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

EFFECTIVE OCTOBER 1, 2010

Note: This manual applies to Federal agency drug testing programs that come under Executive Order 12564 dated September 15, 1986, section 503 of Public Law 100-71, 5 U.S.C. section 7301 note dated July 11, 1987, and the Department of Health and Human Services Mandatory Guidelines for Federal Workplace Drug Testing Programs (73 FR 71858) dated November 25, 2008 (effective October 1, 2010).

This manual does not apply to specimens submitted for testing under U.S. Department of Transportation (DOT) Procedures for Transportation Workplace Drug and Alcohol Testing Programs (49 CFR Part 40).

The current version of this manual and other information including MRO Case Studies are available on the Drug Testing page under *Medical Review Officer (MRO) Resources* on the SAMHSA website:

http://www.workplace.samhsa.gov

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 drug test results in the context of information obtained from the donor interview. The Department of Health and Human Services (HHS) requires the Medical Review Officer (MRO) to fulfill this important function.

The HHS Mandatory Guidelines for Federal Workplace Drug Testing Programs (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 regarding the pharmacology and toxicology of illicit drugs;

- Training in the collection procedures used to collect Federal agency specimens; the interpretation of test results reported by laboratories; chain of custody, reporting, and recordkeeping requirements for Federal agency specimens; the HHS Mandatory Guidelines for Federal Workplace Drug Testing Programs; and procedures for interpretation, review, and reporting of results as specified by the Federal agency or agencies for which the individual may serve as MRO; and

- Satisfactorily passed an examination administered by an HHS-approved organization (i.e., a nationally recognized entity that certifies MROs or a subspecialty board for physicians performing a review of Federal employee drug test results). HHS publishes an annual list of approved organizations in the Federal Register.

The MRO serves as the common point of contact between all participants in a drug test (i.e., the donor, the collector, the test facility, 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 an instrumented initial test facility (IITF) or laboratory for which the MRO is reviewing drug test results, and

- The MRO must not derive any financial benefit by having an agency use a specific test facility or have any agreement with an IITF or laboratory that may be construed as a potential conflict of interest.

The purpose of these prohibitions is to prevent any arrangement between an IITF or laboratory and an MRO that could possibly influence the MRO and prevent him or her from reporting a problem identified with the test results or testing procedures.

The MRO has the following responsibilities:

- Review all specimens reported as positive, adulterated, substituted, invalid, or rejected for testing, and report the verified result to the Federal agency;

- Ensure that specimens reported as negative or as negative and dilute are properly reviewed (i.e., at least 5% personally and the remainder by staff under the MRO's direct, personal supervision) and reported to the Federal agency;

- Review the results of all Federal agency blind samples and perform the initial investigation into discrepant results;

- Discuss potential invalid results with the laboratory to determine whether further testing at another HHS-certified laboratory is warranted;

- Conduct or facilitate a medical evaluation of the donor when a collector reports that the donor was unable to provide a urine specimen;

- Perform an initial investigation of problems identified in the drug testing process and notify the appropriate regulatory authority of findings;

- Monitor the frequency of errors and notify responsible parties to take corrective action to prevent recurrence; and

- Maintain records and confidentiality of drug test information.

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

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 Custody and Control Form (CCF) for their agency workplace drug testing programs.

The following are examples of employers prohibited from using the Federal CCF:

- Private-sector employee drug testing programs, other than testing conducted under the Department of Transportation (DOT) regulations

- State workplace drug testing programs

- Department of Justice drug testing programs

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

The **2010 Federal CCF** has an **effective date of October 1, 2010**.

The **2000 Federal CCF** was published in the Federal Register on June 23, 2000 (65 FR 39155), with **an effective date of August 1, 2000**. To allow for depletion of existing supplies of the 2000 Federal CCF, OMB permitted the use of this Federal CCF in Federal workplace drug testing programs **through September 30, 2011**. Therefore, for one (1) year after the implementation of the revised 2010 Federal CCF on October 1, 2010, regulated specimens may be collected,

tested, and reported using the 2000 Federal CCF.

From October 1, 2010 through September 30, 2011, Federal agencies may use either Federal CCF for their workplace drug testing programs. However, because the two forms differ, the laboratory reporting the primary specimen may need to add additional information to the 2000 Federal CCF as described in *Chapter 4, Section A, Administrative Review of Documents* –see Item 6: Use of the 2000 Federal CCF.

As of October 1, **2011**, the 2010 Federal CCF will be the only Federal CCF for regulated specimens. If a regulated specimen is received at a test facility with the 2000 Federal CCF after September 30, 2011, the test facility (IITF or laboratory) must treat this as a correctable discrepancy as described in *Chapter 4, Section A, Administrative Review of Documents* –see Item 5(b): Actions Based on Administrative Review.

Links to both the **2010 Federal CCF** and the **2000 Federal CCF** are on the SAMHSA website **http://www.workplace.samhsa.gov/**

Federal CCF Description (2010 Federal CCF and 2000 Federal CCF)

Both are five-part forms and the function of each copy is the same:

Copy 1 – Test Facility Copy – sent to the IITF or laboratory with the specimen bottles

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 (ID) number. The CCF includes labels with the same ID number that the collector places on the specimen bottles (primary - Bottle A and split - Bottle B) to link the specimen to information on the CCF.

At the end of the collection, the collector separates the CCF and distributes the copies. Copies 2 through 5 (i.e., MRO, collector, employer, and donor copies) include donor information that is not provided on Copy 1 (i.e., test facility copy). Copy 1 is sealed and shipped with the specimen bottles to the test facility (i.e., IITF or laboratory).

The IITF or laboratory annotates the chain of custody section on the CCF to document receipt of the specimen. The IITF uses a separate transmittal chain of custody form (i.e., IITF Supplemental Custody and Control Form - see example in Appendix C) to document the transfer to the laboratory. The IITF sends the original Federal CCF Copy 1 and the supplemental form with the specimen to the laboratory. When testing has been completed, the IITF or laboratory records the results for a primary specimen (Bottle A) on the CCF by marking the appropriate result boxes and includes any additional comments concerning the specimen's testing or processing on the "Remarks" line. The original Federal CCF Copy 1 is retained in the specimen records at the test facility that reported the result. The IITF or laboratory reports results to the MRO as described below.

For negative and negative/dilute results, the IITF or laboratory is allowed to report results using a computer-generated report.

For rejected for testing specimens, the IITF or laboratory must send a copy or a legible image of the test facility copy of the Federal CCF (Copy 1) to the MRO. The IITF or laboratory is allowed to send a computer-generated report *in addition to* the Federal CCF.

For positive, adulterated, substituted, and invalid results, the laboratory must send a copy or a legible image of the test facility copy of the Federal CCF (Copy 1) to the MRO. The laboratory is allowed to send a computer-generated report *in addition to* the Federal CCF.

For specimens other than negative, laboratories are required to report all results for a specimen as supported by their data. Therefore, the MRO may receive a Federal CCF marked with more than one of the following results:

- Positive for one or more drugs (with the analyte concentration recorded on the Remarks line),
- 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 and value, as appropriate, 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.

Chapter 3. Urine Drug Testing

A. Federal Workplace Drug Testing Overview

Drugs

Federal agencies must test each specimen for marijuana and cocaine, and may test each specimen for opiates, amphetamines, and phencyclidine. **Appendix A** lists the analytes (i.e., drugs and drug metabolites) and test cutoffs specified by the Mandatory Guidelines.

Testing for an additional drug is allowed for the following reasons:

1. A Federal agency may test a specimen for another drug, on a case-by-case basis, when the agency is conducting a specimen collection for reasonable suspicion, post-accident, or unsafe practice testing. The specimen may be tested for any drugs listed in Schedule I or II of the Controlled Substances Act (other than drugs listed in Appendix A or when used pursuant to a valid prescription or when used as otherwise authorized by law). Information on drug schedules is available on the Drug Enforcement Administration website, http://www.justice.gov/dea/.

2. A Federal agency may routinely test its Federal employees for a drug or drug class other than those listed in Appendix A when the agency has been granted a waiver by the Secretary of HHS to do so.

For any circumstance where testing for an additional drug is justified or authorized as described above, 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 additional drug is specified on the Federal CCF (i.e., the "Other" checkbox is marked and the specific drug name is written on the appropriate line in Step 1). The collector attaches the Federal agency memorandum to the Federal CCF prior to transferring the specimen to an HHS-certified laboratory (not an IITF). If the memorandum is not provided, the laboratory must not test for the additional drug noted on the Federal CCF.

It is incumbent upon the Federal agency to ensure that the laboratory has validated initial and confirmatory drug tests for the additional drug(s). If an immunoassay test is not available for the initial test of the additional drug(s), the Federal agency may request the laboratory to perform the drug test for a specimen using the same confirmatory test on two separate aliquots.

Specimen Validity

Specimen validity testing must be performed for each Federal agency specimen. At a minimum, creatinine and pH must be determined for each specimen, specific gravity must be determined for each specimen with creatinine less than 20 mg/dL, and one or more tests for oxidizing adulterants must be performed. Federal agencies may order specimen validity tests in addition to those outlined above routinely (i.e., on every primary specimen) or on an individual specimen basis. Laboratories may also perform additional specimen validity tests when a specimen exhibits abnormal physical characteristics or abnormal drug test results (e.g., abnormal immunoassay absorbance reading, reduced internal standard recovery upon confirmatory drug testing). Specimen validity tests must be performed for split specimens (Bottle B) when a laboratory fails to reconfirm a drug analyte reported positive in the primary specimen (Bottle A).

Specimen Collection

The MRO must be very familiar with the specimen collection procedures required by the Mandatory Guidelines. At this time, urine is the only specimen allowed for Federal agency workplace drug testing. Each Federal agency specimen is collected as a split specimen. The collector prepares a split specimen by pouring the urine from the collection container into two bottles, which are then labeled as Bottle A (the primary specimen) and Bottle B (the split specimen). The HHS Urine Specimen Collection Handbook (available at http://www.workplace.samhsa.gov) contains guidance for collectors to supplement the collection procedures required by the Mandatory Guidelines.

Security and Chain of Custody

The Mandatory Guidelines specify requirements for collection sites, IITFs, and laboratories to ensure the security and integrity of specimens and to maintain confidentiality of donor and drug test information. Collection sites, IITFs, and laboratories must be secured, with access limited to authorized personnel, to prevent unauthorized access to specimens, aliquots, and records.

A permanent site used solely for specimen collections must be secured at all times. At facilities

that are not dedicated specimen collection sites, access to the area used for specimen collections must be restricted to only authorized personnel during the collection. Individual areas within an IITF or laboratory (e.g., receiving/accessioning area, testing areas, sample preparation area, specimen and records storage areas) are usually separately secured, to limit access to staff with job duties in the area. All visitors to secured areas within a test facility must be escorted and their access must be documented.

All Federal agency 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. The collector initiates the chain of custody documentation for the specimen using the Federal CCF, and must maintain line-of-sight custody or provide for the secure storage of specimens from the time the specimen is collected until the bottles are sealed in a shipping container prior to transfer. Since specimens are sealed in packages that would indicate any tampering during transit to the test facility, there is no requirement for delivery service personnel (e.g., couriers, express carriers, postal service personnel) to document chain of custody.

