

**Department of Health and Human Services
Substance Abuse and Mental Health Services Administration
Center for Substance Abuse Prevention**

Medical Review Officer Manual

for

Federal Agency Workplace Drug Testing Programs

**November 1, 2004
(Effective Date)**

This manual provides additional guidance to supplement the medical review officer requirements contained in the Mandatory Guidelines for Federal Workplace Drug Testing Programs that were published in the Federal Register on April 13, 2004 (69 FR 19644), with a November 1, 2004, implementation date.

Note: This manual does not apply to specimens collected under the Department of Transportation Procedures for Transportation Workplace Drug and Alcohol Testing Programs (49 CFR Part 40).

Previous Versions of this Manual are Obsolete

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Chapter 1. The Medical Review Officer (MRO)

The final review of results is an essential component of any drug testing program. A positive laboratory test result does not automatically identify an employee or job applicant as an illegal drug user, nor does a laboratory result of invalid, substituted, or adulterated automatically identify specimen tampering. An individual with a detailed knowledge of possible alternative medical explanations must interpret non-negative results in the context of information obtained from the donor interview. HHS requires the Medical Review Officer (MRO) to fulfill this important function.

The HHS Mandatory Guidelines define an MRO as a licensed physician holding either a Doctor of Medicine (M.D.) or Doctor of Osteopathy (D.O.) degree who has:

- Knowledge about and clinical experience in controlled substance abuse disorders,
- Detailed knowledge of alternative medical explanations for laboratory positive drug test results,
- Knowledge about issues relating to adulterated and substituted specimens, and
- Knowledge about possible medical causes for specimens reported as having an invalid result.

MRO training programs are available from various professional organizations to ensure that MROs are familiar with current regulations and receive the latest information on interpreting test results. Although HHS does not require formal certification for MROs at the present time, training courses have served a very important role in providing continuing education for MROs.

The MRO serves as the common point of contact between all parties involved in a drug test (i.e., the donor, the collector, the laboratory, and the Federal agency's designated representative). The MRO may be an employee or a contractor for a Federal agency; however, the following restrictions apply:

- The MRO must not be an employee or agent of or have any financial interest in the laboratory for which the MRO is reviewing drug testing results, and
- The MRO must **not** derive any financial benefit by having an agency use a specific drug testing laboratory or have any agreement with the laboratory that may be construed as a potential conflict of interest.

The purpose of these prohibitions is to prevent any arrangement between a laboratory and an MRO that would prevent the MRO from reporting a problem identified with a laboratory's test results or testing procedures.

The MRO has the following responsibilities:

- Determine that the information on the Federal Drug Testing Custody and Control Form (Federal CCF) is correct and complete,
- Interview the donor when required,

- Make a determination regarding the drug test results,
- Report the result to the Federal agency, and
- Maintain records and confidentiality of the information.

HHS recommends that each MRO use the guidance contained in this manual to ensure consistency and to improve the overall quality of the review process.

The following professional organizations offer courses and information for licensed physicians who are interested in the MRO specialty:

American College of Occupational and Environmental Medicine (ACOEM)
1114 North Arlington Heights Road
Arlington Heights, IL 60004-4770
Telephone: 847- 818-1800
Fax: 847-818-9266
<http://www.acoem.org/>

American Society of Addiction Medicine (ASAM)
4601 North Park Avenue, Upper Arcade #101
Chevy Chase, MD 20815
Telephone: 301- 656-3920
Fax: 301-656-3815
<http://www.asam.org/>

American Association of Medical Review Officers (AAMRO)
P.O.Box 12873
Research Triangle Park, NC 27709
Telephone: 1-800-489-1839
Fax: 919-490-1010
<http://www.aamro.com/>

Note: The listing of these organizations is not an endorsement by the Federal government.

Chapter 2. The Federal Drug Testing Custody and Control Form

Federal agencies are required to use the Office of Management and Budget (OMB) approved Federal CCF for their agency workplace drug testing programs.

The following employers are prohibited from using the Federal CCF:

- g conducted by DOT-regulated employersPrivate-sector companies
- States
- Department of Justice programs
- Non-DOT testin

The Federal CCF is usually provided by the laboratory that will test the specimen and is also available from other sources (e.g., forms suppliers, collectors, MROs).

A sample of the Federal CCF is on the SAMHSA website at <http://workplace.samhsa.gov>. All discussions in this manual refer to this version of the Federal CCF (OMB Number 0930-0158).

The Federal CCF consists of 5 copies that are distributed by the collector as follows:

Copy 1 - Laboratory Copy – sent to the laboratory with the specimen bottle(s)

Copy 2 - MRO Copy – sent to the MRO

Copy 3 - Collector Copy – retained by the collector

Copy 4 - Employer Copy – sent to the Federal agency

Copy 5 - Donor Copy – given to the donor when the collection process is complete

Each Federal CCF is printed with a unique specimen identification number. The Federal CCF includes labels with the same ID number that the collector places on the specimen bottle(s) to link the specimen to information on the CCF. Information that is pre-printed or written on the Federal CCF includes:

- Name, address, and contact information for the collection site, collector, Federal agency/employer, MRO, and testing laboratory,
- Donor identifying information,
- Reason for test, and
- Test(s) to be performed.

The collector initiates the chain of custody documentation for the specimen using the Federal CCF. The term “chain of custody” refers to documentation of all handling of a specimen. Chain of custody documents provide evidence that the specimen was secure and its integrity was maintained from the time of collection to its final disposition.

The Federal CCF is sealed and shipped with the specimen bottle(s) to the laboratory. The laboratory staff member who receives and processes the specimen for testing (i.e., the accessioner) verifies the information that is on the bottle(s) and on the Federal CCF and signs the Federal CCF. Thereafter, laboratory staff members document the chain of custody of the specimen and all aliquots taken for testing using internal laboratory forms.

The laboratory must be in a secure facility, with access limited to authorized personnel. Individual areas within the laboratory (e.g., receiving/accessioning area, testing areas, sample preparation area, specimen storage areas) are usually separately secured, to limit access to staff with job duties in the area. All visitors to secured areas must be escorted and their access must be documented.

Certified laboratories must ensure the security and integrity of regulated specimens, and follow

strict chain of custody procedures to provide a forensically acceptable record of the specimen's handling. This requires that all specimens be kept in secured storage or in the line of sight custody of an authorized individual, with appropriate chain of custody entries (i.e., signature, date, and action/purpose of each custody transfer) made at the time of actions. In addition, laboratories are required to maintain the confidentiality of donor information by restricting access to records of regulated specimens.

When a specimen's testing is complete, the certifying scientist at the laboratory reviews all data and associated documentation for the specimen including the Federal CCF. The certifying scientist annotates the specimen's results by marking the appropriate boxes on the Federal CCF, and including any additional comments concerning the specimen's testing or processing on the "Remarks" line. By signing the certification statement on the Federal CCF, this individual attests that the specimen was handled and tested in accordance with Federal requirements.

For non-negative results, the laboratory must send the laboratory copy of the Federal CCF (Copy 1) or a legible image of Copy 1 to the MRO. The laboratory is allowed to send a computer-generated report *in addition to* the Federal CCF.

- The copy of the Federal CCF (Copy 1) will be marked with one or more of the following non-negative results:
 - Positive for one or more drugs,
 - Adulterated (with the adulterant or pH value recorded on the "Remarks" line),
 - Substituted (with the creatinine and specific gravity values recorded on the "Remarks" line), or
 - "Invalid result" (with the reason for the invalid result recorded on the "Remarks" line).
- **These are separate results.** For example, "invalid result" does not refer to the drug(s)/drug metabolite(s) marked positive. The MRO should contact the laboratory if there is any confusion about the reported results.

For negative results, the laboratory is allowed to report the results using a computer-generated report (i.e., the completed Federal CCF is retained by the laboratory).

Chapter 3. Urine Drug Testing

A Federal agency may collect urine specimens using either a single specimen collection procedure or a split specimen collection procedure. The collector prepares a split specimen by pouring the urine from the collection container into two bottles, which are then labeled as the A Bottle and the B Bottle. All specimens (including all aliquots taken from the original specimens) are handled using strict chain of custody procedures to provide a clear record of each specimen's handling from the time it was collected until final disposition by the laboratory.

HHS-certified laboratories may routinely only test Federal agency specimens for amphetamines, marijuana, cocaine, opiates, and phencyclidine. However, testing for an additional drug may occur for one of the following reasons:

- There is reasonable suspicion/cause or a post-accident incident for which testing for another drug listed in Schedule I or II of the Controlled Substances Act is justified (see *Section B, Drug Information, below*); or
- A Federal agency was granted a waiver by the Secretary of HHS to routinely test its employees for another drug or drug class.

For any circumstance where testing for an additional drug is justified or authorized, the Federal agency must prepare a memorandum explaining why the specimen is being tested for the additional drug. The memorandum is given to the collector and the collector then marks the **Other** box in Step 1 on the Federal CCF and specifies the name of the drug(s) to be tested. The memorandum from the Federal agency is attached to the Federal CCF when the urine specimen is transferred to the laboratory. If the memorandum is not provided to the laboratory, the laboratory must not test for the additional drug noted on the Federal CCF.

For forensic as well as scientific acceptability, laboratories are required to perform initial and confirmatory tests on a specimen to support a non-negative result. Initial drug and specimen validity tests are performed on all specimens. Those specimens that have negative initial drug test results and acceptable initial specimen validity test results are reported as negative. Specimens that are presumptive drug positive, substituted, or adulterated are subjected to confirmatory testing using a different test method that is usually more specific than the initial test.

The donor is given the opportunity to request a retest when his or her specimen is reported as positive, substituted, or adulterated. The retest (i.e., an aliquot of the single specimen collection or Bottle B of a split specimen collection) is performed at a second certified laboratory.

If the donor chooses not to request specimen retesting, a Federal agency may have a single or split specimen retested as part of a legal or administrative proceeding to defend an original positive, adulterated, or substituted result.

Laboratories are required to maintain the following specimens in a secure frozen storage area for at least one year after reporting the result:

- Drug positive specimens
- Substituted specimens
- Adulterated specimens
- Invalid specimens
- Split specimens (B Bottles) of the primary specimens listed above
- Any specimens or specimen aliquots received from another laboratory for retesting

A Federal agency may request the laboratory to retain a specimen for a longer period (e.g., specimens under legal challenge).

Laboratories may discard rejected specimens after reporting them as rejected to the MRO.

A. Test Methods

An MRO is not required to be as technically knowledgeable of the analytical procedures and data as a laboratory certifying scientist. However, the MRO must know what tests were used to generate the specimen results that he or she reviews and should understand the general

scientific principles of the technologies.

Certified laboratories are required to use immunoassay for **initial drug tests** and to use gas chromatography/mass spectrometry (GC/MS) for **confirmatory drug tests**.

Immunoassay

Immunoassays are immunochemical testing methods that use antigen activity to identify drug analytes. Antibodies to the drug analyte (i.e., the antigen) are produced. A known amount of the antibody is added to a specimen along with drug that has been labeled with an enzyme or radioactive label. The drug in the specimen competes with the labeled drug for the antibody, to form an antigen-antibody complex. Various methods are used to measure the amount of drug present in the specimen. Immunoassays are used as initial drug tests, the preliminary test to identify presumptive positive specimens. The method is not specific enough to use as a confirmatory test. For example, many structurally similar drugs may cross-react with an immunoassay reagent, giving a positive result. Specimens that are positive by immunoassay are tested using GC/MS as a confirmatory test, to specifically identify and quantitate the drug or drug metabolite.

Table 1 provides brief descriptions of common immunoassays used for drugs of abuse.

Gas Chromatography/Mass Spectrometry (GC/MS)

Gas chromatography is a chromatographic technique for separating and analyzing mixtures of chemical substances in a gas or vapor mobile phase by adsorption on a stationary phase. GC/MS is a combined technique coupling a mass spectrometer (MS) with a GC instrument. Urine specimens must undergo a specimen preparation process (i.e., extraction) prior to GC/MS analysis. After the GC has separated the analytes in a specimen, the specimen enters the MS, which identifies and quantitates the separated analytes. The MS creates charged particles (ions) and separates them according to their mass-to-charge (m/z) ratios. The ions form unique mass spectra, which are used to identify analytes.

While the Guidelines do not specify the methods to be used for **initial and confirmatory specimen validity tests**, laboratories are required to use a pH meter for the initial and confirmatory pH tests and a refractometer measuring to at least four decimal places for the initial and confirmatory specific gravity tests. Laboratories must use appropriate, validated methods for all specimen validity tests.

Table 2 provides brief descriptions of some methods that may be used for specimen validity tests.

B. Drug Information

The Federal Government classifies controlled substances under 5 schedules established under the Controlled Substances Act (CSA):

Schedule I:

- The drug or other substance has a high potential for abuse.
- The drug or other substance has no currently accepted medical use in treatment in the United States.
- There is a lack of accepted safety for use of the drug or other substance under medical supervision.

Schedule II:

- The drug or other substance has a high potential for abuse.
- The drug or other substance has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions.
- Abuse of the drug or other substances may lead to severe psychological or physical dependence.

