological matrix.

This is generally performed using a variety of chemicals that help eliminate possible interfering substances, and allow the drug or drug class in question to dissolve in a solvent, which can then be measured on the instrument. The traditional way of extracting a drug from a biological matrix employed the use of organic solvents for extraction, back extraction into an aqueous phase, a pH adjustment, and then a final extraction into an organic solvent. Some laboratories still use this method, even though it is more cumbersome and time consuming than the more modern way. However, there is nothing forensically wrong with using the old method; and often, especially when dealing with an unknown substance in the biological matrix, a liquid-liquid extraction is employed.

A newer method, called SPE (solid-phase extraction), is more efficient. SPE techniques use a disposable tube containing bonded silica sorbents to trap and release components of a specimen. The efficiency and selectivity of the method depends on the type of SPE sorbent used, as well as the relative physical or chemical properties of the sorbent, the solvent used for extraction, and the group of drugs targeted. There are a variety of different commercial SPE cartridges available, such as copolymer/anion exchange, bonded or nonbonded silica, reverse phase, or anion exchange. The sole purpose of these methods is to extract out, as selectively as possible, only the specific drug or drug class to be analyzed. Once extracted, the sample may be ready for analysis, or may go to an additional step called “derivitization.”

The derivitization step is often performed on a drug or drug class that may (depending on the instrument used) benefit from the addition of the attachment of the derivitizing agent to the test molecule. Derivitization often enhances the quality of the analysis and enables the identification of the drug. Once this step, if required, is performed, the sample is ready for analysis on the instrument.

43.4 The Instruments

There are a variety of laboratory instruments capable of identifying and quantifying the drugs that may be found in a biological specimen. Most procedures call for the use of mass spectrometry. Mass spectrometry separates matter by molecular and atomic mass. Mass spectrometry is arguably the most versatile technology used in analytical analysis today, in that it enables the analyst to determine chemical and structural information about the different types of molecules found in the specimen.

There are many techniques that combine the power of mass spectrometry with other instruments to achieve the goals of selectivity, specificity, and sensitivity. The most common—by far—are the instrument combinations known as the GC/MS, LC/MS, and GC/MS/MS.

A. GC/MS

The gas chromatograph/mass spectrometer (GC/MS) utilizes the gas chromatograph (GC) to separate the components (drugs) of a mixture by injecting the mixture into a metal or glass column inside the instrument. The instrument's inner capillary column is coated with a chemical and packed with sand-like, chemical-coated particles. The column is contained in a heated oven designed to liquefy the coating. When a sample is injected onto the column, the injection port is at a temperature capable of volatilizing the sample (transforming it into a gas). A carrier gas pushes the volatilized sample through the column.

The chemical makeup of each of the mixture's compounds and each component's interaction with the liquefied chemicals in the column determine how long the component will take to travel the entire length of the column. Some molecules will make a slow migration through the column, and some will travel quickly through the column relatively unhindered. In any event, each component of the mixture will travel as a group through the column. The amount of time the compound is retained in the column is called the retention time (RT) of the compound. As each compound exits the column, a detector recognizes the passing of a compound and records the event on chart paper.

A drug may be identified in a specimen by comparing the retention time of any instrumental response from the analysis of the specimen with that of a calibrator or control sample, using just a GC alone. The quantity is determined by measuring the magnitude of the response. However, with the GC/MS, the GC functions as a separating mechanism and the identification and quantification is mainly the responsibility of the MS.

The MS creates gas phase ions, separates these ions in accordance to mass or time, and measures the quantity of ions of each mass-charge ratio. Gas phase ions can be prepared by a variety of methods. Perhaps the most common methods are chemical ionization (CI) and electron impact (EI). As each component exits the GC column, it enters the MS. In CI, molecules are ionized by reaction between the analyte molecules and a reagent ion to form ions by proton or hydride transfer. The other method, EI, uses an electron beam to ionize gas-phase molecules. CI is sometimes used instead of EI because it provides increased sensitivity and provides more specific molecular-weight information. However, the method is technique intensive. Hardware limitations also make EI more common.

In EI, the MS bombards the drug with electrons and shatters the structure into pieces, depending on the weak points in the drug's structure. Theoretically, since each drug structure is different, each different drug will break at differ-

ent points on the molecule and thus shatter into predictable pieces. The size and quantity of the pieces form a "fingerprint" of the drug. If one looks at all the pieces and their relative size, one can identify the drug in the sample.

The data set produced by looking at all the fragmentation pieces of the molecule is called a "scan." (See Figure 43.1.) Scans are sometimes used when the identity of the molecule causing the instrument response is unknown and does not match any of the known drugs analyzed with the specimen. The fragmentation pattern of the specimen can be identified by the pattern produced, and the relative sizes of each of the fragments can be compared with one another. Identification can be performed by computation or by library match. In manual computation, the analyst must determine the chemical structure of the molecule by determining the source of the fragment. For example, a fragment with one carbon and three hydrogen atoms will have a mass of 15 ($C = 12, H = 1; 12 + 3 = 15$), and a fragment of 15 will be seen on the chromatogram. A trained mass spectrometrists will be able to look at an ion chromatogram, with all the ion fragments, and determine the molecular structure of the drug. An easier way, however, is to compare the pattern of the fragments with a known library match. Library databases can be purchased or created in-house. However, library matches are rarely 100 percent accurate, and most library programs will

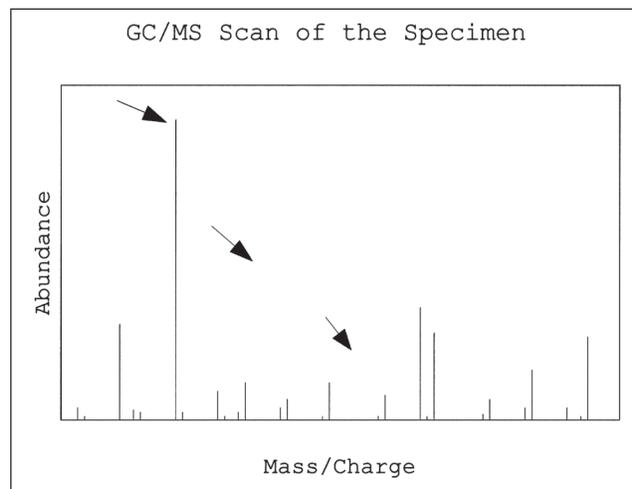


Figure 43.1 GC/MS scan of the specimen
A "scan" records all (each 0.1 amu) of the fragments created from the ionization of the molecule creating a "fingerprint" of the drug. In SIM, the analyst chooses a few relatively unique fragments to represent the identification (arrows). Each fragment must be present at an abundance relative with each other—and in correct proportion, as established by a known drug calibrator—to constitute an identification.

give the analyst the best match, leaving the decision up to the analyst whether an eighty or ninety percent match constitutes an identification. Scans can be performed to identify a drug, but not to quantify the amount of drug present.

Determining the amount of drug present in the specimen is performed using selected ion monitoring (SIM). In the SIM method, the analyst selects only specific ions (rather than all the ions, as in the scan method). The benefit to using the SIM method is the ability to perform quantitations, greater instrument sensitivity, better chromatography, and better accuracy and precision. It is up to the laboratory method to decide which ions to use for identification, but they should be unique (in order to differentiate between the target drug and any similarly structured drugs).

In a typical analysis, the analyst will choose a "target" or "parent" ion for quantifying a drug and "qualifier" ions to assist in identify the drug. These qualifier ions are two more pieces from the electron fragmentation that must be in correct proportion to the target ion in order for the identification to be made. (See Figure 43.2.) The calibrators will establish what the proportion will be for the method. When analyzing an unknown specimen, the analyst/method allows the relative sizes of the qualifier ions to the target ion to differ by about twenty percent. Thus if the qualifier ion is generally eighty percent as abundant as the target ion, a range of sixty-four percent to ninety-six percent is acceptable when analyzing an unknown

specimen. Taken together, with the retention time as recorded by the gas chromatograph and the presence of a target ion and the qualifier ions in proper proportion, these methods can identify a drug with fairly high certainty.

B. Quantifying a drug using the GC/MS

Quantifying a drug on the GC/MS is generally performed by the use of an internal standard. An internal standard is used to monitor the efficiency of the extraction procedure, or to insure that the amount detected is not due to an erroneous injection. The internal standard is usually a compound closely related in structure to the drug being sought, since it must have a retention time within a few minutes of the target drug. However, the analyst must be careful and select an internal standard that will not likely be found in the sample to be analyzed. In the GS/MS, the internal standard is usually a deuterated version of the target drug.

The internal standard is typically added at the beginning of the extraction procedure. Since the internal standard is added to an aliquot of the specimen at the beginning of the analysis, there exists from the start of the analysis a relationship of the internal standard to the drug that never changes. No matter if one drop or one cup of the extracted sample is tested, the ratio of drug to internal standard will remain constant. By plotting the ratio obtained by the instrument for a suspect's sample against a variety of standards of known

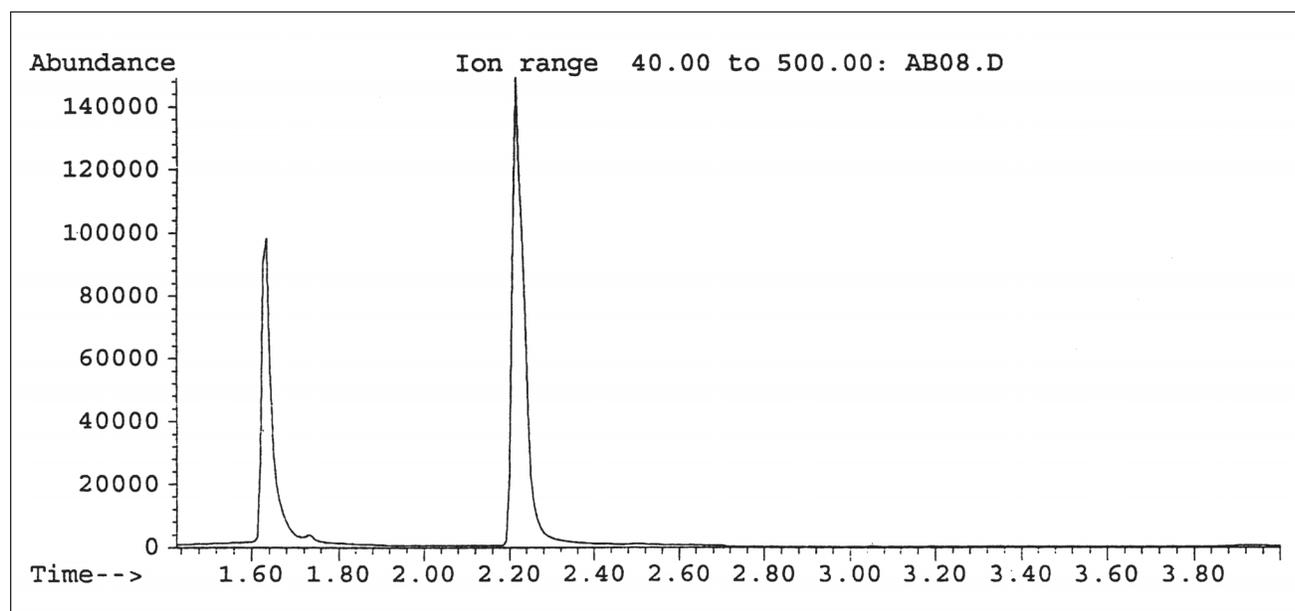


Figure 43.2 The total ion chromatogram

Once the specific ions to be monitored are selected by the analyst via SIM, the resulting chromatograms show only the fragments selected. A total ion chromatogram (TIC) will be generated, representing the total abundances of all the selected ions at different retention times. For example, in this figure, a major compound at 12.86 minutes and another at 13.82 minutes are seen by the instrument.

drug concentrations and their respective ratios, one can determine the amount of drug present in the sample.

In order for the specimen to be quantitated, there needs to be a relationship established between the instrument response and the concentration of the specimen. To establish this relationship, a series of samples of known concentrations, called calibrators, must be created and tested. This is performed by taking a solution of the target drug and spiking the same type of biological fluid as the specimen to be tested with the drug at various concentrations. A calibrator or control without drug must also be tested. These calibrators are extracted in the same manner and around the same time as the specimen to be tested, and have the same amount of internal standard as the test specimen.

A "target" ion, generally the most abundant ion in the molecule, is chosen to be used to quantify the drug. The more abundant the target ion, the higher the concentration of the calibrator/sample. Since an internal standard is used, the ratio of the target ion of the internal standard to the target ion of the calibrator is used to help eliminate the possibility of an incomplete or overstated injection onto the GC/MS.

After the analysis of the calibrators, the relationship of the calibrator/internal standard instrument responses versus the calibrator concentration can be plotted. A straight line will be generated by the analyst or performed automatically by the computer-assisted instrument. (See Figure 43.3.)

The line generated is tested by the use of a quality control. The quality control is a sample of known concentration, which is created separately from a different solution than the calibrators. The result of the quality control, utilizing the line plotted by the calibrators, must fall within specified guidelines, generally no more than \pm twenty percent of the true value.