IITFs and laboratories annotate the appropriate chain of custody section of the Federal CCF upon receipt of the specimen, and continue chain of custody documentation using internal forms. At the test facility, all specimens and all aliquots taken from each specimen are kept in secured storage or in the line of sight 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. When an IITF forwards a specimen to a laboratory for testing, the IITF initiates a separate chain of custody form (i.e., IITF Supplemental Custody and Control Form) to document the transfer to the laboratory. This form is sent with the specimen to the laboratory and is used by the laboratory to continue the chain of custody documentation. An example form is provided in **Appendix C** of this Manual.

Specimen and Records Storage

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

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

A Federal agency may request the laboratory to retain a specimen for a longer period (e.g., specimens under legal challenge). The agency's request must be in writing and must specify the period of time for specimen retention.

IITFs and laboratories may discard negative, negative-dilute, and rejected specimens after reporting them to the MRO.

Collection site records (e.g., collector copies of the Federal CCF) must be maintained for at least two years by the collector or collector employer. IITFs and laboratories must maintain records generated to support test results for a minimum of two years. A Federal agency may request the test facility to maintain a copy of the documentation package for a specimen that is under legal challenge (see Chapter 6, Section D, *Donor Rights to Information*). The agency's request must be in writing and must specify the period of time for record retention.

Testing

Test facilities must be certified by HHS in order to test Federal agency workplace specimens. HHS publishes a monthly list of certified test facilities in the Federal Register. The two types of test facilities allowed under the Mandatory Guidelines are Initial Instrumented Test Facilities (IITFs) and laboratories.

IITFs perform only the first tests for a specimen, and are allowed to report specimens as negative, negative and dilute (with creatinine greater than 5 mg/dL), and rejected for testing. All other federally regulated specimens must be forwarded to an HHS-certified laboratory for testing.

Laboratories perform all tests for a specimen (initial and confirmatory) and are the only facilities that may report specimens as positive, adulterated, substituted, invalid, and dilute (with creatinine less than or equal to 5 mg/dL).

For forensic as well as scientific acceptability, laboratories are required to perform initial and confirmatory tests using separate aliquots of a specimen to support a positive, adulterated, or substituted result. The confirmatory test uses a different test method that is usually more specific than the initial test. Laboratories must also test two separate aliquots of a specimen prior to reporting the specimen as invalid. Specimen reporting criteria are in **Appendix A**.

The MRO is not allowed to request retesting of a primary specimen (Bottle A). Primary specimens may be reanalyzed only:

- When a Federal Agency has requested reanalysis as part of a legal or administrative proceeding to defend an original positive, adulterated, or substituted result.

- When the MRO (on behalf of the donor) has requested analysis of the primary specimen (Bottle A) for adulteration and/or substitution because a second HHS-certified laboratory failed to reconfirm the drug(s) reported in the primary specimen, and reported that the split specimen (Bottle B) was adulterated or substituted.

- When HHS has directed the laboratory to reanalyze the specimen.

When the primary specimen (Bottle A) is positive, adulterated, or substituted, the donor is given an opportunity to request testing of the split specimen (Bottle B) at a second HHS-certified laboratory. Split specimens are tested using only the confirmatory test(s) needed to reconfirm the primary specimen result(s), and split specimen test results are not subject to the HHS test cutoffs. Chapter 4, Section E, *Interpretation and Result Verification,* has additional information concerning testing of split specimens for amphetamines. If the laboratory fails to reconfirm one or more drug analytes reported as positive in the primary specimen (Bottle A), the laboratory performs specimen validity tests for the split specimen (Bottle B).

If the split testing laboratory believes that the analyte (i.e., drug, drug metabolite, adulterant) is present in the split specimen (Bottle B), but cannot reconfirm its presence, the laboratory must consult with the MRO to decide whether to send the specimen to a third HHS-certified laboratory for additional confirmatory testing. The third laboratory should be selected such that it uses a confirmatory test method more similar to that used by the first laboratory (i.e., the laboratory that reported the primary specimen result).

If a donor chooses not to have the split specimen (Bottle B) tested, a Federal agency may have the split specimen tested as part of a legal or administrative proceeding as part of a legal or administrative proceeding to defend an original positive, adulterated, or substituted result.

B. Test Methods

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

Initial drug tests

IITFs and laboratories are required to use **immunoassay** for initial drug tests. Immunoassays are immunochemical testing methods that use antigen (drug) and antibody binding to identify drug analytes. The antibodies are produced to be drug-specific. A known amount of antibody is added to a specimen, along with a drug that has been labeled to distinguish it from the drug in a donor's urine specimen. The labeled drug and the unlabeled drug (if any) compete for the antibody, to form an antigen-antibody complex. The ratio of the labeled and unlabeled drug bound to the antibody allows the measurement of the amount of drug in the donor's urine specimen. Immunoassays are used as initial drug tests to identify specimens that require further testing. 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 must be further tested using a different analytical method as a confirmatory test.

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

Confirmatory Drug Tests

Laboratories are required to use a confirmatory drug test method different from the initial test method (i.e., immunoassay), to specifically identify and quantify the drug or drug metabolite. The analytical method used for the confirmatory drug test must combine **chromatographic separation and mass spectrometric identification**. For confirmatory drug testing, the Mandatory Guidelines require laboratories to use a combined analytical method coupling a chromatographic instrument with a mass spectrometer. Chromatographic techniques such as gas chromatography (GC) and liquid chromatography (LC) are used to separate and analyze mixtures of chemical substances. After the chromatographic instrument has separated the analytes in a specimen, the specimen enters the mass spectrometer (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. Urine specimens must undergo a specimen preparation process (i.e., extraction) prior to GC/MS analysis and may require preparation prior to LC/MS analysis.

Specimen Validity Tests

The Mandatory Guidelines specify test method requirements for some specimen validity tests (e.g., refractometry for specific gravity testing, pH meter tests for the initial and confirmatory pH tests). However, it is not possible to provide guidance on test methods for all substances that may be used to adulterate a urine specimen. As new adulterants are identified, IITFs and laboratories are permitted to implement appropriate tests for their analysis. There may be more than one acceptable test method for a particular measurand. *All* specimen validity tests must be scientifically and forensically supportable.

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

C. Drug Information

The Federal Government classifies controlled substances under five schedules established under the Controlled Substances Act (CSA). Information on drug schedules is available on the DEA website (http://justice.gov/dea/).

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 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 that specifically identifies the major marijuana metabolite, delta-9-tetrahydrocannabinol-9-carboxylic acid (commonly referred to as THCA or THC-COOH).

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 THCA 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. 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 to 30 minutes, and may persist for 2 to 4 hours. Intoxication temporarily impairs concentration, learning, and perceptual-motor skills. Reduced functional ability lasts for at least 4 to 8 hours after a dose of marijuana, beyond the user's perception of the high.

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 marijuana is used at the usual doses.

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, putting THC into the bloodstream and causing 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 bloodstream at very low levels, permitting metabolism and eventual excretion. THC is metabolized extensively in the liver and the major metabolite is delta-9-tetrahydrocannabinol-9-carboxylic acid (THCA or THC-COOH).

The immunoassay procedures detect multiple metabolites of marijuana, while the confirmatory test specifically identifies and quantitates delta-9 THCA. To be reported positive, a specimen must test positive at or above the 50 ng/mL cutoff for the initial test and have a concentration of the 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 to 5 days. 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. Crack is smoked because, unlike cocaine hydrochloride, free base cocaine survives

high temperatures and is absorbed into the bloodstream as rapidly as if it were injected. Cocaine is rapidly metabolized to its major metabolite, benzoylecgonine. The Federal drug testing program requires analysis for the cocaine 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 can usually be detected in urine for two to three days after a single dose using a test cutoff of 300 ng/mL. The detection window may be longer using the 150 ng/mL initial test cutoff and 100 ng/mL confirmatory test cutoff specified by the Mandatory Guidelines. Cocaine and benzoylecgonine are not significantly stored in the body. Therefore, even after heavy, chronic use, urine specimens may be negative when collected several 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, drugs that in moderate doses dull the senses, relieve pain, and induce deep sleep. Excessive doses of such drugs cause stupor, coma, or convulsions. 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. Depending on concentration and preparation, codeine medications are available as a prescription drug (Schedule II and Schedule III) and over-the-counter (Schedule V). Codeine is commonly used in analgesic, antitussive, and anti-diarrheal agents.

- Heroin (diacetylmorphine) – is a semisynthetic opiate obtained by reacting natural morphine with acetic anhydride. 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 miosis, 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.

2. Metabolism and Excretion

Morphine is rapidly absorbed and excreted as:

- unchanged morphine

- glucuronide conjugates

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

- minor metabolites (e.g., normorphine, morphine-3-ethereal sulfate, morphine-3,6-diglucuronide)

Morphine and its metabolites can be detected in urine up to about 4 days after morphine use. Morphine is ***not*** metabolized to codeine.

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

- unchanged codeine,
- morphine

- glucuronide conjugates

    - codeine-6-glucuronide
    - morphine-3-glucuronide
    - morphine-6-glucuronide
    - minor metabolites (e.g., norcodeine, normorphine, morphine-3-ethereal sulfate, morphine-3,6-diglucuronide)

The presence of both codeine and morphine in urine indicates 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-acetylmorphine (6-AM), within minutes of administration, and 6-AM is further metabolized to morphine. Therefore, heroin itself is rarely detected in urine. 6-AM is most likely to be detected within the first 24 hours post-administration because of heroin's 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.

Additional issues regarding opioids:

- Poppy seeds are a significant dietary source of morphine and/or codeine. 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).
    - 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.

- In October 2010, HHS revised the Mandatory Guidelines to require laboratories to test all Federal agency specimens for heroin metabolite (6-AM) regardless of morphine concentration, by performing a 6-AM initial test and confirmatory test. The requirement was implemented because data from laboratories indicated that 6-AM could be present in specimens with morphine less than 2000 ng/mL.

- Synthetic or semi-synthetic narcotics do <u>not</u> metabolize to codeine, morphine, or 6-acetylmorphine. These include, *but are not limited* to:

    - alphaprodine
    - hydromorphone
    - oxymorphone

- hydrocodone
- dihydrocodeine
- oxycodone
- propoxyphene
- methadone
- meperidine
- fentanyl
- pentazocine
- buprenorphine
- tramadol

- Products containing codeine or morphine are available by prescription or over-the-counter (OTC). MROs should have access to references with up-to-date information on such products. (*Some example references are listed at the end of this manual*.)

Note: Further information regarding the interpretation and reporting of opiates is found in Chapter 4, Section E, *Interpretation and Result Verification*.

Amphetamines

Amphetamine and Methamphetamine

1. Background

Amphetamine and methamphetamine are substances regulated under the CSA 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 five 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).

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 unchanged if urine is acidic, while 1 to 2 percent 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 an OTC product such as the Vicks® VapoInhaler® that contains l-methamphetamine (also called *l*-desoxyephedrine or levmetamfetamine), 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.

Products containing amphetamine and/or methamphetamine and substances that are metabolized to amphetamine and/or methamphetamine are available by prescription or OTC. MROs should have access to references with up-to-date information on such products. (*Some example references are listed at the end of this manual*.)