Schedule III:

- The drug or other substance has a potential for abuse less than the drugs or other substances in schedules I and II.
- The drug or other substance has a currently accepted medical use in treatment in the United States.
- Abuse of the drug or other substance may lead to moderate or low physical dependence or high psychological dependence.

Schedule IV:

- The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule III.
- The drug or other substance has a currently accepted medical use in treatment in the United States.
- Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III.

Schedule V:

- The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule IV.
- The drug or other substance has a currently accepted medical use in treatment in the United States.
- Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule IV.

The President's Executive Order 12564 defines "illegal drugs" as those under Schedule I or Schedule II. The U.S. Drug Enforcement Administration (DEA) enforces the provisions of the CSA.

Cannabinoids (Marijuana)**1. Background**

Cannabinoid-containing compounds come from the hemp plant, *Cannabis sativa*. The principal psychoactive agent in cannabinoids is delta-9-tetrahydrocannabinol (THC). Certified laboratories are required to use confirmatory testing for cannabinoids that specifically identifies delta-9-THC.

Cannabinoid-containing compounds are found in two forms, marijuana and hashish. Marijuana is a mixture of crushed leaves, flowers, and sometimes the stems of the cannabis plant. Hashish contains the dried resinous secretions of the cannabis plant and, in general, has a higher concentration of THC than marijuana.

Marijuana is a Schedule I drug. Medical marijuana is a controversial issue, and there has been some scientific evidence that smoked marijuana is beneficial for patients with debilitating

symptoms such as unmanageable pain and vomiting. However, use of marijuana is not an acceptable alternative medical explanation for a positive confirmed drug test result in federally-regulated drug testing programs.

Dronabinol is chemically synthesized delta-9-tetrahydrocannabinol (THC). It is the sole pharmaceutical source of THC and is available as Marinol® (Roxane Laboratories). The drug has psychoactive effects that may present safety issues.

Nabilone (Cesamet®) is a synthetic cannabinoid available in Europe. This drug does not metabolize to delta-9-THC. Therefore, the use of Nabilone is not an acceptable medical explanation for a positive confirmed drug test.

Cannabinoids produce a pleasant euphoria or "high" and a sense of relaxation and well-being that is commonly followed by drowsiness. The initial psychoactive effects of smoking THC occur within minutes, reach a peak within 10-30 minutes and may persist for 2-4 hours. Intoxication temporarily impairs concentration, learning, and perceptual-motor skills. Reduced functional ability lasts for at least 4-8 hours after a dose of marijuana. Psychomotor performance may be impaired long after the acute subjective effects have ended. In one study, experienced pilots demonstrated impaired performance in a flight simulator for 24 hours after a dose, long after the subjective "high" had disappeared⁹. Functional impairment is not well understood in cases of prolonged, heavy marijuana use, because behavioral and physiological tolerance develops.

In addition to tolerance, a mild abstinence syndrome may follow abrupt termination of very high dose, chronic marijuana use. Withdrawal signs include irritability, sleep disturbance, diminished appetite, gastrointestinal distress, salivation, sweating, and tremors. Marijuana abstinence syndromes are uncommon when used at the doses usually taken in this country.

Routes of administration:

- Marijuana – smoking (preferred), and oral (i.e., eating)
- Hashish – smoking (preferred), and oral (i.e., eating)

2. Metabolism and Excretion

Cannabinoids are usually smoked. Trans-pulmonary absorption occurs quickly and causes a direct psychoactive response in the brain. Cannabinoids are sometimes eaten because the drug also is absorbed through the gastrointestinal tract; however, gastro-intestinal absorption occurs much more slowly. THC is distributed into different parts of the body where it is metabolized, excreted, or stored. The THC that is stored in fatty tissue gradually reenters the blood stream at very low levels, permitting metabolism and eventual excretion. THC is metabolized extensively in the liver and the major metabolite is 11-nor- Δ^9 -tetrahydrocannabinol -9-carboxylic acid (delta-9 THCA).

The immunoassay procedures detect multiple metabolites of marijuana, while the GC/MS procedures specifically identify and quantitate delta-9 THCA. To be reported positive under the HHS Guidelines, a specimen must test positive at or above the 50 ng/mL cutoff for the initial test and have a concentration of delta-9 THCA that is equal to or greater than the 15 ng/mL confirmatory cutoff level. Infrequent marijuana use may cause positive initial test results for 1-5 days². With repeated smoking, THC accumulates in fatty tissue. Chronic smokers slowly release THC over a longer time and may continue to produce detectable levels of drug for longer periods of time.

Cocaine

1. Background

Cocaine is an alkaloid from the coca plant that is usually sold as cocaine hydrochloride, a fine, white crystalline powder. "Freebasing" is a method used to chemically alter cocaine hydrochloride to remove the hydrochloride salt. "Crack" is one form of free base cocaine that has become popular in recent years. It is sold as small lumps or shavings and is the product of a manufacturing process that uses sodium bicarbonate or ammonia rather than a flammable solvent. Because it survives high temperatures, crack is smoked, resulting in absorption into the bloodstream that is as rapid as injection. Cocaine is metabolized within hours of administration and; therefore, the Federal drug testing program requires analysis for cocaine as its major metabolite benzoylecgonine.

Cocaine has only a limited legal use in the United States as a topical anesthetic in ear, nose, and throat surgery. It is a widely used drug of abuse and is classified as a Schedule II drug.

Cocaine produces psychomotor and autonomic stimulation with a euphoric subjective "high." Larger doses may induce mental confusion or paranoid delusions. Serious overdoses cause seizures, respiratory depression, cardiac arrhythmias, and death.

Short-term tolerance (tachyphylaxis) develops when several doses of cocaine are administered over a brief period. Among chronic users, the stimulant effect may seem progressively weaker, and exhaustion, lethargy, and mental depression appear. Cocaine abusers often report vocational impairment due to exhaustion even though they do not use the drug at work.

Patients withdrawing from cocaine experience moderate lethargy and drowsiness, severe headaches, hyperphagia, vivid dreams, and some mental depression. These symptoms usually subside within a few days to a few weeks.

Routes of administration:

- Intranasal (i.e., snorting) is the most common
- Smoking the "freebase" or "crack" form of the drug
- Intravenous injection

2. Metabolism and Excretion

Cocaine is rapidly and extensively metabolized by liver and plasma enzymes to its major metabolite benzoylecgonine. Benzoylecgonine is more persistent and can usually be detected for up to 2 days after a single dose. Cocaine and benzoylecgonine are not significantly stored in the body. Therefore, even after heavy, chronic use, urine specimens will be negative when collected a few days after last use.

Opiates

1. Background

The term "opiate" specifically refers to natural alkaloids extracted from the opium poppy. The term "opioid" refers to synthetic opiates and opiate-like drugs in addition to the naturally occurring opiates. Opioids are classified as narcotics. The Federal agency drug testing

program's focus is on illicit use of morphine, codeine, and heroin:

- Morphine – is the most abundant naturally occurring opiate and is considered the prototype of the opioid class of drugs. Morphine is available as a prescription drug (Schedule II) and is used primarily for its potent analgesic properties.
- Codeine – can be naturally occurring; however, it can also be synthesized chemically by 3-O-methylation of morphine. Codeine medications are available by prescription and over-the-counter (Schedule III, Schedule IV, and Schedule V), depending on concentration and preparation. Codeine is commonly used in analgesic, antitussive, and anti-diarrheal agents.
- Heroin (diacetylmorphine) – is a semisynthetic opiate obtained by reacting natural morphine with acetic acid. Heroin has no legitimate medical use in the United States and is only available illegally (Schedule I). Heroin is not easily detected in urine and therefore usage is determined by detection of its intermediate metabolite 6-acetylmorphine (6-AM).

Cognitive and psychomotor performance can be impaired by opiates, although the duration and extent of impairment depend on the type of opiate, the dose, and the experience and drug history of the user. Ingestion of low to moderate amounts produces a short-lived feeling of euphoria followed by a state of physical and mental relaxation that persists for several hours. Opioid intoxication may cause meiosis, a dull facies, confusion or mental dullness, slurring of speech, drowsiness, or partial ptosis (i.e., nodding, the head drooping toward the chest and then bobbing up).

It is common for opioid abusers to develop tolerance and therefore continually increase the dose taken in an attempt to maintain the euphoric effect. All opiates are physically and psychologically addictive, and produce withdrawal symptoms that differ in type and severity. Flu-like symptoms are common during opiate withdrawal (e.g., watery eyes, nausea and vomiting, muscle cramps, and loss of appetite).

Routes of administration:

- Morphine – injection, intranasal (i.e., snorting), oral (i.e., tablets), and smoking
- Codeine – injection and oral (i.e., tablets, elixir)
- Heroin – intravenous injection, intranasal (i.e., snorting), and smoking

Additional issues regarding opioids:

- Poppy seeds are a significant dietary source of codeine and/or morphine.
- In December 1998, HHS revised the Mandatory Guidelines for Federal Workplace Drug Testing Programs to increase the initial testing and confirmatory cutoffs for opiates (i.e., from 300 ng/ml to 2000 ng/ml) and require laboratories to test all morphine positive specimens for heroin metabolite (6-AM). These measures were taken to eliminate most specimens that test positive due to poppy seed ingestion or due to the use of legitimate morphine or codeine medication.
- Synthetic or semi-synthetic narcotics do not metabolize to codeine, morphine, or 6-acetylmorphine. These include, *but are not limited to*:
 - alphaprodine (Nisentil®)

- hydromorphone (Dilaudid®)
- oxymorphone (Numorphan®)
- hydrocodone (Hycodan®, Lorcet-HD®, Vicodin®)
- dihydrocodeine (Synalgos®)
- oxycodone (Percodan®, Percocet®, Tylox®)
- propoxyphene (Darvon®)
- methadone (Dolophine®)
- meperidine (Demerol®)
- fentanyl (Duragesic®, Sublimaze®)
- pentazocine (Talwin®)
- buprenorphine (Buprenex®, Subutex®)

Table 3 provides a representative sample of the prescription and non-prescription products that contain codeine or morphine.

Note: Further information regarding the interpretation and reporting of opiates is found in the Interpretation and Result Verification Section (i.e., Chapter 5, Section C.)

2. Metabolism and Excretion

Morphine is rapidly absorbed and excreted as:

- unchanged morphine
- glucuronide conjugates
 - morphine-3-glucuronide (primary metabolite)
 - morphine-6-glucuronide

Morphine and its metabolites can be detected in urine up to about four days after its use. Morphine is ***not*** metabolized to codeine.

Codeine (methyldmorphine) is also rapidly absorbed and is excreted as:

- unchanged codeine
- morphine
- glucuronide conjugates
 - codeine-6-glucuronide
 - morphine-3-glucuronide
 - morphine-6-glucuronide

The presence of both codeine and morphine in urine indicate the recent use of codeine; however, morphine alone may be detected as a remnant of codeine that has been completely metabolized.

Heroin (diacetylmorphine) is deacetylated to its primary metabolite 6-AM (also known as 6-monoacetylmorphine, 6-MAM) within minutes of administration. Therefore, heroin itself is rarely detected in urine. 6-AM is mostly likely to be detected within the first 24 hours post-administration because of its rapid metabolism to morphine. Codeine may be found in the urine of heroin users as a result of codeine present as a contaminant in the morphine used to synthesize the heroin.

Amphetamines

1. Background

Amphetamine and methamphetamine are substances regulated under the Controlled Substances Act as Schedule II stimulants. Both drugs have been used for treating attention deficit disorder in children, obesity, and narcolepsy.

Amphetamine and methamphetamine are central nervous system stimulants that initially produce euphoria, a feeling of well-being, increased self-esteem and appetite suppression followed by restlessness and irritability. A single therapeutic dose often enhances attention and performance, but exhaustion eventually occurs and performance deteriorates as the effects wear off. Frequently, repeated high dose use produces lethargy, exhaustion, mental confusion, and paranoid thoughts.

Tolerance can develop to the effects of amphetamine and methamphetamine. A typical therapeutic dose is 5 milligrams. Individuals who abuse these drugs are reported to inject up to one gram in a single intravenous dose. Physical dependence is modest. Lethargy, drowsiness, hyperphagia, vivid dreams, and some mental depression may persist for a few days to several weeks after abrupt termination of repeated high doses.

Amphetamine and methamphetamine exist in two isomeric 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. As do many pharmacological enantiomers, the *d*- and *l*- isomers have distinct pharmacological properties. In this case, 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. Illegally manufactured amphetamine and methamphetamine are principally found as the *d*-isomer. However, significant amounts of the *l*- isomer of each substance may be present depending on the starting materials used by the clandestine laboratories.

Routes of administration:

- Amphetamine – oral (i.e., tablets or capsules), intravenous injection, smoking, and intranasal (i.e., snorting)
- Methamphetamine - oral (i.e., tablets or capsules), intravenous injection, smoking, and intranasal (i.e., snorting)

Table 4 provides a representative sample of products containing amphetamines.

2. Metabolism and Excretion

Nearly half of a methamphetamine dose is recovered from urine unchanged. A small percentage is demethylated to amphetamine and its metabolites. The excretion rate of methamphetamine is also increased when urine is acidic.

