U.S. Department of Justice
Office of Justice Programs
National Institute of Justice

NATIONAL INSTITUTE OF JUSTICE
Research Report

A Comparison of Urinalysis Technologies for Drug Testing in Criminal Justice

Prepared jointly by
the **National Institute of Justice** and
the **Bureau of Justice Assistance**

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A Comparison of Urinalysis Technologies for Drug Testing in Criminal Justice

November 1991

NCJ 132397

by Christy Visher, Ph.D.

Prepared jointly by
the **National Institute of Justice** and
the **Bureau of Justice Assistance**

Christy Visher, Ph.D., is a Senior Research Associate with the National Institute of Justice.

Foreword

This report exemplifies how National Institute of Justice (NIJ) staff research complements external research conducted by universities, agencies, and private firms. NIJ staff conduct research and evaluation in areas particularly relevant to public policy. These studies are timely and responsive to current priorities.

This unique comparison study of drug-testing technologies measures the accuracy of the urinalysis testing methods commonly employed within the criminal justice system. The study, which was co-funded by the Bureau of Justice Assistance (BJA), reflects NIJ's continuing emphasis on science and technology in providing reliable, useful information to criminal justice professionals. Dr. Christy Visher, a Senior Research Associate with NIJ, analyzed the data for this study and wrote this report.

With expanded use of drug testing in the criminal justice system, Federal, State, and local agencies need comparative information on the use and accuracy of urinalysis technologies. Information is needed on the different types of testing technologies available and on the frequency of errors occurring in drug testing. Moreover, technologies vary in ease of use, relative costs, and suitability as a screening test.

The primary goal of this study is to give justice agencies and professionals the information they need to decide on urinalysis technologies. The author considers the following questions:

- How accurate are the urinalysis testing technologies?
- Do existing Federal guidelines for drug testing in the workplace meet the needs of the criminal justice system?
- Is any one technology consistently accurate enough to eliminate the need for confirmation by an alternative method?
- Do technologies exist that can be used by paraprofessionals in a criminal justice operational environment?

The answers contained here provide criminal justice officials with the information they need to make informed decisions about the advantages and shortcomings of each of the technologies.

Charles B. DeWitt, Director
National Institute of Justice

Acknowledgments

The Bureau of Justice Assistance (BJA) and the National Institute of Justice (NIJ) funded, designed, and monitored this study. Karen McFadden, Project Monitor for BJA, was primarily responsible for the study's design and implementation. John Spevacek was Project Monitor for NIJ; he assisted in interpreting the data and drafting sections of the report.

This study would not have been possible without the important contributions of two consultants. Leslie Bernstein, School of Medicine, University of Southern California, compiled the laboratory data, performed preliminary analysis, and provided statistical consultation. Mildred Henderson, who served as a technical consultant to the study, gathered information about the onsite testing facility and the standard operating procedures at BPL Toxicology Laboratory, and drafted the sections on immunoassay and chromatography procedures.

Several agencies and organizations participated in the study. The Public Health Foundation of Los Angeles County, Inc., served as a pass-through agency for the project funding. The State of California Department of Corrections, Alhambra Parole Office, conducted onsite urinalysis of the urine specimens. San Diego Association of Governments (SANDAG) provided additional urine specimens from a group of arrestees for the study. BPL Toxicology Laboratory analyzed specimens using RIA, TLC, and GC/MS technologies. We would also like to thank Abbott Laboratories, Roche Diagnostic Systems, Inc., and Syva Company for providing free reagents, instrumentation, and training for the study.

Hugh Alcott, California Department of Corrections; Susan Pennell, San Diego Association of Governments; and Jay Weiss, BPL Toxicology Laboratory, deserve special thanks for their roles in carrying out the study.

Others who provided consultation and advice throughout the study include Lt. Commander Walter Vogel of the Armed Forces Institutes of Pathology, the Department of Defense; Robert Stephenson of the National Institute on Drug Abuse (NIDA), U.S. Department of Health and Human Services; and Michael Walsh, formerly of NIDA.

Eric Wish, Bernard Gropper, Virginia Baldau, and Edwin Zedlewski offered very helpful reviews of the report.

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Introduction

It was once widely believed that drug users engaged primarily in minor property crimes to finance their habits. Current research shows that while this link exists, drug users also commit serious property offenses and some violent crimes. Not surprisingly, 80 to 90 percent of persons charged with drug offenses test positive at arrest for one or more illegal substances, as do 50 to 70 percent of arrestees charged with property offenses and many violent crimes.[1]

In addition, a strong consensus has emerged in the research literature that the most frequent serious offenders are also the heaviest drug users. Studies of male offenders show that criminal activity tends to increase and decrease with level of drug use. Moreover, a 1986 survey of inmates from State correctional facilities found that 43 percent of State prison inmates were using illegal drugs on a daily or near daily basis in the month before their incarceration.[2]

Faced with large numbers of offenders who use illegal drugs, criminal justice agencies have found drug testing to be one way to improve decisions and perhaps to reduce criminal activity. For example, urine testing can help officials to identify suspected drug-abusing offenders and evaluate their potential for treatment as well as to monitor the drug use of individuals under legal supervision. Periodic urine testing may deter drug use, which may also lead to less frequent criminal activity. Urine-testing programs are currently being implemented at several stages: At arrest, during the pretrial release period, and during probation and parole.

Indeed, the Office of National Drug Control Policy recognized the value of using drug testing to identify drug-involved offenders when it wrote:

> Drug testing through urinalysis is the only reliable and practical method currently available for determining whether someone in custody or under correctional supervision has been using illegal drugs. Testing within the criminal justice system can serve as an "early warning system" that provides another method of keeping offenders in check while they are on pretrial or post-conviction release. (*National Drug Control Strategy, 1990*, p. 25.)

As urinalysis becomes standard procedure in criminal justice agencies, it is important to understand more about the various drug-testing technologies. Criminal justice professionals need comparative information about the use and accuracy of urinalysis technologies. For instance, does the chosen technology affect the results? Does the accuracy of the test vary by type of drug? How do the various technologies compare in regard to ease of use, suitability for screening, and relative costs?

These and other questions were addressed in a joint study comparing several technologies that could be used in the criminal justice system to screen offenders for drug use. This report presents findings of this study, which was funded by the Bureau of Justice Assistance (BJA) and the National Institute of Justice (NIJ), which are part of the Office of Justice Programs in the U.S. Department of Justice.

The primary objective of the study was to compare four analytical procedures or technologies routinely used to detect drugs of abuse in urine. Researchers sought to assess the relative accuracy and usefulness of each test within routine criminal justice contexts. More than 2,000 urine specimens were gathered from criminal justice populations in an actual operational environment. Further, the study followed testing procedures similar to those of criminal justice agencies in which either paraprofessional technicians test offender urine specimens for drugs of abuse onsite, or professional laboratory technologists conduct tests at a toxicology laboratory. Both procedures were used in this study.

Four technologies were evaluated: EMIT™, TDX™ FPIA (fluorescence polarization immunoassay), Abuscreen™ RIA (radioimmunoassay), and thin-layer chromatography (hereafter referred to as EMIT, TDX, RIA, and TLC, respectively). These technologies were compared with gas chromatography/mass spectrometry (GC/MS), generally accepted as the standard reference technology because it combines high specificity, good sensitivity, and accuracy.[3]

The intent of the study is to provide information that was not previously available through a single study. Comparing analysis and results from each technology will provide answers to such questions as:

- How accurate are the technologies? Does one technology result in more false positive or false negative errors than others?

- Do the existing Federal guidelines for drug testing in the workplace, especially for drug concentration cutoff levels, meet the needs of the criminal justice system?

- Is there a technology that, when compared to GC/MS, is consistently accurate enough to eliminate the need for routine confirmation by an alternate method?

- Do technologies exist that can be used by paraprofessionals in a criminal justice operational environment?

This report also provides the criminal justice professional with comparative information about the technologies used in the study, including (1) the principles of the technologies, (2) the accuracy of results in comparison to the GC/MS standard, (3) the adaptability of the technologies to onsite use, and (4) the instrumentation required to conduct the tests.[4]

The study findings and their implications for criminal justice policy regarding offender urine testing will help criminal justice professionals make informed decisions about which technology or technologies are best suited to their operations and requirements.

Agencies and organizations involved in the study

The principal agencies and organizations involved in the Drug Testing Technologies study were the Bureau of Justice Assistance and the National Institute of Justice, both part of the U.S. Department of Justice; the U.S. Department of Defense (DOD); the National Institute on Drug Abuse (NIDA) of the U.S. Department of Health and Human Services; the Public Health Foundation of Los Angeles County, Inc.; the State of California Department of Corrections, Alhambra Parole Office; and the San Diego Association of Governments (SANDAG). Also participating in the study were BPL Toxicology Laboratory; Abbott Laboratories; Roche Diagnostic Systems, Inc.; and Syva Company.

- **Bureau of Justice Assistance and National Institute of Justice.** BJA and NIJ funded, designed, and monitored the study. These agencies were responsible for developing and conducting the study, compiling and analyzing study data, and formatting and distributing the findings.

- **Department of Defense (DOD).** DOD personnel served as advisers to the study. For many years, DOD has been actively involved in detecting, treating, and eliminating drug abuse among military personnel. Officials provided technical assistance in the development and implementation of the study and in the analysis and reporting of study data. In addition, the Armed Forces Institute of Pathology provided proficiency samples for GC/MS analysis throughout the study as part of the study's quality control activities.

- **The Public Health Foundation of Los Angeles County, Inc.** Consultants from this nonprofit organization received, maintained, and compiled data and helped BJA and NIJ track the study's progress.