Table 3 lists some substances known to metabolize to amphetamine and methamphetamine.

Methylenedioxymethamphetamine (MDMA) and Methylenedioxyamphetamine (MDA)

1. Background

3,4-Methylenedioxymethamphetamine (MDMA, “Ecstasy,” “Adam,” “E,” “XTC”) and its major, active metabolite, 3,4-methylenedioxyamphetamine (MDA, EA-1299, “Love”), are psychoactive amphetamines regulated under the Controlled Substances Act as Schedule I drugs. Both MDMA and MDA are available as illicit parent drugs.

MDMA and MDA are central nervous system stimulants and are used recreationally as hallucinogens.

Both MDMA and MDA can exist as *d*- and *l*-enantiomers (see above definition under *Amphetamine and Methamphetamine*). Both enantiomeric forms of MDMA and MDA are illicit and categorized as Schedule I.

Routes of administration:

- MDMA - oral (i.e., tablets) is the most common.
- MDA - oral (i.e., tablets) is the most common although the drug also may be administered intravenously.

A tablet contains approximately 100 mg, although street samples vary in dose and potency, and a typical oral dose is one to two tablets. Effects last for 3 to 6 hours. These include feelings of energy, altered sense of time, and pleasant sensory experiences with enhanced perception. Negative symptoms include tachycardia, dry mouth, jaw clenching, and muscle aches.

2. Metabolism and Excretion

MDMA is metabolized primarily by demethylation to form the active metabolite, MDA, and breaking the methylenedioxy bridge to form hydroxymethoxy- and dihydroxy- derivatives.

The anticipated time to a negative result after the last use of MDMA or MDA is approximately 1 to 2 days.

Methylenedioxyethylamphetamine (MDEA)

1. Background

3,4-Methylenedioxyethylamphetamine (MDEA, MDE, “Eve”) is closely related structurally to MDMA and MDA. MDEA is a Schedule I drug.

Like MDMA and MDA, MDEA is widely abused for its hallucinogenic properties. The illicit forms of the drug may also contain MDMA and MDA.

MDEA can exist as *d*- and *l*-enantiomers (see above definition under *Amphetamine and Methamphetamine*). Both enantiomeric forms of MDEA are illicit and categorized as Schedule I.

Routes of administration:

- MDEA - oral (i.e., tablets or capsules) is the most common.

2. Metabolism and Excretion

Like MDMA, MDEA is metabolized through N-dealkylation (de-ethylation) to the active metabolite, MDA, and by oxidative cleavage of the methylenedioxy ring to HMEA (4-hydroxy-3-methoxyethylamphetamine). The metabolism of a single dose results in a 32-hour urine that contains about 19% as the parent drug (MDEA), 28% as MDA, and 32% as HMEA, with trace

amounts of at least eight other metabolites. The anticipated time to a negative result after the last use of MDEA is approximately 1 to 2 days.

Note: Further information regarding the testing, result interpretation, and reporting of amphetamines is found in Chapter 4, Section E, *Interpretation and Result Verification*.

Phencyclidine (PCP)

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 as an injectable short-acting anesthetic in humans and animals. 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 4 to 19 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 reenters 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.

D. 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 test facility 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 Mandatory 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 initial 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 method. Currently, GC/MS assays for marijuana metabolite (THCA) and opiates appear to be affected by adulterants more than GC/MS assays for other drugs.

When an IITF is unable to obtain a valid initial drug test result or when the IITF drug or specimen validity tests indicate a possible unidentified adulterant, the IITF sends the specimen to an HHS-certified laboratory for testing. 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 must contact the MRO prior to reporting a specimen as invalid, to discuss 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 suspected 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.

Note*:* Laboratories are not required to contact the MRO when a specimen meets criteria for reporting as invalid based on creatinine and specific gravity results, on pH, or on a confirmatory nitrite test concentration below 500 mcg/mL. It is unlikely that testing by another certified laboratory would provide different results.

Because it is not possible to provide specific program guidance for *all* substances that may be used as adulterants, HHS allows certified IITFs and laboratories to test for any adulterant. However, HHS has included specific requirements in the Mandatory Guidelines for pH analysis and for the analysis of the known adulterants listed below. **Appendix A** describes Specimen

Reporting Criteria from the Mandatory Guidelines.

The **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.

Research has shown that a specimen's pH may increase up to 9.5 in vitro when the specimen is subjected to high temperatures for an extended time. Therefore, conditions during specimen transport and storage may cause pH to be within the invalid range (i.e., greater than or equal to 9 and less than 11.0). Note*:* see Table 5, *MRO Actions for Primary Specimen Reports (Bottle A),* concerning specimens reported as invalid based on pH between 9.0 and 9.5.

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. HHS set an initial test cutoff level of 50 mcg/mL for chromium (VI). Because the presence of chromium (VI) in a urine specimen is indicative of adulteration, laboratories report a specimen as adulterated when chromium (VI) is present at any concentration at or above the confirmatory test limit of quantitation (LOQ).

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 which suspend respectively, a gas, an immiscible liquid, or a solid in water or some other liquid. Surfactants tend to clump together when in solution, forming a surface between the fluid and air, with their hydrophobic components in the air and their hydrophilic components in the fluid. Often, surfactants will form "bubbles" within the fluid: a small sphere of hydrophobic “heads” surrounding a pocket of air containing the hydrophilic “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). HHS set an initial test cutoff level of 100 mcg/mL dodecylbenzene sulfonate equivalents. Laboratories report a specimen as adulterated when a surfactant is verified as present at or above a concentration equivalent to 100 mcg/mL dodecylbenzene sulfonate using a confirmatory test.

Halogens are the four elements fluorine, chlorine, bromine, and iodine. Halogen compounds have been used as oxidizing 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 (e.g., NaCl, KCl, NaI) which may be present in a urine specimen. An oxidative halogen present at any concentration at or above the confirmatory test LOQ 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 present at any concentration at or above the confirmatory test LOQ 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 is 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 present at any concentration at or above the confirmatory test LOQ is evidence of adulteration.

E. Dilution/Substitution

A donor may attempt to decrease the concentration of drugs or drug metabolites that may be present in his/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 these 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., 32º to 38ºC/90º to 100ºF). Some include prosthetic devices to deceive the observer during an observed collection.

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

Creatinine is endogenously produced and cleared from the body by the kidneys. It is a normal constituent in urine. Normal human urine creatinine concentrations are at or above 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 dissolved 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 and IITFs are required to measure the creatinine concentration in all regulated specimens, and to test specific gravity for specimens with creatinine concentration 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 Specimen Reporting Criteria from the Mandatory Guidelines.

Chapter 4. The MRO Review and Reporting Process

The MRO must review all positive, adulterated, substituted, and invalid test results before reporting the results to the Federal agency's designated representative. Staff under the direct, personal supervision of the MRO may review and report negative and negative-dilute specimen results. The MRO must review at least five percent of the specimen results reported by staff to ensure that staff are properly performing the review process.

The MRO process consists of:

- Administrative review of documents,
- Interview with the donor (as required),
- Handling split specimen (Bottle B) test requests (as required),
- Result interpretation and verification, and
- Reporting the drug test 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

NOTE: The following Federal CCF description and instructions are for the **2010 Federal CCF**.

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 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 MRO verifies the following items on 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 ID number.

c. Each test facility is identified by one of the following:

- A specific IITF or 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 test facility to which the specimen will be delivered), or

- A corporate name and telephone number at the top of the Federal CCF (Note: the test facility that reports the specimen results to the MRO will annotate Copy 1 to include the specific name and address in the "Test Facility" line in Step 5a).

d. The Federal CCF was properly completed:

- Step 1 contains:

  - Federal agency name and address and employer identification number (as appropriate),
  - MRO name, address, telephone number, and fax number,
  - Donor identification (e.g., social security number, employee identification number),
  - Testing authority (i.e., HHS, NRC, specific DOT agency, USCG),
  - Reason for the test,
  - Drug 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, (Note split specimen collections are required for Federal agency specimens.)
  - 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 test facility.

- 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. Test Facility Report - Federal CCF (Copy 1) and/or Computer-Generated Electronic Report

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

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

The following items are verified for the report(s) for a specimen:

a. The specimen ID number on the test facility copy of the Federal CCF (Copy 1) and/or any other report matches that on the MRO copy (Copy 2) for the identified donor.

b. Copy 1 (the test facility copy) of the Federal CCF was properly completed:

- Step 4 contains:
  - IITF or laboratory accessioner's printed name,
  - Accessioner's signature,
  - Date of receipt, and
  - Documentation of the primary (Bottle A) specimen bottle seal condition upon receipt at the test facility.
- Step 5a contains:
  - Primary specimen (Bottle A) test results,
  - Certifying technician or certifying scientist's printed name,
  - Certifying technician or 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, substituted, rejected for testing, invalid result, or dilute (see Table 4)
    - Observations or explanatory comments recorded by IITF and/or laboratory staff concerning the specimen, and

- Name and address of the test facility reporting the specimen results (if not at the top of the Federal CCF).

- If the split specimen (Bottle B) was tested, Step 5b contains:

  - Name and address of the split testing laboratory
  - Results for the split specimen, with the certifying scientist's signature and printed name and the date of certification
  - A reference to the separate laboratory report in the Reason line in Step 5b of the CCF.

c. For a split specimen (Bottle B), the laboratory's Split Specimen Report was properly completed and contains, at a minimum, the following:

- Laboratory name and address

- MRO name and fax number

- Specimen ID number

- Laboratory accession number

- Donor identification (social security number or employee ID number), if provided

- RECONFIRMED result

  - For RECONFIRMED drug results: the specific drug analyte(s) reconfirmed
  - For RECONFIRMED adulterated results: ADULTERATED with the measurand(s) reconfirmed
  - For RECONFIRMED Substituted: SUBSTITUTED with the creatinine and specific gravity values

- FAILED TO RECONFIRM result

  - For FAILED TO RECONFIRM drug results: the specific drug analyte(s) not reconfirmed
  - For FAILED TO RECONFIRM adulterated results: NOT ADULTERATED with the measurand(s) not reconfirmed
  - For FAILED TO RECONFIRM substituted results: NOT SUBSTITUTED

- For FAILED TO RECONFIRM drug results: the specimen validity tests performed, the results of all specimen validity tests (screening/differential, initial, confirmatory), and the determination based on specimen validity testing (i.e., ADULTERATED with adulterant/reason, SUBSTITUTED with confirmatory creatinine and specific gravity values, INVALID with required comment)

- Certification statement

- Certifying scientist signature, printed name, and certification date

- Required comments/explanatory remarks for RECONFIRMED results, and

- Required comments/explanatory remarks for FAILED TO RECONFIRM results

d. Memoranda for the record from the collector, IITF, or laboratory to address any correctable discrepancies identified. (See below Item 3, *Federal CCF or Specimen Errors*).

e. The computer-generated electronic report (if any) contains the HHS-required information as follows:

- Test facility name and address,

- Federal agency name,

- MRO name,

- Specimen ID number,

- Donor identification from the Federal CCF (e.g., social security number, employee ID number),

- Collector name and telephone number,

- Reason for test (if provided),

- Date of collection,

- Date received at IITF and/or laboratory,

- Certifying technician or certifying scientist's name,

- Date certifying technician or certifying scientist released the results,

- CCF result(s) annotated, and

- Additional comments concerning the specimen's testing and processing, as listed in the "Remarks" line of the Federal CCF.

f. The information on the computer-generated electronic report (if any) is consistent with that on the test facility copy of the Federal CCF (Copy 1).