Once a relationship has been created between drug concentration versus instrument response and the line is validated by the acceptability of the quality-control result, the analyst can begin to analyze the specimen of unknown concentration. This analysis results in the determination of the instrument response, the abundance of target ions of the unknown specimen, and the target ions of the specimen's internal standard. Utilizing the line generated by the analysis of the calibrators, the analyst can then mathematically determine the concentration of the drug in the sample. (See Figure 43.4.)

C. The GC/MS/MS

The GC/MS/MS is similar to the description for the GC/MS above, but a third step is added. The initial fragmentation goes through yet another fragmentation to produce daughter fragments. This method is often used for better selectivity and specificity, but is not as common as the GC/MS because of the cost of the instrument.

D. The LC/MS

Liquid chromatography (LC) is a separation technique whereby the test specimen is forced over a chemical system contained in a column by means of a flowing solvent stream rather than via gas (as with the GC). As with a GC, the individual compounds in the mixture travel at different rates down the column, depending on the chemical interaction of the mixture with the chemical system contained in the column.

The solvent system can be of a single buffered solvent (isocratic) or be a combination of several solvent systems (gradient). The benefit of a gradient system is the versatility in analyzing a wide range of compounds, and the ability to produce a higher concentration of the drug. Gradient is most often used when the specimen contains unknown drugs. The isocratic method is faster, and thus is more attractive to laboratories that analyze large quantities of specimens.

LC can be used alone with the traditional ultraviolet, visible, fluorescence, or electrochemical detector, or coupled with a MS. Use of LC/MS is steadily increasing in the field of toxicology, partly due to the ease in sample preparations, and partly because of the instrument's simple extractions and lack of need for derivitization.

43.5 Sources of Instrumental Error

Regardless of the instrument chosen, there are many opportunities for error to be introduced into the testing process. The magnitude of the error is dependent on the type and degree of error allowed by the analyst of the method employed. Regardless of the source, appreciable error results in uncertainty of the identification and quantitation of the drug in the specimen and may directly impact litigation.

Errors in sample preparation, including extraction, directly affect the resulting numerical result. Improperly prepared calibrations and changes in the amount of sample used for extraction introduce the greatest magnitude of error. For these reasons, the quality-control sample must always be used to ensure that the calibrators were properly made. Likewise, the internal standard must be added as soon as possible in the preparation steps.

Errors in analysis can be introduced in many ways. One way is by the improper selection of calibrators to create the concentration/instrument response relationship. The calibration line does not always travel through zero, and may not be linear at all levels. Of special concern is when the drug concentration of the unknown specimen is greater than the highest calibrator used to create the linear relationship, since the relationship can only be shown to be linear through the range of the calibrators. After the highest or lowest calibrator, the line may cease to be linear and may curve. Thus, it is important to elicit the experimental upper range of linearity from

the testing laboratory. It should be noted that although the laboratory has scientifically determined this upper level in the past, only the calibrators used at the time of the test can determine the working parameters of the instrument at the time of the subject's test.

To overcome the problem of a sample being higher than the calibrators, some laboratories dilute the sample, or use less sample volume, and then multiply the calculated concentration by the dilution factor. This dilution step, unfortunately, introduces another possible source of experimental error.

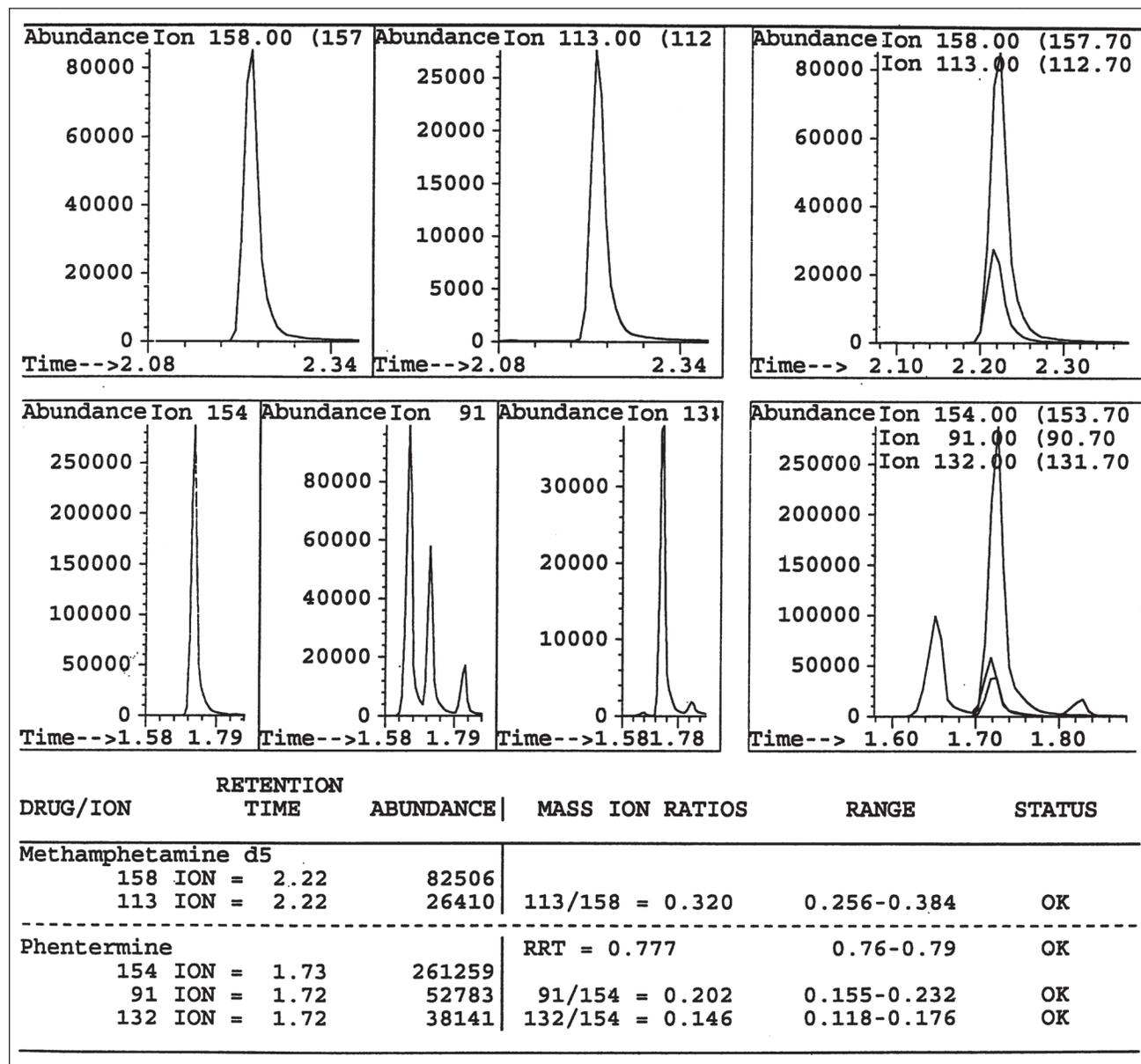


Figure 43.3 Sample data sheet

The peaks seen on the TIC (Figure 43.4) chromatogram represent the instrument's response and detection of a compound with any or all of the selected ions at different retention times. On the left side of Figure 43.4, the abundances of the selected ions of the TIC peak with retention time at 13.813 and 13.833 are shown. On the right side of Figure 43.4, the deuterated (D3) morphine internal standard and the morphine in the specimen are shown. The ratio of the response (Resp) of the D3-morphine target ion (470302) and the specimen target ion response (278222) determine the resulting concentration of 0.056 ug/mL for the specimen. Note that the target ion has a ratio of 100, and the qualifier ions (432 and 199 for D3-morphine, and 429 and 196 for morphine) must be between the upper and lower established ranges to constitute an identification.

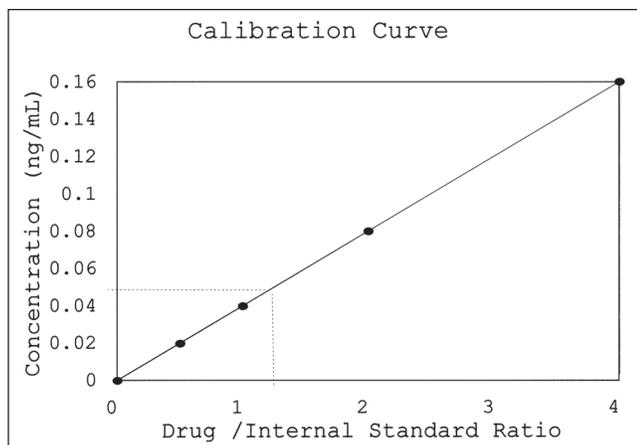


Figure 43.4 Calibration curve figure

A relationship between (1) the concentration of the calibrator prepared by the analyst and (2) the ratio of the instrument's response of the drug—divided by the instrument's response of the internal standard—is plotted. A straight line is drawn to establish a linear relationship. The concentration of drug in the specimen can then be determined by measuring the drug/internal standard instrument response and mathematically or visually determining the corresponding concentration. In this example, an specimen with a drug/internal standard response ratio would be about 0.06 ng/mL. All modern GC or LC/MS systems are computerized to perform this function automatically.

Sometimes the concentration of the drug in the subject's sample is too minute for the limit of detection for the method and instrument used. Although the GC/MS is state of the art, there is a level of target molecule so low that the instrument cannot identify or consistently quantify the sample. These levels are respectively called the "limit of detection" and the "limit of quantitation."

The analyst must be careful to measure the amount of response properly so that a proper ratio can be determined. Typically, the responses should be Gaussian in shape, or much like a sharp triangle. However, when the chromatography starts to deteriorate, "shoulders" and other bumps start to distort the Gaussian peak. When this happens, area is added to the peak, and is erroneously attributed to the amount of drug.

43.6 Types of Errors

Errors can include the following:

- improper sampling of the aliquot from the sample vial,
- error in spiking calibrators from which the instrument response line will be generated,

- improper addition of the internal standard,
- poor chromatography,
- inadequate testing of other drugs to eliminate interference or misidentification,
- improper range of calibrators,
- lack of proper controls,
- lack of linearity of the concentration/instrument response curve, and
- carryover or contamination from the sample analyzed immediately preceding.

43.7 Discovery

Discovery of the proper laboratory data is essential for determining the exact quantity of drug found in a biological specimen. The following data should be discovered:

A. Sample collection

- documentation of the time of the incident/death
- documentation of the location of the sample draw (arm, heart, femoral artery, and so on)
- postmortem: time of autopsy
- method of body storage prior to autopsy
- damage to stomach and other internal organs

B. Standard operating procedure

Standard operating procedure (SOP) for evaluating analysis QA/QC should include the following:

1. Testing and certification

- results of the last two proficiency tests given by an outside organization, if any
- results of in-house blind QA tests given in the last twelve months
- results of any proficiency tests given to the analyst in this case

2. Screening test

- all screening test results for the subject's specimen
- all quality controls and calibrator results for the run in which the specimen was tested
- the identification of the manufacturer of the reagent kit used in the analysis
- the manufacturer's product insert provided with the kit
- the method used by the laboratory in the analysis
- procedures used that differ from the manufacturer's method

- results of specificity tests performed by the laboratory for the drug in question

3. Confirmation

- identification of the type of instrument and detector used
- all GC, GC/MS, and/or LC/MS data (chromatograms and ion identification) of the subject's specimen
- all GC, GC/MS, and/or LC/MS data (chromatograms and ion identification) of the calibrators/controls
- the GC, GC/MS, and/or LC/MS method identifying the chromatography, RT and ion ratio acceptability
- all specificity data for the drug in question on the GC, GC/MS, LC/MS
- the extraction procedure and sample preparation method
- the run list identifying the position of the subject's sample in the order of analysis

43.8 Summary

Proper analysis of the biological specimen for drugs is crucial to the litigation of drug-related cases. The identity and quantity of the drug found in the specimen should always be critically reviewed and questioned. Whether representing a plaintiff or defendant, the data gleaned from a close review may make or break a case.

Analysis of the sample generally starts with a screening of the specimen by use of a presumptive test, followed by extraction of the drug from the biological matrix and analysis on a confirming instrument, such as the GC-MS. It is critical that each of these steps follow acceptable forensic and scientific standards to ensure the identity and integrity of the analysis.

Generally, the specimen will go through a screening or presumptive test to determine whether it contains a specific drug or drug class. The screening test must have quality controls, calibrators, and negative controls that meet the defined criteria as established by the laboratory. Ideally, the specimen should be tested in duplicate. Specimens tested in singlet have the potential of error because of incorrect sampling by the analyst, because of cross-reactivity with other drugs in the sample (which can cause false positives), as well as unexplained, randomly occurring errors. Thus, specimens tested in singlet may be quick and inexpensive for the laboratory, they do not rise to the certainty required in court. The most that can be said about a result from a presumptive screening test is that there is a potential of the target drug class being present in the specimen.