- **State of California Department of Corrections, Alhambra Parole Office.** The California State Department of Corrections requires adult parolees with known histories of drug abuse to submit to urine drug testing as a condition of parole. Technicians at the Alhambra Parole Office collected specimens from this office's parolees and conducted onsite urinalysis for the identification of drugs using EMIT and TDX technologies, reported test results to the study's statistical consultant, and prepared urine specimens for transport to the BPL Toxicology Laboratory.

- **San Diego Association of Governments.** SANDAG coordinates the San Diego Drug Use Forecasting Program, which collects voluntary urine specimens each quarter from a sample of anonymous arrestees. SANDAG provided urine specimens from arrestees tested during one quarter for the study.

- **U.S. Department of Health and Human Services, National Institute on Drug Abuse.** NIDA is the agency responsible for setting mandatory guidelines for Federal workplace drug-testing programs and establishing standards for certification of laboratories engaged in such testing. NIDA staff provided consultation on the study and reviewed findings.

- **BPL Toxicology Laboratory.** The BPL Toxicology Laboratory in Tarzana, California, has extensive experience in conducting urinalysis for the criminal justice system as well as other public and private sector clients nationwide. BPL received study specimens from the Alhambra Parole Office; analyzed specimens for drugs using RIA, TLC, and GC/MS technologies; and reported test results to the study's statistical consultant.

- **Abbott Laboratories.** Abbott Laboratories in North Chicago, Illinois, is devoted to the discovery, development, manufacture, and sale of a broad and diverse line of human health care products and services. Abbott developed the TDX procedure used by the Alhambra Parole Office. The firm also developed and supplied the instruments, reagents, and materials used in the TDX tests.

- **Roche Diagnostic Systems, Inc.** Roche Diagnostics of Montclair, New Jersey, develops, manufactures, and markets clinical and analytical systems and specialty kits that help determine and monitor the medical status and well-being of individuals. Roche developed the RIA procedure used by the BPL Toxicology Laboratory. The corporation also developed and supplied the instruments, reagents, and materials used in the RIA tests.

- **Syva Company.** Syva Company in Palo Alto, California, develops, manufactures, and markets diagnostic tests and instrument systems for drugs-of-abuse testing, therapeutic drug monitoring, and infectious disease diagnosis. Syva developed the EMIT procedure used by the Alhambra Parole Office. They developed and supplied the instruments, reagents, and materials used in the EMIT tests.

Study Procedures

Technicians used five different analytical procedures—EMIT, TDX, RIA, TLC, and GC/MS—to analyze urine specimens and determine whether certain classes of drugs were present. Specifically, the specimens were tested for any of the five drugs of primary concern to the criminal justice community—opiates, cocaine, phencyclidine (PCP), amphetamines, and marijuana (or their metabolites). When any of the drugs were present, technicians obtained a measure of the concentration of the drug in nanograms per milliliter. Thus, each specimen was tested 25 times (5 tests for each of 5 drugs).

The technologies and analytical procedures chosen for this study have either been widely used throughout the criminal justice system or have been approved by the Food and Drug Administration (FDA). When the study began in 1988, all five immunoassay technologies tested had been approved by the FDA. New drug testing technologies were continually being approved by the FDA and introduced into the commercial market, and, as the study progressed, several gained approval. These include (1) ONTRAK™, a rapid agglutination procedure developed by Roche Diagnostic Systems, Inc., for onsite use and (2) accuPinch™, an enzyme immunoassay, developed by Hycor Biomedical, Inc., that can analyze a specimen in 7 minutes. The study did not evaluate these two products. It was also unable to test a third technology currently on the market, Toxi-Lab™, a thin-layer chromatography method that uses specialized procedures and prepackaged materials. In addition to these three technologies, other procedures not included were gas chromatography (without the mass spectrometer), high-performance liquid chromatography (HPLC), and high-performance thin-layer chromatography (HPTLC). Although some are based on technologies similar to those used in the study (thin-layer chromatography and immunoassay), they involve substantially different methods and procedures; thus, the results reported here do not apply to these products.[5]

Given that each urine specimen was analyzed by 5 procedures for 5 different drugs, the volume of urine needed for 25 separate tests was significant. While examining other current technologies would have been informative, the sheer volume of urine required limited the number of technologies and procedures included in the study.

During the course of the study, urine specimens were collected from 2,470 adult parolees within the State of California Department of Corrections, Parole Division, Alhambra Parole Office. Urine specimens were also collected from 198 arrestees in San Diego, California. As a condition of parole, the California Department of Corrections routinely tests adult parolees with known histories of identified drug abuse, and the study was incorporated into the Department's regu-

lar operating procedures. Each urine specimen was analyzed for the presence or absence (and concentration, if present) of opiates, cocaine, PCP, amphetamines, and marijuana. Part of the analysis was conducted in the Alhambra Parole Office laboratory using both EMIT and TDX onsite technologies. (Urine specimens from San Diego were shipped to the Alhambra laboratory.)

Manufacturers trained onsite technicians to conduct tests and interpret test results following appropriate package insert instructions. The manufacturers also supplied and/or installed instruments, reagent kits, controls, and standards at no cost.

The Parole Office technicians reserved a sample from each urine specimen, which was transported daily to the BPL Toxicology Laboratory. BPL analyzed each specimen and reported the absence or presence (and concentration, if present) of opiates, cocaine, PCP, amphetamines, and marijuana using the RIA technology developed and supplied by Roche Diagnostic Systems, Inc., TLC, and the GC/MS analytical procedures. The technologists met the State of California standards for toxicology laboratory technologists.

Roche Diagnostic Systems, Inc., trained the BPL technologists to conduct and interpret the RIA tests. Technicians conducted TLC and GC/MS tests according to BPL's *Standard Operating Procedures* manual. Each laboratory forwarded test results on an ongoing basis to the study's statistical consultant for review and analysis. Neither laboratory had access to or knowledge of the other laboratory's findings.

Urinalysis technologies

Urinalysis technologies for detecting drugs of abuse are based on two major analytic principles, *immunoassay* and *chromatography*. Three of the procedures tested in this study—EMIT, TDX, and RIA—are variations of immunoassays. Immunoassays are used for initial screening of specimens. The other two study procedures—TLC and GC/MS—are based on chromatography principles. Chromatographic methods can be used for screening or confirmation. The five technologies used in the study are briefly described in this section. Appendix A provides a more detailed explanation of these technologies.

Urinalysis technologies are often described and compared in terms of their sensitivity and specificity, and manufacturers may even use these terms when marketing their products. A procedure's *sensitivity* refers to its ability to detect a given substance in positive specimens. Highly sensitive tests can detect relatively low concentrations of drugs. Less sensitive procedures, on the other hand, may fail to detect a drug at a given concentration, thus producing more false negative results;

for example, a less sensitive procedure may report a negative result when the drug or drug metabolite[6] is actually present in the specimen.

A procedure's *specificity*, another measure of the test's validity, refers to the ability to discriminate between the drug or drug metabolites of interest and other substances. A highly specific procedure for a particular drug produces few false positives; in other words, few specimens test positive that are in fact negative for the drug of interest. False positives may occur because a particular procedure detects components that mimic the substance of interest.

Immunoassays

Immunoassays are generally considered to have moderate to good sensitivity, and hence can detect small amounts of a drug in urine. The specificity of an immunoassay is more variable and depends on the procedure used and the drug being detected. In principle, an immunoassay test is designed to identify a specific drug or drug metabolite. In practice, however, immunoassay tests involve chemical reactions that may make it difficult to distinguish a specific drug from other substances, such as prescription drugs with similar chemical properties; hence, false positive test results may occasionally occur. Because of this possibility, manufacturers of immunoassays recommend a confirmatory procedure that is more specific to a particular drug or its byproducts, generally one of the chromatographic methods.[7]

The Enzyme Multiplied Immunoassay Test (EMIT) procedure is marketed by Syva Company for either commercial laboratories or onsite settings. The onsite version can be performed by trained paraprofessionals using inexpensive materials and standard urinalysis equipment. Laboratories can also purchase testing instruments from the manufacturer; costs vary, depending on the size of the machine and the options purchased.

Abbott Laboratories' TDX method is relatively inexpensive and sensitive, and can be easily adapted to onsite use by paraprofessionals. Instrumentation is available only from Abbott, and cost depends on the sophistication of the equipment purchased.

The RIA, marketed by Roche Diagnostic Systems, Inc., is similar to the other immunoassays. The product is not readily suited to onsite testing, however, because this procedure uses radioactive materials and requires instruments that are generally operated by licensed technicians in commercial laboratories. Further, while reagents are inexpensive, the instrumentation costs can be expensive.

Chromatography

Chromatography is a method of chemical analysis that separates, identifies, and measures the various substances in a specimen (for instance, drugs in urine). The process either extracts these substances or causes them to attach to some other type of material or particles.

Standard thin-layer chromatography (TLC). This drug test is used frequently in treatment programs and some criminal justice agencies because urine specimens can be screened for several drugs with one test. One drawback of this technology, however, is that the test is not as sensitive as the immunoassays. Further, standard TLC is not typically used onsite because interpreting test results requires considerable technical expertise and instrumentation.

Gas chromatography/mass spectrometry (GC/MS). This is believed to be the most conclusive method of confirming the presence of drugs of abuse in urine. Manufacturers of the immunoassays often recommend that initial positive results be confirmed by GC/MS. The technique is time consuming because it uses two procedures to detect a foreign substance. Moreover, separate tests are usually needed to identify each targeted drug. GC/MS testing equipment is complex and expensive, and operation requires specialized training.

Study Design

Primary objective was to compare leading technologies

The primary objective of the study was to compare and contrast four urine-testing technologies commonly used in situations where authorities must screen many people for illegal drugs. Because of its recognized accuracy, GC/MS was used as the standard against which results from the four other technologies were compared.