Amphetamine is excreted as both unchanged amphetamine and as hydroxylated metabolites. Typically, about one-quarter of an administered dose is excreted as unchanged amphetamine, but this varies widely with urinary pH; the drug stays in the body longer when urine is alkaline, allowing re-absorption and thus allowing more of it to be metabolized. In 24 hours, about 80

percent of a dose will be excreted if urine is acidic, while less than half is excreted if urine is alkaline.

A single therapeutic dose of amphetamine or methamphetamine can produce a positive urine for about 24 hours depending upon urine pH and individual metabolic differences. High dose abusers may continue to generate positive urine specimens for 2 to 4 days after last use.

Generally, the amphetamine/methamphetamine result reported by the laboratory does not indicate the specific enantiomer because the laboratory procedure is set up to only identify and quantitate the presence of amphetamine and/or methamphetamine. In order to determine which enantiomer is present, an additional analysis must be performed.

The enantiomer identification may be useful in determining if a donor has been using a Vicks Inhaler®, a prescription medication, or abusing an illegal drug; however, the presence of the *l*-isomer of either amphetamine or methamphetamine does not by itself rule out illegal use.

Phencyclidine

1. Background

Phencyclidine (PCP), an arylcyclohexylamine, was first synthesized in the 1950's as a general anesthetic. Street names include Angel Dust, Crystal, Killer Weed, Supergrass, and Rocket Fuel. PCP's synthesis is relatively simple for clandestine laboratories. Phencyclidine's use as a human anesthetic was discontinued because it produced psychotic reactions (i.e., "emergence delirium"), but the drug remains in use as a veterinary tranquilizing agent. PCP is currently a Schedule II controlled substance.

PCP has a variety of effects on the central nervous system. Intoxication begins several minutes after ingestion and usually lasts eight hours or more. PCP is well known for producing unpredictable side effects, such as psychosis or fits of agitation and excitability. The severe debilitating physical and psychological effects of PCP abuse and the extremely unpredictable behavior caused by the drug clearly have drastic effects on performance.

Intoxication may result in persistent horizontal nystagmus, blurred vision, diminished sensation, ataxia, hyperreflexia, clonus, tremor, muscular rigidity, muteness, confusion, anxious amnesia, distortion of body image, depersonalization, thought disorder, auditory hallucinations, and variable motor depression or stimulation, which may include aggressive or bizarre behavior.

Ketamine is the only analog of PCP that has any legitimate use. It is currently used in veterinary treatment. Ketamine does not cross-react with PCP initial or confirmatory testing.

Routes of administration:

- Smoking (preferred)
- Oral
- Intranasal (i.e., snorting)
- Intravenous injection

2. Metabolism and Excretion

PCP is well absorbed by any route and is excreted as unchanged PCP and as conjugates of

hydroxylated PCP. About 10 to 15 percent of the PCP dose is excreted in the urine as unchanged drug. PCP is a weak base which concentrates in acidic solutions in the body. Because of gastric acidity, PCP repeatedly re-enters the stomach from plasma, and is re-absorbed into plasma from the basic medium of the intestine.

Generally, PCP is considered detectable in urine for several days to several weeks depending on the frequency of use.

C. Adulterant Information

“Adulterated” is the term used for a specimen that has been altered by the donor in an attempt to defeat the drug test. The goal is to affect the ability of the laboratory to properly test the specimen for drugs and/or to destroy any drug or drug metabolite that may be present in the specimen. Many substances can be used to adulterate a urine specimen *in vitro*, including common household products, commercial chemicals, and commercial products developed specifically for drug test specimen adulteration. Adulterants are therefore readily available, may be easily concealed by the donor during the collection procedure, and can be added to a urine specimen without affecting the temperature or physical appearance of the specimen. To identify adulterated specimens, HHS requires certified laboratories to perform a pH test and a test for one or more oxidizing compounds on all regulated specimens. Laboratories are also allowed to test regulated specimens for any other adulterant, providing they use initial and confirmatory tests that meet the validation and quality control requirements specified by the HHS Guidelines.

An adulterant may interfere with a particular test method or analyte, but not affect others. For example, an adulterant may cause false negative marijuana (cannabinoids) results using a particular immunoassay reagent, but not affect the test results for other drugs. The same adulterant may not affect the test results obtained using a different immunoassay reagent or different immunoassay method. It is also possible for an adulterant to cause false positive drug test results, rather than the intended false negative. The initial drug test required for Federal workplace programs (immunoassay) is more sensitive to adulterants than the required confirmatory drug test (GC/MS). Currently, the GC/MS assays for marijuana metabolite (THCA) and opiates appear to be affected by adulterants more than GC/MS assays for other drugs.

When a laboratory is unable to obtain a valid drug test result or when drug or specimen validity tests indicate a possible unidentified adulterant, the laboratory reports the specimen to the MRO as “invalid result” (see Interpretation and Result Verification section below). When an MRO receives an “invalid” specimen report, it is incumbent upon him/her to discuss with the laboratory whether additional tests should be performed by the laboratory or by another certified laboratory. It may be possible to obtain definitive drug test results for the specimen using a different drug test method or to confirm adulteration using additional specimen validity tests. The choice of the second laboratory and/or additional tests will be dependent on the suspect adulterant and the validated characteristics of the different drug tests. Laboratory staff should be knowledgeable of their tests’ validated characteristics including effects of known interfering substances, and be able to recommend whether additional testing is worthwhile.

HHS allows certified laboratories to test for any adulterant. It is not possible to provide specific program guidance for all substances that may be used as adulterants; however, HHS has included specific requirements in the Guidelines for pH analysis and for the analysis of known adulterants listed below:

pH of human urine is usually near neutral (pH 7), although some biomedical conditions affect

urine pH. HHS set the program cutoffs for pH based on a physiological range of approximately 4.5 to 9. Specimens with pH results outside this range are reported as invalid. An extremely low pH (i.e., less than 3) or an extremely high pH (i.e., at or above 11) is evidence of an adulterated specimen.

Nitrite is an oxidizing agent that has been identified in various commercial adulterant products. Nitrite (NO_2) is produced by reduction of nitrate (NO_3). Nitrite in high concentrations is toxic to humans especially infants, causing methemoglobinemia by oxidizing the iron in hemoglobin. Nitrate and, to a lesser extent, nitrite are present in the environment. Nitrite may be present in human urine from the following sources:

- Food: Sodium nitrite is used as part of the curing process for meat (e.g., ham, wieners). Nitrates are present in vegetables (e.g., celery, spinach, beets, radishes, cabbage).
- Drinking water: Water sources may become contaminated with nitrate and nitrite due to run-off from farms using nitrogen fertilizers, from septic systems, and from livestock feedlots. The levels of nitrate and nitrite in public drinking water supplies are monitored because of the potential health threat to infants under six months of age.
- Occupational exposure: Workers in explosives and pharmaceuticals manufacturing may be exposed to nitrates.
- Medications: Organic nitrate and nitro compound drugs (e.g., used for angina, congestive heart failure, ulcers) metabolize to inorganic nitrite ion. Inorganic nitrite/nitrate salts have limited medical uses (e.g., used for cyanide poisoning).
- Endogenous production: The enzyme nitric oxide synthase (NOS) catalyzes the endogenous formation of nitric oxide radical, which oxidizes to nitrite and nitrate. This may result in normal human urine containing a small amount of nitrate with an extremely small ratio of nitrite.
- Pathological conditions: Some infectious and inflammatory conditions (e.g., sepsis, asthma, rheumatoid arthritis, tuberculosis, inflammatory bowel disease, Alzheimer's disease, multiple sclerosis) induce another enzyme (i.e., inducible NOS) that catalyzes the formation of nitric oxide radical.
- Medical treatments: Some medical treatments (e.g., Interleukin-2 in cancer treatment) can induce NOS and result in nitrite in the urine.
- Urinary tract infections: Some urinary tract infections are caused by bacteria that, if present in large numbers, may reduce nitrate to nitrite by microbial action.

Because low levels of nitrite may be present in human urine due to the reasons listed above, HHS set a cutoff level of 500 mcg/mL for adulteration and 200 mcg/mL for invalid results. **These concentrations are well above levels seen in human urine.** Therefore, these reasons do **not** explain a nitrite adulterated result.

Chromium (VI) is a strong oxidizing agent that has been identified in various commercial adulterant products. The most common forms of the element chromium are chromium (0), chromium (III), and chromium (VI). All have industrial uses. Both chromium (III) and chromium (VI) are used for chrome plating, dyes and pigments, leather tanning, and wood preserving.

Chromium (III) is an essential nutrient and is always present in humans. Chromium (VI) is toxic and has been shown to be a human carcinogen. The presence of chromium (VI) in a urine specimen is indicative of adulteration. HHS set an initial test cutoff level of 50 mcg/mL for chromium (VI).

Surfactants, including ordinary detergents, have been used to adulterate urine specimens. Surfactants have a particular molecular structure made up of a hydrophilic and a hydrophobic component. They greatly reduce the surface tension of water when used in very low concentrations. Foaming agents, emulsifiers, and dispersants are surfactants that suspend an immiscible liquid or a solid, respectively, in water or some other liquid. Surfactants tend to clump together when in solution, forming a laminar surface between the fluid and air with their hydrophobic components along the surface and their hydrophilic components in the fluid. Often surfactants will form "bubbles" (micelles) within the fluid: a small sphere of hydrophilic "heads" surrounding a pocket containing the hydrophobic "tails." They can also form bubbles in air (i.e., two nested spheres of surfactant with a thin layer of water between them, surrounding a pocket of air) and can form "antibubbles" in fluid (i.e., a layer of air surrounding a pocket of water).

Halogens are the four elements fluorine, chlorine, bromine, and iodine. Halogen compounds have been used as adulterants. The term "halogen" (from the Greek *hals*, "salt," and *gennan*, "to form or generate") was given to these elements because they are salt formers. None of the halogens can be found in nature in their elemental form. They are found as salts of the halide ions (F-, Cl-, Br-, and I-). Fluoride ions are found in minerals. Chloride ions are found in rock salt (NaCl), the oceans, and in lakes that have a high salt content. Both bromide and iodide ions are found at low concentrations in the oceans, as well as in brine wells. The assays used by certified laboratories identify halogen compounds that act as oxidants. These do not include the halogen salts that may be present in a urine specimen. The presence of an oxidative halogen in a urine specimen is evidence of adulteration.

Glutaraldehyde is a clear, colorless liquid with a distinctive pungent odor sometimes compared to rotten apples. One of the first effective commercial adulterants was found to contain glutaraldehyde. Glutaraldehyde is used as a sterilizing agent and disinfectant, leather tanning agent, tissue fixative, embalming fluid, resin or dye intermediate, and cross-linking agent. It is also used in X-ray film processing, in the preparation of dental materials, and surgical grafts. Glutaraldehyde reacts quickly with body tissues and is rapidly excreted. The most common effect of overexposure to glutaraldehyde is irritation of the eyes, nose, throat, and skin. It can also cause asthma and allergic reactions of the skin. Glutaraldehyde at any detectable level in a urine specimen is evidence of adulteration.

Pyridinium chlorochromate is a strong oxidizing agent that has been identified in some commercial adulterants. This compound is confirmed by urine drug testing laboratories using a confirmatory test for pyridine. Pyridine is a colorless liquid that can be prepared from crude coal tar or from other chemicals. Pyridine formed from the breakdown of natural materials results in very low levels in air, water, and food. It is used as a solvent, and also used in the preparation of medicines, vitamins, food flavorings, paints, dyes, rubber products, adhesives, insecticides, and herbicides. There is little information on the health effects of pyridine, although some animal studies and human case reports have noted liver damage from exposure to pyridine. Human exposure may occur by various means (e.g., inhalation or dermal exposure of workers in industries that make or use pyridine, inhalation of pyridine released into air from burning cigarettes or hot coffee, exposure to air or water contaminated from hazardous waste sites or landfills). The U.S. Food and Drug Administration (FDA) allows its use as a flavoring agent in food preparation. Pyridine at any detectable level in a urine specimen is evidence of

adulteration.

D. Dilution/Substitution

A donor may attempt to decrease the concentration of drugs or drug metabolites that may be present in his or her urine by **dilution**. Deliberate dilution may occur *in vivo* by consuming large volumes of liquid, often in conjunction with a diuretic, or *in vitro* by adding water or another liquid to the specimen. Donors also have been known to **substitute** urine specimens with drug-free urine or other liquid during specimen collection. Due to donor privacy considerations, collections for federally regulated drug testing programs are routinely unobserved. Therefore, dilution and substitution may be undetected by collectors and be viable methods for defeating drug tests. There are products on the market today purporting to “cleanse” the urine prior to a drug test; many of which are diuretics. There are also products designed specifically for urine specimen substitution, including drug-free urine, additives, and containers/devices to aid concealment. Many such devices have heating mechanisms to bring the substituted specimen’s temperature within the range set by HHS to determine specimen validity at the time of collection (i.e., 32° to 38°C/90° to 100°F). Some include prosthetic devices to deceive the observer during a direct observed collection.

To identify diluted and substituted specimens, HHS developed criteria for evaluating specimens for the following human urine characteristics:

Creatinine is a protein produced by muscle and cleared from the body by the kidneys. It is a normal constituent in urine. Normal human urine creatinine concentrations are greater than 20 mg/dL. Abnormal levels of urine creatinine may result from excessive fluid intake, glomerulonephritis, pyelonephritis, reduced renal blood flow, renal failure, myasthenia gravis, or a high meat diet.