3. Federal CCF or Specimen Errors

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

a. **Fatal flaws** that result in specimen rejection by the IITF or laboratory and test cancellation by the MRO:

- Specimen ID numbers on the Federal CCF and the label/seal of either the primary (Bottle A) or split specimen (Bottle A) do not match, or the number is missing on either the Federal CCF or the primary or split specimen bottle label/seal,

- The specimen bottle label/seal is missing or broken on the primary specimen (Bottle A) 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,

- There is insufficient specimen volume for testing in the primary specimen (Bottle A), and the split specimen (Bottle B) cannot be redesignated as the primary specimen,

- The accessioner at the IITF did not mark the Bottle A seal condition on the CCF and the split specimen (Bottle B) cannot be redesignated as the primary specimen,

- The accessioner at the laboratory failed to mark the primary bottle seal condition,

- The collector used a non-Federal form or an incorrect version of the Federal CCF (and the specimen was NOT tested in accordance with Mandatory Guidelines requirements - unless the IITF or laboratory obtains approval from HHS to report the results to the MRO), or

- The donor has requested testing of the split specimen (Bottle B), and the split specimen is not available, has a broken/missing bottle seal, or has insufficient volume for testing.

b. **Correctable discrepancies** that result in specimen rejection and/or cancellation unless corrected by a memorandum for the record (MFR) from the collector or IITF (as applicable):

    - The collector failed to sign the CCF (but the printed name is present).

    - The collector used a non-Federal form or an incorrect version of the Federal CCF (and the specimen was tested in accordance with Mandatory Guidelines requirements).

    - The IITF redesignated the primary specimen (Bottle A) and split specimen (Bottle B), but failed to include a comment on the Federal CCF.

c. **Federal CCF omissions and discrepancies** that are considered insignificant when they are infrequent (i.e., when a collector or an IITF or laboratory staff member does not make the error more than once a month). Examples include, *but are not limited to*:

    - Incorrect IITF or laboratory name and address,

    - Incomplete/incorrect/unreadable employer name or address,

    - No MRO name,

- Incomplete/incorrect MRO address,
- Transposition of numbers in the donor's ID number,
- Missing/incorrect telephone or fax number,
- A "reason for test" box is not marked,
- A "drug tests to be performed" box is not marked,
- The single or split specimen collection box is not marked,
- The "observed" box is not marked for an observed collection,
- No collection site address,
- No collection date/time,
- No courier entry,
- Incorrect name of delivery service,
- Donor name included on the test facility copy of the CCF,
- No temperature marked and no explanatory comment in the Remarks line,
- Signature present without printed name (i.e., of collector, accessioner, certifying technician or certifying scientist), or
- Certifying technician or certifying scientist initialed instead of the signing the CCF for a rejected specimen.

d. **Administrative errors** 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*:

- The donor's signature is missing on the MRO copy of the Federal CCF and the collector failed to provide a statement that the donor refused to sign the form,
- No certifying scientist signature on the CCF for a positive, adulterated, substituted or invalid specimen, or
- The electronic report from the IITF or laboratory did not contain all required data elements for a positive, adulterated, substituted, invalid or rejected specimen.

e. **Report discrepancies** may be identified by an IITF or laboratory after a report has been sent to the MRO, or may be identified by an MRO during administrative review. Examples include incorrect or outdated CCF information (e.g., account number), data entry errors due to illegible or misread CCF information, data review or transcription

errors by the certifying technician or certifying scientist, or a discrepancy between the Federal CCF and electronic report. The IITF or laboratory must reissue the report and/or send an MFR to document the correct information in the specimen records.

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. IITF and 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., quantitative results, creatinine and specific gravity values supporting a substituted result, the basis for reporting a specimen as adulterated, the basis for reporting a specimen as invalid, the reason for rejection – see **Table 4** at the end of this Manual).

The MRO evaluates whether the information provided on the Federal CCF Remarks lines has 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/she either attempts to obtain an MFR or cancels the test.

5. Actions Based on Administrative Review

a. When a **fatal flaw** is identified (as defined in Item 3.a above):

- If an IITF or laboratory identifies the error, the IITF or laboratory rejects the specimen and reports the specimen as rejected for testing to the MRO. The reason for rejection is included on the CCF and any other report to the MRO.

- If the MRO receives a rejected for testing specimen report or identifies a fatal flaw during review, the MRO cancels the test.

- 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.

b. When a **correctable discrepancy** (as defined in Item 3.b above) by the collector or IITF is identified by either the IITF, the laboratory, or the MRO, the responsible party is notified to provide an MFR to address the error:

- For a missing collector signature:

  - If the collector **provides** an MFR, the IITF or laboratory includes a copy of the MFR with the report to the MRO. The MRO reports the verified result to the Federal agency and maintains the MFR in the files for the specimen.

  - If the collector **does not provide** an MFR, the IITF or laboratory holds the specimen for a minimum of five business days after requesting the MFR, then reports the specimen as rejected for testing and discards the specimen. The reason for rejection is included on the report(s) to the MRO. The MRO cancels the test and notifies the Federal agency of the cancelled test and the reason for

- For a regulated specimen submitted with a non-Federal form or an incorrect Federal CCF (e.g., the 2000 Federal CCF as of October 1, 2011):

    - If the collector provides an MFR AND the specimen was tested in accordance with the Mandatory Guidelines, the IITF or laboratory will report the specimen based on test results. The MRO reports the verified result to the Federal agency and maintains the MFR in the files for the specimen.

    - If the collector provides an MFR BUT the specimen was tested as non-regulated using procedures different from those specified in the Mandatory Guidelines, IITFs and laboratories have been instructed to contact HHS for guidance. The IITF or laboratory reports the specimen per HHS and submits the written HHS instruction on reporting the specimen to the MRO with the specimen report. If the specimen is reported as rejected for testing, the IITF or laboratory discards the specimen and includes the reason for rejection on the report(s) to the MRO. The MRO cancels the test and notifies the Federal agency of the cancelled test and the reason for cancellation. If the IITF or laboratory reports the specimen based on test results, the MRO reports the verified result to the Federal agency and maintains the MFR in the files for the specimen.

    - If the collector does not provide an MFR for either situation described above, the IITF or laboratory holds the specimen for a minimum of five business days after requesting the MFR, then reports the specimen as rejected for testing and discards the specimen. The reason for rejection is included on the report(s) to the MRO. The MRO cancels the test and notifies the Federal agency of the cancelled test and the reason for cancellation.

- For a regulated specimen received at an HHS-certified laboratory with redesignated primary (Bottle A) and split specimen (Bottle B) bottles and no IITF explanatory comment on the Federal CCF:

    - If the IITF provides an MFR, the laboratory includes a copy of the MFR with the report to the MRO. The MRO reports the verified result to the Federal agency and maintains the MFR in the specimen records.

    - If the IITF does not provide an MFR, the laboratory holds the specimen for a minimum of five business days after requesting the MFR, then reports the specimen as rejected for testing and discards the specimen. The reason for rejection is included on the report(s) to the MRO.

c. When a **significant administrative error** is identified by the MRO (as defined in Item 3.e above), the MRO notifies the responsible party to provide an MFR to address the error. If the MFR is not provided within 5 days after this notification, the MRO must cancel the test.

d. When a report discrepancy is identified (as defined in item 3.f above), the IITF or laboratory must reissue a report and/or provide an explanatory MFR, depending on the significance of the discrepant information. A reissued report will be either:

- A **corrected report** when the IITF or laboratory has changed specimen identification or results (e.g., corrected donor ID or test facility accession number; a positive result changed to negative; a positive result for a different drug; a substituted result changed to invalid). The reissued report must be identified as a "corrected report," and have the re-transmission date on the report.

- An **amended report** when the IITF or laboratory has changed information other than the specimen identification or result s (e.g., employer name, account number) or has provided additional information for a reported specimen (e.g., additional quantitative results, methamphetamine enantiomer results for a specimen reported as positive for methamphetamine). The report will be reissued with the revised/new information.

The MRO must document and monitor the frequency of errors made by collectors, IITF staff, and laboratory staff. HHS-certified IITFs and laboratories have been instructed to note and report to the MRO when an identified error was caused by the collector. HHS-certified laboratories have also been instructed to note and report to the MRO when they have identified procedural or documentation errors made by IITF staff. The MRO also may identify errors during his/her administrative review. The MRO must maintain a record of such errors. When the MRO documents frequent errors (i.e., more than once a month) by an individual collector or staff member at an IITF or laboratory:

a. The MRO notifies the responsible party of the errors.

b. The collector/collection site, IITF, or laboratory takes appropriate corrective actions (e.g., revises procedures, retrains the individual and other staff) 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/her records.

6. Use of the 2000 Federal CCF

The Federal CCF implemented August 1, 2000 may be used for federally regulated drug testing specimens **through September 30, 2011**. The MRO uses the same procedures as above for administrative review this CCF Version. In addition, due to differences between this CCF and the 2010 Federal CCF, the following information should be added to the 2000 CCF:

a. Copy 1: The employer, Federal agency representative, or collector should write the testing authority (i.e., HHS, NRC, specific DOT agency, USCG) in Step 1. Note: No action is taken by the MRO if this information is omitted.

b. Copy 1, Step 4: the IITF accessioner must mark through "laboratory" and annotate "IITF" on the accessioner chain of custody section in Step 4.

c. Copy 1, Step 5a: If a specimen is reported positive for a drug analyte that is not printed on the Federal CCF, the laboratory certifying scientist must mark the "positive for" checkbox and record the analyte name and concentration on the Remarks line. Note: the MRO must obtain an MFR from the certifying scientist if the positive analyte information on the Federal CCF is not consistent with the laboratory's computer-generated electronic report (if provided).

As of October 1, 2011, the 2010 Federal CCF must be used for all Federal agency workplace specimens. The use of the 2000 Federal CCF for a specimen collected as of October 1, 2011 is a correctable discrepancy (see above for actions to be taken for specimens with an incorrect Federal CCF).

B. Donor Interview

The MRO must contact the donor and interview the donor when the donor's specimen is reported by the laboratory as positive, adulterated, substituted, and/or 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/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 five days, and

    - Inform the MRO once the donor has been so instructed or if 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 five days after being contacted by the Federal agency.

The Interview Process

1. Positively identify the donor by requesting the donor to provide identifying information (e.g., employee identification number, social security number) 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 that the drug use was associated with a valid medical procedure, or is taking a medication that may have interfered with the drug test), 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, adulterated, or substituted results:** Inform the donor that he/she may have the split specimen (Bottle B) tested at a second certified laboratory. The split specimen test request must be made within 72 hours of the interview with the MRO. Note: donors are not allowed to request split specimen (Bottle B) testing when the primary specimen (Bottle A) was reported as invalid.

   a. If the donor requests split specimen (Bottle B) testing, use the procedures described in Chapter 4, Section D (Split Specimen Tests) to direct the laboratory to send the split specimen to another certified laboratory for confirmatory testing.

   b. If the donor does not request testing of the split specimen (Bottle B), document that the donor was informed of and declined the opportunity to test the split specimen.

   c. **For invalid results:** Note: donors are not allowed to request split specimen (Bottle B) testing when the primary specimen (Bottle A) was reported as invalid.