When a specimen indicated the presence of a drug present at or above a specified GC/MS concentration level, the specimen was considered positive for that drug. If the GC/MS results showed a drug concentration below the cutoff, the specimen was considered negative for the drug in question. The specimens were also tested using the four other technologies—EMIT, TDX, RIA, and TLC—and were considered positive or negative depending on the concentrations specified for each of the respective technologies.

The results based on the four technologies were then compared individually to the GC/MS results to determine the accuracy of the other technologies. Four outcomes were possible:[8]

- *True positive:* Both results, GC/MS and the other technology, are positive.
- *True negative:* Both results, GC/MS and the other technology, are negative.
- *False negative:* GC/MS is positive, but the other technology is negative.
- *False positive:* GC/MS is negative, but the other technology is positive.

Determining whether a urine specimen is positive or negative for a specific drug depends on more than simply the drug's presence or absence. Technicians must determine the *amount* of drug present in the specimen and whether this amount is above a specified cutoff level. Concentrations of drugs in urine are measured in nanograms per milliliter of liquid (ng/mL). The nanogram—one-billionth of a gram—indicates the amount of the drug or drug metabolite measured in the urine specimen. Because urine testing for illegal drugs is a relatively new science, there are no accepted scientific standards for determining whether a urine specimen should be classified as positive or negative for a particular drug. The cutoff concentration level is primarily based on the accuracy of the test in measuring a specific amount of a drug.[9]

In 1988, the National Institute on Drug Abuse of the U.S. Department of Health and Human Services established standards to guide the Federal Government in developing procedures for Federal employee drug testing.[10] The NIDA guidelines

specify all urinalysis testing policies and protocols to be used when testing Federal employees for illegal drugs. The guidelines cover collecting urine specimens; preparing, handling, and shipping specimens for analysis; chain of custody requirements; screening and confirmation protocols; and reporting results. The NIDA guidelines also include specific drug concentration levels and cutoffs that determine whether a urine specimen is to be declared positive or negative for five drugs (marijuana, cocaine, opiates, PCP, and amphetamines). Only initial screening test levels for immunoassays and confirmatory test levels for GC/MS are specified.

Drug testing in the criminal justice system was specifically *excluded* from the NIDA guidelines. Nonetheless, the criminal justice system—as well as the private sector, commercial laboratories, and manufacturers of drug-testing products—has relied on the NIDA guidelines for direction in establishing and implementing drug-testing programs. In effect, these guidelines have become the standard for most urine screening of individuals for detection of illegal substances.

The immunoassays are usually calibrated or preset by their manufacturers to detect substances at the screening test concentrations in the NIDA guidelines, with some exceptions.[11] Detecting drugs using TLC is based on a different principle, but rough drug concentration levels can be determined by laboratory technicians.

NIDA's cutoff levels were also evaluated

Another purpose of the study was to examine the extent to which the NIDA guidelines may classify some positive specimens as negative because the drug concentration level in the specimen is below the official cutoff; this practice yields many false negative test results. Some research suggests that the relatively high screening and confirmation cutoffs in the NIDA guidelines may not detect the presence of drugs in 20 to 30 percent of positive urine specimens. In fact, researchers using blind procedures in one NIDA-sponsored study found that 30 percent of positive urine samples were falsely identified as negative when using the NIDA guidelines.[12]

In general, *lower* screening or confirmation cutoffs lead to more positive test results because a urine specimen can contain a smaller amount of the drug (fewer nanograms per milliliter) and still be considered positive.

Because the cutoff levels in the NIDA guidelines are widely accepted, this study's primary findings for marijuana, cocaine, and opiates are based on the screening and GC/MS confirmation cutoffs approved by NIDA. The results for PCP and amphetamines using EMIT are based on different cutoffs because tests using the NIDA guidelines were not available at the time of the study. The screening and confirmatory cutoffs (GC/MS) approved by NIDA for Federal employee testing

Table 1
NIDA and Study Cutoffs for Immunoassays and GC/MS (by ng/mL)

Drug	*Immunoassays* NIDA	*GC/MS* NIDA	*GC/MS* Alternate
Marijuana	100	15	10
Cocaine	300	150	50
Phencyclidine	25[a]	25	10
Opiates	300	300	50
Amphetamines	1,000[b]	500	50

[a] for EMIT, 75 ng/mL
[b] for EMIT, 300 ng/mL

and the immunoassay cutoffs used in this study are listed in table 1 in nanograms per milliliter. Table 1 also includes an alternate set of GC/MS cutoffs that permit the detection of drugs at a level near the limits of the technology. These lower cutoffs, selected in consultation with Federal drug-testing experts, will be used to explore how much drug use may be undetected in criminal justice populations.

For example, in this study a screened urine specimen that contains at least 300 nanograms of cocaine metabolites will be designated as a presumptive positive. It will be considered conclusively positive if a second GC/MS test shows a concentration of at least 150 nanograms of cocaine/metabolite. The drug concentration levels for GC/MS are lower than the levels for screening except for opiates and PCP, for which they are identical. GC/MS uses lower cutoff levels because it allows a much more specific test of the presence of particular metabolites.

Study Findings

The statistical analysis is based on 2,470 urine specimens from parolees (90 percent male). The specimens were provided by the California Department of Corrections between May and August 1988. In February 1989, an additional 198 specimens were collected from males arrested in San Diego and added to the initial data base. Thus, the total sample of 2,668 specimens represents a population of persons at an elevated risk for using illicit drugs. Table 2 shows the percentage of the study sample found positive for each of the five drugs; findings were based on the GC/MS test using the cutoff levels in the NIDA guidelines.

Table 2
Percentage of Study Sample Positive for Drugs Based on GC/MS Test*

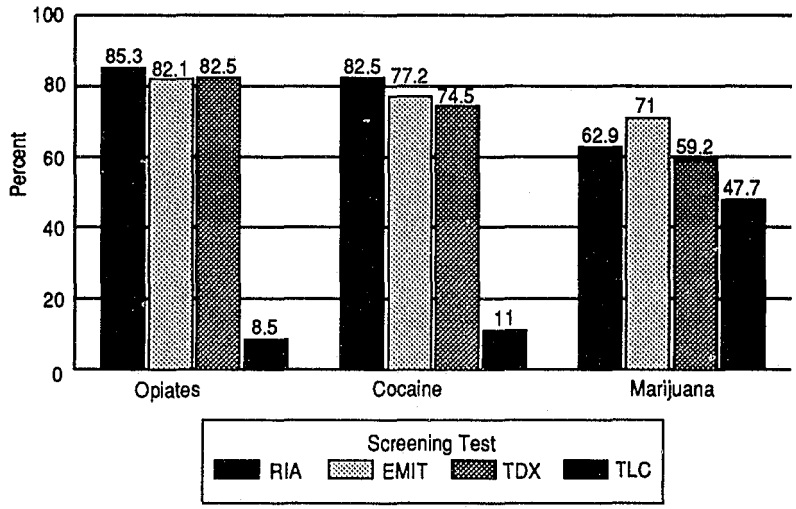
Drug Type	Percent Positive
Marijuana	34.0%
Cocaine	27.5%
PCP	7.7%
Opiates	7.1%
Amphetamines	3.6%

* Refer to table 1 for the exact NIDA-specified GC/MS cutoff levels for each of the drugs.

Clear accuracy differences between types of tests

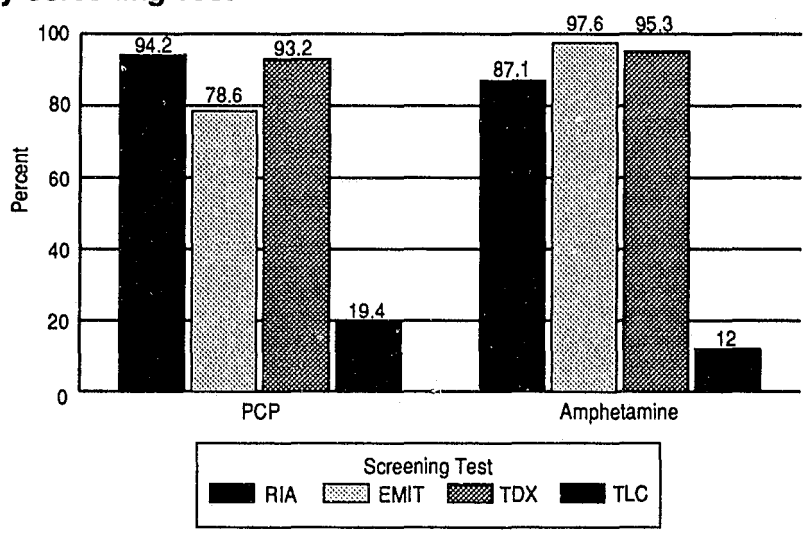
Clear differences exist between the accuracy of the three immunoassays and thin-layer chromatography. (Tables presenting the data for all tests and all drugs appear in appendix B.) The TLC test was inadequate in identifying drug users and did not identify the majority of specimens containing drugs. Specifically, the TLC technology identified approximately 8 percent of the positive opiate specimens, 11 percent of the positive cocaine specimens, 19 percent of the positive PCP specimens, 48 percent of the positive marijuana specimens, and 12 percent of the positive amphetamines specimens (see figures 1 and 2). Positive specimens were determined by GC/MS using the cutoff levels in the NIDA guidelines.