The extraction of the drug from the specimen is necessary to prepare it for the confirmation step. A series of standards and controls should be extracted concurrently with the sample specimen. The use of an internal standard in the extraction procedure is the most common and recommended practice. Use of an internal standard helps eliminate extraction errors, since any error in the extraction of the target drug from the specimen will likely be reflected in an equally poor extraction of the internal standard. A poor recovery of the internal standard alerts the analyst to a possible extraction error.

After extraction, the specimen extract is analyzed on a confirmation instrument, generally a GC/MS. The GC/MS will identify and quantitate the drug in the specimen. However, the accuracy of the measurement is only as good as the method used by the laboratory. The selected method must have been rigorously validated in the laboratory prior to use to help eliminate the possibility of misidentification. Calibration standards and controls must be used in the analysis to ensure that the measurement is correct.

If the presumptive screening result and the GC/MS result are consistent, and if all standard scientific criteria are met, the specimen result is then reported. Toxicology experts then interpret the results to determine the levels of the drug and corresponding effects.

Interpretation of the results is dependent on the quality and quantity of the data given to the expert to review. The expert must be given all the screening and confirmation data from the specimen, as well as from the standards and controls used in the analysis. A copy of the laboratory's SOP should be reviewed to ensure that the proper steps were taken. The laboratory's validation data should be reviewed to ensure that the method used has the necessary level of sensitivity and accuracy for the test.

Finally—but perhaps most importantly—the identity and integrity of the specimen must be documented through each step.

Endnotes

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Chapter 44

Drug Testing in the Workplace

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44.1 Introduction

Illegal drug use has increased in an alarming rate. In the period between 1955 and 1980, the United States experienced a twenty-fold increase in the use of illegal drugs. The highest drug-use rates are among persons aged sixteen to twenty-five—the emerging workforce in America. In a 2000 federal survey, about 14 million Americans were determined to have used illegal drugs within one month of the survey.¹

Abuse of drugs and alcohol are two of the most costly activities to the American society. In 1993, the societal cost reached \$400 billion.² The corporate world incurs a large share of this cost in the form of lost productivity, untimely deaths, and illnesses associated with drug use, to the tune of almost \$81.6 billion a year.³ Increased absenteeism, workplace accidents, workers’ compensation claims, medical costs, and decreased productivity all negatively affect the economy and American businesses.⁴

A survey by Hazelden Foundation determined that more than 60 percent of adult Americans know individuals who have gone to their place of business under the influence of either drugs or alcohol.⁵ In fact, it is estimated that 70 percent of all illegal drug users are currently employed and affecting the efficiency of the workplace.⁶ Drug-impaired employees are not only costly to the business owner and industry, they also can pose a substantial safety risk to themselves, to their co-workers, and to the general public. As an apparent response to these alarming statistics, over 80 percent of American companies now conduct some type of workplace testing.⁷

44.2 Non-Regulated Testing

The interest of an employer in the productivity and welfare of his employees is not a new concept. As early as 1914, industry attempted to regulate the “sobriety” of their employees. In the 1940s, accidents and absenteeism in the Kaiser shipyards were so prevalent that Kaiser created an in-house healthcare system, financed by payroll deductions. These early attempts of identifying drug-use risk factors and drug-testing by industry leaders, however, were fundamentally flawed—the plans were unregulated, lacked clear policy statements, and had no standards of performance.

44.3 Regulated Testing

In 1983, the Department of Transportation (DOT), in conjunction with the National Institute on Drug Abuse (NIDA), drafted a drug program for regulated testing. This program was initiated in response to concerns of the National Traffic Safety Board over the increase in drug- and alcohol-related

accidents in that industry.⁸ However, it was not until 1986, when President Reagan's Commission on Organized Crime released a report connecting drug use with trafficking and organized crime, did regulated testing get into full swing.⁹ In the report, the commission called upon the president to issue a policy statement expressing the unacceptability of drug use among federal employees, and to outline the measures necessary to achieve the commission's goals.

In response, on September 15, 1986, President Reagan signed Executive Order 12564, the first step towards the ultimate goal of a "Drug-Free Federal Workplace." The order recognized the impact of drug use in the workplace, and established the unprecedented rule of prohibiting federal employees from using illegal drugs on- or off-duty. The order states, in part,

The Federal Government, as the largest employer in the Nation, can and should show the way towards achieving drug-free workplaces through a program designed to offer drug users a helping hand and, at the same time, demonstrating to drug users and potential drug users that drugs will not be tolerated in the Federal workplace (Ibid)

On July 11, 1987, Congress passed legislation affecting the implementation of the order. Congress' goals were to establish uniformity among the drug-testing plans of the various agencies, ensure reliable and accurate drug testing, allow employees access to drug-testing records, provide confidentiality of drug-testing results, and centralize oversight of the drug-testing program.¹¹ This legislation was made under Section 503 of the Supplemental Appropriations Act of 1987.¹²

The act placed the burden of providing mandatory guidelines on the Department of Health Services (HHS). The HHS was directed to establish "comprehensive standards for all aspects of laboratory drug-testing and laboratory procedures to be applied in carrying out Executive Order Numbered 12564, including standards which require the use of the best available technology for enduring the full reliability and accuracy of drug tests and strict procedures governing the chain of custody of specimens collected for drug-testing."¹³ The Secretary of the HHS was required to set the mandatory standards for all aspects of laboratory drug testing, including who would be tested, when the tests would be conducted, what drugs would be covered, and how the tests would be conducted. Testing was authorized for applicants, random testing of employees in designated "sensitive" positions, reasonable-suspicion testing, accident or unsafe-practice test-

ing, voluntary testing, and testing as part of or as a follow-up to counseling or rehabilitation.

In 1988, the first guidelines were published by the U.S. Department of Health and Human Services Administration (HHS) in the document titled "Guidelines for Federal Workplace Drug-testing Programs." In 1994, the guidelines were revised and republished.¹⁴ They established the testing criteria, the allowable specimen matrix, and the limited number of drugs that may be tested in the specimen.¹⁵ The following entities are mandated to follow the guidelines:

- Executive agencies, as defined in 5 U.S.C. § 105
- Uniformed services, as defined in 5 U.S.C. § 2101(3), except for the armed forces, as defined in 5 U.S.C. § 2101(2)
- Any other employing unit of the federal government, except for the U.S. Postal Service, the Postal Rate Commission, and employing units of the judicial and legislative branches
- Laboratories that possess or seek certification to perform urine drug testing for federal agencies under a drug-testing program conducted under Executive Order 12564
- The intelligence community, as defined by Executive Order 12333, to the extent agreed to by the head of the affected agency

HHS established the National Laboratory Certification Program (NLCP) to certify laboratories before they are permitted to test specimens collected for federal agency drug-testing programs. The DOT, the Department of Energy (DOE), and the Nuclear Regulatory Commission (NRC) also require the industries they regulate to use these certified laboratories for their workplace drug-testing programs. The DOT, in particular, has followed the guidelines very closely in their drug-testing program. The DOT's program was codified in the Federal Register (49 C.F.R. Part 40) and became applicable nationwide in the passage of the Omnibus Transportation Employee Drug-testing Act of 1991.¹⁶

44.4 Voluntary Programs

Many private companies perform functions that do not require mandatory adherence to the Federal HHS guidelines, yet still have a regulated internal program. One such voluntary program, administered by the College of American Pathologists, is called the Forensic Urine Drug-testing Program (FUDT). The FUDT program establishes the minimum criteria for reliable urine drug-testing procedures, which parallel the general consensus of the scientific community. While

participation in the FUDT program is voluntary, many laboratories have an interest in being accredited by FUDT, since the program is one of the few non-governmental programs available to forensic laboratories.

Lack of formal regulation has some benefits and drawbacks. The most notable drawback is the possible development of a workplace drug-testing program that lacks procedural oversight and mandatory adherence to basic forensic-testing standards. Lack of adherence to scientifically accepted standards in a company's policies and procedures could increase employee-based legal challenges to any enforcement and sanctions incurred through the administration of the program. However, non-regulated testing allows employers to conduct more extensive testing of an employee's biological sample. For example, regulated testing may narrow the groups of drugs to be tested to five major drugs of abuse: cocaine, phencyclidine, opiates, amphetamines, and cannabinoids. Regulated testing often limits the sample matrix to urine, and dictates the methods of testing. Non-regulated testing may allow testing for a multitude of drugs, including prescription drugs, in a variety of testing matrices such as blood, hair, sweat, urine, or saliva.

Regardless of whether the private company chooses to follow the federal program, a private program, or one of their own, certain program guidelines should be followed. Only by establishing a comprehensive program, can an effective program be created.

44.5 Establishment of a Workplace Program

The decision to develop and implement a drug-free workplace program begins with the establishment of policies guiding the program to the ultimate goal of increased safety and productivity in the workplace. Guidance for the components of a complete program can be found in Section 503 of the Supplemental Appropriations Act of 1987 (Section 503). Section 503 requires that all agencies establish a reliable workplace drug program containing five major components: a written policy statement, provision for supervisor training, provision for employee education, provision for employee assistance, and the guidelines for drug testing.¹⁷

All five steps are not necessary in non-regulated testing, but establishment of all five steps make the policy clear, and may minimize legal ramifications on any employer-based action taken when an employee violates the program.

A. Written policy

A written policy statement provides the basis for an agency or company's program. Thus, an obvious starting point for

the establishment of an effective program is a written policy documenting the requirements of the employer, program-adherence expectations, and ramifications of non-compliance with the policy. For federal programs, the act requires the agency to state why the drug-free program is being implemented, provide a clear description of what behaviors are prohibited, and provide a thorough explanation of the consequences of violating the policy. Regardless of whether the employer is or is not mandated to follow the steps established by the act, the following program components must be included:

- The rationale for the establishment of a policy
- A clear description of the prohibited substances and behaviors
- The type of required drug testing, and the circumstances (random, post-accident, reasonable cause, etcetera) prompting drug-testing
- Procedures for the determination of a policy violation
- The consequences for the violation of the policy (and any available appeals processes)
- A statement of when the policy will be enforced
- The documentation of what types of employees will be covered by the policy (safety-sensitive employees, contractors, pre-employment, all employees, and so forth)
- The treatment and rehabilitation services available to the employee
- Issues of employee confidentiality

B. Employee assistance programs

Employee Assistance Programs (EAPs) provide drug-abuse education to company managers and counseling for employees seeking assistance for drug- or alcohol abuse problems. An EAP program is a benefit to the employer, in that it allows managers to become educated in drug-abuse issues, while keeping them separated from the actual counseling process. An EAP is also an excellent benefit to the employee, since it often becomes an alternative to dismissal, and can provide resources for treatment facilities and counseling.

An EAP is a necessary component of any effective program, and is a requirement in HHS-regulated testing. The act states that an agency must provide an EAP to help resolve poor work performance due to alcohol or drugs, as well as for personal problems. A successful EAP must provide treatment and rehabilitation to employees who have tested positive on a drug test or who have referred themselves for assistance. In addition, an EAP should disseminate knowledge on drug abuse and effects, and reinforce the impact of drug use in the workplace. Above all, any effective EAP program must as-

sure the employee that all functions provided by the EAP, including test results and medical treatment, will be conducted with confidentiality.

C. Employee awareness training

Policies that are established and enforced in a draconian manner are often not financially beneficial to the employer. Legal consequences and the cost of training and hiring new employees make the establishment of an employee-education program beneficial. Aside from educating the employee on the contents of the program and the new company policy, basic information on alcohol and drug abuse in the workplace is recommended. The act requires that the EAP administrator provide employee education to all federal employees. A model program under the act would include education on the types and effects of drugs, symptoms of drug use, effects of drugs on performance, the role of the EAP, treatments available, and confidentiality issues. Employee awareness programs should also include the recognition of substance abuse in the family or coworkers, the safety hazards of drug abuse in the workplace, and the available resources for addiction assistance in the company and community.

D. Supervisor training

Supervisors provide the first line of drug detection in employees. The act requires that federal agencies provide and implement training to assist their supervisors in recognizing illegal drug use.¹⁸ In addition, an agency must develop a training package or course covering the following issues:

- Employee problems with drugs and alcohol
- The role of EAP and the EAP supervisor
- Recognition of employees with drug or alcohol problems
- Documentation of performance or behavior problems
- Skills in confronting employees
- Agency procedures regarding referral to the EAP
- Disciplinary action and removal from safety-sensitive positions (Section 5 of the Executive Order)
- Reintegration of the employee into the workforce
- Written materials for the supervisor

Supervisors should be trained to recognize and understand drug-abuse and job-performance issues. The monitoring of job performance, rather than the diagnosis of drug abuse or drug-abuse counseling, is the main purview of the supervisor. Documentation of performance problems will prompt the employee's referral to the available assistance. The act requires the supervisor's training to include the

organization's policy, the supervisor's specific responsibilities, and how to deal with employees who have performance problems. In addition, the supervisor should be trained on how to monitor employee job performance, document performance issues, enforce the policy, and make referrals for testing based on reasonable suspicion.