C. Refusal to Test

The Mandatory Guidelines specify the circumstances under which a collector or an MRO reports a refusal to test to the Federal agency. The Federal agency will take disciplinary action against the donor, up to and including dismissal. The MRO reports a refusal to test to the Federal agency in the following instances:

1. The drug test result is verified by the MRO as adulterated or substituted.

2. The donor admits to the MRO that he or she adulterated or substituted the specimen.

3. The donor refuses to participate at any point in the drug testing process, including failure to undergo a medical evaluation as directed by the MRO as part of the verification

process or by the Federal agency (e.g., when the donor failed to provide a sufficient specimen).

- EXCEPTION: for a Federal agency applicant/pre-employment test, if the donor does not undergo a medical evaluation and there has been no offer of employment contingent upon the drug test, the MRO cancels the test.

When the MRO reports a refusal to test based on the donor's refusal to participate during the drug testing process, the MRO must immediately notify the Federal agency's designated representative (e.g., by telephone or secure fax machine).

D. Split Specimen Tests

Note: Donors are not allowed to request split specimen (Bottle B) testing of primary specimens (Bottle A) reported as invalid.

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

1. The MRO must inform the donor that he or she has the opportunity to request testing of the split specimen (Bottle B) when the MRO informs the donor that his or her primary specimen (Bottle A) is being reported as positive, adulterated, or substituted to the Federal agency. The donor has 72 hours from the time he or she is notified to request the split specimen test. The MRO must document the donor's verbal request in the MRO records.

2. The MRO must request testing of the split specimen (Bottle B) 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 (Bottle A) was tested and must contain the following information:

    a. MRO name and address (use MRO letterhead),
    b. Laboratory name and address (i.e., Laboratory A) where the primary specimen analysis was performed,
    c. Specimen ID number on the Federal CCF,
    d. Laboratory accession number (i.e., the number assigned by Laboratory A to the specimen when it was accessioned),
    e. Request for confirmatory testing for the drug/metabolite, adulterant, or substitution reported by Laboratory A, and
    f. Name and address of the HHS-certified laboratory (i.e., Laboratory B) selected to test the split specimen (Bottle B).

3. Laboratory B may be selected by the MRO, the Federal agency, or the donor. In most instances where split specimen (Bottle B) testing is requested, the first laboratory will have blanket purchase agreements with two or three other certified laboratories to make the billing and payment process easier.

4. 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 reports to the Federal agency and the donor that the test is cancelled and the reason for cancellation.

- The MRO directs the Federal agency to immediately collect another specimen **under direct observation**, with no notice given to the donor until immediately before the collection.

- If the test is cancelled because no other certified laboratory tests for the specific adulterant, the MRO notifies the appropriate regulatory office.

5. The second HHS-certified laboratory reports split specimen (Bottle B) test results directly to the MRO using the laboratory's Split Specimen Report, along with Copy 1 of the Federal CCF. The MRO must take actions in response to the split testing laboratory's reported results as outlined in **Table 6**.

6. The MRO reports the result to the Federal agency and the donor.

E. Interpretation and Result Verification

Chapter 3, Section C, Drug Information 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.

SAMHSA has developed MRO Case Studies to illustrate MRO interpretation and result verification in various real-life scenarios. SAMHSA will review and update the case studies periodically based on reported incidents and issues raised in forensic workplace drug testing. The MRO Case Studies are available on the SAMHSA website http:/www.workplace.samhsa.gov.

- The results reported by the test facility,

- 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 (Bottle A) results.

Table 6 describes MRO actions to be taken for split specimen (Bottle B) results.

IITF and Laboratory Results

IITF and laboratory staff are available to answer MRO questions concerning *reported* drug test results. However, IITFs and 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 IITFs and laboratories to report Federal agency specimen results. These criteria are described in **Appendix A**.

After receiving a drug test report, the MRO should contact the IITF and/or laboratory whenever additional information is needed. For example, the MRO may wish to clarify the IITF's or laboratory's administrative and analytical procedures or obtain 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 for a split specimen) must be made by the MRO in writing. The written request may be mailed, faxed, or electronically sent to the test facility.

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 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, on pH, or on a confirmatory nitrite test concentration below 500 mcg/mL are exceptions to this rule.** The laboratory is <u>not</u> required to contact the MRO 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 positive, adulterated, substituted, or invalid 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.

<u>Prescriptions</u>

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. Additional guidance is provided in Chapter 6, Section C, *Occupational and Public Safety*.

State Initiatives and Laws

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 CSA, 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.

Interpretation of Results

Dilute Specimens

A dilute finding may be reported 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 and drinking large amounts of fluid,
- Taking a diuretic, or
- Drinking fluids immediately before providing the specimen.

A certifying technician at an IITF may report a specimen as dilute in conjunction with a negative drug test only when the creatinine test result is greater than 5 mg/dL. When creatinine is less than or equal to 5 mg/dL, the IITF must send the specimen to an HHS-certified laboratory for testing.

A certifying technician or certifying scientist at a laboratory may report a specimen as dilute in conjunction with a positive or negative drug test.

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, MRO Actions for Primary Specimen Reports (Bottle A)***.

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/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 that the Federal agency 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 that the donor 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 that the donor 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.

Invalid Specimens

The MRO is required to contact the donor and give the donor an opportunity to explain any reason for the invalid result (e.g., provide information on medications or a medical condition). **For invalid results based on pH between 9.0 and 9.5**, the MRO must consider whether there is evidence of elapsed time and high temperature that could have account for the result. The MRO must contact the collection site, IITF, and/or laboratory to discuss time and temperature issues. The MRO must take the following actions for a specimen with an invalid result:

1. If the donor's medical explanation is legitimate OR if time and temperature conditions appear to account for pH between 9.0 and 9.5, report the test as canceled with the reason for the invalid result and inform the Federal agency that a recollection is not required because there is an acceptable reason for the invalid result. **Exception:** if a

negative result is required (e.g., for a Federal agency applicant/pre-employment, return to duty, or follow-up test) – follow procedures as described in item 4 below.

2. If the donor's medical explanation is not legitimate OR if time and temperature conditions do not appear to account for pH between 9.0 and 9.5, 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.

3. If a specimen is recollected using direct observation and is invalid for:

   a. The same reason reported for the first specimen – report the test as canceled with the reason for the invalid result and inform the Federal agency that a recollection is not required because there is an acceptable reason for the invalid result. **Exception:** if a negative result is required (e.g., for a Federal agency applicant/pre-employment, return to duty, or follow-up test) – follow procedures as described in item 4 below.

   b. A different reason than reported for the first specimen – *do not contact the donor*. 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. Review and report the test based on the reported result of the specimen from the second observed collection using the above procedures. If the specimen from the second observed collection is reported as invalid for a different reason than the specimen from the first observed collection and there is no acceptable explanation, follow procedures as described in item 4 below.

4. Determine if there is clinical evidence that the donor is a current illicit drug user when:

   a. The donor has an invalid result with an acceptable explanation as described in item 1 above, and a negative result is required (e.g., for a Federal agency applicant/pre-employment, return to duty, or follow-up test)

   b. The donor has two specimens reported as invalid for the same reason as described in item 3(a) above, and a negative result is required (e.g., for a Federal agency applicant/pre-employment, return to duty, or follow-up test)

   c. The donor's second specimen collected under direct observation as described in item 3(b) above is invalid for a different reason than the specimen from the first observed collection and there is no acceptable explanation (e.g., time and temperature that account for pH between 9.0 and 9.5)

5. Arrange for a medical evaluation of the donor

   a. The MRO must personally conduct the medical evaluation or ensure that the medical evaluation is conducted by another licensed physician that is acceptable to the MRO. If appropriate, the MRO may also consult with the donor's physician to gather information needed to make the determination.

   b. The physician conducting the medical evaluation may conduct medically approved procedures to determine clinical evidence of current drug use.

6. The MRO reports in writing to the Federal agency as follows:

a. **Negative** when the medical evaluation reveals no clinical evidence of drug use. The MRO report must include the following information: written notations regarding the medical evaluation, explanation of the reason for the medical evaluation, and the basis for determining that no signs and symptoms of drug use exist.

b. **Test cancelled** when the medical evaluation reveals clinical evidence of drug use. The MRO must inform the Federal agency that the canceled test does not serve the purpose of a negative test result (i.e., the donor may not begin or resume performing safety-sensitive functions, because a negative drug test result is needed). The MRO report must include the following information: written notations regarding the medical evaluation, explanation of the reason for the medical evaluation, and the basis for determining that signs and symptoms of drug use exist.

Marijuana

Medical 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 I drug, and marijuana use is not an acceptable medical explanation for a positive drug test result in any 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.

All Federal drug testing programs – whether they are the programs under the regulatory and legal auspices of the Department of Health and Human Services, the Department of Defense, the Department of Transportation, or the Nuclear Regulatory Commission – have taken the identical stance: Use of Schedule I drugs by individuals in federally regulated workplaces is unacceptable, and any individual who tests positive for a Schedule I drug will have a positive drug test on his or her record.

Prescription THC

Dronabinol is chemically synthesized delta-9-tetrahydrocannabinol (THC). It is available under the trade name Marinol® in 2.5, 5, or 10 mg soft gelatin capsules for oral administration. Marinol® 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 Marinol® should be warned not to drive, operate complex machinery, or engage in hazardous activity.

At this time, there are no other prescription or OTC 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/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/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.

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 approximately two or three days prior to when the urine specimen was collected. Use at an earlier time may not cause a positive urine test.

Topical Anesthetics

Cocaine is structurally unique and does not resemble any of the other topical anesthetics, such as lidocaine, benzocaine, etc. Although these compounds have analgesic properties, there is no structural similarity to cocaine or its metabolite (benzoylecgonine), nor are any of these compounds metabolized to cocaine or its metabolites. 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

"crack" smoke do not produce a urine positive for cocaine using the HHS cutoffs for initial and confirmatory testing.

When a donor claims that his/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 medical 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 "Health 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/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 medical explanation for the presence of benzoylecgonine 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 a legitimate source as follows:

- Consumption of poppy seeds or
- Legitimate use of al drug product that contains codeine or morphine

Signs and Symptoms of Opiates Abuse

The MRO relies on his/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/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.

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 around the time the urine was collected.

Legitimate Codeine or Morphine Use

A donor who tests positive for codeine or morphine may have legally used the drug (see Chapter 3, Section C, Drug Information).

HHS included additional criteria in the Mandatory Guidelines to distinguish between specimens testing positive due to opiates abuse and specimens testing positive due to food sources or legitimate medical use. 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 or 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 <u>not</u> 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.

  An MRO may request quantitative information from the laboratory on the presence of opiate analytes (i.e., morphine, codeine, 6-AM) below the cutoff for specimens that have been reported positive for one or more opiate analytes. This information may be helpful to the MRO in assessing the medical explanation provided by the donor. The requests may be for an individual specimen or a blanket request for all quantitative results when one or more opiate analyte is positive.