Figure 1
Percent of Positive Samples* Correctly Identified as Positive by Screening Test



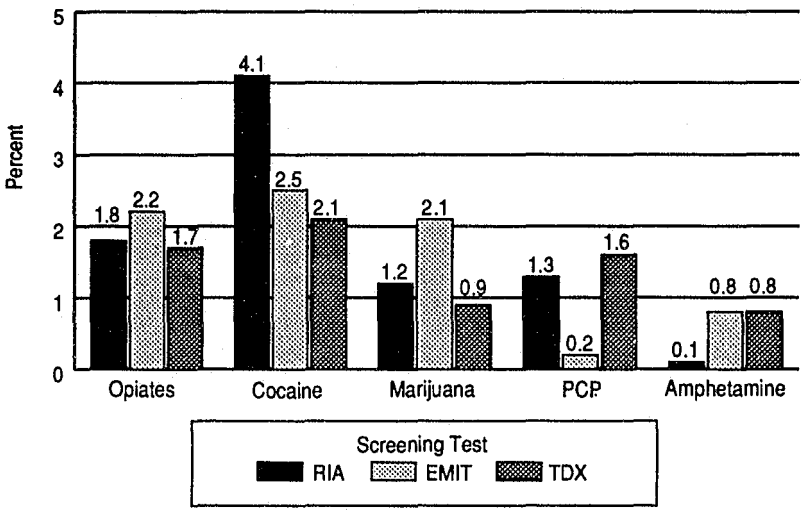
* Positive samples determined by GC/MS; see text for details.

Figure 2
Percent of Positive Samples* Correctly Identified as Positive by Screening Test



* Positive samples determined by GC/MS; see text for details.

Figure 3
False Positive Rates* by Drug Type



* Negative by GC/MS but positive by screening test; see text for details.

False positive rates

The most common concern voiced about drug testing—whether in the criminal justice system, the military, or the civilian workplace— is the possibility that an individual will be falsely accused of using drugs because of a positive urine test when in fact the individual has not used drugs. These errors are known as false positives. Manufacturers of the immunoassays compared in this study are also concerned about these errors; hence, their tests are purposely designed to *reduce false positive errors.*

When results for the five drug types were combined, the average false positive rate was about 1 to 2 percent (see figure 3).[13] That is, in a hypothetical sample of 1,000 persons *all testing positive* for drug use by one of the screening tests, 10 to 20 may have incorrect positive results. In comparison to other drugs tested, the error rate for false positives was somewhat greater for cocaine and slightly less for PCP and amphetamines. The TLC test also has a low rate of false positives, but this finding is not surprising given the relative overall inability of this technology to detect drug use. It must be noted that these false positive rates are based on the screening test alone; in an actual testing program, confirmation with GC/MS would be expected to eliminate virtually all false positive results.

False negative rates

Because of the concern about false positive results, less attention has been paid to testing errors that falsely identify a positive specimen as negative. In this study, *false negative rates* were more variable across type of drug and testing method. As discussed above, the results of the study show a clear distinction between the three immunoassays and TLC in their ability to identify positive urine specimens accurately, and thus avoid false negative results. For the three immunoassays, the average false negative rate for the five drug types was about 20 percent using the cutoff levels in the NIDA guidelines. That is, of a hypothetical 1,000 urine specimens that are positive, 200 might actually yield negative test results.[14]

The false negative rate was higher than this average for cocaine and especially for marijuana, but lower for PCP and amphetamines. Thus, the immunoassay screening technologies failed to detect 29 to 41 percent of the specimens positive for marijuana, but only missed 2 to 21 percent of the specimens positive for PCP and amphetamines. Overall, this study's data show that using the available immunoassay techniques as screening tests (and the cutoff levels in the NIDA guidelines) may result in about one in five urine specimens that are actually positive for one of the five drugs examined here being declared negative.

However, these false negative results are unlikely to affect the ability of the criminal justice system to detect drug users if tests are performed repeatedly on individual offenders. The most common use of drug testing in the criminal justice system is to monitor an offender's compliance with pretrial, probation, or parole conditions by testing for illegal drugs on a regular basis. With this type of drug testing program, the likelihood of repeated negative test results when an individual is a regular drug user is statistically very low.[15]

A final note about error rates

The study findings on false positive and false negative rates should not be the sole criterion for selecting an immunoassay for use in a drug-testing program. Many factors contribute to these findings and, in some cases, a simple comparison of the percentage of test results found in error may be misleading. For example, analysis of data from the RIA test indicates that the 4.1 percent false positive rate for cocaine occurred, in part, because the GC/MS cutoff level used to determine whether a specimen was positive or negative (150 ng/mL) was lower than the screening cutoff level (300 ng/mL). A majority of the 78 RIA false positive specimens did contain cocaine (at a level above 300 ng/mL), but the reported GC/MS concentration level for the same specimens was below 150 ng/mL. Thus, the specimens were declared negative. This type of test result occurred more frequently for RIA than for the other immunoassays.[16]

The amphetamine data offer a further example of why error rates should not be the sole criterion for selecting a screening test. The false positive *rates* for amphetamines among the three immunoassays are very low and not statistically different (0.8, 0.8, 0.1), but the *number* of false positive test results varies from 2 (RIA) to 20 (EMIT, TDX). (See data in appendix B.) In this case, the rate is misleading because of the small number of specimens in the study sample that were positive for amphetamines.

Overall results by drug type

As a group, the three immunoassays—EMIT, TDX, and RIA—were much more accurate than TLC. In general, there are small differences among the immunoassays by drug type. In comparing the immunoassays, however, the data indicate that *no one type of immunoassay was consistently superior to the others in identifying positive and negative specimens across the five drug types.*

Cocaine, marijuana, and opiates. Considering the results for cocaine, marijuana, and opiates, the three drugs most commonly used by drug-involved offenders, the three immunoassays together correctly identified an average of 75 percent of the positive specimens and 98 percent of the negative specimens. Stated differently, the immunoassay tests resulted in a false negative rate of about 25 percent and a false positive rate of about 2 percent (see figures 1 and 3 and table 3).

The immunoassays were most accurate in detecting opiates, cocaine, and marijuana, in that order. The tests often missed marijuana, which is discussed later in this report. False positive rates were highest for cocaine and lower for opiates and marijuana.

PCP. The study population's use of PCP was considerably lower than for marijuana and cocaine, but similar to use of opiates. When technicians used the highly accurate GC/MS test at a cutoff level of 25 ng/mL, 200 persons tested positive for PCP. As was the case with the other drugs, TLC correctly identified only a minority—19 percent—of these specimens (figure 2).

In sharp contrast to TLC, the three immunoassays identified more than 75 percent of the specimens that were positive for PCP (see figure 2 and table 3). Two of the immunoassays (TDX and RIA) recommended or preset a cutoff level of 25 ng/mL, the screening cutoff for PCP in the NIDA guidelines. The third immunoassay (EMIT) used a preset cutoff of 75 ng/mL. These cutoff differences may account for the slight variations in detecting PCP. Using a relatively high cutoff level—a concentration of 75 ng/mL, for example—would reduce the technology's ability to identify positive specimens because more of the drug would have to be present before the test could detect it. False positive rates for the immunoassays testing for PCP were quite low—less than 2 percent—for all three immunoassays (see figure 3).

Table 3
False Positive and False Negative Rates for Immunoassay Screening Methods by Drug Type*

	EMIT		*TDX*		*RIA*	
Drug/Drug Class	**False Positive Rate†**	**False Negative Rate‡**	**False Positive Rate**	**False Negative Rate**	**False Positive Rate**	**False Negative Rate**
Cocaine	2.5%	22.8%	2.1%	25.5%	4.1%	17.5%
Opiates	2.2	17.9	1.7	17.5	1.8	14.7
Marijuana	2.1	29.0	0.9	40.8	1.2	37.1
PCP	0.2	21.4	1.6	6.8	1.3	5.8
Amphet-amines	0.8	2.4	0.8	4.7	0.1	12.9

* These summary results are based on data in appendix B, using the cutoff levels for immunoassays and GC/MS stated in the NIDA guidelines, with the exceptions noted in table 1.

† The percentage of negative urine specimens, as determined by GC/MS, which are positive (falsely) by the screening test. See text for further discussion.

‡ The percentage of positive urine specimens, as determined by GC/MS, which are negative (falsely) by the screening test. See text for further discussion.

Amphetamines. Comparing the ability of urinalysis technologies to identify illegal amphetamine use posed several problems. At the time the study was conducted, illegal use of amphetamines, including methamphetamine, was primarily confined to a few metropolitan areas in the West and Southwest regions of the United States.[17] Although the study population was drawn from California, initial analysis revealed a very low rate of amphetamine use in the specimens obtained from the parole sample (18 of 2,470 or 0.7 percent). Thus, researchers expanded the study by adding a sample of persons arrested in San Diego, a city known to have high rates of illegal amphetamine use.

With these additions, technicians found that a total of 95 out of 2,668 urine specimens were positive for amphetamines or methamphetamine based on GC/MS (using the NIDA cutoff of 500 ng/mL). "Ice" is the street name for an illegal substance that has appeared in Hawaii and is reportedly available in some west

coast cities; though this substance appears primarily as methamphetamine in urine, approximately 4 to 7 percent of methamphetamine is metabolized as amphetamine. Screening tests can detect ice if the technology is designed to recognize both amphetamines and methamphetamine.

Because of the small number of positive specimens, however, the study's results for amphetamines are not as conclusive as those for the other four drug types. In addition, urine-screening tests for amphetamines have historically been considered less accurate than tests for other drugs. Existing tests for amphetamines are continually being revised, and new technologies have appeared since the study began.

The three immunoassays were surprisingly accurate in correctly identifying illegal amphetamines or methamphetamine use when it was actually present, based on the GC/MS test.[18] The screening tests correctly identified nearly 9 of every 10 positive specimens. In sharp contrast, TLC only identified 12 percent of the positive amphetamine specimens (see figure 2). False positive rates were less than 1 percent (see figure 3 and table 3). As was the case with PCP, the slight differences in the amphetamine results for the immunoassays may be due to differences in screening cutoff levels among the three tests. The NIDA guidelines specify 1,000 ng/mL as the cutoff level for detection of amphetamines using urine-screening tests. At the time of the study, the EMIT test for amphetamines was based on a fixed cutoff of 300 ng/mL, and the RIA test used a cutoff of 1,000 ng/mL. Although the TDX amphetamine test may be set lower than 1,000 ng/mL, the 1,000 ng/mL cutoff was used in the study for TDX, since the cutoffs in the NIDA guidelines were the basis for the study design.