E. Drug testing

A standard drug-free workplace program must allow for drug testing, since any sanctions against an employee for mere suspicion of drug use or influence may not stand up to legal review. Drug testing may take place prior to hiring, upon reasonable suspicion, for cause, post-accident, randomly, periodically, or post-rehabilitation. Executive Order 12564 defines illegal drugs as any drug on Schedule I or II of the Controlled Substance Act. Since it is impractical to test for all the drugs listed in these schedules, the guidelines require that random drug-testing programs shall test urine for marijuana and cocaine, at a minimum. The agency may add to the minimum list by also testing for opiates, amphetamines, and phencyclidine; or request a waiver from the HHS to routinely test drugs other than the five listed. However, when testing for reasonable suspicion, accident, or unsafe practice testing, other drugs in Schedule I or II may be tested.¹⁹

In nonregulated testing, the employer and the testing laboratory have wide discretion in choosing the methods used and the drugs tested in a biological specimen. HHS restricts the matrix to urine. However, non-regulated programs may allow for testing of an unlimited number of drugs in a variety of matrices, including sweat, saliva, and hair.

44.6 The Drug-Testing Process

A vital part of any drug-free workplace program is the collection of the chosen biological matrix, the analytical testing of the matrix for a series of illegal drugs, and the accurate reporting of the results. Non-regulated testing laboratories are not limited to testing only urine, and may use any method for testing. Their only oversight is the opinion in the relevant scientific community. Regulated testing, on the other hand, may take the form of the private CAP-FUDT program or the HHS Guidelines.

Federal agencies of the executive branch must comply with Executive Order 12564 (1986), which establishes the on and off-duty abstinence from illegal drugs a condition for employment in a federal job. Federal grantees and contractors with contracts valued at \$100,000 or more must comply with the Drug-Free Workplace Act of 1988. In addition, laboratories, which perform testing on federal employees, must

be certified by the NLCP under the HHS. In the transportation industry (DOT), employers must comply with the Omnibus Transportation Employee Testing Act of 1991 by establishing an alcohol and drug program for safety-sensitive employees. The NRC has established standards for nuclear power producers, and employers with Department of Defense (DOD) contracts must also establish a drug-free program for employees in “sensitive” jobs.

Private programs and the federal programs have some similarities—they are dedicated to maintaining a high analytical standard. All programs must require the laboratory to have in place a Standard Operating Procedure (SOP) manual that includes a description of the laboratory’s chain-of-custody procedures, analytical testing procedures, quality control and quality-assurance programs, equipment and maintenance, accessioning and security, personnel qualifications and training, and reporting procedures. The laboratory must also be subject to inspections by the administering program, which must send proficiency samples to the laboratory on a regular basis.

The following drug-testing guidelines contain the basic scientific concepts of the testing process and also provide some examples of the basic requirements of different programs. However, the complete guidelines for the College of American Pathologists Forensic Urine Drug-Testing program (CAP-FUDT), the federal program as outlined in the federal mandatory guidelines, and the DOT program will not be provided here. Drug-testing programs are always subject to change with increasing needs and technology. Therefore, for a more thorough list of requirements, clarification on each activity, and new changes, the latest revision of the original documents should be consulted.

A. Collection

The collection of the specimen is a vital part of the workplace testing process. It is the foundation of the process, and can affect the reliability and effectiveness of the entire program. During the entire drug-testing process the integrity and identity of the specimen must be maintained—from the collection of the specimen to the reporting of the specimen results. The manner in which the specimen is collected, the safeguards against specimen tampering during the collection of the specimen, the correct identification of the specimen, and the accompanying chain of custody are all factors impacting the identity and integrity of the specimen.

A chain of custody must be maintained to document the location of the specimen at all times. In order to maintain the integrity of the specimen, the chain of possession of the specimen must remain intact and must not be broken at any time. The common acceptable chain-of-custody formation

is generally called the “Z” formation. A “Z” formation (representing a “Z” character when the chain-of-custody documentation form has two entries per line) takes the following form: A to B, B to C, C to D, and so on. The following represents an unacceptable chain of custody: A to B, C to D, etcetera. In the latter example, there is no documentation of where “B” placed the specimen and from where “C” received the specimen—the chain has been broken. The HHS requires that their standardized Custody Control Form (CCF) be used and that the control and accountability of specimens be maintained at all times. Every individual in the chain must be identified, and documentation of the individual handling the specimen—as well as the date and purpose for access to the specimen—must be contained on the chain-of-custody document.²⁰

The integrity of a urine drug test hinges on the proper collection of the specimen. The DOT has set into place strict requirements for the collection of specimens. All procedures for Department of Transportation (DOT) collection must be performed as per 49 C.F.R. Part 40.21 The correct collection procedure must be followed, a proper chain-of-custody form must be used at all times (CCF), the identity and integrity of the sample must always be maintained, and the collector must meet the training requirements of Section 40.33 of Part 40.

The DOT’s collector training requirements are extensive and thorough. As of August 1, 2001, the collector must be trained in a series of procedures and must meet the requirements of 40.33 of Part 40. The collector must show knowledge and compliance in the following areas:

- Knowledgeable about the current “DOT Urine Specimen Collection Procedures Guidelines” published by the DOT
- Qualification training in the proper collection procedures, completion of the CCF, procedures in solving problem collections (e.g., “shy bladder”), correction of correctable flaws and identification of fatal flaws (for example, the specimen ID on the donor’s bottle does not match the CCF or the seal is broken) during collection.
- Demonstration of collection proficiency by completing five consecutive error-free mock collections by a qualified collector
- Attendance of a refresher training at least every five years
- Attendance of a refresher course within thirty days if an error in a collection results in the cancellation of a test (fatal or uncorrected flaws)

- Maintenance of documentation showing compliance with the requirements in § 40.33 of Part 40

Each agency or company must have designated collection sites. These sites must be secure, accessible only to designated personnel, and have the proper procedures in place to ensure the integrity and identity of the urine specimen. Such procedures include the deterrence of possible dilution of the sample by the donor, the presentation of a photo-identification card by the donor upon arrival, the removal of any clothing that may conceal adulteration materials, the washing of the donor's hands prior to urination, the elimination of access of the donor to water during the physical voiding of the bladder, and the collector's observation of the donor prior to urination. All collections must be performed in accordance with applicable regulations and must ensure the privacy of the donor by the use of a donor number rather than the donor's name.

Many programs require or allow the collection of "split specimens." Split specimens allow a portion of the collected sample to be poured into an addition container for independent testing or to preserve the specimen in the event that the original or first container becomes destroyed or contaminated. An example of a split collection procedure can be found in the DOT agency drug-testing requirements. In the DOT program, all specimens must be split-specimen collections. At least 45 mL of urine must be collected; 30 mL must be poured by the collector into Bottle "A," the primary testing bottle, and at least 15 mL must be poured into Bottle "B." The donor may urinate into a specimen container or a designated Bottle "A." The collection site person then pours the urine into two specimen bottles that are labeled Bottle "A" and Bottle "B" or, if Bottle "A" was used to collect the specimen, pours an appropriate amount into Bottle "B".

During the physical collection of the specimen, the donor is given a clean specimen bottle and allowed privacy to complete the voiding of the bladder. On receiving the voided specimen from the donor, the collector must ascertain that a sufficient amount of urine has been voided. The specimen temperature should always be checked immediately. A urine temperature less than 90–100° F indicates that dilution or substitution of the specimen may have occurred. If not enough urine has been voided, and the urine temperature is within range, most programs allow the donor to drink fluids and attempt another collection in the same manner as described above. All specimens—even those suspected of being adulterated or diluted—are considered evidence, and must be sent to the laboratory for testing.

After collection, the specimen is checked for color and any signs of contaminants. Any signs inconsistent with a valid sample must be noted on the chain-of-custody collection form. The specimen bottle is sealed with tamper-evident tape by placing the tape over the cap and down the sides of the bottle. An identification label containing the date, the donor's specimen number, and other identifying information (other than the donor's name) is placed on the bottle. The donor then signs the chain-of-custody form, verifying the collection process.

The privacy of the donor during collection is maintained unless certain criteria are met. Under certain circumstances, direct observation of the actual collection may be allowed. For example, employers may specify a direct collection when it is determined that there is no valid medical reason for the specimen to have been considered "invalid," when the donor's test is a return-to-duty test, or a follow-up test. The collector must conduct a direct observation of urine collection if the specimen temperature is out of range, or there is evidence of specimen tampering or adulteration.

B. Accessioning

The accessioning procedure is the gateway to the laboratory testing process. The biological specimen must arrive at the laboratory with the shipping package intact, a proper chain-of-custody form, and the specimen correctly identified. Broken specimen containers or seals or gaps in the chain of custody all call into question the integrity of the specimen. Specimens without all the indicia of reliability should not be tested.

When the specimen is received, laboratory personnel must inspect the package for evidence of possible tampering, and must compare information on specimen bottles to the information on the accompanying CCF. Most drug-testing programs have requirements in place for the acceptance or rejection of specimens during the accessioning process. Some flaws are not considered "fatal" and may be easily corrected by affidavit from the collector. At present, HHS is reviewing their policies and has proposed a list of minor issues that may appear on the CCF that do not need to be corrected by affidavit. The DOT requires that certified laboratories follow the requirements in Section 40.83 of 49 C.F.R., Part 40, in receiving and processing the sample for testing. The laboratory must inspect the CCF and the specimen and note if there are "fatal" or correctable flaws. Some types of identified fatal flaws are:

- The specimen ID numbers on the specimen bottle and CCF do not match

- The specimen bottle “A” seal is broken or shows evidence of tampering. Exceptions are when split specimens can be redesignated as Bottle “A.”
- The collector’s printed name and signature is omitted from the CCF
- Specimen bottle “A” has insufficient urine. Exceptions are when split specimens can be redesignated as Bottle “A.”

Fatal flaws are not correctable, and the specimen must be rejected for testing.²¹ Nonfatal flaws can be corrected within five days by affidavit.

Since the accessioning area receives and maintains the urine specimens, the area must be secure and limited to authorized individuals. Entry and exit from the area must be documented. Authorized visitors are allowed in the accessioning area, but must be escorted at all times.

C. Drugs to be tested

Non-regulated testing has no restriction on which drugs or drug classes that a laboratory may test in a specimen. Generally, in regulated testing, only five classes of drugs are covered: phencyclidine, opiates, amphetamines, cocaine, and cannabinoids. The HHS requires that an “Agency requesting the authorization to include other drugs shall submit to the Secretary in writing the agency’s proposed confirmatory test methods, testing levels, and proposed performance test program.”

When performing an analysis for a particular drug or drug class, a laboratory must clearly establish the criteria for the determination of a positive or negative result, including a proper “cutoff point,” below which the specimen

result must be reported as “negative.” In nonregulated testing, the laboratory has a broad discretion in determining what cutoff level will be used and how the ultimate result will be reported. A nonregulated laboratory may allow the cutoff to be determined by the lower limit of detection of the instruments used, or may allow the reported result to be worded in vague terminology such as “possible presence” or “indicated.” In regulated testing, however, cutoffs for screening and confirmation are mandatory (Table 44.1).

D. Initial test/immunoassay testing

Laboratory analysis of a donor’s urine sample is performed in two separate stages. The first analysis is generally called an “initial test,” “screening,” or “presumptive” test. Non-regulated programs may allow a laboratory to use thin-layer chromatography or similar technology to screen the urine specimen. HHS and DOT guidelines mandate that immunoassay techniques be employed. The requirements do not specify which initial immunoassay product to use, as long as the product meets all the requirements of the Food and Drug Administration for commercial distribution.

Most commercially available immunoassay kits have initial tests for the drugs typically covered by the regulated programs. Immunoassays are useful in separating out the negative specimens from those that may be positive for a particular drug or drug class. The technology does not yet rise to the certainty standard as required by a confirmation test, mainly because there is considerable cross-reactivity with drugs other than the target drug.

There are a variety of different types of immunoassay techniques on the market. Some common technologies utilized are radioimmunoassay (RIA), enzyme immunoassay

Table 44.1

| Drug or Metabolite: | Initial Test (ng/mL): | Confirmation Tests (ng/mL): |
|---|-----------------------|---|
| Marijuana metabolites Delta-9-tetrahydrocannabinol-9-carboxylic acid | 50 | 15 |
| Cocaine metabolites Benzoylecgonine | 300 | 150 |
| Phencyclidine Amphetamines: ∞ amphetamine ∞ methamphetamine | 25 1000 | 25 500 500 (with amphetamine present at a concentration ≥ 200 ng/mL) |
| Opiate metabolites: ∞ codeine ∞ morphine ∞ 6-acetylmorphine | 2000 | 2000 2000 10 (only tested if morphine ≥ 2000 ng/mL) |

(EIA), kinetic interaction of microparticles in a solution (KIMS), and fluorescence-polarization immunoassay (FPIA). Some immunoassay techniques are more specific to a specific target drug than others. However, all immunoassay techniques use an antibody-antigen relationship to identify a drug class in a sample.

b-lymphocytes and plasma cells create an antibody protein in an immune response to an introduced antigen. This created antibody is able to identify and bind to any similar antigen that is introduced into the host. Commercial immunoassay kits contain a substrate with antibody to a specific class of drugs, and also the target drug, which is "labeled" with a tracer. In radioimmunoassay kits the label is radioactive iodine or carbon. In fluorescence immunoassays, the label is a fluorochrome, and in enzyme immunoassays the label is a lysozyme or other enzyme. One of the most popular enzyme immunoassay kits used by many NLCP laboratories is the enzyme multiplied immunoassay test (EMIT) developed by Syva Corporation.