<u>6-Acetylmorphine Positive Specimens</u>

When a laboratory reports a specimen as positive for the heroin metabolite (6-acetylmorphine), this is proof of heroin use. There is no legitimate medical explanation for a 6-AM positive result.

6-AM is metabolized to morphine, so morphine is positive (i.e., at or above the program cutoff of 2000 ng/mL) in most positive 6-AM specimens. There are reasons that morphine may be below the program cutoff of 2000 ng/mL but present in the specimen (e.g., if the donor used heroin close to the time of collection, if the donor has a metabolic defect in the metabolism of 6-AM resulting in prolonged excretion, if a donor's morphine metabolic pathways have been altered, or if another substance interacted with 6-AM or morphine). These are atypical specimens.

At this time, there is no scientific evidence to support that a specimen could contain 6-AM at or above 10 ng/mL with no morphine present. Beginning October 1, 2010, DOT is gathering information on any evidence of such specimen results in federally regulated workplace drug testing programs. As described below, MROs and laboratories who identify 6-AM positive

specimens with no morphine present must notify DOT.

When a laboratory reports a specimen as **positive for 6-AM and not also positive for morphine**, it is recommended that the MRO request the quantitative results for the other opiates (codeine and morphine) present in the specimen. As noted above, MROs may submit individual requests or a blanket request to receive opiates quantitative results below the cutoff when one or more opiate analytes is positive.

When the MRO has requested the quantitative codeine and morphine results for a 6-AM positive specimen:

1. If the opiates initial test was negative and the laboratory had not performed a confirmatory test for opiates (codeine and morphine) using a mass spectrometric (MS) method prior to reporting the specimen, the laboratory will notify the MRO. The MRO should then request that MS analysis be performed to provide the additional interpretive information for the 6-AM result. **Note:** The MRO may submit a blanket request for the laboratory to test all confirmed positive 6-AM specimens using the opiates mass spectrometric test regardless of the opiates initial test result. The laboratory will report as positive ONLY those drug analytes with a positive initial test and a positive confirmatory test. Therefore, if the opiates initial test was negative, the laboratory certifying scientist will NOT mark the "positive for" opiates checkbox on the Federal CCF

2. The certifying scientist will annotate the additional opiate results requested by the MRO on the Remarks line of the CCF as described below. The additional results will also be included on the electronic report for the specimen (if any).

    - If the laboratory quantitated codeine or morphine above the assay limit of quantitation (LOQ), the laboratory reports the quantitative result to the MRO. The MRO reports the specimen as positive for 6-AM.

    - If the laboratory identified codeine or morphine above the limit of detection (LOD) but the quantitative result was below the LOQ, the laboratory reports "codeine present" or "morphine present" to the MRO. The MRO reports the specimen as positive for 6-AM.

    - If the laboratory did not identify codeine above the LOD, the laboratory reports "codeine not present." The MRO reports the specimen as positive for 6-AM.

    - If the laboratory did not identify morphine above the LOD, the laboratory reports "morphine not present." The laboratory and the MRO must notify DOT. The MRO will not report the specimen to the Federal agency until after his/her discussion with DOT.

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 below in Section F, *Reporting*, and in Chapter 6, Section C, *Occupational and Public Safety*.

Amphetamines

An MRO may request the quantitative results of amphetamine analytes below the cutoff for a specimen reported positive for one or more amphetamine analytes. This information may be helpful to the MRO in assessing the medical explanation provided by the donor.

Amphetamine and Methamphetamine

Depending on the amphetamines confirmatory test 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 100 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.

3. When the MRO requests that a split specimen (Bottle B) be tested for amphetamine and/or methamphetamine, the second laboratory performs confirmatory testing for both amphetamine and methamphetamine, but reports only the analyte(s) reported positive by the first laboratory (as specified in the MRO retest request). The second laboratory reports analytes as reconfirmed or failed to reconfirm. The following rules apply:

    - The second laboratory does NOT apply the HHS cutoff (250 ng/mL) to split specimens. The laboratory must use its established limit of detection (LOD) or limit of quantitation (LOQ) as the decision point for determining whether a drug has been reconfirmed in the retest specimen.

    - The laboratory must identify the presence of amphetamine (at or above the laboratory's established LOD for the assay) in order to report methamphetamine as reconfirmed.

An MRO may request the quantitative result of amphetamine or methamphetamine below the cutoff for a specimen reported positive for the other analyte. This information may be helpful to the MRO in assessing the medical explanation provided by the donor.

<u>Enantiomers</u>

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 confirmatory tests 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 an aliquot of the specimen to another certified laboratory for *d*- and *l*-enantiomer testing. The MRO may order enantiomer testing for all specimens with positive amphetamines initial test results, all specimens with a positive methamphetamine confirmatory test result, or request such testing on a case-by-case basis (i.e., when the MRO receives a methamphetamine positive result from a laboratory).

Enantiomer test results may 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. One example is selegiline, 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 test is specific for methamphetamine and amphetamine. Specimens containing sympathomimetic amines will not be reported positive by the laboratory after conducting the confirmatory test. Some OTC products (e.g., inhalers such as Vicks® VapoInhaler®) contain *l*-methamphetamine (also called *l*-desoxyephedrine or levmetamfetamine). Enantiomer analysis may be used to verify that a positive methamphetamine result was due to the use of such products. 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 OTC drug and a contaminant of the analytical procedure. If there is greater than 80% *l*-methamphetamine, the results are considered to be consistent with OTC use. If there is more than 20% *d*-methamphetamine present, the results indicate the use of some source other than the OTC product, and the result is verified as positive. This is a very conservative interpretation.

Methylenedioxymethamphetamine (MDMA), Methylenedioxyamphetamine (MDA), Methylenedioxyethylamphetamine (MDEA)

When a laboratory reports a specimen as positive for MDMA, MDA, and or MDEA, this is proof of the use of an illicit substance. The MRO verifies the result as positive.

Phencyclidine

A positive phencyclidine (PCP) result is evidence of illegal drug use. There are no prescription

or OTC 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 a confirmatory test as required by the Mandatory Guidelines. The MRO verifies the result as positive.

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 4 and 5.**

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 social security number 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, IITF, 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.

For positive, adulterated, or substituted specimens, the MRO must send a hardcopy of either the completed MRO copy of the Federal CCF or the separate letter/memorandum.

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

Confidentiality

The Mandatory Guidelines require the MRO to:

1. Report the verified result(s)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:

   a. information related to the donor's medical condition,

   b. medications,

   c. medical diagnosis, and

   d. 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 donor 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,
- IITF personnel,
- Laboratory personnel, and
- Collectors.

The Mandatory Guidelines require MROs to retain drug test records for a minimum of two years from the date of collection.

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

- Documentation to support an alternative medical explanation for the drug test 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
- Documentation of 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 for 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.

Chapter 6. Additional MRO Responsibilities

A. Federal Agency Blind Samples

Federal agencies are required to have blind samples submitted with donor specimens to each IITF and laboratory to which the collector sends employee specimens for the Federal agency. Each Federal agency must send at least 3% blind samples along with its donor specimens based on the projected total number of donor specimens collected per year. Efforts should be made to submit some of the blind samples each quarter. Blind samples are helpful in determining the acceptability of the entire testing process (i.e., from the collector's submission of a specimen to a test facility until a result is reported to the MRO).

The Mandatory Guidelines include requirements for blind samples as follows:

1. A blind sample that is positive must be prepared with one or more of the drugs or metabolites specified in the Mandatory Guidelines at a concentration between 1.5 and 2 times the initial drug test cutoff (see Appendix A, *Specimen Reporting Criteria*);

2. A blind sample that is positive must be validated by the supplier as to content using appropriate initial and confirmatory tests;

3. A blind sample that is negative (i.e., certified to contain no drug) must be validated by the supplier as negative using appropriate initial and confirmatory tests;

4. A blind sample that is adulterated must have the characteristics to clearly show that it is an adulterated sample at the time it is validated by the supplier;

5. A blind sample that is substituted must have the characteristics to clearly show that it is a substituted sample at the time it is validated by the supplier;

6. The supplier must provide information regarding the shelf life of the blind sample.

The blind samples may be purchased by the Federal agency and supplied to the collector, or purchased by the collector and submitted to an IITF or 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/she will have the information necessary to determine if the correct result was reported. On the MRO copy of the Federal CCF, the collector indicates that the sample is a "blind sample" where the donor would normally provide a signature (Step 5 on Copy 2 of the Federal CCF).

An incorrect result does not automatically indicate that the IITF or 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 an IITF or laboratory reports a result different from the one expected based on information provided by the supplier of the blind sample, the MRO must conduct an initial investigation to determine the cause of the error. The Mandatory Guidelines require the MRO to:

1. Contact the supplier of the blind sample and attempt to determine if the supplier made a mistake when preparing the blind sample.

2. Contact the collector and attempt to determine if the collector made a mistake when preparing the blind sample for transfer to the IITF or laboratory.

3. If there is no obvious reason for the inconsistent result, notify both HHS and the Federal agency for which the blind sample was submitted.

When contacted by an MRO, HHS will investigate the blind sample error to determine the exact cause of the incorrect result. HHS will provide a report of investigative findings and corrective

actions taken by the HHS-certified IITF or laboratory to the Federal agency. HHS will also ensure notification of all other Federal agencies for which the IITF or laboratory performs testing, and will coordinate any action necessary to prevent recurrence of the error.

B. Insufficient Specimen

When a collector reports that a donor did not provide a sufficient amount of urine for a drug test, the MRO consults with the Federal agency. The Federal agency must immediately direct the donor to obtain, **within five days**, a medical evaluation from a licensed physician, acceptable to the MRO, who has expertise in the medical issues raised by the donor's failure to provide a specimen. The MRO may conduct the evaluation if he or she has the appropriate expertise.

The purpose of the evaluation is to determine whether the donor has an ascertainable physiological condition (e.g., urinary system dysfunction) or a medically documented pre-existing psychological disorder that, with a high degree of probability, could have prevented him or her from providing a sufficient amount of urine during the collection. If so, the physician must further determine whether the medical condition is a permanent or long-term disability that would prevent the donor from providing sufficient urine for an extended or indefinite time. Examples include:

- Destruction of the glomerular filtration system leading to renal failure,
- Unrepaired traumatic disruption of the urinary tract, or
- A severe psychiatric disorder focused on genitourinary matters.

Unsupported assertions of "situational anxiety" or dehydration are not considered valid reasons and shall be regarded as a refusal to test. When a donor has difficulty providing sufficient urine during a collection, the donor is given the opportunity to attempt to provide a specimen during a period of time up to three hours. The collector will give the donor a reasonable amount of liquid to drink over this period (e.g., an 8 ounce glass of water every 30 minutes, but not to exceed a maximum of 40 ounces over three hours).

If a physician other than the MRO is performing the evaluation, the MRO provides the following information to the referral physician:

1. The circumstances necessitating the medical evaluation (i.e., that the donor was required to provide urine for a federally regulated drug test, but was unable to provide at least 45 mL of urine as required for the test).