Specific gravity is a measure of the density of a substance compared to the density of water. For urine, the specific gravity is a measure of the concentration of particles in the urine. Normal values for the specific gravity of human urine range from approximately 1.0020 to approximately 1.0200. Decreased urine specific gravity values may indicate excessive fluid intake, renal failure, glomerulonephritis, pyelonephritis, or diabetes insipidus. Increased urine specific gravity values may result from dehydration, diarrhea, excessive sweating, glucosuria, heart failure, proteinuria, renal arterial stenosis, vomiting, and water restriction.

Laboratories are required to test the creatinine in all regulated specimens, and to test specific gravity for specimens with creatinine less than 20 mg/dL. There are established program cutoffs for identifying invalid, dilute, or substituted specimens based on the paired creatinine and specific gravity test results. **Appendix A** describes Laboratory Reporting Criteria from the HHS Guidelines.

Chapter 4. The MRO Review and Reporting Process

The MRO must review all **non-negative** test results (i.e., positive, adulterated, substituted, invalid) and all **negative and dilute specimens** before reporting the results to the Federal agency’s designated representative. **Negative** specimen results may be reviewed and reported by staff under the direct, personal supervision of the MRO.

The MRO process consists of:

- Administrative review of documents,
- Interview with the donor (as required),
- Handling retest requests (as required),
- Result interpretation and verification, and
- Reporting of results to the Federal agency's designated representative.

No regulatory requirements exist requiring MROs to use specific procedures to review drug tests; however, using a standard procedure better ensures that the MRO review for each specimen is complete and thorough. A simple checklist can be helpful in assuring consistency and completeness of the process.

A. Administrative Review of Documents

1. MRO Copy of the Federal CCF (Copy 2)

The collector is required to send the MRO Copy of the Federal CCF (Copy 2) to the MRO within 24 hours or one business day after the collection. If the MRO receives a laboratory test report for a specimen without having received the MRO copy of the Federal CCF, the MRO must contact the collector. If the MRO copy is not available, the MRO must obtain another legible copy of the Federal CCF (e.g., collector or employer copy) that has been signed by the donor and has the donor's name and telephone number(s).

The following items are verified for Copy 2 of the Federal CCF:

- a. The correct OMB-approved Federal CCF was used to document the specimen collection.
- b. The Federal CCF contains the specimen identification number.
- c. The testing laboratory is identified by one of the following:
 - A specific laboratory name and address at the top of the CCF,
 - A list of addresses with check boxes at the top of the Federal CCF (the collector checks the box for the laboratory to which the specimen will be delivered), or
 - A corporate name and telephone number at the top of the Federal CCF and the specific laboratory address in the "Test Lab" line in Step 5a.
- d. The Federal CCF was properly completed:
 - Step 1 contains:
 - Federal agency name and address,
 - MRO name, address, and telephone number,
 - Donor identification (e.g., SSN, employee identification number),
 - Reason for the test,
 - Tests to be performed, and

- Collection site information (i.e., address, telephone number, and fax number)
- Step 2 documents that:
 - The temperature of the specimen was or was not within the required temperature range,
 - The collection was a split specimen or single specimen collection,
 - No specimen was collected and why (if applicable),
 - A direct observed collection was performed and why (if applicable), and
 - Comments on the "Remarks" line (as appropriate) recording the collector's observations or explanatory comments concerning the donor, the specimen, or collection events.
- Step 4 contains:
 - Collector's printed name,
 - Collector's signature,
 - Date and time of the collection, and
 - Specific name of the delivery service that was used to transfer the specimen to the laboratory.
- Step 5 contains:
 - Donor's printed name,
 - Donor's signature,
 - Date signed,
 - Donor's daytime telephone number,
 - Donor's evening telephone number, and
 - Donor's date of birth.

2. Laboratory Report - Federal CCF (Copy 1) and/or Computer-Generated Electronic Report

Certified laboratories report drug test results only to the MRO. The laboratory and the MRO must have procedures in place to ensure the confidentiality of the reports (i.e., hardcopy and electronic). The laboratory may send drug test reports by:

- Courier,
- Mail,
- Secure fax, and
- Secure electronic transmission.

The following items are verified for the laboratory report for a specimen:

- a. The specimen identification number on the laboratory copy of the Federal CCF (Copy 1) and/or on any other laboratory report matches that on the MRO copy (Copy 2) for the identified donor.
- b. The Federal CCF was properly completed:
 - Step 4 contains:
 - Accessioner's printed name,

- Accessioner's signature, and
 - Documentation of the bottle seal condition upon receipt at the laboratory.
- For a single or primary (Bottle A) specimen, Step 5a contains:
 - Test results,
 - Certifying scientist's printed name,
 - Certifying scientist's signature,
 - Date of result certification,
 - Comments on the "Remarks" line (as appropriate):
 - Quantitative test results
 - Comments as required by HHS for specimens reported as "adulterated," "rejected for testing," or "invalid result"
 - Observations or explanatory comments recorded by laboratory staff concerning the specimen, and
 - Name and address of the testing laboratory (if not on the top of Copy 1).
 - For a retest specimen, Step 5b contains:
 - Test results,
 - Certifying scientist's printed name,
 - Certifying scientist's signature,
 - Date of result certification,
 - Comments on the "Remarks" line (as appropriate):
 - Quantitative test results
 - Comments as required by HHS for specimens that failed to reconfirm
 - Observations or explanatory comments recorded by laboratory staff concerning the specimen, and
 - Name and address of the testing laboratory.
- c. The laboratory has included a memorandum from the collector to address any correctable flaws identified. See Section 3 below.
- d. The computer-generated electronic report (if any) contains the HHS-required information as follows:
- Laboratory name and address,
 - Federal agency name,
 - MRO name,
 - Specimen identification number,
 - Donor identification from the Federal CCF (e.g., SSN, employee ID number),
 - Collector name and telephone number,
 - Reason for test (if provided),
 - Date of collection,
 - Date received at laboratory,
 - Certifying scientist's name,
 - Date certifying scientist released the results,
 - Test results, and
 - Additional comments concerning the specimen's testing and processing, as listed in the "Remarks" line of the Federal CCF.
- e. The information on the computer-generated electronic report (if any) is consistent with

that on the laboratory copy of the Federal CCF (Copy 1).

3. Federal CCF or Specimen Errors

A laboratory or an MRO may identify errors made on a Federal CCF, or a laboratory may identify a problem with a specimen during processing. The various types of errors are outlined below:

- a. **Uncorrectable errors** that result in specimen rejection by the laboratory and test cancellation by the MRO:
 - Specimen ID number on the Federal CCF and bottle label/seal do not match or the number is missing on either the Federal CCF or the specimen bottle label/seal,
 - Specimen bottle label/seal is missing or broken on the specimen from a single specimen collection or on a primary specimen (Bottle A) of a split specimen collection and the split specimen (Bottle B) cannot be redesignated as the primary specimen,
 - The collector's signature and printed name are omitted from the CCF, or
 - There is insufficient specimen volume for testing.
- b. **Correctable errors** that result in specimen rejection and/or cancellation unless corrected by a memorandum for the record (MFR) from the collector:
 - The collector failed to sign the CCF (but the printed name is present), or
 - The collector used a non-Federal form or an expired version of the Federal CCF.
- c. **Federal CCF omissions and discrepancies** that are considered insignificant when they are infrequent (i.e., when a collector does not make the error more than once a month). Examples include, *but are not limited to*:
 - No collection date/time,
 - No courier entry,
 - No specific delivery service name, or
 - Donor name included on the laboratory copy of the CCF.
- d. **Administrative errors made by laboratory staff** that are judged by the MRO to have a significant impact on the forensic defensibility of the results unless corrected by an MFR. Examples include, *but are not limited to*:
 - No accessioner signature on the CCF,
 - No documentation of bottle seal condition on the CCF, or
 - No certifying scientist signature on the CCF.

4. Federal CCF Remarks

Collectors are required to include comments on the "Remarks" line in Step 4 (the collector's section) of the Federal CCF to document any unusual donor behavior or incidents occurring during the collection. Laboratory staff are required to include comments on the "Remarks" line in Step 5a of the Federal CCF to document any issues concerning the specimen (e.g., redesignation of the A and B Bottles), as well as explanatory reporting comments required by the program (e.g., the basis for reporting a specimen as adulterated, the basis for reporting an "invalid result," reason for rejection).

The MRO evaluates whether information provided on the Federal CCF "Remarks" lines have a significant impact on the forensic defensibility of the drug test results. If the MRO believes the forensic defensibility of the results is affected, he or she either attempts to obtain an MFR or cancels the test.

5. Actions Based on Administrative Review

When an **uncorrectable error** is identified (see Item 3.a above):

- a. If the laboratory identifies the error, the laboratory rejects the specimen for testing and reports the specimen as rejected to the MRO. The reason for rejection is included on the laboratory report(s) to the MRO.
- b. If the MRO receives a rejected for testing report or identifies an uncorrectable error during review, the MRO cancels the test.
- c. The MRO reports the cancellation and the reason to the Federal agency, which then determines whether or not to immediately collect another urine specimen from the donor.

When a **correctable documentation/specimen error** (see Item 3.b above) by the collector is identified by either the laboratory or the MRO, the collector is notified to provide an MFR to address the error:

- a. If the collector **provides** an MFR:
 - The laboratory includes a copy of the MFR with the report to the MRO.
 - The MRO reports the verified result (see Section D below) to the Federal agency and maintains the MFR in the files for the specimen.
- b. If the collector **does not provide** an MFR:
 - The laboratory holds the specimen for a minimum of 5 business days after requesting the MFR, then reports the specimen as rejected and discards the specimen. The reason for rejection is included on the laboratory report(s) to the MRO.
 - The MRO cancels the test and notifies the Federal agency of the cancelled test and the reason for cancellation.

When the laboratory and/or MRO document **frequent insignificant errors** by an individual

collector (see Item 3.c):

- a. The MRO notifies the collector/collection site of the errors.
- b. The collector/collection site takes appropriate corrective actions (e.g., revises procedures, retrain the individual and other collectors at the collection site) and submits a copy of documentation of the action(s) to the MRO.
- c. The MRO maintains the documentation of error notification and corrective action response in his or her records.

B. Donor Interview

The MRO must contact the donor and interview the donor when the donor's specimen is reported by the laboratory as non-negative (i.e., positive, adulterated, substituted, invalid).

The MRO must attempt contact as soon as possible after receiving the report (usually within 24 hours). The MRO copy of the Federal CCF will contain daytime and evening telephone numbers for the donor.

The MRO should establish guidelines as to what constitutes a reasonable effort to contact a donor. **All attempts made to contact the donor must be documented.**

If the MRO, after making all reasonable efforts, has been **unable to contact the donor within 14 days** after the date on which the MRO received the test result from the laboratory:

1. The MRO must inform the Federal agency of his or her inability to contact the donor.
 - a. The MRO must not reveal the test result or any information about the drug test.
 - b. The Federal agency must:
 - Confidentially direct the donor to contact the MRO within 5 days, and
 - Inform the MRO once the donor has been directed to contact the MRO or if the Federal agency was unable to contact the donor.
2. The MRO may verify a test result without having communicated directly with the donor (i.e., a non-contact determination) for the following reasons:
 - a. The donor expressly declines the opportunity to discuss the test result, or
 - b. The Federal agency has contacted the donor and instructed the donor to contact the MRO, but the donor has not contacted the MRO within 5 days after being contacted by the Federal agency.

The Interview Process

1. Request the donor to provide information that will verify the donor's identity (e.g., employee identification number, SSN) to ensure that it agrees with the information documented on the Federal CCF. (This step may be done by staff under the MRO's

supervision; however, the MRO must personally perform all other steps of the interview process as listed below).

2. Inform the donor, prior to obtaining any information, that confidential medical information provided during the review process may be disclosed to the Federal agency.
3. Inform the donor of the laboratory reported test result(s).
4. Take action based on the donor's response:
 - a. If the donor admits use of an illegal drug consistent with the test results or admits that he or she tampered with the specimen, advise the donor that the test result will be reported to the Federal agency.
 - b. If the donor does not admit use of an illegal drug or specimen tampering, ask the donor if there is any possible medical explanation for the test result:
 - If the donor provides a possible medical explanation (e.g., claims that a positive result was due to a legally prescribed medication or that the drug use was associated with a valid medical procedure), require the donor to provide appropriate supporting documentation within a specified time.
 - If the donor has no valid medical explanation for the result, advise the donor that the test result will be reported to the Federal agency.
5. **For positive, substituted, or adulterated results:** Inform the donor that he or she may have the specimen retested at a second certified laboratory. The retest request must be made within 72 hours of the interview with the MRO. (Note that donors are not allowed to request retesting of specimens reported as invalid.)
 - a. If the donor requests a retest, use the procedures described in Section C (Handling Retest Requests) to direct the laboratory to send the retest specimen to another certified laboratory for confirmatory testing.
 - b. If the donor does not request a retest, document that the donor was informed of and declined the opportunity for a retest.

C. Handling Retest Requests

Note: Donors are not allowed to request retesting of specimens reported as invalid.