The EMIT uses a technique known as competitive binding. The drug (antigen) labeled with the enzyme competes with any drug found in the subject's sample for a limited supply of antibodies. When the labeled drug in the kit is bound with the antibody, the enzyme activity is inhibited. The more drug in the subject's sample, the less antibodies available to bind to the kits enzyme-labeled antigen. By measuring the magnitude of enzymatic change on a substrate, the amount of drug in the donor's sample can be determined. For example, a donor's sample with no target drug will enable most of the kit's enzyme-labeled drug to be bound to the antibodies and result in an inhibition of the enzyme's activity. When the enzyme activity is inhibited, the substrate in the kit, NAD, cannot be oxidized into NADH. The result is a small absorbance change of 340 nm, measured spectrometrically. Conversely, a large amount of drug in a subject's sample will leave few antibodies for the kit's enzyme-labeled drug, and many enzymes will be able to convert NAD to NADH and result in a large absorbance change.

Using the initial cutoffs as outline in Table 44.1, specimens that test below the cutoff level on all initial tests will be signed out as negative, with no further testing permitted on the specimen. For positive test results, multiple re-screening may be an option, as long as quality-control and guideline cutoffs are used. Some laboratories use a second initial test that is more specific for the drug in question, thus eliminating a possible false positive on the broader, first initial test. For example, if a particular assay tends to flag positive for structural amphetamine analogues, a more specific second immunoassay test may be performed.

When conducting an initial test, every batch is required to contain an appropriate number of calibrators, negative urine samples, controls, and blind samples to ensure the accuracy of test results, along with the donor specimens. Results lower than the cutoff are considered "negative" and are not tested any further; positive results are sent on for confirmation. The laboratory must perform a "confirmation" test on a gas chromatograph (GC), gas chromatograph/mass spectrometer (GC/MS), or an equivalent instrument, to identify what substance has caused the positive initial test result.

E. Confirmation tests

Once an initial screen indicates that the specimen may be positive for a particular drug or drug class, a confirmation test is performed. Only those specimens confirmed positive by a test utilizing an analytical technology different from the screening test may be reported as positive. Non-regulated testing has the option of using a variety of confirmation methods, some of which may not be considered acceptable with the scientific community majority. Under regulated testing, laboratories must use gas chromatography/mass spectrometry (GC/MS) for the confirmation method.

The GC/MS is, in effect, the combination of two instruments. The gas chromatograph (GC) separates the components (drugs) of a mixture by injecting the mixture into a column inside the instrument. The column contains chemicals, which slow the migration of some of the compounds, and allows other compounds to travel relatively unhindered. The chemical makeup of each of the mixture's compounds and their interactions with the chemicals in the column determines how long the component will take to travel the entire length of the column. As each compound or drug exits the column, it enters the mass spectrometer (MS).

The MS bombards the drug with electrons and shatters the structure into pieces, depending on the weak points in the drug's structure. Theoretically, since each drug structure is different, each different drug will break at different points on the molecule, and, thus, shatter into predictable pieces. The size and quantity of the pieces form a "fingerprint" of the drug. A proficient scientist can reconstruct the structure of the molecule merely by evaluating the totality of the ions produced by the electron bombardment. For quantitation, a laboratory does not look at the entire scope of ions that are produced by the molecule, but rather chooses several unique ions to represent an identification. The abundance of one ion, generally the "target" or "quantifying ion," is measured to determine the amount of drug in the specimen. The measured relative abundance of two other ions ("qualifier ions") is chosen to help assure the proper identification of the drug. Using

both the retention time as recorded by the gas chromatograph and the presence of a target ion and the qualifier ions, a drug can be identified to a fairly high certainty.

As with any instrument, the quality and worth of the data achieved through the GC/MS is a function of how the instrument is maintained and operated. Confirmation methods must be validated to ensure the reliable analysis of specimens. Validation of the method includes the determination of carryover, linearity, precision, specificity, accuracy, limit of quantitation, and limit of detection of the method. Confirmations must be by quantitative analysis, and fall within the linear region of the standard curve. Tests that exceed the linear range must be documented in the laboratory record as “exceeds the linear range of the test.” Periodic procedure re-validations should also be performed.

The calibrators that establish the quantitation of the result and the controls that check the proper results of the calibrators must be used in the analytical run and fall within acceptable ranges of accuracy. The appropriate number of calibrators, negative urine samples and controls must be used. Some laboratories establish a three-point calibration curve with each batch analysis. However, some laboratories use a single-point calibration and check a stored, historical calibration curve with the appropriate quality-control samples. Quality-control requirements for a confirmation test include certified negative urine samples, positive calibrators, controls containing the specific drug to be tested, and at least one control at or near the cutoff.

F. Reporting and storage of samples

After analysis, the final test result must be reviewed and approved by a person authorized to review the analytical data for accuracy. In regulated programs, this duty is assigned to a “certifying scientist.” The certifying scientist reviews all the data of the initial and confirmation test and chain of custody and determines if the result is justified. This initial review is then sent to the MRO within an average of five working days after the laboratory receives the specimen. The completed CCF is sent by fax, mail, or courier, or electronically to a MRO—not to the employer. The laboratory may transmit results to the MRO by facsimile or computer, although this must be done in a manner designed to ensure confidentiality of the information.

Confidentiality of records is protected under the Privacy Act, 5 U.S.C. § 552a et. seq. and Section 503(e) of the act. Results may not be disclosed without written permission of the employee, unless the disclosure is to the MRO, the EAP administrator who is providing counseling to the employee, a supervisory or management official in the

agency, or pursuant to a court order. An applicant for employment is not entitled to the results of the drug test, but an employee may obtain information by written request.

Results may not be provided verbally over the telephone. Quantitative results are not routinely sent, except for when the sample is positive for morphine or codeine at a level of 15,000 ng/mL or above. All other reports for quantitation require a letter from the MRO asking for the quantitation results. All confirmed positive specimens must be maintained in long-term frozen storage for a minimum of one year. All records must be maintained for two years.

44.7 Additional Program Aspects

A. The medical review officer (MRO)

The DOT and Federal Mandatory Guidelines require that a medical review officer (MRO) review positive results. A MRO is a licensed physician, responsible for receiving laboratory results generated by an agency’s drug-testing program, with knowledge of substance-abuse disorders, and appropriate medical training to interpret and evaluate an individual’s positive test result. The MRO is typically a licensed physician (doctor of medicine or osteopathy) who has been specially trained to review and evaluate the laboratory’s implementation of the relevant program’s testing of urine samples and controlled substance-abuse disorders. The MRO must not have a conflict of interest with the employer’s laboratory.

The DOT program requires that when a positive result is reported, the MRO use due diligence to contact the employee directly and confidentially to determine whether the employee wishes to discuss the result. After three unsuccessful attempts to contact the employee, the MRO requests that the designated employer representative (DER) contact the employee and have the employee call the MRO. Positive results can be verified without interviewing the employee if more than ten days have passed since the reported result and there has been no success in contacting the employee. Interviews are also not required when more than seventy-two hours have passed since the employee was told to contact the MRO, or if the employee refuses to speak with the MRO.

The MRO verifies a confirmed positive test for PCP, cocaine, amphetamines, and marijuana, unless a legitimate medical explanation exists for the presence of the drug in the employee’s urine. If the employee can present proof of a legitimate explanation for the positive test, the test will be deemed negative. However, the MRO may still raise fitness-for duty issues with the employer. If the sample contained 6-acetylmorphine (6-AM), the test is verified posi-

tive. If, however, the test is negative for 6-AM, the result will still be verified positive if the morphine or codeine is at 15,000 ng/mL or above. All other positive opiates test must be accompanied by clinical evidence of unauthorized use of opiate or opium derivatives. Adulterated or substituted test results are treated as a verified positive if, after interviewing the employee, there is no medical reason for the result.

B. Public interest exclusions (PIE)

To help protect the public against service agents that fail to meet the DOT regulations, the federal government has instituted a PIE proceeding policy. PIE proceeding may be initiated against a MRO, a laboratory, a SAP, a collector, or any service agent that is non-compliant with the program's provisions. The issuing party has the burden of proving by a preponderance of the evidence that the agent was in serious non-compliance of the regulations. The duration of a PIE can last about one to five years.

C. Blind performance testing

Blind quality-control specimens are used as a test of the entire testing process. The current guidelines require each Federal agency to ensure that a minimum of 3 percent blind quality-control samples is submitted with the donor specimens. An employer may provide blind samples to the collector, who submits the quality-control sample as if it were a donor specimen. The collector will generate a fictitious social security number or employee identification number, complete a CCF, and properly label a specimen bottle. Only the MRO's copy of the CCF, copy four, will have the designation "Quality Control Sample" in the donor's name section. The MRO is to determine whether the laboratory reported the correct result when second copy of the CCF is received from the laboratory after the laboratory's analysis.⁹If the laboratory reports a result different from the one expected, the MRO must contact the laboratory to determine if there is a reason why the laboratory did not report the correct result. The MRO may request the laboratory to retest the specimen or to have an aliquot sent to another certified laboratory for confirmatory testing. If the retest result does not confirm the original result, the laboratory likely made an error.

A false negative result is not considered as serious as a false positive. If the retest result has confirmed that a false positive was reported by the laboratory on a blind quality-control sample, the employer and the regulatory office will be contacted, so that an investigation can be conducted. If a specific cause for the false positive is identified, the laboratory will be required to take corrective action to prevent the recurrence of the error.

D. Alcohol testing

Not all drug-testing programs allow for the testing of ethyl alcohol. By a 1994 amendment to 49 C.F.R. Part 40, alcohol testing for the DOT is now mandated. These are separate regulations from the drug-testing requirements, and a MRO review is not required. Alcohol testing may be done in four situations: post-accident, reasonable suspicion, random testing, return-to-duty, and follow up. At this time, pre-employment testing is not required. Alcohol screening tests may be performed on breath or saliva. If the alcohol concentration result is greater than 0.02 percent (g/100mL), a confirmation test must be performed on a specified breath-alcohol testing device within thirty minutes of the screening test. Specially trained screening test technicians (SSTs) or breath alcohol technicians (BATs) may perform breath-alcohol testing procedures. Only a qualified BAT may conduct a confirmation test. A confirmation test device must be on the NHTSA conforming products list (CPL) for evidential testers. The screen test may be on the CPL list for evidential and non-evidential devices.

All confirmation results must be printed in triplicate, and the printed record must include the printed results, date and time, a sequential test number, and the name and serial number of the EBT. Confirmation tests on an evidential breath tester (EBT) must be performed after a fifteen-minute observation period, to ensure that alcohol in the oral cavity does not contaminate the breath test. Before beginning the test, an air blank must be conducted on the EBT.

A positive result is any confirmation test that is a 0.04 percent or higher. Employees who have a positive test must be removed from safety-sensitive duty and referred to a substance abuse professional (SAP). A test result between 0.02–0.039 percent is considered neither positive nor negative. The employee at this level must be removed from safety sensitive functions until they are below a 0.02 percent, or their next duty period (at least eight hours). Below 0.19 percent, the test is considered negative and the employee may return to work.

44.8 Special Drug-Testing Issues

A. Type of matrix

Determining what matrix to use to detect the use or presence of drugs depends on the concentration of the drug used, route of administration, distribution in tissues, and metabolism and excretion of the drug. Drug distribution in interstitial and cellular fluids is dependent on physiological and physicochemical properties of the drug. For example, lipid-insoluble drugs cannot permeate cell membranes easily and, thus, are restricted in their distribution and sites of action. Some drugs bind to plasma proteins, such as the

binding of acidic drugs to plasma albumin or the binding of basic drugs to “-1 acid glycoprotein. Lipid-soluble drugs, such as cannabinoids, accumulate in tissues and fat cells, which act as a reservoir, prolonging drug action and subsequent elimination from the body. These factors, as well as many more, affect the concentration and detection levels of various drugs in different matrices.

Generally, the purpose for the testing and the information desired often dictates the type of sample preferred. If the employer wishes to test an employee “for cause” or post-accident, a blood sample may be far superior to a hair or urine sample, provided the employee is available close to the time of the accident or occurrence. However, if the employer wishes to determine if the employee or hiring candidate has a long-term history of drug use, a hair sample might be the best option.

The following is an overview of the benefits and drawbacks of different sample matrices for the presence of drugs of abuse in workplace testing.

1. Hair testing

Hair serves as a repository for drugs, drug metabolites, vitamins and minerals and other substances, which are delivered to the hair root by the blood supply. Most of the drug is deposited in the central part of the hair, called the cortex.²² It takes approximately three to five days for the hair to extrude from the scalp to enable it to be cut for collection. The amount of sample required for testing varies, but generally sixty to 360 hairs are required, depending on the length of the hair and the testing technology used. Hair testing can be performed by the analysis of the whole shaft of hair, or segmented to assist in the determination of the dates of ingestion. Segmentation is not very useful, since not all individuals grow hair at the same rate and not all hair on one person’s head is in the growth cycle phase at the same time.