2. The consequences of a refusal to take a drug test for the Federal agency. (See Chapter 4, Section C, *Refusal to Test.*)

3. Instructions for submitting a written statement to the MRO with a recommendation for the MRO determination and the basis for the recommendation:

    a. The statement must not include any detailed information on the employee's medical condition beyond that necessary to explain the recommendations.

    b. The recommendation for the MRO determination must be <u>either:</u>

- That there is not an adequate basis for determining that the donor's medical condition has or, with a high degree of probability, could have precluded the employee from providing a sufficient amount of urine, or

- That the donor's medical condition has or, with a high degree of probability, could have precluded the employee from providing a sufficient amount of urine.

c. In the second case above, the physician must also indicate whether the donor has permanent or long-term medical disability (as described above) that would prevent him or her from providing sufficient urine for a drug test for an extended or indefinite time and, if so, the basis for this determination.

In making a determination based on the medical evaluation, the MRO must seriously consider and assess the recommendations made by the referral physician.

The MRO reports in writing to the Federal agency as follows:

1. **Refusal to Test** when the MRO determines that there is no adequate basis for determining a medical condition interfered with the collection.

2. **Test cancelled** when the MRO determines that the donor's medical condition interfered with the collection. The Federal agency takes no further action and the donor remains in the random testing pool, unless a negative result is required (e.g., for a Federal agency applicant/pre-employment, follow-up, or return-to-duty test). In such cases, the Federal agency takes action as required in the Federal agency plan or as described below.

Permanent or Long-Term Medical Condition and Required Negative Test

Additional actions are required when the MRO determines that a donor has a permanent or long-term medical condition that would likely prevent provision of a sufficient specimen for an extended or indefinite time, and the reason for the drug test was:

- Federal agency applicant/pre-employment,

- Follow-up, or

- Return-to-duty.

In these cases, the MRO must conduct a medical evaluation or, alternatively, ensure that a medical evaluation is conducted by another licensed physician acceptable to the MRO, to determine if there is clinical evidence of drug use. The MRO also consults with the donor's physician and/or the referral physician (i.e., who evaluated the donor after the failure to provide a sufficient specimen).

The MRO reports in writing to the Federal agency as follows:

1. **Negative** when the medical evaluation reveals no clinical evidence of drug use. The MRO report must include the following information concerning the medical evaluation(s) of the donor: the basis for determining that the donor has a permanent or long-term medical condition that makes provision of a sufficient urine specimen impossible, and

the basis for determining that no signs and symptoms of drug use exist.

2. **Test cancelled** when the medical evaluation reveals clinical evidence of drug use. The MRO report must include the following information concerning the medical evaluation(s) of the donor: the basis for determining that the donor has a permanent or long-term medical condition that makes provision of a sufficient urine specimen impossible, and the basis for determining that signs and symptoms of drug use exist. The Federal agency is not authorized to allow the donor to begin or resume official functions because a negative test is required.

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 CSA 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 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 which 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 a documentation package. A donor or Federal agency will occasionally request an IITF and/or 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. The documentation package may also be referred to as a "data package" or "litigation package." The request must always be submitted to the test facility through the MRO.

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

1. A cover sheet that provides a brief description of the drug testing procedures and specimen validity tests performed on the donor's specimen;

2. A table of contents page that lists by page number all documents and materials in the package;

3. A copy of the Federal CCF with any attachments, internal chain of custody documents for the specimen, memoranda (if any), and a copy of the electronic report (if any) generated by the IITF or laboratory;

4. A brief description of the initial drug tests and specimen validity tests procedures, instrumentation, batch quality control requirements, and copies of the test data for the donor's specimen with all calibrators and controls identified and copies of all internal chain of custody documents related to these tests;

5. For a laboratory: a brief description of confirmatory drug tests and confirmatory validity tests procedures, instrumentation, batch quality control requirements, and copies of the test data for the donor's specimen with all calibrators and controls identified and copies of all internal chain of custody documents related to these tests;

6. A copy of the résumé or curriculum vitae for the certifying technician or certifying scientist that certified the test result; and

7. A copy of the résumé or curriculum vitae for each of the IITF's Responsible Technicians or each of the laboratory's Responsible Persons.

Appendix A. Specimen Reporting Criteria

Initial test analyte	Initial Test Cutoff	Confirmatory test analyte	Confirmatory Test Cutoff
Marijuana metabolites	50 ng/mL	THCA[1]	15 ng/mL
Cocaine metabolites	150 ng/mL	Benzoylecgonine	100 ng/mL
Opiate metabolites Codeine/Morphine[2]	2000 ng/mL	Morphine	2000 ng/mL
		Codeine	2000 ng/mL
6-Acetylmorphine (6-AM)	10 ng/mL	6-AM	10 ng/mL
Phencyclidine	25 ng/mL	Phencyclidine	25 ng/mL
Amphetamines[3]	500 ng/mL	Amphetamines:	
Amphetamine/Methamphetamine[4]		Amphetamine	250 ng/mL
		Methamphetamine[5]	250 ng/mL
MDMA[6]	500 ng/mL	MDMA	250 ng/mL
		MDA[7]	250 ng/mL
		MDEA[8]	250 ng/mL

[1]Delta-9-tetrahydrocannabinol-9-carboxylic acid (THCA)
[2]Morphine is the target analyte for codeine/morphine testing.
[3]Either a single initial test kit or multiple initial test kits may be used provided the single kit detects each target analyte independently at the specified cutoff.
[4]Methamphetamine is the target analyte for amphetamine/methamphetamine testing.
[5]To be reported positive for methamphetamine, the specimen must also have an amphetamine concentration equal to or greater than 100 ng/mL.
[6]Methylenedioxymethamphetamine
[7]Methylenedioxyamphetamine
[8]Methylenedioxyethylamphetamine

Negative
An IITF or a laboratory will report a urine specimen as negative when the specimen has valid negative results at any point in the testing process:

- All immunoassay results below the initial test cutoffs

Or

- Confirmatory test results below the confirmatory test cutoffs

And

- Specimen validity test results in the acceptable range.

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 confirmatory drug test result (i.e., on a separate aliquot) was at or above

the confirmatory test cutoff for the specific drug/drug metabolite.

Dilute

An **IITF** will report a urine specimen as **dilute** in conjunction with a negative drug test when:

- The creatinine concentration is greater than 5 mg/dL and less than 20 mg/dL

And

- The specific gravity is greater than 1.0010 and less than 1.0030.

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

- 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 and 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 confirmatory test result is greater than or equal to 500 mcg/mL,
- Chromium (VI) is present,
- A halogen (e.g., bleach, iodine, fluoride) is present,
- Glutaraldehyde is present,
- Pyridine (pyridinium chlorochromate) is present,
- A surfactant is present,

- The specimen contains a substance that is not a normal constituent of human urine (at or above the LOQ of a confirmatory test for the specific substance), or

- The specimen contains an endogenous substance at a concentration that is not a normal physiological concentration (at or above the LOQ of 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.

    - 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.

    - 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.

Note*:* see Table 5, *MRO Actions for Primary Specimen Reports (Bottle A),* concerning specimens reported as invalid based on pH between 9.0 and 9.5.

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.

    - 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 by testing two separate aliquots using the same chromium (VI) colorimetric test with a cutoff greater than or equal to 50 mcg/mL chromium (VI).

5. The possible presence of a halogen (e.g., bleach, iodine, fluoride) is determined by testing two separate aliquots using the same halogen colorimetric test with a cutoff greater than or equal to the LOQ, or relying on the odor of the specimen as the initial (first) test and testing one aliquot using the halogen colorimetric test.

6. The possible presence of glutaraldehyde is determined by testing two separate aliquots using the same aldehyde test (aldehyde present) or testing two separate aliquots using the immunoassay drug tests to verify characteristic immunoassay responses on one or more of the tests.

7. The possible presence of an oxidizing adulterant is determined by testing two separate aliquots 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 LOQ).

8. The possible presence of a surfactant is determined by testing two separate aliquots using the same surfactant colorimetric test with a greater than or equal to 100 mcg/mL dodecylbenzene sulfonate-equivalent cutoff, or using a foam/shake test for the initial (first) test and testing one aliquot using the surfactant colorimetric test.

9. Interference with the immunoassay drug test occurs on two separate aliquots (i.e., valid immunoassay drug test results cannot be obtained)

Note*:* Some substances may interfere with some immunoassay tests. Cross-reactivity information is included in package inserts provided by the immunoassay reagent manufacturer. Laboratories are required to contact the MRO prior to reporting a specimen as invalid based on immunoassay interference, and laboratory personnel should be knowledgeable of possible interferents.

10. Interference with the confirmatory drug test occurs on two separate aliquots and the laboratory is unable to identify the interfering substance.

A laboratory will report an invalid result for a urine specimen when the laboratory identifies an abnormal physical characteristic and:

- The laboratory cannot test the specimen due to the abnormal physical characteristic.
- The physical appearance of the specimen is such that testing the specimen may damage the laboratory's instruments.
- The physical appearance of Bottles A and B is clearly different (note the laboratory tests the A Bottle).
- The laboratory suspects tampering, but has no evidence of a specific substance.
- The laboratory suspects a specific substance (e.g., bleach or glutaraldehyde based on odor), but does not test for that substance and is unable to locate an HHS-certified laboratory to perform the testing.
- The MRO does not authorize the laboratory to send the specimen for additional/different specimen validity testing.

Appendix B. Glossary

The following definitions are excerpted from the HHS Mandatory Guidelines for Federal Workplace Drug Testing Programs (73 FR 71858) dated November 25, 2008.

Accessioner. The individual who receives the specimens at the laboratory or IITF and signs the Federal drug testing custody and control form.

Adulterated Specimen. A specimen that has been altered, as evidenced by test results showing either a substance that is not a normal constituent for that type of specimen or showing an abnormal concentration of an endogenous substance.

Aliquot. A fractional part of a specimen used for testing, representing the whole specimen.

Alternate Responsible Person. The person who assumes professional, organizational, educational, and administrative responsibility for the day-to-day management of the HHS-certified laboratory when the responsible person is unable to fill these obligations.

Alternate Responsible Technician. The person who assumes professional, organizational, educational, and administrative responsibility for the day-to-day management of the HHS-certified IITF when the responsible technician is unable to fill these obligations.

Batch. A number of specimens that are being handled and tested as a group.

Calibrator. A solution of known concentration in the appropriate matrix that is used to define expected outcomes of a measurement procedure or to compare the response obtained with the response of a test specimen aliquot/sample. The concentration of the analyte of interest in the calibrator is known within limits ascertained during its preparation. Calibrators may be used to establish a calibration curve over a concentration range.

Cancelled Test. The result reported by the MRO to the Federal agency when a specimen has been reported to the MRO as invalid result (and the donor has no legitimate explanation) or rejected for testing, when a split specimen (Bottle B) fails to reconfirm, or when the MRO determines that a fatal flaw or unrecovered correctable error exists in the forensic records.

Carryover. The effect that occurs when a sample's result (e.g., drug concentration) has been affected by a preceding sample during analysis.

Certifying Scientist (CS). The individual responsible for verifying the chain of custody and scientific reliability of any test result reported by an HHS-certified laboratory.