Other issues in using screening tests

One purpose of this study was to determine the extent to which drug use may be missed using the standards in the NIDA guidelines. In a second set of analyses for this study the confirmation cutoffs for each drug were purposely set at very low levels to ensure the detection of a drug if it was present at all (see "alternate" cutoffs listed in table 1).[19] A comparison of the numbers of specimens labeled positive using NIDA cutoffs and alternate cutoffs for GC/MS provides some information on this question. As shown in table 4 (and as would be expected) a lower cutoff results in more specimens being labeled as positive.

Table 4
Number of Positives by GC/MS

Drug Type	NIDA Cutoff	Alternate Cutoff
Opiates	190	300
Cocaine	733	943
Marijuana	906	999
PCP	206	235
Amphetamines	95	119

Another way to assess this issue is to examine what would happen if the cutoff levels for the screening tests were lowered as well. If the drug concentration level at which a specimen is considered positive or negative is too high, the screening assay may report a false negative test result for some positive specimens. As noted earlier, the immunoassays were more likely to miss the presence of cocaine and marijuana in urine specimens than the other three drugs tested. In many of these specimens, the drug in question was present in the specimen, but at a concentration lower than the NIDA cutoff for screening tests. The three immunoassays, when compared to the GC/MS test result using the NIDA cutoffs, missed 30 to 40 percent of the specimens that were positive for marijuana, 18 to 25 percent of the positive cocaine specimens, and 15 to 18 percent of the positive opiate specimens.

Two results were reported for each urine specimen analyzed in the study: (1) a positive or negative designation (based on the NIDA cutoff levels discussed earlier) and (2) a quantitative report of the drug concentration present in nanograms per milliliter. These data allow us to provide a rough and preliminary look at the effects of lowering cutoffs for some drugs.

The appropriate drug concentration level for determining if a urine specimen is positive for marijuana has been the subject of several studies and much debate. NIDA guidelines have approved a screening cutoff level for marijuana of 100 ng/mL. However, tests with lower cutoff levels are also being used. An EMIT test for marijuana detection is available with cutoff levels of 100, 50, and 20 ng/mL, and several TDX tests for detecting marijuana are available with a user-defined cutoff range of 10 to 200 ng/mL. Analysis of data gathered in this study indicated that if the screening cutoff level for marijuana were lowered to 50 ng/mL, the number of specimens positive for marijuana might increase as much as 40 percent (see table 5).[20]

Table 5
Changes in Numbers of Marijuana Positives for Different Screening Cutoff Levels

Technology	Drug Concentration Cutoff for Screening Tests: NIDA (100 ng/mL)	Suggested (50 ng/mL)	Percent Change
GC/MS*	999	999	—
RIA	572	785	+ 37%
TDX	536	761	+ 42%
EMIT	650	673	+ 4%†

* The GC/MS cutoff is 10 ng/mL.

† The EMIT test for marijuana (using a fixed cutoff of 100 ng/mL) does not allow a clear determination of the expected change in number of positive test results.

Table 6
Changes in Numbers of Cocaine Positives for Different Screening Cutoffs

Technology	Drug Concentration Cutoff for Screening Tests: NIDA (300 ng/mL)	Suggested (200 ng/mL)	Percent Change
GC/MS*	943	943	—
RIA	661	711	+ 6%
TDX	562	614	+10%
EMIT	589	700	+19%

* GC/MS cutoff is 50 ng/mL.

For cocaine, the potential change in the number of positive test results that would result from lowering the screening cutoff level is much smaller. The screening cutoff level in the NIDA guidelines for cocaine is 300 ng/mL. The data from this study suggest that if this cutoff were lowered to 200 ng/mL, 6 to 19 percent of the specimens previously labeled negative for cocaine at the higher cutoff would be labeled as positive (table 6), depending on the type of immunoassay used for screening.

Table 7
Changes in Numbers of Opiate Positives for Different Screening Cutoffs

Technology	Drug Concentration Cutoff for Screening Tests: NIDA (300 ng/mL)	Suggested (200 ng/mL)	Percent Change
GC/MS*	300	300	—
RIA	193	217	+12%
TDX	180	200	+11%
EMIT	186	212	+14%

* GC/MS cutoff is 50 ng/mL.

For opiates, lowering the cutoff level might raise the number of positive test results, but no more than 15 percent. The screening cutoff level in the NIDA guidelines for opiates is 300 ng/mL. Based on the study data, if this screening cutoff were lowered to 200 ng/mL, approximately 11 to 14 percent of the specimens that were negative for opiates at the higher cutoff would be labeled as positive (see table 7), depending on the type of immunoassay used for screening.

These findings show that some of the false negative test results might be considered positive for the drug or drug metabolite in question if screening cutoff levels were lowered. The impact on drug-testing programs could be substantial in the case of marijuana because more of the persons being tested might have positive results. Only a small number of additional cocaine or opiate users probably would be identified, however, if the cutoff levels for these drugs were lowered.

The projections for marijuana, cocaine, and opiates are only an approximation of what might be expected if screening cutoff levels were lowered. Analyses are based on statistical manipulation of data gathered in the study, not on actual comparison of test results using screening tests with different cutoff levels. The estimates depend, in part, on the drug concentration level in the population being tested. If, for example, urine specimens from parolees have lower drug concentrations on average than arrestees, then a change in the cutoff level would be expected to have a greater effect for parolees than arrestees. A change in cutoff levels might not greatly affect the number of positive specimens in a population in which drug concentrations levels are high, that is, routinely above the NIDA cutoff levels.

Some criminal justice users of urine screening methods may wish to set cutoff levels in their testing program lower than the NIDA guidelines. Manufacturers of urinalysis technologies for drug testing may or may not specify a particular cutoff level for determining whether a specimen is positive or negative. Some screening tests (for example, TDX) allow the operator to select a cutoff level within a specified range, although the cutoff level may be preset before the test kit is distributed. Other screening tests (EMIT, for instance) have a fixed cutoff level—usually the screening cutoff level recommended by NIDA—at which a specimen is to be considered positive or negative. These types of tests perform most accurately at the specified cutoff level.

Several issues should be considered if criminal justice agencies have the option of selecting specific cutoff levels or choosing a test with a cutoff lower than the NIDA guidelines. Using lower cutoff levels will likely identify more drug users, particularly those using marijuana. This may be useful if the purpose of the test is to distinguish those who may need drug treatment. Other consequences of selecting lower cutoffs might include increased demand for drug treatment, an increased need for additional supervision of drug-using offenders, and a greater need for jail and prison space for probation and parole revocations.

Others might argue, however, that the cutoff levels in the NIDA guidelines are appropriate because these levels identify the vast majority of drug-involved offenders in pretrial, probation, and parole testing. Moreover, in some jurisdictions, criminal justice testing programs are constrained by "scientifically acceptable" cutoff levels that may have already been established by either State law or regulation.[21]

At a minimum, cutoffs should be set at levels that the manufacturer will legally defend. Further, the procedures outlined by the manufacturer, such as preparation of reagents, should be strictly followed to obtain maximum accuracy. Using established cutoff levels, such as those recommended by NIDA, ensures continuity of drug-testing procedures between jurisdictions and uniform testing of all offenders. Little research is available to guide the criminal justice community—or the private sector, for that matter—on how much of a given drug should be present in a urine specimen before the specimen should be declared positive. For most purposes, the cutoff levels approved by NIDA for screening and confirmation of urine specimens will meet the objectives of drug-testing programs in the criminal justice system.

Changes in NIDA guidelines. The NIDA guidelines for establishing cutoff levels for workplace drug testing are currently being evaluated. One consideration is whether cutoff levels for some illegal substances should be lowered. Modifying the NIDA guidelines entails discussion of both scientific concerns about the accuracy of testing methods at lower cutoff levels and policy implications that might result from such changes. Any official change in the NIDA guidelines will likely affect further development and marketing of urinalysis technologies for drug testing, which may also affect urine-testing programs in criminal justice settings.

The issue of confirmation

It is reasonable to ask if any single urine-screening technology examined in this study is sufficiently accurate to make confirmation of positive results unnecessary. As this study has shown, none of the technologies provides 100-percent correct results when compared to the highly accurate GC/MS technology. Of greatest concern to the criminal justice system should be the 1 to 2 percent of the specimens that were *falsely identified as positive* by the four screening technologies. No single technology emerged as superior in the ability to reduce these errors.

Although the rate of false positives is low, confirmation of screened positives using an alternative technology is recommended by the NIDA guidelines to avoid testing errors. Because of the expense and time involved in confirmatory testing, in many criminal justice settings an individual's admission of drug use after being confronted with a positive drug test is considered a "confirmation." If a positive drug test is *contested*, however, a second, confirmatory test is essential, especially if one positive drug test will result in serious punitive action. Users of urine tests must weigh the costs of confirmation of positive results and the need for a rapid test result against the consequences of possible testing errors.[22]

Because of the possibility of false results, screening test manufacturers generally include instructions stating that all positives designated as such by their product should be confirmed by a method based on a different chemical principle. For instance, all three manufacturers of the immunoassays examined in this study state that GC/MS is the preferred confirmatory method. Other chromatographic technologies, such as gas chromatography and high performance thin-layer chromatography (HPTLC), can also be used for confirmation.

Repeat testing of urine specimens by the same method or confirmation of screened positives using a similar technology (for example, using another type of immunoassay if the initial screen was also an immunoassay) probably will not eliminate all erroneous results.[23] Repeat testing by the same technology may eliminate faulty procedural results, but not the errors inherent in the technology; hence, this practice should not be considered "confirmatory."