The following are rules for handling retest requests for positive, adulterated, or substituted specimens:

1. The donor has 72 hours from the time the MRO notified the donor that his or her specimen was reported positive, adulterated, or substituted to request the retest.
2. The MRO must request the retest of a single specimen or the test of the split (Bottle B) specimen in writing (i.e., a memorandum or letter format). The written request may be mailed, faxed, or electronically sent to the laboratory where the primary specimen was tested and must contain the following information:

- MRO name and address (use MRO letterhead),
 - Laboratory name and address (i.e., Laboratory A) where original analysis was performed,
 - Specimen ID Number on the Federal CCF,
 - Laboratory Accession Number (i.e., the number assigned by Laboratory A to the specimen when it was accessioned),
 - Request for confirmatory retest for the drug/metabolite, adulterant, or substitution reported by Laboratory A, and
 - Name and address of the HHS-certified laboratory (i.e., Laboratory B) selected to retest the specimen (i.e., aliquot of a single specimen or the split (Bottle B) specimen).
1. Laboratory B may be selected by the MRO, the Federal agency, or the donor. In most instances where retesting is requested, the first laboratory will have blanket purchase agreements with 2 or 3 other certified laboratories to make the billing and payment process easier.
 2. If the specimen cannot be tested by a second laboratory (e.g., insufficient volume, lost in transit, Bottle B not available, no other certified laboratory tests for the specific adulterant), the MRO shall direct the Federal agency to immediately collect another specimen **using a direct observed collection procedure**.
 - If the test is cancelled because no other certified laboratory tests for the specific adulterant, the MRO notifies the appropriate regulatory office.
1. The second HHS-certified laboratory reports retest results directly to the MRO using Copy 1 of the Federal CCF.
 2. The MRO reports the result to the Federal agency and the donor.

D. Interpretation and Result Verification

The Drug Information section above provides information on the drugs specified in the HHS Mandatory Guidelines for testing in Federal agency workplace programs, including the current CSA schedules, signs/symptoms of abuse, and metabolism information.

The MRO interprets drug test results based on:

- The laboratory results,
- The donor's explanation and supporting documentation, and
- The MRO's medical assessment of the donor's behavior and physical symptoms during the donor interview.

The MRO must report only verified results to the Federal agency. The MRO must not inform the Federal agency when a positive, adulterated, or substituted result was verified as negative.

Table 5 describes MRO actions to be taken for primary specimen results.

Table 6 describes MRO actions to be taken for retest specimen results.

Laboratory Results

Laboratory staff is available to answer MRO questions concerning *reported* drug test results. However, laboratories are strictly prohibited from providing any information about a specimen's result prior to completion of testing and are prohibited from providing any drug test results over the telephone.

The Mandatory Guidelines provide specific reporting criteria for certified laboratories to report Federal agency specimen results. These criteria are described in **Appendix A**. The laboratory must report all non-negative results for a specimen, as supported by data.

After receiving a drug test report, the MRO should contact the laboratory whenever additional information is needed. For example, the MRO may wish to clarify the laboratory's administrative and analytical procedures, or obtain quantitative results or other information that could be useful in evaluating the validity of a donor's explanation. General information may be given over the telephone. Requests for information about a specific specimen (e.g., quantitative results) must be made by the MRO in writing. The written request may be mailed, faxed, or electronically sent to the laboratory.

The term "invalid result" is used when a scientifically supportable negative test result cannot be established for a specimen due to an unidentified adulterant, an interfering substance, an abnormal physical characteristic, or an endogenous substance at an abnormal concentration (see criteria in Appendix A).

When the MRO receives a report of "invalid result," the MRO must discuss the result with the laboratory to determine if additional testing by another certified laboratory could provide a definitive result (i.e., negative, positive, or adulterated). **Specimens reported as invalid based on creatinine and specific gravity results or on pH are exceptions to this rule.** The MRO is not required to contact the laboratory when a specimen is reported as invalid for these reasons. It is unlikely that testing by another certified laboratory would provide different results.

Donor Explanation

As noted previously, one of the purposes for a donor interview is to allow a donor the opportunity to provide an alternative explanation for a non-negative drug test result. For the explanation to be accepted, the donor must provide acceptable supporting documentation to the MRO. If the alternative explanation for a positive, adulterated, or substituted result is acceptable and supported by documentation as outlined below, the MRO must verify the result as negative.

Prescriptions

If the donor claims to have taken a prescribed medicine that contains either the drug reported positive or a substance that can metabolize to that drug, the donor must provide one of the following:

- A copy of the prescription,
- The medicine container with the appropriately labeled prescription (or the label

from the container), or

- A copy of the medical record documenting the valid medical use of the drug during the time of the drug test.

The MRO may contact the prescribing physician or the pharmacist who filled the prescription to verify the information provided by the donor.

If the donor has been taking a prescription medication that contains a drug with a high potential for abuse for a long time, there must be appropriate justification for the long term use. The MRO must contact the prescribing physician to express concern that the continued use of the medication may present a significant safety problem for the donor while on the medication.

State initiatives and laws which make available to an individual a variety of illicit drugs by a physician's prescription or recommendation do not make the use of these illicit drugs permissible under the Federal Drug-Free Workplace Program. These State initiatives and laws are inconsistent with Federal law and put the safety, health, and security of Federal workers and the American public at risk.

The use of any substance included in Schedule I of the Controlled Substance Act, whether for non-medical or ostensible medical purposes, is considered a violation of Federal law and the Federal Drug-Free Workplace Program. These drugs have no currently accepted medical use in treatment in the United States and their use is inconsistent with the performance of safety-sensitive, health-sensitive, and security-sensitive positions, and with drug-free workplace programs.

The MRO must not accept a prescription or the verbal or written recommendation of a physician for a Schedule I substance as a valid medical explanation for the presence of a Schedule I drug or metabolite in a Federal employee/applicant specimen.

E. Interpretation of Results

Dilute Specimens

A laboratory may report a specimen as dilute in conjunction with a positive or negative drug test. A donor may produce urine that meets the program criteria for dilution under some conditions including:

- Working in hot weather conditions drinking large amounts of fluid,
- Taking a diuretic, or
- Drinking fluids immediately before providing the specimen.

The MRO actions to be taken in response to a dilute specimen report depend on whether the drug test result is positive or negative. These MRO actions are shown in **Table 5**.

Substituted Specimens

The HHS criteria for identifying substituted specimens are based on the physiological ranges for creatinine concentration and specific gravity value of normal human urine. If the donor denies

substituting the specimen, he or she is given the opportunity to prove the ability to produce urine that meets substitution criteria as described below.

1. If the donor claims to have consumed a large quantity of fluids prior to providing the urine specimen:
 - a. The MRO requests the Federal agency to have the donor provide another specimen collected using a direct observed collection procedure and have the collector document that the donor drank a similar quantity of fluids prior to providing the specimen.
 - b. If the creatinine and specific gravity results for the second specimen are similar to the results for the first specimen, this is considered a legitimate explanation for the substituted result.
2. If the donor claims to have a pre-existing, documented medical condition that causes the donor's urine to meet both the creatinine and specific gravity criteria for a substituted specimen, the MRO requests the donor to provide a copy of the medical record to support that claim.
3. If the donor claims to have personal characteristics (e.g., race, gender, weight, diet, working conditions) such that his or her urine normally satisfies the substitution criteria:
 - a. The MRO requests the donor to demonstrate that he or she can normally produce a substituted specimen.
 - b. The demonstration must provide a reasonable basis to conclude that the donor's personal characteristics are a legitimate medical explanation.

Adulterated Specimens

The MRO is required to contact the donor and give the donor an opportunity to explain the adulterated result and to demonstrate that the presence of the adulterant occurred through normal physiological means. However, the program criteria for adulteration definitively prove adulteration. There is no valid medical explanation for a urine specimen to meet the criteria for an adulterated result under the HHS Mandatory Guidelines.

Amphetamines

Depending on the amphetamines confirmation method (e.g., derivatization procedure, instrument parameters) used by a laboratory, it is possible for some structurally similar compounds (i.e., sympathomimetic amines) to be converted to methamphetamine during GC/MS analysis. HHS instituted the following assay validation and reporting requirements that prevent the possibility of false positive methamphetamine results due to this conversion:

1. Laboratories are required to quantitate at least 200 ng/mL amphetamine in a specimen in order to report a positive methamphetamine result. As described previously, methamphetamine metabolizes to amphetamine. This occurs quickly, via a simple demethylation reaction. Because the sympathomimetic amines are not converted to amphetamine, the presence of amphetamine is supporting evidence for methamphetamine use.

2. Certified laboratories are required to validate all assays prior to use with Federal agency specimens. For amphetamines confirmatory assays, each laboratory must document the assay's ability to identify and accurately quantitate methamphetamine and amphetamine in the presence of high levels of sympathomimetic amines and also demonstrate that these compounds are not misidentified as methamphetamine or amphetamine (i.e., by analyzing samples containing sympathomimetic amines without methamphetamine or amphetamine). These experiments must be performed on at least an annual basis, to verify the assay's continued performance.

Enantiomers

Most immunoassays used as the initial test in Federal workplace drug testing programs are focused on *d*-methamphetamine. However, the *l*-methamphetamine enantiomer and amphetamine enantiomers cross-react with the immunoassay reagents. Amphetamines GC/MS assays identify both amphetamine and methamphetamine and do not distinguish between enantiomers. Therefore, there is a possibility that a laboratory positive result could be reported for *l*-methamphetamine and/or *l*-amphetamine.

Laboratories may employ a chiral GC/MS assay that distinguishes between the *d*- and *l*-enantiomers and determines the relative percentages of each. HHS does not require each certified laboratory to have this capability. Upon written request of the MRO, the laboratory may perform the test or send a specimen to another certified laboratory for *d*- and *l*-enantiomer testing.

When the MRO receives a methamphetamine positive result from a laboratory, he or she may order enantiomer testing to aid in result interpretation, as described below:

1. Prescription Drug Products. There are prescriptions that contain amphetamine or methamphetamine. Enantiomer analysis may be used to verify that a positive methamphetamine result was due to use of a legal drug. For example, Selegiline is a brain monoamine oxidase inhibitor used in the adjunctive treatment of Parkinson's disease and for depression. Selegiline is metabolized to *l*-methamphetamine and *l*-amphetamine. A *d*- and *l*-isomer differentiation will reveal the presence of only *l*-methamphetamine and *l*-amphetamine after the ingestion of Selegiline.
2. Non-Prescription Drug Products. Some non-prescription products contain sympathomimetic amines which can cause a positive result on an initial immunoassay test. The confirmatory GC/MS test is specific for methamphetamine and amphetamine. Specimens containing sympathomimetic amines will not be reported positive by the laboratory after conducting the confirmatory test. The Vicks Inhaler⁷ is the only over-the-counter drug that contains *l*-methamphetamine. Enantiomer analysis may be used to verify that a positive methamphetamine result was due to its use. There may be a trace amount of the *d*- isomer present because a very slight amount of *d*-methamphetamine may be present as a contaminant in the Vicks Inhaler⁷ and a contaminant of the analytical procedure. If there is greater than 80% *l*-methamphetamine, the results are considered to be consistent with Vicks Inhaler⁷ use. If there is more than 20% *d*-methamphetamine present, the results indicate the use of some source other than the inhaler and the result is verified as positive. This is a very conservative interpretation.

Cocaine

There are no prescription medications that contain cocaine. However, the medical community uses TAC (tetracaine, adrenalin, cocaine) as a topical preparation prior to various surgical procedures and may use cocaine by itself as a topical vasoconstrictive anesthetic for various ear, nose, throat, and bronchoscopy procedures. If cocaine is used, the licensed physician performing the procedure would document its use in the donor's medical record. The medical use must have occurred within 2 to 3 days prior to when the urine specimen was collected. Use at an earlier time will not cause a positive urine test.

Topical Anesthetics

Cocaine is structurally unique and does not resemble any of the other topical anesthetics, such as Novocain⁷, Xylocaine⁷ (lidocaine), benzocaine, etc. Although these compounds have analgesic properties, there is no structural similarity to cocaine or its metabolite (benzoylecgonine). Specimens containing these substances will not be reported positive by the laboratory for benzoylecgonine.

Passive Inhalation of Crack Cocaine

Comprehensive scientific studies have demonstrated that individuals passively exposed to Δcrack[@] smoke do not produce a urine positive for cocaine using the HHS cutoffs for initial and confirmatory testing.

When a donor claims that his or her positive benzoylecgonine test was due to passive inhalation, the MRO should allow the donor to describe the circumstances pertaining to how and when the passive exposure occurred. Passive inhalation is not an acceptable alternative explanation for the presence of benzoylecgonine in the donor=s urine.

Coca Leaf Tea

In the early 1980s, health food stores sold a tea under the trade name ΔHealth Inca Tea.[@] It was discovered that this tea contained decocanized coca leaves with detectable amounts of cocaine present and the U. S. Food and Drug Administration banned the importation of this tea into the United States. Therefore, any tea sold using the name "Health Inca Tea" should not contain any cocaine.

When a donor claims that his or her positive benzoylecgonine test was due to drinking a beverage with coca leaves as an ingredient, the MRO should allow the donor to explain where and when the tea was purchased. Drinking "Health Inca Tea" or other beverage purporting to contain coca leaves is not an acceptable alternative explanation for the presence of benzoylecgonine in the donor's urine.