A major benefit of using hair as a drug-testing sample is the ability to determine long-term drug abuse. Unlike urine or blood, hair represents a more lengthy record of drug exposure. The amount of hair growth per month depends on the health and sex of the individual and the anatomical location of the hair. In general, the average rate of growth for head hair is about one centimeter (0.4 inch) per month.²³ For example, if a two-inch length of hair is tested, it may represent drug use over the past five months. While it may be possible for an employee to maintain sober for a short period of time in order to test negative in an anticipated urine test, it would be more difficult for an employee to abstain for several months.

Drugs become incorporated into hair from three major sources—the blood supply, the sweat and sebum, and from

passive exposure to the smoke or solid form of the drug.²³ In general, hair testing is less susceptible to intentional adulteration or substitution by the donor; the donor is always in sight of the collector. However, there have been other contentions of contamination of the hair from external sources: Environmental drug contamination from exposure to methamphetamine or cocaine smoke has been shown to be present in children exposed to drug smoke in the home environment.²⁴

Studies have shown that despite a washing procedure prior to testing, environmental contamination of the hair may still cause a false-positive test result.²⁵ Smith and Kidwell performed a study where cocaine-using adults and their non-using children were tested for drug use and exposure. Hair from the adult subjects showed cocaine in 92 percent of the cases and hair from the children was positive in 88 percent of the cases.²⁶ In addition, hair is continuously in contact with body sweat. Sweat also contains drugs, which may be incorporated into the hair matrix after the hair has extruded from the skin. One study demonstrated that deuterated cocaine may be found in previously drug-free hair when volunteers, who were administered deuterated cocaine, held the hair in their hands for thirty minutes.²⁸ This positive result persisted even after the standard pre-test washing procedure.

Other issues in the hair-testing arena are the different amounts of uptake in the hair depending on ethnicity, and hair color.²⁷ Studies by Henderson et al. have shown a bias in ethnic hair types to the incorporation of the hair to cocaine vapor. The order of the degree of incorporation was largest for Asian hair, followed by African hair, and finally Caucasian hair.²⁸ Hair color bias was also demonstrated in a study by Reid et al., in which binding of benzoylecgonine was different for black, brown and blond hair types.²⁹

Hair testing has enjoyed some popularity in a variety of arenas, including family law, insurance cases, custody cases, pre-employment, law enforcement, and the military. In workplace testing, hair is most often used for pre-employment testing only, since it best represents a history of drug use over a long period of time. If a company’s goal is to determine long-term drug use, a hair sample may be the best matrix.

2. Saliva testing

Saliva is an oral liquid composed of water (90 percent) and various other substances, such as mucins and enzymes. Saliva testing is simple to perform, and the easiest noninvasive method available. Saliva is a substance that most reliably can be correlated to blood concentrations for certain drugs.³⁰ Additionally, saliva differs from urine in that saliva contains higher concentrations of the

parent drug than inactive metabolites. However, there are a variety of factors that affect the concentration of drugs in the saliva.

It is well known that an increase in saliva pH can alter the partitioning of certain drugs from the blood into the saliva.³¹ Many drugs are weak acids or bases. The distribution of a weak electrolyte is determined by its pKa and the pH gradient across the membrane. For drugs with a pKa less than 5.5, saliva concentrations are not pH dependent and the concentration will correlate with the plasma portion of the blood. However, drugs with a pKa greater than 5.5 are highly pH dependent. For example, cocaine (pKa 8.6) concentration in saliva may change by a factor of twelve if the saliva pH changes from 6.5 to 7.6.³²

Saliva is a good matrix for the determination of drug use during a twelve to twenty-four-hour period of time.³³ As compared to hair, saliva would not be useful for determination of a historical drug use pattern, but may be useful for testing employees prior to their engagement in safety-sensitive functions.³³

3. Sweat testing

Sweat is a body fluid that was not, until recently, fully utilized in the drug-testing arena. Sweat is mainly produced by eccrine in the transdermal layer of the skin surface or apocrine glands in specific regional areas in the body. Sweat is about 99 percent water and 1 percent sodium chloride and other trace materials. Researchers have known since 1911 that drugs are excreted in the sweat.³⁴

Over the years, there have been several devices that have been used to collect sweat. However, many of these devices consisted of a pad covered by an occlusive membrane, which would trap both water and solute. This type of patch design could not always eliminate bacterial growth under the patch or allow the skin under the patch to remain healthy for long-term application. However, more recent technological developments have enabled the invention of an absorbent pad covered by a non-occlusive membrane, which facilitates comfort to the wearer by allowing oxygen, water, and carbon dioxide to pass through the patch.³⁵ The invention of a "sweat patch" collection device developed by Sudormed™ and marketed by PharmChem™ Laboratories under the trade name Pharm-Chek™ is such a device. After approval by the Food and Drug Administration, the patch was introduced in the drug-detection and testing arena.

The Pharm-Chek™ patch is left on the subject for about a week, upon which time it is removed. The removed patch is placed in a vial with elution buffer to extract the drug from the patch. Testing is performed in the conventional immunoassay screening procedure and confirmation

of positive results is completed with a GC/MS procedure. Benefits of sweat testing are that it is non-invasive, and that it can detect use—even a one-time use—for a longer period of time than can urine.³⁶ Other benefits include the detection of parent compounds rather than the more polar metabolites, and the tamper-evident membrane that will likely tear if there is an attempt to tamper with the patch after it is applied. These facts have made the device popular in the drug-treatment field, as well as in custody cases, probation, parole, and in the social-service arena.

While the use of sweat as a testing matrix may be suitable for pre-employment testing, the sweat patch would likely be unsuitable in "for cause" or in post-accident testing. Concentration of the drug in the sweat patches is expressed as ng/mL of buffer eluate. This convention of reporting makes it difficult to interpret or correlate the concentration with blood levels or to determine the degree of "under the influence." In addition, certain drugs tend to deposit in adipose tissue, making an issue of "recent use" more difficult to interpret.³⁷

The manufacturer claims that the "patch is carefully designed so that contaminants from the environment can not penetrate the adhesive barrier from the outside, and therefore the patch can be worn during most normal activities (bathing and swimming, for example) without affecting the integrity of the test."³⁸ Several scientific articles have mirrored that opinion in stating that the molecular pore structure of the plastic membrane will exclude substances greater in molecular size than vapor-phase isopropanol.³⁹ However, there have been questions of contamination of the patch, during application and removal of the patch, or external contamination. Early studies indicate that the cleaning solution used (70-percent isopropanol) on the skin prior to the application of the patch does not adequately clean external contaminants from the skin.⁴⁰ A 1999 study by the Naval Research Laboratory concluded that "the potential for external contamination of the skin (CFWI) as well as contamination of the patch membrane (CFWO) can occur and generate false results."⁴¹

4. Blood

Blood is a valuable matrix, especially for post-accident drug-use determinations. A 1985 DOT study evaluated existing data on the concentrations of a variety of drugs in drivers to assess the ability of different matrices to detect drug impairment. The study concluded that urine testing would be suitable for establishing the need to obtain and analyze blood specimens for THC (the active ingredient in marijuana), and that blood is the only body fluid that may serve in a limited manner to relate drug levels to impairment.⁴² A blood sample

showing presence of a significant concentration of a drug that impairs the safe operation of large machinery can be beneficial to the ultimate determination of impairment. Other factors that may affect the ultimate determination of impairment are whether the blood is drawn from the employee during the expected timeframe of active drug action, and whether the employee exhibits consistent signs of the expected effects. Another benefit is the plethora of studies and literature delineating therapeutic versus toxic concentrations of drugs in whole blood or plasma.

The major disadvantage to blood testing is the invasiveness of the collection process, the increased hazardous exposure of the collector to possible virulent blood, and the lower concentration of drugs found in the blood, as compared to urine.

5. Urine

HHS currently mandates that only urine may be tested. However, even in non-regulated testing, urine appears to be most popular. Since most workplace testing is either random testing or pre-employment, recent use is the information sought, not drug impairment. Urine is suitable for the determination of recent use, especially during the past seventy-two hours. The time frame in which a drug may be detected depends on several factors, including the amount of drug initially consumed, the frequency of drug use, the lipid-solubility of the drug in question, and the half-life (T_{1/2}) of the drug. For example, some drugs, such as the cannabinoids, can be detected for over a month, if the donor is a frequent user. Another benefit to using urine for drug testing is that drug concentration in urine is ten to one-hundred times more concentrated than in the blood, making detection easier using conventional drug-testing instruments.

In urine collection, the substitution of another substance as urine, the addition of chemicals to the urine, or the dilution of the specimen with water are common methods of tampering with the specimen during collection. Adulteration of urine samples to mask drug use or cause a false-negative result when tested can be achieved in vivo or in vitro. In-vivo adulteration is caused by the consumption of some substance that will dilute the urine or change the amount of drug excreted into the urine of drugs. Consumption of large amounts of water or the use of diuretics will increase the amount of urine produced and will cause the drug concentration in the urine to be lowered. Consumption of a substance that makes the pH more alkaline will slow down the excretion of amphetamines and result in a lower amount in the urine per unit time. Both of these methods will effectively lower the concentration in the urine and

may result in the drug concentration falling below the cutoff value of the test.

The addition of chemicals directly into a specimen may create a false negative in an otherwise positive specimen. Chemicals may interfere with the screening kit's reagents, causing the test to report the specimen as negative when it is truly positive. Some common chemicals used include detergents, vinegar, and bleach. The addition of plain water to the sample cup dilutes the specimen and lowers the concentration of the drugs in the specimen. The dilution may be so great, that the specimen may test below the laboratory's cutoff concentration for determining which specimens are to be considered positive. The substitution of another substance, or another person's urine, results in the false specimen being called negative for drugs.

When choosing a program or laboratory, the employer must evaluate the safeguards in place at the collection site and the testing laboratory. During the actual voiding of the specimen, the employee must not have access to water to dilute the specimen. Turning the water line to the sink off during voiding, or having the employee void where no sink is accessible is necessary. The placement of bluing agent in the toilet enables the collector to check the color of the sample to make sure the specimen was not diluted with water from the toilet. A temperature indicator on the specimen cup allows the collector to check the temperature of the specimen immediately after the voiding to ascertain if the temperature is consistent with body temperature. The HHS guidelines call for the collector to check the temperature of the urine within four minutes of collection. The temperature of the urine must be within 90–100°F. Despite these precautions, a negative urine specimen may be heated to body temperature by the concealment on or in the donor and substituted for the donor's urine at the time of collection. The collector's evaluation of specimen temperature, color, or smell during the collection process may still not be sufficient to detect donor adulteration. The laboratory, then, has the task of determination of the adulteration of a specimen.

In an effort to ascertain whether a specimen has been tampered with during collection, the laboratory should test the urine for creatinine levels, specific gravity, nitrites and/or pH. If the specimen falls outside the normal ranges expected for normal urine, the integrity of the specimen might have been compromised. Unregulated laboratories often do not have criteria in place for the determination of an adulterated or dilute specimen. However, regulated programs have addressed this issue. The DOT requires specimen validity testing, and the HHS program strongly encourages the practice, through their publication of Program Document #35 for re-

porting urine specimen validity test results.⁴³ The publication discusses the issues of adulterated, diluted, and substituted urine specimens. Under the reporting guidelines, a specimen is considered “substituted” if the urine creatinine concentration is < 5 mg/dL and the urine specific gravity is < 1.001 or > 1.020 . A specimen is considered dilute if the creatinine is less than 20 mg/dL and the specific gravity is less than 1.003. A sample is considered adulterated if the pH is less than or equal to three or greater than or equal to eleven, or if it contains exogenous substances, such as nitrites.

Natural polyuria can occur in medical conditions such as diabetes insipidus or nephrogenic diabetes.⁴⁴ However, scientific research of medical conditions resulting in severe overhydration (polyuria) and water-loading studies has indicated that guidelines can be established to enable a laboratory to detect a specimen condition that is not consistent with normal human urine. Analytical criteria for laboratories testing federal and federally regulated specimens are outlined in Program Document #37.⁴⁵ To report a specimen as “substituted,” creatinine must be quantitatively measured on two different aliquots, both using a cutoff of 5 mg/dL, with the results reported to the first decimal place. Specific gravity must be determined by refractometry on at least one of these aliquots, using cutoffs of 1.001 or 1.020, and reported to the third decimal place.

Occasionally, the donor may have trouble urinating because of what is termed “shy bladder,” or merely be unable to provide a sufficient amount of urine for the test. If this is the case, the specimen must be discarded and the collector must attempt another collection. Consumption of copious amounts of water may encourage the production and collection of sufficient urine. The DOT guidelines direct the donor to consume approximately forty ounces of fluid during a three-hour period following the unsuccessful collection. However, an employee’s decision not to drink fluids in a “shy bladder” situation will not be regarded as a refusal to test. If the employee still cannot provide a specimen, the procedure is halted and the collector must make a notation on the CCF and notify the DER and MRO within twenty-four hours. The DER must then direct the employee to obtain a medical evaluation from a licensed physician within five days to explain the medical condition that would have precluded the employee from providing an adequate specimen. If a medical condition does exist, the MRO must determine whether there is clinical evidence that the employee is an illicit drug user. Evidence of a dilute specimen allows the employer to ask the employee to take another test immediately. Positive specimens that are determined to be dilute are treated as a valid positive test.