Criminal justice agencies involved in drug testing may benefit from preparing a detailed plan that outlines testing procedures, drug-testing technologies, and agency policy. The plan should also specify at what drug concentration levels a specimen will be considered positive and how positive results will be confirmed.[24]

Laboratory versus onsite testing

The study also addressed whether accuracy was significantly greater when specimens were analyzed in a full-service laboratory, as compared to analysis using onsite technology. The results of the three immunoassays were essentially equivalent: The one immunoassay technology carried out in a laboratory (RIA) was no more accurate than two immunoassays (EMIT and TDX) performed in an onsite testing facility.[25]

Although the quality of services varies among onsite testing facilities, many of these facilities are as professional as full-service laboratories. Onsite facilities frequently follow documented chain-of-custody procedures for handling urine specimens, provide training for personnel, and design ongoing programs to monitor the accuracy of their testing procedures, which are often called "proficiency programs." The onsite facility used in this study met these criteria.

To ensure the quality of onsite drug testing, criminal justice agencies must establish procedures and protocols for specimen testing and quality assurance. If these procedures and protocols are developed and maintained, the testing results can be as accurate as those produced in a commercial laboratory.

Study Conclusions and Policy Implications

This study was designed to provide guidance on urinalysis technologies for drug testing in the criminal justice system, including arrestees; those on pretrial release, probation, and parole; and incarcerated offenders. Some of the findings may be dependent upon the higher levels of illegal drug use in these populations than in the general population. Results should not be generalized to other types of populations, including military personnel, Federal employees, pilots, railroad employees, job applicants, or other such populations. For many of these groups, drug-testing policies are governed by guidelines specific to their needs.

The study arrived at several principal conclusions and related policy implications for using urinalysis technologies for drug testing in the criminal justice system. These are summarized below.

- Standard thin-layer chromatography was found to be seriously deficient in detecting the five substances examined in this study. Therefore, TLC is unlikely to be useful for screening or confirming urine specimens for illegal drug use within criminal justice populations.

- When using the Federal guidelines for establishing cutoff levels for screening tests (or the manufacturer cutoff, if different), none of the immunoassay technologies examined—EMIT, TDX, and RIA—is superior to the others in detecting all five drugs. Although there are some small differences by drug type, these differences are unlikely to help agencies choose a technology, because populations are usually screened for several drugs.

- The three immunoassays examined in this study—EMIT, TDX, and RIA—are about equally effective in limiting false positives for the substances tested. Overall, about 1 to 2 percent of screened specimens were falsely identified as positive, using the screening cutoff levels in the NIDA guidelines.

- Although using an immunoassay as a drug-screening technology generates few false positive errors, confirmation of screened positives by a method based on a different chemical principle, preferably GC/MS, should be required if the individual contests the positive result, or if one positive drug test will result in serious punitive action.

- Using the three immunoassays examined in this study, approximately 20 percent of specimens identified as positive for illegal drugs (based on GC/MS and NIDA cutoff levels for screening and confirmation) were actually found to be negative. Some of these false negative results, however, resulted from the higher screening cutoff levels. *Repeated* drug testing of an individual—on a weekly or monthly basis, for example—will most likely detect illegal substances in a regular drug user.

- To ensure the highest level of accuracy, users of urine-screening technologies should carefully follow manufacturers' instructions for determining whether a urine specimen is positive or negative.

- The choice of cutoff levels for determining positive and negative results in a specific jurisdiction should reflect the needs of the testing program, any potential legal restrictions, and the capability of the screening test. The screening cutoff levels in the NIDA guidelines for the five most prevalent drug types ensure uniformity in screening criminal justice populations for drug use. If use of the lower screening cutoffs is desired, cutoffs should be set at levels which the manufacturer will legally defend.

- Given the number of false negative results in screening urine for marijuana, manufacturers of urine-screening technologies should make available screening tests that can detect marijuana at a lower concentration level of 50 ng/mL. Lowering the cutoff may reduce the rate of false negative results for marijuana.

- Drug tests performed in an onsite testing facility using technologies designed for onsite use can be just as accurate as testing performed in a full-service laboratory. Accuracy depends on maintaining appropriate procedures and protocols such as chain of custody, quality control program, and personnel training.

Glossary

Chromatography: A procedure used to identify substances, such as drugs of abuse, in urine. The procedure is based on separating or extracting the substances, allowing them to move or migrate along a carrier, and then identifying them based on their characteristic locations on the carrier.

Enzyme Immunoassay (EIA): An immunoassay procedure used to identify drugs of abuse in urine by attaching an enzyme tag to the drug in question.

Confirmation Tests: A second test used to confirm positive results from an initial screening test. A confirmation test uses a method more specific than a screening test and provides a greater margin of certainty.

Cutoff Level: The concentration of a drug in urine, usually in nanograms per milliliter (ng/mL), used to determine whether a specimen is positive (at or above the cutoff level) or negative (below the cutoff level) for the drug in question.

False Positive: A test result indicating positive for a given drug when that drug is actually absent *or* below the designated cutoff level. For this study, a positive test result by EMIT, RIA, TDX, or TLC but negative by GC/MS (evaluated individually for each drug and each test using the cutoff levels in the NIDA guidelines).

False Positive Rate: The percentage of negative urine specimens, as determined by GC/MS, which are positive (falsely) by a specific screening method (computed separately for each drug).

False Negative: A negative test result for a given drug when that drug is present in a sample and at a concentration above the cutoff level for the test. For this study, a negative test result by EMIT, RIA, TDX, or TLC, but positive by GC/MS (evaluated individually for each drug and each test using the cutoff levels in the NIDA guidelines).

False Negative Rate: The percentage of positive urine specimens, as determined by GC/MS, that are negative (falsely) by a specific screening method (computed separately for each drug).

Fluorescence Polarization Immunoassay (FPIA): An immunoassay procedure used to identify drugs of abuse in urine by attaching a tag that glows or fluoresces to the drug in question.

Gas Chromatography/Mass Spectrometry (GC/MS): A chromatographic procedure used to identify drugs of abuse in urine using a helium or nitrogen carrier to move the drug in question to a detector for identification and measurement. The detector, a mass spectrometer, identifies the drug by its mass to charge ratio.

Immunoassay: A procedure used to identify substances, such as drugs of abuse in urine, based on the competition between tagged and untagged antigens to combine with antibodies. The uncombined, tagged antigen is an indicator of the drug present in the urine specimen.

Laboratory Testing: The testing of urine specimens by professional technologists or technicians at a commercial laboratory.

Onsite Testing: The testing of urine specimens within criminal justice facilities using paraprofessional technicians.

Proficiency Sample: A urine specimen that has a known concentration of a specific drug that is tested by a laboratory to determine the accuracy of its testing procedures.

Proficiency Program: An ongoing process in which a series of proficiency samples are sent to a laboratory on a regular basis. The laboratory is rated on its accuracy in identifying the presence and concentration of the drug.

Radioimmunoassay (RIA): An immunoassay procedure used to identify drugs of abuse in urine by attaching a radioactive tag to the drug in question.

Screening Test: An initial test used to detect drugs of abuse in urine. Screening tests are rapid and less expensive, but generally not as accurate as confirmation tests.

Sensitivity: The ability of a procedure to detect minute amounts of substances. A highly sensitive procedure will rarely fail to detect a substance if it is present, thus few false negative results will occur.

Specificity: The ability of a procedure to differentiate between chemically similar substances. A highly specific procedure is rarely positive for a given drug if the substance is truly absent; thus few false positive results will occur.

Thin-Layer Chromatography (TLC): A chromatographic procedure used to identify drugs of abuse in urine using a thin layer of material such as silicon as a carrier. The separated substances are dyed, and the resultant color and migration patterns are used to identify the drugs in question.

Threshold: The lowest levels of a substance detectable by a given test. Cutoff levels are usually set above the threshold to balance the resulting false positive and false negative errors and maximize the overall accuracy of test results.

Urinalysis: The chemical analysis of urine to determine the presence or absence of substances. In the criminal justice setting, the substances being determined are drugs of abuse.

References and Related Documents

[Many of these items are available from the National Criminal Justice Reference Service, P.O. Box 6000, Rockville, MD 20850, 800–851–3420 or 301–251–5500.]

Blanke, Robert (1988). "Assessment of Laboratory Quality in Urine Drug Testing: A Proficiency Testing Pilot Study." *Journal of the American Medical Association*, Vol. 260, No. 12, Sept. 23/30, pp. 1749–1754.

Bureau of Justice Assistance (1988). *Urinalysis as Part of a Treatment Alternatives to Street Crime (TASC) Program.* Washington, D.C.: Bureau of Justice Assistance.

Bureau of Justice Assistance (1991). *American Probation and Parole Association's Drug Testing Guidelines and Practices for Adult Probation and Parole Agencies.* Washington, D.C.: Bureau of Justice Assistance.

Bureau of Justice Assistance (1989). *Estimating the Costs of Drug Testing for a Pretrial Services Program.* Washington, D.C.: Bureau of Justice Assistance.

Bureau of Justice Statistics (1988). "Drug Use and Crime." *Special Report.* Washington, D.C.: Bureau of Justice Statistics.

Carver, John A. (1986). "Drugs and Crime: Controlling Use and Reducing Risk Through Testing." *Research in Action.* Washington, D.C.: National Institute of Justice.

Dembo, Richard, Linda Williams, Eric D. Wish, and James Schmeidler (1990). "Urine Testing of Detained Juveniles To Identify High-Risk Youth." *Research in Brief.* Washington, D.C.: National Institute of Justice.

Hoyt, David, Robert Finnigan, et al. (1987). "Drug Testing in the Workplace—Are Methods Legally Defensible?" *Journal of the American Medical Association*, Vol. 258, No. 4, July 24/31, p. 504–509.