Marijuana

There has been much discussion in the political and medical fields over the years concerning the benefits of medicinal marijuana. At this time, marijuana remains a Schedule 1 drug and marijuana use is not an acceptable medical explanation for a positive drug test result in the Federal agency drug testing program. A prescription or written recommendation from a licensed physician or medical professional does not exempt the donor from this rule. If the donor admits the use of medical marijuana, the MRO verifies the result as positive.

Prescription THC

Dronabinol is chemically synthesized delta-9- tetrahydrocannabinol (THC). It is available under

the trade name Marinol⁷ in 2.5, 5, or 10 mg soft gelatin capsules for oral administration. Marinol⁷ may be used for stimulating appetite and preventing weight loss in patients with a confirmed diagnosis of AIDS and treating nausea and vomiting associated with cancer chemotherapy. Additionally, a few individuals have been permitted by a court order to use THC for the management of glaucoma. Patients that are prescribed Marinol⁷ should be warned not to drive, operate complex machinery, or engage in hazardous activity.

There are no other prescription or over-the-counter medications that contain cannabinoids or any other substances that might be identified as or metabolized to THC or its acid metabolite.

When a donor claims to have a prescription for Dronabinol or a court order allowing the use of THC, the MRO should allow the donor the opportunity to provide the supporting documentation.

Passive Inhalation or Unknowing Ingestion of Marijuana

Passive inhalation and unknowing ingestion (i.e., an inadvertent exposure to marijuana) are frequent excuses for positive urine tests. Passive inhalation of marijuana smoke does occur and can result in detectable levels of THC and its metabolites in urine. Clinical studies have shown, however, that it is highly unlikely that a non-smoking individual could unknowingly inhale sufficient smoke by passive inhalation to result in a high enough drug concentration in urine for detection at the cutoff levels used in the Federal agency program. Similarly, it is extremely difficult to achieve detectable levels through unknowing ingestion of plant material (e.g., leaves, stems) or marijuana in food products. Studies have also shown that any measurable peak concentration in urine occurs within several hours after the exposure.

When a donor claims that his or her positive THCA test was due to passive inhalation or unknowing ingestion, the MRO should allow the donor to describe the circumstances pertaining to how and when the exposure/ingestion occurred. Generally, the circumstances will not approximate what would be needed to explain the presence of THC in the donor=s urine.

Hemp Products

The Drug Enforcement Agency (DEA) issued its final rule clarifying control of natural and synthetic tetrahydrocannabinol (THC) effective April 21, 2003 (21 CFR Part 1308). The rule states that it is illegal for anyone to manufacture, distribute or market products used, or intended for use, for human consumption that contain any amount of THC. Personal care products (e.g., shampoos, lotions) are not considered to fall in this category, because they are not intended for human consumption and studies have shown that use of these products does not cause urine specimens to test positive for THC under the Federal Guidelines. Other “non-consumable” hemp items (e.g., clothing, industrial solvents, and animal feed mixtures) are considered non-controlled substances and are not subject to any of the CSA requirements regardless of their THC content.

When a donor claims that his or her positive THCA test was due to ingestion or use of a legal hemp product, the MRO should allow the donor to explain where and when the product was purchased and used. Generally, the circumstances will not approximate what would be needed to explain the presence of THCA in the donor=s urine.

Opiates

The opiate drug class poses some unique challenges with regard to interpreting a positive test result. A positive result for codeine or morphine may be from the following:

- A drug product that contains codeine or morphine (see **Table 3** for some

examples), or

- Poppy seeds.

Eating a normal dietary amount of poppy seeds can cause a urine specimen to test positive for morphine and codeine. The concentration of morphine can be substantial, with usually very low concentrations or no detectable codeine. In many instances, a donor will not know that poppy seeds can cause a positive test or realize that he or she had eaten poppy seeds at the time the urine was collected.

HHS included additional criteria in the Mandatory Guidelines to distinguish between specimens testing positive due to opiates abuse and specimens testing positive due to legitimate medical use or food sources. The criteria are as follow:

- When a laboratory reports a specimen as positive for codeine and/or morphine and the quantitative results for both codeine and morphine are less than 15,000 ng/mL:
 - If there is clinical evidence of illegal use of any opium, opiate, or opium derivative (e.g., morphine/codeine) listed in CSA Schedule I or II, the MRO verifies the result as positive.
 - If there is no clinical evidence of illegal use, the MRO verifies the result as negative.
- When a laboratory reports a specimen as positive for codeine and/or morphine and the codeine and/or morphine result is greater than or equal to 15,000 ng/mL:
 - If the donor does not present a legitimate medical explanation for the presence of morphine or codeine (e.g., a valid prescription), the MRO verifies the result as positive. Consumption of food products is not a legitimate medical explanation for the donor having morphine or codeine at or above this concentration.
 - If the donor presents a legitimate medical explanation for the presence of morphine or codeine (e.g., a valid prescription), the MRO verifies the result as negative.
- When a laboratory reports a specimen as positive for the heroin metabolite (6-acetylmorphine), this is proof of heroin use. The MRO verifies the result as positive.

The MRO relies on his or her medical knowledge to identify signs and symptoms of abuse during the donor interview. Clinical evidence of illegal use may include, *but is not limited to*:

- A donor's admission that he or she took a prescription medication containing codeine or morphine that was prescribed to another individual,
- Recent needle marks, or
- Behavioral and physiological signs of acute opiate intoxication or withdrawal.

An MRO may have a blanket written request on file at the laboratory to routinely receive the quantitative values associated with positive codeine and morphine results. The MRO also may

request quantitative information on the presence of codeine below the cutoff for specimens that have been reported positive for morphine only. This information may be helpful to the MRO in assessing the medical explanation provided by the donor.

Other Narcotic Analgesics

Occasionally, a donor will reveal information regarding the use of a narcotic analgesic (that does not contain codeine or morphine) believing that this medication was the reason for the positive codeine or morphine. Assuming that it was a legally prescribed medication, this confidential medical information cannot be provided to the Federal agency and is not an explanation for the positive codeine or morphine. Since the use of a narcotic analgesic may have a possible effect on the ability of the donor to perform a specific task (e.g., driving a vehicle), it may be appropriate to discuss the use of the medication with the prescribing physician. Additional guidance on reporting such information is provided in Section F below and in Section C of Chapter 6.

Phencyclidine

A positive phencyclidine (PCP) result is evidence of illegal drug use. There are no prescription or over-the-counter medications that contain PCP, there are no legal medical uses of PCP, and there are no other substances that can be misidentified as PCP using GC/MS.

Retest Results

After a second certified laboratory tests an aliquot of the single specimen or the split (Bottle B) specimen, the MRO must take actions in response to the second laboratory's reported results as outlined in **Table 6**.

If the second laboratory believes that the analyte (i.e., drug, drug metabolite, adulterant) is present in the retest specimen, but cannot reconfirm its presence, the laboratory must consult with the MRO to decide whether to send the specimen (i.e., the remaining aliquot of a single specimen or Bottle B of a split specimen) to a third certified laboratory for additional confirmatory testing. (If there is an insufficient quantity of urine remaining in the aliquot of the single specimen at the second laboratory, the MRO may request the first laboratory to obtain another aliquot from the original specimen bottle and send it to the third laboratory.) The third laboratory should be selected such that it uses a confirmation method more similar to that used by the first laboratory (i.e., the laboratory that reported the non-negative result for the primary specimen).

F. Reporting

After the review and verification processes have been completed, the MRO reports the final, verified result(s) for a specimen to a Federal agency. Reporting instructions are detailed in **Tables 5 and 6**.

The MRO must send the report using one of the following methods, in a manner designed to ensure confidentiality of the information:

- Secure fax,
- Courier,
- Mail, or

- Secure electronic transmission.

The report may be:

- A legible image or copy of the completed Copy 2 of the Federal CCF, or
- A separate letter or memorandum for each specimen that contains the following:
 - Donor's name and SSN or employee ID number,
 - Specimen ID number from the Federal CCF,
 - Result for the test as indicated on the Federal CCF,
 - Relevant comments provided by the collector and/or laboratory on the Federal CCF,
 - Relevant information from the MRO (e.g., documentation of attempts to contact the donor, a statement of the donor's refusal to cooperate with the medical review process),
 - Information provided by the donor (especially at the donor's request) to the report (*Note: this must not include specific confidential medical information*),
 - MRO's printed name and signature, and
 - Date reported.

The MRO must not disclose any numerical values to the Federal agency.

Confidentiality

The Mandatory Guidelines require the MRO to:

1. Report the final result of the drug test to a Federal agency in a manner designed to ensure the confidentiality of the information, and
2. Maintain the confidentiality of the information received during the review process, including:
 - information related to the donor's medical condition,
 - medications,
 - medical diagnosis, and
 - medical history.

Despite this general requirement to maintain the confidentiality of medical information, there are certain circumstances in which the MRO may provide such information to other parties. In these instances, prior to the medical interview the MRO must inform the donor that disclosure of information learned as part of the medical review process may occur if:

- There is a significant safety hazard associated with donor performing assigned duties,
- Medical disqualification of the donor exists under applicable regulations, or
- The Federal agency's regulations specify requirements for disclosure of such information under other circumstances.

When the MRO releases otherwise confidential information due to such concerns, the MRO must attempt to release as little specific information as possible and release such information only to parties that clearly “need-to-know.” Such parties include:

- Physicians responsible for medical certification of the donor,
- Federal agency officials as required by regulation, or
- Designated Federal agency representatives.

Diagnoses or other specific details of medical information do not need to be provided to non-medical personnel. For example, Federal agency representatives may only need to be informed that a safety hazard may exist and that the MRO will provide specific information to the physician responsible for making medical qualification decisions regarding the donor. In general, unless required by regulation or law, the MRO must only discuss specific medical information with other physicians or qualified health professionals.

Chapter 5. Documentation and Recordkeeping

Accurate recordkeeping is essential in documenting all aspects of the MRO review process. All MRO activities should be properly documented, to provide a record that procedures used were consistent with the Mandatory Guidelines. The MRO should maintain documentation of all communications (written and oral) with:

- Donors,
- Federal agency representatives,
- Laboratory personnel, and
- Collectors.

Although the Mandatory Guidelines do not specify the length of time that MROs must retain drug test records, it is recommended that they be maintained for a minimum of two years from the date of collection, or as otherwise provided by law or contract with the Federal agency.

Documentation for each specimen must be retained in the donor files and normally includes such things as:

- Documentation to support an alternative medical explanation for a non-negative result (e.g., copies of prescriptions, labels from prescription bottles, notes that a prescription was verified at a pharmacy or by the treating physician),
- Letters or notes received from an employee, relative, or physician providing treatment, or
- MRO actions regarding the test (e.g., attempts to contact the donor, documentation of the donor interview, any checklists used by the MRO and MRO staff for the record).

Some MROs may serve as primary care providers and retain medical records related to that

function. MRO records must be separated from other medical and personnel records kept on an individual.

A donor has the right, upon written request, to records relating to his or her drug test. In addition, information can be requested by a subpoena or court order. If an MRO has any concern regarding the release of information associated with drug testing results, the MRO may want to obtain a legal opinion.

The maintenance of donor confidentiality is particularly important with respect to confirmed non-negative drug test results, and especially for those that may be verified by the MRO as negative due to a valid medical explanation.

Chapter 6. Additional MRO Responsibilities

A. Federal Agency Blind Samples

Federal agencies are required to have blind samples submitted with donor specimens. Blind samples are helpful in determining if the entire testing process (i.e., from the collector's submission of a specimen to a laboratory until a result is reported to the MRO) satisfies all requirements.

To ensure that the blind samples purchased from different sources are acceptable, Federal agencies must use only samples certified by the sample suppliers. Samples must be certified:

1. To have the stated results as verified by the program-required method(s) of analysis:
 - a. Negative (verified by immunoassay and GC/MS),
 - b. Drug positive (verified by immunoassay and GC/MS),
 - c. Adulterated (verified by initial and confirmatory specimen validity testing methods as appropriate), and
 - d. Substituted (verified by confirmatory creatinine and specific gravity tests).
2. To have acceptable performance demonstrated up to the stated expiration date and documented by stability studies.

The blind samples may be purchased by the Federal agency and supplied to the collector, or purchased by the collector and submitted to a laboratory with an agency's specimens. Each blind sample is submitted as if it were a donor specimen. This requires the collector to complete a Federal CCF and to properly label the specimen bottle(s) containing the sample. Since there is no donor associated with a blind sample, the collector generates a fictitious social security number or employee identification number and fictitious initials to be written on the specimen bottle label/seal.

The collector or the Federal agency, whichever purchased the blind samples, must forward information to the MRO, so he or she will have the information necessary to determine if the laboratory reported the correct result. On the MRO Copy of the Federal CCF, the collector indicates that the sample is a "blind QC sample" where the donor would normally provide a

signature (Step 5 on Copy 2 of the Federal CCF).

An incorrect result reported by the laboratory does not automatically indicate that the laboratory made an analytical error. For example, there could have been a problem with the sample itself (e.g., stability, concentration) or the collector did not properly submit the sample.