B. Alternate sources of drug exposure

The main focus of drug-testing programs is to detect illegal drug use by the employee. However, some positive urine drug tests may have their origins in the use of a legal substance, rather than in the use of an illegal substance or in the unintentional exposure to substances used by another. Passive inhalation of smoked drugs, dermal absorption, food-stuff ingestion, or a laboratory’s technical inability may be just a few of the other reasons for a positive urine test.⁴⁶ Thus, it is imperative that the employer or MRO be versed in the alternative explanations for positive drug-test results, prior to the imposition of any sanctions.

Use of certain beauty products, health oils, and food products are typical routes of drug exposure. The use of hemp products, such as hemp-seed oil or tea, has shown to cause a positive urine test for cannabinoids.⁴⁷ In one study, a forty-nine-year old man consumed a total of 30mL of cold pressed hemp-seed oil a day for four days. Urine samples were collected periodically from the start of the first ingestion through 177 hours. Urine specimens from collections between hours forty-five through 142 were determined to contain THCCOOH from 12–68 ng/mL.^{48,49}

In the 1980s, health food stores sold a tea under the trade name “Health Inca Tea.” Health Inca Tea containing about 1.87 mg of cocaine per cup was found to produce positive benzoylecgonine screening results twenty-one and twenty-six hours after ingestion.⁴⁹ This tea no longer contains cocaine, since the FDA banned the importation of any tea containing residual cocaine into the United States.

The ingestion of poppy seeds can cause a positive urine test for opiates. The type of poppy seeds used, the concentration of morphine and codeine per gram of seeds, and the amount of seeds ingested play an important role in the amount of morphine ultimately found in the urine. Numerous studies have been undertaken to determine whether poppy seeds can cause a positive urinalysis result. In one study, ingestion of three poppy seed bagels resulted in 214 ng/mL codeine and 2797 ng/mL morphine at three hours.⁵⁰ In another study, the ingestion of twenty-five grams of poppy seeds from four brands of poppy seeds, containing between seventeen and 294 mcg of morphine per gram, resulted in serum levels of up to 131 ng/mL and urine detectability over forty-eight hours.⁵¹ The vast majority of the searched literature indicates that depending on the cutoff level utilized by the laboratory, the detection of morphine in the urine does not necessarily indicate an illegal drug use.

The HHS also recognizes that a positive for codeine or morphine may be a result of the donor consuming “normal dietary amounts” of poppy seeds. The MRO is directed to

report the result as negative unless clinical evidence of abuse or illegal use of opiates is verified.⁵³ The guidelines state the MRO “shall determine that there is clinical evidence—in addition to the urine test—of illegal use of any opium, opiate, or opium derivative” Since 6-acetylmorphine metabolite comes only from heroin, its presence confirms the illegal use of heroin, not the legal consumption of poppy seeds. In addition, the guidelines permit an MRO to have a blanket written request on file at the laboratory to routinely receive the quantitative values associated with a positive codeine and morphine result, or request quantitative information on the presence of codeine below the cutoff for specimens that have been reported positive for morphine only.

Passive inhalation or absorption of drugs can also occur. Secondary smoke contains active ingredients and pyrolysis products of the burning substance. The lungs have a large surface area and an abundant blood flow, enabling the drug to pass readily into the blood stream. Passive inhalation can occur with any smoked substance—marijuana, PCP, cocaine, methamphetamine, so on. The level of drug ultimately found in the bystander from the smoke depends on the proximity of the subject to the smoke, the ventilation in the confined area, the amount of smoke, the concentration of the substance smoked, and the chemical nature of the substance.

The combustion of cannabis results in the conversion of various chemical precursors to form the active constituent of marijuana, THC. Most of the dose enters the smoker’s lungs during inhalation, but a small amount is released into the environmental air. The concentration of THC in the air is directly related to the THC concentration in the cigarette and the size of the room where the smoke is released. The amount of THC absorbed by the passive inhaler depends on several factors. Not only is the size of the room in which the smoke is confined important, but also the number of “joints” smoked, and the number of hours exposed to the smoke. It is shown that a casual contact with marijuana smoke in a room containing approximately four smoking cigarettes may result in the passive inhaler testing positive for marijuana use by urine analysis. In a study by Dr. E. Cone et al. several volunteers were subjected to two differing concentrations of THC smoke in a confined room.⁵² The study took place over six days, and the exposure time was limited to one hour per day. Individuals exposed to concentrations of THC smoke from sixteen cigarettes reached RIA levels of up to 100 ng/mL, and up to 87 ng/mL on the GC/MS.⁵² A subject confined to a medical ward tested positive for marijuana metabolites due to passive inhalation and tested positive for marijuana in the urine

in concentrations up to 260 ng/mL.⁵³ The detection of cannabinoids in the blood and urine were also found by Morland et al, eliciting the conclusion the “the demonstration of cannabinoids in blood or urine is no unequivocal proof of active cannabis smoking.”⁵⁴ HHS recognizes that passive inhalation of marijuana smoke does occur and can result in detectable levels of THC and its metabolites in urine. However, HHS also takes the position that it is unlikely that a nonsmoking individual could unknowingly passively inhale smoke that results in a drug concentration in urine at or over the cutoff levels used in the federal program. As such, HHS directs the MRO to report the result as “positive” for cannabinoids.

Passive exposure is not limited to the cannabinoids. There are numerous articles citing incidences of passive exposure by children and infants exposed to cocaine (crack) vapor which resulted in a positive urine test for benzoylecgonine.⁵⁵ A study conducted at NIDA’s Addiction Research Center has demonstrated that individuals passively exposed to “crack” smoke did not produce a urine positive for cocaine using the guidelines’ established testing levels.⁵⁶ In another unrelated study, a seventy-three-kilogram man exposed to vapors produced by the volatilization of 200 mg of cocaine “free-base” for thirty minutes prompted the authors to conclude that “passive exposure to free-base cocaine vapor can produce low-positive results” and that is was “probable that a longer exposure period, larger cocaine dose, or a more efficient (lower) vaporization temperature would lead to higher urinary benzoylecgonine concentrations.”⁵⁷

Accidental exposure of police officers to cocaine in work-related situations led the authors to conclude that “passive microingestion of cocaine needs to be considered when examining persons who are in cocaine intensive environments.”⁵⁸ Passive exposure of crime-lab personnel to cocaine during processing and analysis was also discovered by Le et al., prompting the authors to emphasize the use of protective equipment and short exposure times.⁵⁹

The issue of passive exposure to phencyclidine (PCP) has not been studied extensively in the literature. However, there have been numerous laboratory studies determining levels of animal exposure to PCP pyrolysis products. In addition, the literature cites a few instances of accidental or occupational exposure to PCP. A woman living above an illegal PCP synthesis laboratory developed psychiatric manifestations of PCP exposure and levels of PCP in her blood.⁶⁰ In another study, law-enforcement personnel handling illegal PCP have been shown to have PCP in their blood and urine for at least six months after their last-known occupational exposure.⁶¹

It is clear that when reviewing a case for the possibility of a positive result due to passive exposure that the circumstances around the exposure be carefully evaluated. Casual contact in a social setting, or a one-time exposure, may yield only a low positive test. However, individuals exposed to either large amounts of smoke, smoke with a high concentration of drug, or lower amounts on a daily basis for a long period of time, may result in higher results. Lipid-soluble drugs pose a special problem in that daily exposure of even low amounts of smoke over a long period of time may result in the accumulation of drug in the body and result in a highly positive test.

C. Amphetamine testing issues

Analysis of the phenethylamines, or amphetamines, has always posed a challenging problem to toxicologists and drug-testing personnel. A positive amphetamine test result could occur because of a medical use of amphetamines, use of a legal drug that metabolizes to an amphetamine or methamphetamine, identification of enantiomers of methamphetamine, and the conversion of ephedrine or pseudoephedrine to methamphetamine during the GC/MS testing process.

Conversion of ephedrine to methamphetamine during the testing process has been shown to occur. In 1990, a certified laboratory reported a false-positive result in the analysis of a proficiency sample. Further investigation by the HHS of the laboratory and the NLCP revealed that the misidentification was analytical in nature. Specimens reported positive by the affected laboratory were sent to other laboratories and found not to contain methamphetamine. The culprit in the false identification appeared to be the presence of high levels of ephedrine or pseudoephedrine. Other factors included the use of high injection port temperatures in the GC/MS, and the use of derivitizing agents such as 4-carbethoxyhexafluorobuturyl chloride (CB), heptafluorobutyric anhydride (HFBA), N-trifluoro acetyl-propyl chloride (TPC), or pentafluoropropionic anhydride (PFPA).

In an attempt to eliminate further similar problems, the NLCP now requires that for the laboratory to report a specimen positive for methamphetamine, the specimen must also contain the metabolite, amphetamine, at a concentration equal to or greater than 200 ng/mL. If this criterion is not met, the specimen must be reported negative for amphetamines. Another way to virtually eliminate the problem is for the laboratory to incorporate an extraction procedure utilizing periodate. Periodate oxidizes primary amines, by reacting with $-OH$ and $-NH$ on adjacent carbon atoms. The result is a change in the molecule such that the ion fragments will not be similar to methamphetamine.

Once methamphetamine is identified, the structural form should be elicited. Methamphetamine and amphetamine exist in two structural forms known as enantiomers. Enantiomers are non-superimposable mirror images. The two isomers of each substance are designated as d- (dextro) and l- (levo), indicating the direction in which they rotate a beam of polarized light. The d- isomer of each substance has a strong central-nervous system stimulant effect while the l- isomer of each substance has primarily a peripheral action. A Vicks Inhaler[®] contains l-methamphetamine, affording the possibility that a laboratory positive result could be reported for l-methamphetamine and/or l-amphetamine. Selegiline, a monoamine oxidase inhibitor used in the treatment of Parkinson's disease, is metabolized to l-methamphetamine and l-amphetamine.

HHS dictates that the MRO should request the laboratory to perform a d-, l- isomer differentiation. Following Vicks Inhaler[®] use, there will be close to 100 percent l-methamphetamine with perhaps a small amount of d-methamphetamine, present as a contaminant inhaler. When isomer differentiation is conducted and there is greater than 80 percent l-methamphetamine, the results are considered to be consistent with Vicks Inhaler use.

D. Medical use of drugs

Not all drugs found in the urine are the product of the illegal use. Some drugs can be directly prescribed by a medical professional (see Table 44.2), or can be present as a metabolite of a prescribed substance (see Table 44.3). In certain medical conditions, the use of drugs that are usually illegal may be permitted. Over-the-counter (OTC) preparations may contain drugs that may interfere or be misidentified as the illegal substance. The MRO has the burden of interpreting the results found by a laboratory. As such, the MRO should request the donor to submit a copy of his or her medical record, or evidence of medications taken during the period around the time of the drug test.

Methamphetamine is a sympathomimetic amine legally prescribed for medical conditions such as obesity, narcolepsy, and attention-deficit disorder.⁶² Methamphetamine or amphetamine can be metabolically produced by the ingestion of prescribed drugs as well. Some common drugs that metabolize to amphetamine are found in Table 44.3. Some of these drugs, such as dimethylamphetamine, ethylamphetamine and fenrthylline, are Schedule I drugs in the United States and have no recognized medical usage.⁶³ However, these drugs may be found in other countries.

During the analysis of a urine specimen, the main laboratory focus is to accurately identify methamphetamine or amphetamine in the specimen. However, the MRO must

consider any alternative origins for these drugs. The identification of the legal parent drug, when present, will assist in the determination of the source of the illegal substance. Some of the drugs listed in Table 44.3, such as famprofazone or fenforex, undergo extensive metabolism in the body resulting in very little, if any, parent drug found in the urine specimen. However, if the parent drug is not

present, other metabolic products of the drug may be found. For example, deprenyl will metabolize to methamphetamine, amphetamine, and desmethyldeprenyl. Presence of demethyldeprenyl may indicate deprenyl as the source. Other considerations include evidence of a valid prescription by the donor, and the possible concurrent use of legal drug and illegal amphetamines.