McBay, Arthur (1987). "Drug-Analysis Technology—Pitfalls and Problems." *Clinical Chemistry*, Vol. 33, No. 11(B), pp. 33B–40B.

Mike, Lawrence, and Maria Hewitt (1988). "Accuracy and Reliability of Urine Drug Tests." *University of Kansas Law Review*, Vol. 36, pp. 641–681.

Davis, Kenneth, and Richard Hawks (1986). "Urine Testing for Drugs of Abuse." *Research Monograph #73.* Rockville, Maryland: National Institute on Drug Abuse.

National Institute of Corrections (1989). *Legal Issues in Drug Testing Probation and Parole Clients and Employees*. Washington, D.C.: National Institute of Corrections.

National Institute of Justice. "Drug Use Forecasting (DUF)." *Research in Action* (annual and quarterly reports). Washington, D.C.: National Institute of Justice.

Office of National Drug Control Policy (1989). *National Drug Control Strategy*. Washington, D.C.: U.S. Government Printing Office.

Office of National Drug Control Policy (1990). *National Drug Control Strategy*. Washington, D.C.: U.S. Government Printing Office.

Rosen, Cathryn Jo, and John S. Goldkamp (1989). "The Constitutionality of Drug Testing at the Bail Stage." *Journal of Criminal Law & Criminology*, Vol. 80, No. 1, pp. 114–176.

Smith, Douglas A., Eric D. Wish, and Roger G. Jarjoura (1989). "Drug Use and Pretrial Misconduct in New York City." *Journal of Quantitative Criminology*, Vol. 5, No. 2, pp. 101–126.

Toborg, Mary A., et al. (1989). *Assessment of Pretrial Urine Testing in the District of Columbia*. Washington, D.C.: National Institute of Justice.

Wish, Eric D., Robert Dupont, and Bernard Gropper (1991). *Urine Testing of Offenders: A Manual for Practitioners*. Draft final report. Washington, D.C.: National Institute of Justice.

Wish, Eric D., and Bernard Gropper (1990). "Drug Testing by the Criminal Justice System: Method, Research, and Application." In *Crime and Justice, Vol. 13: Drugs and Crime*. Chicago, Illinois: University of Chicago Press.

Wish, Eric D., Mary A. Toborg, and John P. Bellassai (1988). *Identifying Drug Users and Monitoring Them During Conditional Release*. Washington, D.C.: National Institute of Justice.

Appendix A

Immunoassay technologies

Immunoassays use antibodies to detect the presence of drugs. An antibody is a protein that will react only when combined with a specific substance or group of very similar substances. The substance with which the antibodies react is called the antigen. In using immunoassays for drug testing, the targeted drug acts as the antigen. A label or "tag" is mixed with a specific amount of the drug being tested. The tag is a substance that can be identified and measured after the antigen/antibody reaction takes place. The drug containing the tag is called the "tagged antigen." Commonly used immunoassay tags include radioactive material, enzymes, or fluorescent material (i.e., material that glows). In immunoassays, tagged antigen, urine that may contain the drug in question (untagged antigen), and antibodies that react specifically against the drug being tested are mixed together. The tagged antigen and the untagged antigen compete to react with the antibodies. The amount of unbonded tag that remains after the reaction is complete indicates the presence or absence of the drug.

The immunoassay procedures used in the study differ primarily by the type of tag used and the method of detecting unused, tagged antigens. The onsite testing facility at the Alhambra Parole Office and the BPL Toxicology Laboratory were instructed to provide both a designation of whether the specimen was positive or negative (using the cutoffs in the NIDA guidelines) for the specific drug in question and a quantitative result of the drug concentration level in the specimen in nanograms per milliliter (ng/mL).

Syva's EMIT™ is an enzyme immunoassay technology in which an enzyme (a protein that helps chemical reactions take place both within and outside of the body) is used as the tag. The change in enzyme activity in the tagged antigen, antibody, and urine mixture serves as an indicator of the amount of drug present in the urine sample. An estimate of the drug concentration level in the specimen was determined by following the manufacturer's instructions for obtaining quantitative results.

Abbott's TDX™ is a fluorescence polarization immunoassay (FPIA). It uses a substance, fluorescein, that "glows" or fluoresces as its tag. The tag is subjected to polarized light, and the degree of polarization of the tagged drug is measured to indicate the presence of the drug in the urine specimen being tested. Samples with low concentrations of drug or drug metabolite will produce a high degree of polarization. The test results are reported in qualitative terms (above or below the selected cutoff) as well as semiquantitative terms of numerical concentration of the drug in the specimen.

Roche's Abuscreen™ is a radioimmunoassay. The antigen is tagged with a radioactive substance. Drug presence is indicated by measuring the amount of radioactivity present after the antibody, tagged antigen, and urine sample react with one another. A gamma counter must be used to measure the level of radioactivity in the specimen. Procedures outlined in the manufacturer's package inserts allow laboratory technicians to determine the drug concentration level in the specimen.

In many cases, drug use is inferred by measuring metabolites rather than the substance itself. For some substances, the body produces similar metabolites from use of legal as well as illegal substances. The screening assays may detect many different types of metabolites, some of which may be metabolites of legal substances, or the screening assay may "cross-react" with another substance, giving a false positive result. This raises the problem of ensuring that a urine specimen screened as positive for a substance results from using an illegal substance rather than a legal substance. For instance, some over-the-counter cold remedies may be detected as illegal amphetamine by some screening assays. Confirmation of presumptive positives by an alternate technology that can distinguish between these metabolites, principally GC/MS, is the preferred method of resolving these problems. A positive result by GC/MS is highly unlikely to be erroneous.

The reagents, instruments, and materials used in the three immunoassay procedures—TDX™ FPIA, Abuscreen RIA™, and EMIT™—were developed and/or supplied by Abbott Laboratories, Roche Diagnostic Systems, Inc., and Syva Company, respectively. The location of each manufacturer, a menu of drugs of abuse that can be identified by each technology, and the instruments used by each technology are presented in table A.1. The materials and equipment used in thin-layer chromatography are available through major chemical and laboratory supply companies throughout the country. Each manufacturer supplies a variety of support services to its customers including training, technical assistance, problem resolution, and expert witness assistance.

Thin-layer chromatography

In thin-layer chromatography, a measured amount of an extract of the urine specimen is put onto a glass plate that has been coated with a thin layer of silica or similar material to which components can become attached. The coated plate is put into a container that has a special chemical solution in it. The chemical solution moves up the plate taking the urine components with it, and the urine components are separated according to their different abilities to migrate. The separated components can then be identified by spraying the plate with a solution that causes the components to develop a color. The technician interprets color and migration patterns to determine the presence of specific drugs.

Gas chromatography/mass spectrometry (GC/MS)

GC/MS is a two-part process. In the first part, a gas such as helium or nitrogen transports the urine extract to a column where the chemical components in the materials to be measured are separated. The gas then transports the separated components onto a detector for identification and measurement. The detector in the GC/MS procedure is known as a mass spectrometer. It identifies a substance by its mass-to-charge ratio. The mass spectrum pattern or signature of a substance is specific for that particular substance.

Preparation of the specimen for analysis is also important. Depending on the drug being identified, extraction and hydrolysis procedures are used to extract the drug from the urine specimen. The sample volume, extraction solvent, hydrolysis reagent (whenever needed), internal standard, and derivatization reagent differ from drug to drug.

In this study, the GC/MS test performed by BPL Toxicology Laboratory identified and quantitated the following five drugs (or classes of drugs): 9 tetrahydrocannabinol (THC-marijuana); benzoylecgonine (cocaine); morphine, codeine (opiates); phencyclidine (PCP); and amphetamine, methamphetamine (amphetamines). Commercial control specimens were also included in daily analysis to establish the quantity of the unknown drug and to ensure that the control was within ± 20 percent of its established target value, which is the industry standard for determining the acceptability of GC/MS test results.

Laboratories also use two other procedures, both of which are classified as chromatography procedures. These are gas chromatography as a stand-alone procedure (without the mass spectrometer) and high performance liquid chromatography (HPLC). Either of these procedures may be used by a laboratory as a screening or confirmation technology. Because they require sophisticated equipment and professionally trained technicians, these tests are not adaptable to onsite use. They were not included in this study.

The body metabolizes and excretes different drugs at different rates. Thus, the maximum amount of time (in hours or days) after ingestion that a substance can be detected in urine varies by the type of drug ingested and, in some instances, the amount and frequency of use. The approximate duration of detectability of selected drugs in urine is shown in table A.2. Almost all drugs of abuse can be detected for 48 hours after ingestion. Some drugs, including PCP and marijuana, are stored in the body's fatty tissues and can be detected in urine for several days or weeks, depending on the amount and frequency of use.

Appendix A
Table A.1

Manufacturer	Technology/ Procedure	Drug–of–Abuse Menu	Instrumentation
Abbott Laboratories Abbott Park, IL 60064 1–800–323–9100	TDX™ FPIA	Amphetamine/ Methamphetamine Amphetamine Class Barbiturates Benzodiazepines Cannabinoids Cocaine Methadone Opiates PCP	TDX analyzer manufactured by Abbott.
Roche Diagnostic Systems, Inc. One Sunset Avenue Montclair, NJ 07042 1–800–526–1247	Abuscreen™ RIA	Amphetamines Barbiturates Benzodiazepines Cannabinoids Cocaine LSD Methaqualone Morphine PCP	Abuscreen RIA uses standard equipment found in most labs: pipetting equipment (automated or manual); centrifuge; gamma counter. These instruments are marketed by many manufacturers.
Syva Company 900 Arastradero Road Palo Alto, CA 94303 1–800–227–8994	EMIT™	Amphetamines Barbiturates Benzodiazepines Cocaine metabolite Methadone Methaqualone Opiates PCP Cannabinoids Propoxyphene	EMIT assays can be run on various chemistry analyzers including all Hitachi/BMD analyzers; high volume models; Olympus series; Technicon analyzers; and Roche analyzers. EMIT assays can also be run on the ETS system marketed by Syva Company.