When a laboratory reports a result different from the one expected based on information provided by the supplier of the blind sample, the MRO must contact the Federal agency. The Federal agency will investigate and/or contact the appropriate regulatory office to institute an investigation to determine the exact cause of the incorrect result. When the specific cause is identified, appropriate corrective actions will be taken. The regulatory office will share the findings with the MRO.

B. Shy Bladder

Occasionally, a donor is unable to provide a specimen upon arrival at the collection site because he or she either urinated recently or has Ashy bladder.@ Generally, the term “shy bladder” refers to an individual who is unable to provide a urine specimen either upon demand or when someone is nearby during the attempted urination. The medical term for this condition is paruresis.

When a donor has difficulty providing a urine specimen, the collector gives the donor a reasonable amount of liquid to drink over a period of time (not to exceed 3 hours). Unsupported claims of “situational anxiety” or dehydration are not considered valid reasons for a donor’s failure to provide a urine specimen. When sufficient time has elapsed and fluids have been ingested, the inability to provide a urine specimen shall be regarded as a refusal to take a test.

If it is believed that an individual has a “shy bladder,” the Federal agency must arrange to have the donor evaluated to determine whether the donor’s inability to provide a specimen is genuine or constitutes a refusal to provide a specimen. The evaluation must be performed by a licensed physician (e.g., the MRO, a physician acceptable to the agency, the agency’s occupational health physician) and must take place as soon as practical after the attempted collection.

The examining physician must determine, in his or her reasonable medical judgment, that a medical condition has or, with a high degree of probability, could have precluded the donor from providing a urine specimen (e.g., a urinary system dysfunction or a documented pre-existing psychological disorder). An evaluation must include a review of any pertinent medical records and may include evaluative testing such as blood chemistries for kidney function or other physiologic factors likely to affect urine output.

The examining physician shall provide to the MRO a brief written statement describing his or her conclusion and the basis for it. The written statement shall not include detailed information on the medical condition of the donor. Upon receipt of the written statement from the examining physician, the MRO shall report his or her conclusions to the agency in writing.

C. Occupational and Public Safety

Executive Order 12564 uses the term “illegal drugs” to refer to any controlled substance included in Schedule I or II of the Controlled Substances Act, and not to refer to the use of a controlled substance pursuant to a valid prescription or other uses authorized by law.

The purpose of this policy is to ensure that a workplace drug testing program does not intentionally identify an individual who is receiving valid medical care and, thereby, provide confidential medical information to an agency or anyone else.

There is, however, a public safety issue associated with information that a donor may provide to an MRO during the review of a test result. That is, the donor may be taking a legal prescription medication as treatment for a medical condition and the medication may have possible side effects that may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks (e.g., driving a car or truck, operating machinery).

If the side effects of a legitimately prescribed medication have a possible impact on the safety aspects of the work performed by a donor, the MRO must decide what must be done with the information. Although the Mandatory Guidelines require an MRO to verify a drug test result as a negative result if the donor has legally taken a prescription medication, it is recommended that the MRO contact the prescribing physician to discuss the possible impact that the medication may have on the safety aspects of the work performed by the donor. Additionally, some occupations have restrictions that prohibit an individual from taking specific medications that may, otherwise, be allowable for other occupations. In these instances, the MRO may inform the individual responsible for certifying that the donor is qualified to perform that job that the donor is taking a medication that is restricted for an individual in that occupation or that the medication may affect the individual's ability to perform a safety sensitive occupation.

D. Donor Rights to Information

An employee who is the subject of a drug test may, upon written request through the MRO and the Federal agency, have access to any records relating to his or her drug test, any records relating to the results of any relevant certification, review, or revocation of certification proceedings, and access to a documentation package. A donor or Federal agency will occasionally request the testing laboratory to provide a complete package of analytical data, chain of custody records, and other administrative documents associated with the testing of a particular specimen. This package is generally referred to as a "data package" or "litigation package." The request must always be submitted to the laboratory through the MRO.

A standard data package provided by an HHS-certified laboratory consists of the following items:

- A cover sheet that provides a brief description of the drug testing procedures and specimen validity tests performed on the donor's specimen
- A table of contents page that lists by page number all documents and materials in the package
- A copy of the Federal CCF with any attachments and a copy of the electronic report (if any) generated by the laboratory
- A brief description of the initial drug tests and initial specimen validity tests (e.g., instrumentation, batch quality control, and test data format)
- A brief description of confirmatory drug tests and confirmatory validity tests (e.g., instrumentation, batch quality control, and test data format)
- A copy of the resume or curriculum vitae for the certifying scientist that certified

the test result

- A copy of the resume or curriculum vitae for the laboratory's Responsible Person(s)
- Donor specific information including:
 - Internal chain of custody records for the specimen,
 - Memoranda (if any) generated by the laboratory,
 - Copies of the initial drug and specimen validity test data for the donor's specimen with all calibrators and controls identified and copies of all internal chain of custody documents related to the initial tests, and
 - Copies of the confirmatory drug and specimen validity test data for the donor's specimen with all calibrators and controls identified and copies of all internal chain of custody documents related to the confirmatory tests.

Appendix A. Laboratory Reporting Criteria

Positive

A laboratory will report a urine specimen as positive for a drug/drug metabolite when:

- The specimen's immunoassay result was at or above the initial test cutoff for the drug class
- and**
- The specimen's GC/MS result (i.e., on a separate aliquot) was at or above the confirmatory test cutoff for the specific drug/drug metabolite.

Drug/Metabolite	Initial Test Cutoff	Confirmatory Test Cutoff
Amphetamines	1000 ng/mL	Amphetamine 500 ng/mL
		Methamphetamine 500 ng/mL* *must also contain at least 200 ng/mL amphetamine
Opiates	2000 ng/mL	Codeine 2000 ng/mL
		Morphine 2000 ng/mL
		6-acetylmorphine 10 ng/mL* *must also be positive for morphine
Marijuana (cannabinoids)	50 ng/mL	THCA (marijuana metabolite) 15 ng/mL
Cocaine	300 ng/mL	Benzoylcegonine (cocaine metabolite) 150 ng/mL
Phencyclidine (PCP)	25 ng/mL	Phencyclidine 25 ng/mL

Negative

A laboratory will report a urine specimen as negative when the specimen has valid negative drug test results at any point in the testing process:

- Immunoassay results below the initial test cutoffs
- or**
- GC/MS results below the confirmatory test cutoffs
- and**
- Specimen validity test results in the acceptable range

Dilute

A laboratory will report a urine specimen as **dilute** in conjunction with a positive or negative drug test when on a single aliquot:

- The creatinine concentration is greater than or equal to 2 mg/dL and less than 20 mg/dL
- and**
- The specific gravity is greater than 1.0010 but less than 1.0030

Substituted

A laboratory will report a urine specimen as **substituted** when both the initial and confirmatory tests (i.e., tests on separate aliquots) document that:

- The creatinine concentration is less than 2 mg/dL
- **and**
- The specific gravity is less than or equal to 1.0010 **or** greater than or equal to 1.0200

Adulterated

A laboratory will report a urine specimen as **adulterated** when both the initial and confirmatory test results (i.e., tests on separate aliquots) meet one of the following criteria:

- The pH is less than 3,
- The pH is greater than or equal to 11,
- The nitrite concentration is greater than or equal to 500 mcg/mL,
- Chromium (VI) is present, verified by a specific confirmatory test,
- A halogen (e.g., bleach, iodine, fluoride) is present, verified by a specific confirmatory test,
- Glutaraldehyde is present (verified by a GC/MS confirmatory test),
- Pyridine (pyridinium chlorochromate) is present (verified by a GC/MS confirmatory test),
- A surfactant is present (i.e., dodecylbenzene sulfonate-equivalent concentration is greater than or equal to 100 mcg/mL),
- The specimen contains a substance that is not a normal constituent of human urine (verified by a confirmatory test for the specific substance), or
- The specimen contains an endogenous substance at a concentration that is not a normal physiological concentration (verified by a confirmatory test for the specific substance).

Invalid Result

A laboratory will report an invalid result for a urine specimen when results for two separate aliquots meet one of the following criteria:

1. Creatinine concentration and specific gravity results are discrepant:
 - The creatinine concentration is less than 2 mg/dL on both the initial and confirmatory creatinine tests and the specific gravity is greater than 1.0010 but less than 1.0200 on either or both the initial and confirmatory specific gravity tests, or
 - The specific gravity is less than or equal to 1.0010 on both the initial and

confirmatory specific gravity tests and the creatinine concentration is greater than or equal to 2 mg/dL on either or both the initial and confirmatory creatinine tests;

2. The pH is outside the acceptable range:
 - The pH result is greater than or equal to 3 and less than 4.5 using either a colorimetric pH test or pH meter for the initial test and a pH meter for the confirmatory test, or
 - The pH result is greater than or equal to 9 and less than 11 using either a colorimetric pH test or pH meter for the initial test and a pH meter for the confirmatory test;
3. Nitrite is present, but below the program cutoff for adulteration:
 - Nitrite is greater than or equal to 200 mcg/mL using a nitrite colorimetric test for both the initial and confirmatory tests,
 - Nitrite is greater than or equal to the equivalent of 200 mcg/mL nitrite using a general oxidant colorimetric test for both the initial and confirmatory tests, or
 - Nitrite is greater than or equal to 200 mcg/mL using a nitrite colorimetric test or a general oxidant colorimetric test and is greater than or equal to 200 mcg/mL but less than 500 mcg/mL for a confirmatory test using a different method;
4. The possible presence of chromium (VI) is determined using the same chromium (VI) colorimetric test with a cutoff greater than or equal to 50 mcg/mL chromium (VI) for both the initial and confirmatory tests;
5. The possible presence of a halogen (e.g., bleach, iodine, fluoride) is determined using the same halogen colorimetric test with a cutoff greater than or equal to the LOD for both the initial and confirmatory tests, or relying on the odor of the specimen as the initial test;
6. The possible presence of glutaraldehyde is determined by using the same aldehyde test (aldehyde present) or characteristic immunoassay response on one or more drug immunoassay tests for both the initial and confirmatory tests;
7. The possible presence of an oxidizing adulterant is determined by using the same general oxidant colorimetric test (with a greater than or equal to 200 mcg/mL nitrite-equivalent cutoff, a greater than or equal to 50 mcg/mL chromium (VI)-equivalent cutoff, or a halogen concentration greater than or equal to the LOD) for both the initial and confirmatory tests;
8. The possible presence of a surfactant is determined by using the same surfactant colorimetric test with a greater than or equal to 100 mcg/mL dodecylbenzene sulfonate-equivalent cutoff for both the initial and confirmatory tests, or using a foam/shake test for the initial test;
9. Interference occurs on the immunoassay drug tests on two separate aliquots (i.e., valid immunoassay drug test results cannot be obtained);

Note: Tolectin⁷ (Tolmetin - a non-steroidal anti-inflammatory), Flagyl⁷ (metronidazole - an antifungal and antibacterial agent), Cipro⁷ (ciprofloxacin - an antibacterial agent), Grisactin⁷ (Griseofulvin - a fungistatic antibiotic), and Clonoril⁷ (sulindac - a non-steroidal anti-inflammatory) are some known prescription medications that may interfere with some immunoassay tests.

10. Interference with the GC/MS drug confirmation assay occurs on two separate aliquots of the specimen and the laboratory is unable to identify the interfering substance;.
11. The physical appearance of the specimen is such that testing the system may damage the laboratory's instruments; or
12. If the physical appearances of Bottles A and B are clearly different, the test result for Bottle A is one of the reasons stated in 1 through 10 above and/or the specimen was negative for drugs upon initial testing.

Table 1. Immunoassays

Method	Abbreviation	Description
Enzyme Immunoassay	EIA	An immunoassay based on competition for antibody binding sites between drug in the specimen and drug labeled with an enzyme. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the specimen can be measured in terms of enzyme activity.
Kinetic Interaction of Microparticles in Solution	KIMS	An immunoassay based on the principle of the kinetic interaction of microparticles in a solution where the drug content of the urine is directly proportional to the inhibition of the microparticle aggregation.
Cloned Enzyme Donor Immunoassay	CEDIA	An immunoassay utilizing enzyme fragments engineered by recombinant DNA techniques. Two fragments, the enzyme donor (ED) and enzyme acceptor (EA), are inactive when separated. CEDIA is based on competition for antibody binding sites between drug conjugated with ED and drug in the specimen. Enzyme activity decreases when the ED-drug fragment is bound, so the drug concentration in the specimen can be measured in terms of enzyme activity (i.e., drug concentration and enzyme activity are inversely related).
Fluorescence Polarization Immunoassay	FPIA	An immunoassay based on competition between drug in the specimen and drug labeled with a fluorophore. Light emitted by the fluorescently labeled drug/antibody complex will be more polarized. The specimen's fluorescence polarization value is inversely related to the drug concentration.
Radioimmunoassay	RIA	An immunoassay based on competition between drug in the specimen and drug labeled with a radioisotope. The antibody-antigen complex is precipitated out of solution, separated from the unbound reagents, and measured in a gamma counter. Radioactivity is inversely proportional to drug concentration.
Microplate Enzyme-Linked Immunosorbent Assay	ELISA	A competitive binding enzyme immunoassay using drug-specific antibodies immobilized on the sides of a microplate well.