Table 44.2

| Product | Drug Present |
|--|--|
| Marinol [®] | Cannabinoids |
| Astramorph PF [®] Duramorph [®] MSIR [®] MS Contin Tablets [®] Roxanol [®] Amogel PG [®] Diabismul [®] Donnagel-PG [®] Infantol Pink [®] Kaodene with Paregoric [®] ParegoricQuiagel PG [®] | Morphine |
| Actifed with Codeine Cough Syrup [®] Codimal PH [®] SyrupDimetane-DC Cough Syrup [®] Phenaphen with Codeine [®] Robitussin A-C [®] Triaminic Expectorant with Codeine [®] Tylenol with Codeine(#1, 2, 3, or 4) [®] Kaodene with Codeine [®] | Codeine |
| Desoxyn [®] (Gradumet [®]) | d-methamphetamine |
| Adderall [®] Benzedrine [®] Biphetamine [®] Dexedrine [®] Durophet [®] Obetrol [®] | d-amphetamine or racemic d,l-amphetamine |
| Vicks Inhaler [®] | l-methamphetamine |

Table 44.3

| Product | Metabolizes to |
|---|-----------------------------------|
| Amphetaminil Clobenzorex (Dinintel [®] , Finedal [®]) Ethylamphetamine Fenethylamine (Captagon [®]) Fenproporex (Tegisec [®]) Mefenorex (Pondinil [®]) Mesocarb Prenylamine | Amphetamine |
| Benzphetamine (Didrex [®]) Dimethylamphetamine Famprofazone Fencamine Furfenorex Selegiline (Deprenyl, Eldepryl [®]) | Methamphetamine (and amphetamine) |

Dronabinol is chemically synthesized delta-9-tetrahydrocannabinol (THC). It is sold under the trade name Marinol® in gelatin capsules for oral administration. Marinol is used for stimulating appetite and preventing weight loss in patients with confirmed diagnoses of AIDS, for treating nausea and vomiting associated with cancer chemotherapy, and in the management of glaucoma. The MRO should request that the donor submit a copy of his or her medical record or court order authorizing the legal use of Marinol or marijuana.

There is a variety of prescription and nonprescription drugs that contain morphine, codeine, or the by-products of opium. As mentioned earlier, though, the use of heroin can be differentiated from these other drugs in that the 6-acetylmorphine metabolite comes only from heroin. Its presence in the urine confirms the illegal use of heroin.

44.9 Legal Aspects of Workplace Drug-Testing

The implementation and enforcement of a workplace drug-testing program is always subject to lawsuits by affected employees or state and federal legal guidelines. The development of a program must consider the potential legal ramifications. Legal basis for a workplace program review and criticism may come from several sources, including constitutionality issues (right to privacy, freedom from unreasonable searches, due process), negligence or libel and slander, contract law, and discrimination. Constitutional issues generally arise in the public sector, but may apply to private sector employers under specific circumstances. However, the other three areas are applicable to all employers.

A. Constitutional issues

Opponents of workplace drug testing often argue the fundamental right to privacy and the intrusiveness of the drug-collection procedure. The Fourth Amendment to the Constitution affords an individual the right to be free from an unreasonable search and seizure by the government. Any unreasonable intrusion must be justified by the law. This amendment, in addition to the Fourteenth Amendment's allowance for due process, is the two major constitutional arguments cited in workplace drug-testing litigation.⁶⁴

By implication, the Fourth Amendment affords an individual the right to privacy. The concept of an individual's right for a constitutional-based "zone of privacy" was recognized in the 1965 case *Griswold v. Connecticut* (381 U.S. 479).⁶⁵ In the *Griswold* case, citizens were accorded a "zone of privacy" free of government intrusion, and recognized an individual's right to be "let alone." The United States Supreme Court unanimously held that mandatory drug testing is

a "search," under the Fourth Amendment in the case of *Samuel K. Skinner v. Railway Labor Executives' Association* (489 U.S. 602). However, the court also held that when drug testing was performed within an employment context, the intrusion was justifiable and did not unnecessarily infringe on privacy interests. (*Samuel K. Skinner v. Railway Labor Executives' Association*, 489 U.S. 602, p. 625.) Proponents of workplace drug testing argue that this and other court rulings are not "adequate for describing the employee's claim to privacy in an essentially social and cooperative setting like the workplace."⁶⁶ To date, it appears that the prevalent view in the workforce is that workplace drug testing is not an undue intrusion of privacy rights when the standards for employment are clearly communicated to the prospective employee and there is a subsequent contractual basis for reasonable continued performance monitoring.

The due process provision of the Fourteenth Amendment prohibits states from denying federal constitutional rights, and does not generally apply to private citizens or entities.⁶⁷ The authority of Congress to enforce the Fourteenth Amendment, Section 1983 of Title 42 of the United States Code, prohibits interference with federal rights under color of state law. In fact, in 1966, the Supreme Court stated "In cases under Section 1983, 'under color' of law has consistently been treated as the same thing as 'state action' required under the Fourteenth Amendment."⁶⁸ Therefore, a private employer's action of drug testing, or discharge due to a "dirty" test, can be seen as state action in some circumstances. According to case law, a private employer's action may be considered "state action" and thus regulated under the Fourteenth Amendment if any of the following four are true:⁶⁹

- The employer derives his income from the government.
- The employer is controlled by "extensive and detailed" regulation by the state.
- The function of the employer is "traditionally the exclusive prerogative" of the state.
- There is a "symbiotic relationship" between the employer and the government.

Similarly, the Fourth Amendment applies to government actions and generally not applicable to private-sector drug testing. A warrant is generally required for a search to be considered reasonable under the Fourth Amendment.⁷⁰ However, in regulated industries, an exception to the warrant requirement was developed for searches of premises pursuant to an administrative inspection scheme.⁷¹ There are two requirements that justify the unwarranted administrative search exception.

One is a strong state interest in conducting an unannounced search. Additionally, the pervasive regulation of the industry must have reduced the justifiable privacy expectation of the subject of the search.

B. State and federal mandates

An employer must be aware of the myriad of state and federal mandates that may affect the company's workplace drug-testing policy and implementation of the program. The DOT regulations and the Federal Workplace Act of 1988 have already been briefly discussed. The following are additional mandates to consider:

- The National Labor Relations Act
- Title VII of the Civil Rights Act of 1964
- The Americans with Disabilities Act of 1990
- The Rehabilitation Act of 1973
- State drug-testing laws and city ordinances

Title VII of the Civil Rights Act of 1964 applies to all private-sector employees with fifteen or more employees and prohibits the discrimination against applicants or employees based on race, religion, sex, or national origin.⁷² Disparities in sanctions or reasonable-cause testing, or a drug-testing policy that unfairly impacts a protested class may prompt a Title VII charge. Thus, applying policies evenly and without bias is critical to the successful implementation of a drug-free workplace program.

State drug-testing laws may also place restrictions on an employer's right to implement random drug testing, or to require certain aspects of a program to be in place. For example, the California Department of Health Services prohibits drug tests performed by anyone other than a certified laboratory or licensed physician.⁷³ California also requires that employers with twenty-five or more employees must accommodate employees who wish to participate in a substance-abuse treatment program, provided the accommodation does not place an undue hardship on the employer.⁷⁴ On the other hand, Rhode Island only allows drug testing when "the employer has reasonable grounds to believe based on specific aspects of the employee's job performance and on specific contemporaneous observations, capable of being articulated, concerning the employee's appearance, behavior or speech that the employee's use of controlled substances is impairing his or her ability to perform his or her job."⁷⁵

The confidentiality of medical records and communications in a doctor-patient relationship is generally upheld. A cause of action may be charged and damages may be awarded when there is an improper disclosure of confiden-

tial records or information. State statutes regarding unemployment compensation should also be considered, since a positive drug test may be considered "misconduct" and render a discharged employee ineligible for unemployment compensation. For these reasons, it is highly recommended that employers have a legal professional review the proposed program and policies for compliance with the relevant state and local regulations.

The Americans with Disabilities Act of 1990 (ADA) is applicable to employers with fifteen or more employees.⁷⁶ Title I of the ADA prohibits employment discrimination against "qualified individual with a disability." Among other "qualified individuals," a person who is currently not using drugs and who is participating in or completed a supervised drug-rehabilitation program may also qualify.⁷⁷ The ADA specifically permits employers to adopt drug-testing policies, and expressly excludes drug testing as part of the prohibition against medical inquiries of a "qualified individual's" disability. In fact, a "qualified individual" expressly does not include an individual who is currently engaged in the use of illegal drugs.⁷⁸ The Rehabilitation Act of 1973 is similar to the ADA but protects a narrower class of individuals—"handicapped" persons—from certain types of discrimination by the federal government, federal contractors, and federal grantees.⁷⁹ A "handicapped" person may include an employee who is an "addict" and who has sought treatment voluntarily.⁸⁰ However, occasional users are not considered handicapped and are therefore not protected. Here, as with the ADA of 1990, employers are not prohibited from testing employees.⁸¹

The 1982 National Labor Relations Act (NLRA) was developed to promote, among other things, the flow of commerce and establish legitimate rights of both employers and employees.⁸² Employee drug-testing issues were addressed in this updated version of the 1947 Labor Management Relations Act. Case law has established that drug testing of current employees, not applicants, is a mandatory subject of collective bargaining agreements and union contracts.⁸³

Employers who hire workers who belong to a union or collective-bargaining unit need to consult with union representatives or union bylaws. Incorporation of workplace drug-testing policies that are acceptable to collective-bargaining agreements is the first step towards running a smooth company program.

Clinical Laboratory Improvement Amendments of 1988 (CLIA '88) was created to establish uniform testing standards in the clinical field. Laboratories that are HHS-certified under the NLCP are specifically exempt from the requirements set forth under CLIA '88. The exemption is limited to the certified laboratories' immunoassay and GC/

MS confirmatory testing processes for the five drug classes (HHS-5) stated in the guidelines. Certified laboratories that perform tests with procedures not in accordance with the guidelines or by methods not certified by HHS are subject to the technical and regulatory requirements of CLIA '88.

44.10 Discovery: The “Litigation Package”

By the time cases are filed, specimens may get lost or become unsuitable for re-testing. In these instances, the litigation package—all of the documents pertaining to the case—is the only evidence that can be used to evaluate the reliability of the analysis. The litigation package must include:

1. The CCF. The CCF documents the circumstances around the sample collection, including the identity of the specimen, the condition of the specimen, and the chain of custody. On this form, as well, any irregularities surrounding the collection (for example, the need for an affidavit of correction) or discrepancies in labeling are noted.
2. The preliminary screening data. The screening data will include the results of the calibrators (low/high) and controls (blank/quality control) and the results of the cases in question. Also included should be evidence of integrity testing, such as creatinine, nitrates, or specific gravity. Also recommended are the following:
 - The standard-operating procedure (SOP), including criteria for acceptance of the data for the calibrators, controls and case, and specificity testing (evaluation of other drugs which may cause a false positive).
 - The manufacturer’s assay kit insert describing the required procedure and cross-reactivities of other drugs with the assay.
3. The confirmation data. Confirmation is performed with GC/MS. Data should include the spectrograms for the calibrators and controls as well as the case. Some laboratories use a historical (established monthly etc.) calibration curve, and one calibrator and control. Also recommended for evaluation are the following:
 - The standard-operating procedure (SOP), including the extraction method (chemical preparation of the specimen prior to testing on the GC/MS); criteria for acceptance of the data for the calibrators, controls and case; criteria for acceptable chromatography; specificity (evaluation of other drugs which may cause a false positive) testing; and data

establishing of the limit of detection and limit of quantitation.

- Maintenance and standard tune (evaluation of the working parameters of the machine for the day) data for the GC/MS.

4. Results of proficiency tests (SAMHSA and others) for two years prior and after the case in question. This should include any reports of non-compliance or errors in identification or quantity found.

44.11 Conclusions

The effectiveness of a workplace drug-testing program is evident. It is estimated that between five and sixteen dollars are saved for every dollar employers invest in an EAP.⁸⁴ There are scores of statistics that support the benefits of a drug-free workplace program for both the employer and the employee. A contractor firm in Florida saved \$100,000 on workers’ compensation premiums in 1990, experienced increased productivity, and reduced absenteeism.⁸⁵

Employers reap the benefits of a drug-free workplace through increased employee morale, customer satisfaction, and public image. Accidents, production error, absenteeism, employee theft, employee turnover, and legal expenses all decrease. Employees benefit through increased security, productivity, coworker relations, health, and safety. A thorough drug-free workplace program also gives an employee who may be struggling with substance abuse the resources and assistance to achieve and maintain sobriety and achieve greater career success.

Workplace drug-testing programs need continual revisions to keep up with the advances in technology. Drugs outside the DHHS-5 and the inclusion of matrices other than urine are likely to be considered in the near future. New analytical methods will likely be more specific and sensitive, allowing for more accurate and reliable testing. As the concept of workplace drug testing matures, formal policies and the scope of programs will change. Even at this writing, DHHS and DOT are making or considering changes. The following are program issues that will likely be addressed or implemented in coming years:

- Alternative matrices (sweat patch and saliva, at minimum)
- Mandatory collection of split specimens
- Mandatory testing of the five major drug classes
- Testing for other drugs, such as MDMA
- “Point-of-collection” analysis
- Initial testing facilities that perform validity testing and screening only

- Changes in cutoff levels
- Increased validity testing
- Uniform guidelines encompassing all federal agencies
- Increased training and certification requirements for MROs, SAPs, and collectors

Regardless of the program implemented, voluntary or mandatory, the employer must have all of the basic aspects of a program in place, including a written policy statement, provisions for supervisor training, employee education and assistance, and guidelines for drug testing. Inclusion of all these steps will increase the effectiveness of any program and help to achieve the goal for American commerce and the welfare of the workforce—a drug-free workplace.

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