Table A.2
Approximate Duration of Detectability of Selected Drugs in Urine

Substance	Duration of Detectability*
Amphetamines	48 hours
Methamphetamine	48 hours
Barbiturates	
Short-acting	24 hours
Intermediate-acting	48–72 hours
Long-acting	7 days or more
Benzodiazepines	3 days (therapeutic dose)
Cocaine metabolites	2–3 days
Methadone	3 days (approximate)
Codeine/Morphine	48 hours
Propoxyphene/Norpropoxyphene	6–48 hours
Cannabinoids (marijuana)	
Single use	3 days
Moderate use (4 times per week)	4 days
Heavy use (daily)	10 days
Chronic heavy use	21–27 days
Methaqualone	7 days or more
Phencyclidine (PCP)	8 days (approximate)

Source: Adapted from the *Journal of the American Medical Association's Council on Scientific Affairs*, 1987, p. 3112.

* Interpretation of the duration of detectability must take into account many variables, such as drug metabolism and half-life, subject's physical condition, fluid balance and state of hydration, and route and frequency of ingestion. These are general guidelines only.

Appendix B

Opiates*

Test	*Positives by GC/MS*			*Negatives by GC/MS*		
	GC/MS	Missed by Test	Percent False Negatives	GS/MS	Missed by Test	Percent False Positives
RIA	190	28	14.7	2,454	45	1.8
TLC	189	173	91.5	2,452	8	0.3
EMIT	190	34	17.9	2,454	54	2.2
TDX	189	33	17.5	2,455	42	1.7

* Screening test cutoff = 300 ng/mL; GC/MS cutoff = 300 ng/mL.

Cocaine*

Test	*Positives by GC/MS*			*Negatives by GC/MS*		
	GC/MS	Missed by Test	Percent False Negatives	GC/MS	Missed by Test	Percent False Positives
RIA	733	128	17.5	1,913	78	4.1
TLC	730	650	89.0	1,913	20	1.9
EMIT	732	167	22.8	1,916	48	2.5
TDX	732	187	25.5	1,917	40	2.1

* Screening test cutoff = 300 ng/mL; GC/MS cutoff = 150 ng/mL.

Marijuana*

Test	*Positives by GC/MS*			*Negatives by GC/MS*		
	GC/MS	Missed by Test	Percent False Negatives	GC/MS	Missed by Test	Percent False Positives
RIA	906	336	37.1	1,729	20	1.2
TLC	907	474	52.3	1,729	54	3.1
EMIT	906	263	29.0	1,727	37	2.1
TDX	904	369	40.8	1,726	15	0.9

* Screening test cutoff = 100 ng/mL; GC/MS cutoff = 15 ng/mL.

PCP*

Test	*Positives by GC/MS*			*Negatives by GC/MS*		
	GC/MS	Missed by Test	Percent False Negatives	GC/MS	Missed by Test	Percent False Positives
RIA	206	12	5.8	2,442	31	1.3
TLC	206	166	80.6	2,446	8	0.3
EMIT	206	44	21.4	2,450	5	0.2
TDX	205	14	6.8	2,449	39	1.6

* Screening test cutoff = 25 ng/mL (for EMIT, 75 ng/mL); GC/MS cutoff = 25 ng/mL.

Amphetamines*

Test	*Positives by GC/MS*			*Negatives by GC/MS*		
	GC/MS	Missed by Test	Percent False Negatives	GC/MS	Missed by Test	Percent False Positives
RIA	85	11	12.9	2,515	2	0.1
TLC	83	73	88.0	2,513	7	0.3
EMIT	85	2	2.4	2,515	20	0.8
TDX	85	4	4.7	2,515	20	0.8

* Screening test cutoff = 1,000 ng/mL (for EMIT, 300 ng/mL); GC/MS cutoff = 500 ng/mL.

Notes

1. National Institute of Justice, *DUF 1989 Annual Report*, 1990.

2. Bureau of Justice Statistics, *Drug Use and Crime*, 1988.

3. For example, see National Institute on Drug Abuse, *Technical, Scientific and Procedural Issues of Employee Drug Testing: Consensus Report*, 1990, p. 16.

4. Detailed information regarding the current costs of various testing systems is not presented because costs often vary depending on the quantity being supplied. Also, new testing methods are continually being introduced. Interested readers should contact the vendors of the various testing systems to receive the most up-to-date description of features and costs (addresses and phone numbers appear in table A.1 in appendix A). However, GC/MS is the most expensive of the methods used in this study, and it is likely to remain so in the foreseeable future.

5. Since the study began, Abbott Laboratories has modified some of its assays for marijuana, PCP, and amphetamine, and the products used in this study are, in some cases, no longer marketed by the company. In addition, Syva Company has recently marketed a specialized assay for detecting amphetamines which is supposed to be less reactive to over-the-counter drugs. It is not known how these new or modified products would compare to those used in the study.

6. A drug metabolite is a chemical byproduct of a drug that is formed in the body after ingestion of a specific drug.

7. This study was not designed to investigate the identification of substances other than illegal drugs (e.g., prescription and over-the-counter drugs, specific foods or liquids, etc.), which may produce a positive result on a urine-screening test. The specific cross-reactive elements are known to vary by drug and type of immunoassay being performed. Manufacturers of urine screening assays should be consulted about issues of cross-reactivity that may arise in using their product.

8. The GC/MS technology can be set to detect a wide or narrow range of metabolites for a specific drug. In this study, for opiates, GC/MS identified the presence or absence of codeine or morphine, and for amphetamines, either amphetamine or methamphetamine. These are the most common metabolites of these two drugs in offender populations. It is possible that the immunoassays could detect a metabolite of a specific drug for which GC/MS was not "programmed." Thus, a small number of specimens that we have called "false positive" could be positive for the drug in question, but for a different metabolite than those GC/MS detected.

9. See National Institute on Drug Abuse, "Urine Testing for Drugs of Abuse," *Research Monograph #73*, 1986.

10. "Mandatory Guidelines for Federal Workplace Drug Testing Programs," *Federal Register*, Vol. 53, No. 69 (April 11, 1988): 1970–1989, issued by the U.S. Department of Health and Human Services. These guidelines are commonly referred to as the NIDA guidelines, and this usage has been adopted for this report.

11. The TDX fluorescence polarization immunoassay marketed by Abbott Laboratories has preset cutoffs, but the user may select a different cutoff level within a wide range. The preset cutoffs are generally lower than those in the NIDA guidelines.

12. Davis, K.H., Hawks, R.L., and Blanke, R.V. (1988). "Assessment of laboratory quality in urine drug testing: A proficiency testing pilot study." *Journal of the American Medical Association*, Vol. 260, No. 12, pp. 1749–1754.

13. As a result of the study design, some of the false positive test results may have occurred because of a mismatch between specific metabolites detected by confirmation and screening methods or the use of a confirmation cutoff that does not match the capabilities of the screening method. In an actual testing program, the false positive rates of the screening methods may be slightly lower.

14. The magnitude of the false negative rate is determined by the screening and confirmation cutoff levels, which followed the NIDA guidelines. A close examination of the data reveals that the failure of the immunoassays to identify the specimens designated as positive by GC/MS is due partly to the immunoassay cutoffs. Many of the false negative specimens contained some amount of the drug but not at a high enough concentration to call the specimen positive by the immunoassay. Accordingly, the false negative rate would be reduced by lowering the immunoassay cutoffs.

15. Given that the probability of testing positive by the screening test after taking a detectable level of a drug is 0.8 (false negative rate is 0.2), the probability of *two independent, consecutive negatives* is 0.04 (might occur 4 times in 100); the probability of three consecutive negatives is 0.008 (might occur 8 times in 1,000).

16. Another explanation for these results may be degradation of the urine specimens that could make cocaine metabolites more difficult to detect and measure precisely with screening tests (Robert Dupont, personal communication). Degradation can occur because of inadequate refrigeration or other conditions that can alter the physical properties of the specimen.

17. National Institute of Justice, *Drug Use Forecasting Annual Report, 1989*, 1990.

18. Initial analyses separated results for amphetamines and methamphetamine, but no substantive differences were found; hence, the results are reported for total amphetamines.

19. Table 1 lists the specific cutoff level for each drug.

20. In addition, preliminary findings from a separate National Institute of Justice study show that lowering the screening cutoff level for marijuana from 100 ng/mL to 50 ng/mL (using TDX) might increase the number of positive test results by about 30 percent (Mieczkowski, 1990, Presentation at the Drug Use Forecasting Project Meeting, June 27–29, New Orleans, Louisiana).

21. A discussion of legal issues surrounding drug testing is beyond the scope of this report. A thorough discussion of many of the relevant issues can be found in *American Probation and Parole Association's Drug Testing Guidelines and Practices for Adult Probation and Parole Agencies*, Bureau of Justice Assistance, U.S. Department of Justice, 1991.

22. Any jurisdiction considering the implementation of a drug-testing program should review the most recent case law on the need for confirmation.

23. Although this study was unable to examine the issue of confirmation in detail, analysis was carried out to see if one immunoassay would confirm the results generated by another. For example, we compared the EMIT results to those using TDX and RIA to determine whether the other immunoassays might reveal errors—primarily false positive results—using EMIT. All combinations of immunoassays were examined. Analysis revealed that a second immunoassay does not discover all false positive results from the first test. Moreover, the second immunoassay may produce different errors than the initial screen.

24. For additional information about standards for drug testing in criminal justice agencies and relevant legal issues, see the reference section of this report.

25. However, this issue cannot be resolved fully by this study because none of technologies were carried out in both a laboratory and an onsite testing facility. (The RIA can only be performed in a full-service laboratory.)