Table 2. Laboratory Specimen Validity Test Methods

Method	Analytes	Description
Colorimetry	pH, creatinine, adulterants (general or compound-specific tests)	An analytical procedure based on comparison of the color developed in a solution of a test material with that in a standard solution, quantitated on the basis of the absorption of light. In a colorimetric test method, reagents are added to a sample and a reaction occurs with the analyte of interest, producing a color. Because the intensity of the color is related to the analyte's concentration, the concentration of the analyte is determined by visually measuring the color or electronically measuring the intensity of light at selected wavelengths (i.e., spectrophotometry).
Refractometry	Urine specific gravity	A urine specific gravity refractometer is used to determine the amount of solute (i.e., urinary total solids) in the urine by measuring the index of refraction. The index of refraction is the ratio of electromagnetic radiation in a vacuum to its velocity in the medium of interest. The instrument manufacturer applies a formula to convert from refractive indices to the urine specific gravity values displayed by the refractometer.
Potentiometry	pH	The measurement of the electrical potential difference between two electrodes in an electrochemical cell. A pH meter is a type of potentiometer.
Atomic Absorption Spectrophotometry (AAS)	Adulterants (e.g., chromium VI)	An analytical method in which a sample is vaporized in a flame or graphite furnace. The atoms absorb ultraviolet or visible light and make transitions to higher electronic energy levels. The analyte concentration is determined from the amount of absorption of specific wavelengths.

Method	Analytes	Description
Electrophoresis Capillary electrophoresis (CE)	Adulterants (e.g., nitrite, chromium VI)	A separation technique that is based on the mobility of ions in an electric field. Positively charged ions migrate towards a negative electrode and negatively charged ions migrate toward a positive electrode. Ions have different migration rates depending on their total charge, size, and shape, and can therefore be separated. Capillary electrophoresis (CE) is an electrophoretic method using a small-bore, fused silica capillary tube. The capillary tube allows the use of very high electric fields because the small capillaries efficiently dissipate the heat that is produced. Increasing the electric fields produces very efficient separations and reduces separation times.
Gas Chromatography/Mass Spectrometry (GC/MS)	Adulterants (e.g., glutaraldehyde, pyridine)	(See method description in this manual)
Inductively-Coupled Plasma-Mass Spectrometry (ICP-MS)	Adulterants (e.g., chromium VI, halogens)	An analytical method in which the sample is introduced into a radio-frequency (RF) induced plasma in the form of a solution, vapor or solid. The temperature of the plasma may reach up to 6000 K at the center and 8000 K at its periphery. The high thermal energy and electron-rich environment of the ICP results in the conversion of most atoms into ions. A quadrupole mass spectrometer permits the detection of ions at each mass in rapid sequence, allowing signals of individual isotopes of an element to be scanned.
Multi-wavelength spectrometry (MWS)	Adulterants (e.g., nitrite, chromium VI, halogens, surfactants)	A method that measures multiple wavelengths of light (or other electronic transmissions) to identify an analyte. The method generates corrected absorbance values that are related to the analyte concentration.

Method	Analytes	Description
Ion Chromatography (IC)	Adulterants (e.g., nitrite, chromium VI, halogens)	A form of liquid chromatography that uses ion-exchange resins to separate atomic or molecular ions based on their interaction with the resin. Its greatest utility is for analysis of anions for which there are no other rapid analytical methods. It is also commonly used for cations and biochemical species such as amino acids and proteins.
High-Performance Liquid Chromatography (HPLC)	Adulterants (e.g., nitrite, chromium VI)	A chromatographic technique for separating and analyzing chemical substances in solution. Separation is based on absorption, partition, ion exchange, or size exclusion.

Table 3. Some Products Containing Opiates

Drug	Prescription Products	Non-Prescription Products¹
Codeine	Ambenyl with Codeine®	Kaodene with Codeine®
	Codimal PH7 Syrup®	
	Fioricet with Codeine®	
	Fiorinal with Codeine®	
	Guiatuss A.C. ®	
	Phenaphen with Codeine®	
	Robitussin-DAC®	
	Triacin-C®	
	Tylenol with Codeine®	
Morphine	Avinza®	Donnagel-PG® ²
	Astramorph PF®	Infantol Pink® ²
	Depodur®	Kaodene with Paregoric® ^{2,3}
	Duramorph®	Quiagel PG® ²
	Kadian®	
	MS Contin Tablets®	
	Oramorph SR®	
	Roxanol®	
	Paregoric® ³	

¹Each listed non-prescription product is used as an anti-diarrheal. They are generally available over-the-counter; however, non-prescription sale is prohibited in some States.

²The non-prescription morphine products listed contain opium.

³Paregoric alone is a Schedule III prescription drug, but in combination with other substances is a Schedule V over-the-counter product.

Table 4. Some Products Containing Amphetamines

Substances	Products
Substances known to contain <i>d</i> -amphetamine or racemic <i>d,l</i> -amphetamine	Adderall®
	Dexedrine®
	DextroStat®
Substances known to contain <i>d</i> -methamphetamine	Desoxyn®
Substances known to metabolize to methamphetamine (and amphetamine)	Benzphetamine (Didrex®)
	Dimethylamphetamine
	Famprofazone
	Fencamine
	Furfenorex
	Selegiline (Alzene®, Carbex®, Deprenyl®, Eldepryl®)
Substances known to metabolize to amphetamine	Amphetaminil
	Clobenzorex
	Ethylamphetamine
	Fenethylamine
	Fenproporex
	Mefenorex
	Mesocarb
	Prenylamine

Table 5. MRO Actions for Single Specimen/Bottle A Reports

Laboratory Result	MRO Action
Negative	Report the negative result.
Negative and Dilute	Report the negative result and inform the Federal agency that the next time the donor is selected for a drug test, the agency may require the specimen to be collected using a direct observed collection procedure.
Positive	<p>Contact the donor to determine if he or she has a valid medical explanation for the positive result. If the medical explanation for the positive result appears to be:</p> <p>Legitimate – Verify the result as negative and report a negative result to the agency. <i>(It is recommended that the MRO contact the prescribing physician to discuss the possible impact that the medication may have on the safety aspects of the work performed by the donor. The MRO may inform the Federal agency’s designated representative that the donor is taking a medication that is restricted for an individual in that occupation or that the medication may affect the individual’s ability to perform a safety sensitive occupation.)</i></p> <p>Not legitimate – Report the positive drug result to the Federal agency.</p>
Positive and Dilute	<p>If the positive drug test is verified as negative due to a valid medical explanation – Report the specimen as negative and dilute and inform the Federal agency that the next time the donor is selected for a drug test the agency may require the specimen to be collected using a direct observed collection procedure.</p> <p>If the positive drug test is verified positive – Report the positive result to the Federal agency but do not report that the specimen was also dilute.</p>
Substituted	<p>Contact the donor to determine if he or she has a valid medical explanation for the substituted result. If the medical explanation for the substituted result appears to be:</p> <p>Legitimate – Report a negative result to the Federal agency.</p> <p>Not legitimate – Report a refusal to test (substituted) to the Federal agency.</p>

Laboratory Result	MRO Action
Adulterated	<p>Contact the donor to determine if he or she has a valid medical explanation for the adulterated result <i>(Although the MRO is required to contact the donor and give the donor an opportunity to explain the adulterated result, the program criteria for adulteration definitively proves adulteration. There is no valid medical explanation.)</i> - Report a refusal to test (adulterated) to the Federal agency.</p>
Invalid Result	<p><i>Prior to reporting an invalid result to the MRO, the laboratory must contact the MRO to decide whether additional/different testing would be of use to obtain a definitive result</i></p> <p>Contact the donor to determine if he or she has an explanation for the invalid result.</p> <p>If the medical explanation for a first invalid result appears to be:</p> <p>Legitimate – Report the test as canceled with the reason for the invalid result and inform the Federal agency that a recollection is not required because the explanation provided by the donor for the invalid result is acceptable <i>unless</i> a negative drug test result is required based on the reason for testing (e.g., pre-employment, return to duty, follow-up).</p> <p>Not legitimate – Report the test as canceled with the reason for the invalid result and direct the Federal agency to immediately collect another specimen using a direct observed collection procedure.</p> <p>If a specimen is recollected using direct observation and is invalid due to:</p> <p style="padding-left: 40px;">The same reason reported for the first specimen - Report the canceled test with the reason for the invalid result and recommend to the Federal agency that no further action be taken.</p> <p style="padding-left: 40px;">A different reason than reported for the first specimen - Report the result for the recollected specimen as a refusal to test with the reason for the invalid result. <i>(The reason for reporting a refusal to test rather than reporting another invalid result is that the donor must have managed to defeat the drug test even though a direct observed collection procedure was used.)</i></p>
Multiple Non-Negative Results	<p>Follow the review procedures above as appropriate for each reported result and report all verified results.</p>

Laboratory Result	MRO Action
Rejected for Testing	Report the test as canceled along with the reason for the cancellation and inform the Federal agency that an immediate collection of another specimen is permitted, if a negative drug test result is required based on the reason for testing (e.g., pre-employment, return to duty, follow-up).

**Table 6. MRO Actions for Retest Specimen Reports
(Bottle B or Aliquot of Bottle A)**

Laboratory Retest Result			MRO Action
Reconfirmed	Failed to Reconfirm	Additional Testing Results ¹	
Drug(s)			Report as reconfirmed.
Adulterated			Report as reconfirmed.
Substituted			Report as reconfirmed.
	Drug(s)	Adulterated Substituted	<p>Contact the donor to determine if he or she has an explanation for the adulterated/substituted result.</p> <p>If the explanation for the adulterated/substituted result appears to be:</p> <p>Legitimate - Report as failed to reconfirm (specify drug(s)) and cancel both tests.</p> <p>Not legitimate – Give the donor 72 hours to request that Laboratory A tests Bottle A for the adulterant/substitution.</p> <p>If Bottle A contains the adulterant/is substituted - Report as refusal to test with the reason (adulterant present/substituted)</p> <p>If the donor chooses not to have Bottle A retested - Report as failed to reconfirm (specify drug(s)) and as refusal to test with the reason (adulterant present/substituted)</p> <p>If Bottle A does not reconfirm Bottle B results (i.e., does not contain the adulterant/is not substituted):</p> <p>Cancel both tests,</p> <p>Direct the Federal agency to immediately collect another specimen using a direct observed collection procedure, and</p> <p>Notify the appropriate regulatory office about the failure to reconfirm and cancelled tests.</p>

¹ Laboratory B conducts specimen validity tests to determine whether the failure to reconfirm the drug(s) is because the retest specimen is adulterated/substituted/invalid.

Laboratory Retest Result			MRO Action
Reconfirmed	Failed to Reconfirm	Additional Testing Results ¹	
	Drug(s)	Invalid	<p><i>Prior to reporting as failed to reconfirm and invalid to the MRO, the laboratory must contact the MRO to decide whether testing at a third laboratory would be of use to obtain a definitive result.</i></p> <p>Assuming the invalid result cannot be resolved:</p> <p>Report as failed to reconfirm (specify drug(s)) with the reason for the invalid result, Cancel both tests,</p> <p>Direct the Federal agency to immediately collect another specimen using a direct observed collection procedure, and Notify the appropriate regulatory office about the failure to reconfirm and cancelled tests.</p>
	Drug(s)	<p><u>Not</u> adulterated</p> <p><u>Not</u> substituted</p> <p><u>Not</u> invalid</p>	<p><i>Prior to reporting as failed to reconfirm to the MRO, if the laboratory believes the drug may be present, the laboratory must contact the MRO to decide whether testing at a third laboratory would be useful.</i></p> <p>Report as failed to reconfirm (specify drug(s)), Cancel both tests, and Notify the appropriate regulatory office about the failure to reconfirm and cancelled tests.</p>
	Adulterated		<p>Report as failed to reconfirm (specify adulterant), Cancel both tests, and Notify the appropriate regulatory office regarding the test results for the specimen.</p>
	Substituted		<p>Report as failed to reconfirm (not substituted), Cancel both tests, and Notify the appropriate regulatory office regarding the test results for the specimen.</p>

¹ Laboratory B conducts specimen validity tests to determine whether the failure to reconfirm the drug(s) is because the retest specimen is adulterated/substituted/invalid.

When Laboratory A reported **multiple non-negative results** (i.e., drug-positive, adulterated, substituted) for the primary specimen and Laboratory B **reconfirmed some but not all of the results** for the retest specimen, the MRO takes the following action:

- Report all reconfirmed results (specify drug(s)/adulterant/substituted) and all results that failed to reconfirm (specify drug(s)/adulterant/not substituted).
- For specimens with at least one reconfirmed positive drug, inform the Federal agency that it may take action based on the reconfirmed drug result(s):
 - *Regardless of* Laboratory B's failure to reconfirm the other drug(s) reported positive in the primary specimen
 - *Regardless of* whether Laboratory B found the retest specimen to be adulterated, substituted, or invalid when performing SVT after failing to reconfirm a drug
 - *Regardless of* whether Laboratory B reported the failure to reconfirm a drug because the laboratory was unable to obtain valid confirmatory test results.
- Notify the appropriate regulatory office of the test results for the specimen.

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Additional Resources

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