Certifying Technician (CT). The individual responsible for verifying the chain of custody and scientific reliability of negative, negative/dilute, and rejected for testing results reported by a laboratory or IITF.

Chain of Custody (COC). Procedures to account for the integrity of each specimen or aliquot by tracking its handling and storage from point of specimen collection to final disposition of the specimen and its aliquots.

Chain of Custody Document. A form used to document the security of the specimen and all aliquots of a specimen. The document, which may account for an individual specimen, aliquot, or batch, must include the names and signatures of all individuals who handled the specimen or aliquots and the date and purpose of the access.

Collection Site. A place where donors present themselves for the purpose of providing a specimen.

Collector. A person who instructs and assists donors at a collection site and receives the specimen provided by the donor.

Confirmatory Drug Test. A second analytical procedure performed on a different aliquot of the original specimen to identify and quantify the presence of a specific drug or drug metabolite.

Confirmatory Specimen Validity Test. A second test performed on a different aliquot of the original specimen to further support a specimen validity test result.

Control. A sample used to evaluate whether an analytical procedure or test is operating within predefined tolerance limits.

Cutoff. The decision point or value used to establish and report a specimen as negative, positive, adulterated, substituted, or invalid.

Dilute Specimen. A urine specimen with creatinine and specific gravity values that are lower than expected but are still within the physiologically producible ranges of human urine.

Donor. The individual from whom a specimen is collected.

Failed to Reconfirm. The result reported for a split specimen (Bottle B) when the second laboratory is unable to corroborate the original result reported for the primary specimen (Bottle A).

Federal Drug Testing Custody and Control Form (Federal CCF). The Office of Management and Budget (OMB)-approved form that is used to document the collection, custody, and transport of a specimen from the time the specimen is collected until it is received by the testing site (i.e., certified laboratory, instrumented initial test facility). The form may also be used to report the test result to the Medical Review Officer.

HHS. The Department of Health and Human Services.

Initial Drug Test. The test used to differentiate a negative specimen from one that requires further testing for drugs or drug metabolites.

Initial Specimen Validity Test. The first test used to determine if a specimen is adulterated, diluted, substituted, or invalid.

Instrumented Initial Test Facility (IITF). A permanent location where initial testing, reporting of results, and recordkeeping are performed under the supervision of a responsible technician.

Invalid Result. The result reported by an HHS-certified laboratory in accordance with the criteria established in Guidelines Section 3.8 when a positive, negative, adulterated, or substituted result cannot be established for a specific drug or specimen validity test.

Laboratory. A permanent location where initial and confirmatory testing, reporting of results, and recordkeeping is performed under the supervision of a responsible person.

Limit of Detection. The lowest concentration at which a measurand can be identified, but (for quantitative assays) the concentration cannot be accurately calculated.

Limit of Quantitation. For quantitative assays, the lowest concentration at which the identity and concentration of the measurand can be accurately established.

Lot. A number of units of an item (e.g., drug test kits, reagents, quality control material) manufactured from the same starting materials within a specified period of time for which the manufacturer states that the items have essentially the same performance characteristics and the same expiration date.

Medical Review Officer (MRO). A licensed physician who reviews, verifies, and reports a specimen test result to the agency.

Negative Result. The result reported by an HHS-certified laboratory or an HHS-certified IITF to an MRO when a specimen contains no drug or the concentration of the drug is less than the cutoff concentration for that drug or drug class and the specimen is a valid specimen.

Oxidizing Adulterant. A substance that acts alone or in combination with other substances to oxidize drug or drug metabolites to prevent the detection of the drugs or drug metabolites, or affects the reagents in either the initial or confirmatory drug test.

Performance Testing (PT) Sample. A program-generated sample sent to laboratory or IITF that is used to evaluate performance.

Positive Result. The result reported by an HHS-certified laboratory when a specimen contains a drug or drug metabolite equal to or greater than the cutoff concentration.

Quality Control (QC) Sample. A calibrator or control used to verify that an analytical test is providing accurate test results.

Reconfirmed. The result reported for a split specimen (Bottle B) when the second laboratory is able to corroborate the original result reported for the primary specimen (Bottle A).

Rejected for Testing. The result reported by an HHS-certified laboratory or HHS-certified IITF when no tests are performed for a specimen because of a fatal flaw or an unrecovered correctable error (as described in Guidelines Sections 15.1 and 15.2).

Responsible Person (RP). The person who assumes professional, organizational, educational, and administrative responsibility for the day-to-day management of the HHS-certified laboratory.

Responsible Technician (RT). The person who assumes professional, organizational, educational, and administrative responsibility for the day-to-day management of the HHS-certified IITF.

Sample. A performance testing sample, quality control material used for testing, or a representative portion of a donor specimen.

Specimen. Fluid or material collected from a donor at the collection site for the purpose of a drug test. Urine is the only specimen allowed for Federal workplace drug testing programs.

Split Specimen Collection. A collection in which the urine collected is divided into two separate specimen bottles, the primary specimen (Bottle A) and the split specimen (Bottle B).

Standard. Reference material of known purity or a solution containing a reference material at a known concentration.

Substituted Specimen. A specimen that has been submitted in place of the donor's urine, as evidenced by creatinine and specific gravity values that are outside the physiologically producible ranges of human urine.

Appendix C. IITF Transfer to Laboratory Supplemental Custody and Control Form

Specimen I.D. #:

_____

IITF Accession #: _____

IITF Name: _____
NLCP IITF No. _____

IITF address: _____ ☐ **Bottle A and**

Bottle B included

_____ ☐ **CCF Copy 1**

included

_____

I certify that the specimen identified on the Federal CCF was examined upon receipt, handled using chain of custody procedures, analyzed, and resealed in accordance with applicable Federal requirements.		
		SPECIMEN BOTTLES RELEASED TO:
Signature of Certifying Technician		
	/ /	
(Print) Certifying Technician Name (First, M I, Last)	Date (Mo/Day/Yr)	_____ Name of Delivery Service

RECEIVED AT LABORATORY		
		BOTTLE A SEAL INTACT
Signature of Accessioner		
	/ /	YES ☐ NO ☐
(Print) Accessioner Name (First, M I, Last)	Date (Mo/Day/Yr)	If NO, enter Remark below

Laboratory Remarks:

_____

_____

_____

Date	Specimen Released by	Specimen Received by	Purpose

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 directly 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.
Microplate Enzyme-Linked Immunosorbent Assay	ELISA	A competitive binding enzyme immunoassay using drug-specific antibodies immobilized on the sides of a microplate well.

Other types of immunoassay for drugs and/or metabolites exist and may be used to test Federal agency specimens. Please contact the IITF or laboratory as needed for information on the immunoassay method used for the initial drug test, if not listed above.

Table 2. Some Specimen Validity Test Methods

Method	Measurand	Description
Atomic Absorption Spectrophotometry (AAS)	Adulterant concentration (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 adulterant concentration is determined from the amount of absorption at a specific wavelength.
Characteristic Immunoassay Drug Test Responses	Adulterant concentration (e.g., glutaraldehyde)	Characteristic responses are exhibited by some immunoassay reagents in the presence of some adulterants. This enables IITFs and laboratories to develop criteria for initial drug test data to identify a specific adulterant. If the responses are validated by a laboratory for a specific adulterant, the laboratory may accept the abnormal drug test results as the initial test for that adulterant. For the confirmatory test, laboratories must use a definitive method for identifying the adulterant (e.g., GC/MS for glutaraldehyde).
Colorimetry	pH, creatinine concentration, adulterant concentration (general or 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, producing a color. Because the intensity of the color is related to the measurand, the measurand is determined by visually measuring the color or electronically measuring the intensity of light at selected wavelengths (i.e., spectrophotometry).
Electrophoresis; Capillary electrophoresis (CE)	Adulterant concentration (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)	Adulterant concentration (e.g., glutaraldehyde, pyridine)	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.,

Method	Measurand	Description
		extraction) prior to GC/MS analysis. After the GC has separated the analytes in a specimen, the specimen enters the MS, which identifies and quantifies 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.

Method	Measurand	Description
High-Performance Liquid Chromatography (HPLC)	Adulterant concentration (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.
Inductively-Coupled Plasma-Mass Spectrometry (ICP-MS)	Adulterant concentration (e.g., chromium, halogens, surfactants)	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.
Ion Chromatography (IC)	Adulterant concentration (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.
Multi-wavelength spectrometry (MWS)	Adulterant concentration (e.g., nitrite, chromium VI, halogens, surfactants)	A method that uses multiple wavelengths of light (or other electronic transmissions) to identify a measurand. The method generates corrected absorbance values that are related to the measurand concentration.
Potentiometry	pH, oxidizing adulterant concentration	The measurement of the electrical potential difference between two electrodes in an electrochemical cell. A pH meter is one type of potentiometer. The HHS Guidelines require certified laboratories to use a pH meter for the initial and confirmatory pH tests.
Refractometry	Urine specific gravity	The required test method for 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. An IITF or a laboratory may use a three-decimal place refractometer for a specific gravity screening test. The HHS Guidelines require certified laboratories to use refractometers that report and display specific gravity to four decimal places for the initial and confirmatory specific gravity tests.

Table 3. Some Substances that Metabolize to Amphetamines

Category	Substance
Substances known to metabolize to methamphetamine (and amphetamine)	Benzphetamine
	Dimethylamphetamine
	Famprofazone
	Fencamine
	Furfenorex
	Selegiline
Substances known to metabolize to amphetamine	Amphetaminil
	Clobenzorex
	Ethylamphetamine
	Fenethylline
	Fenproporex
	Mefenorex
	Mesocarb
	Prenylamine

Table 4. Required Comments for IITF and Laboratory Reports

Test Result	Required Comment[1]	Note
Negative and Dilute	Creatinine = (numerical value) mg/dL & SpGr = (numerical value)	IITF forwards to lab if creatinine ≤ 5.0 mg/dL
Positive	(Specify drug analyte) = confirmatory test quantitative result	
Positive and Dilute	(Specify drug analyte) = confirmatory test quantitative result; Creatinine = (numerical value) mg/dL & SpGr = (numerical value)	
Adulterated	pH = (conf. test value)	pH < 3.0 or ≥ 11.0
	Nitrite = (conf. test value) mcg/mL	≥ 500 mcg/mL nitrite
	Surfactant Present; dodecylbenzene sulfonate = (conf. test value) mcg/mL	≥ 100 mcg/mL dodecylbenzene sulfonate
	Chromium (VI) = (conf. test value) mcg/mL	adulterant ≥ LOQ
	(Specify Halogen) = (conf. test value)	
	Glutaraldehyde = (conf. test value) mcg/mL	
	Pyridine = (conf. test value) mcg/mL	
	(Specify Adulterant) Present = (conf. test value)	
Substituted	Creatinine = (conf. test value) mg/dL & SpGr = (conf. test value)	
Invalid Result	Creatinine < 2 mg/dL & SpGr Acceptable	SpGr > 1.0010 & < 1.0200
	SpGr ≤ 1.0010 & Creatinine ≥ 2 mg/dL	
	Abnormal pH = (pH value supporting the invalid result)	pH ≥ 3.0 & < 4.5 or pH ≥ 9.0 & < 11.0
	Nitrite = (conf. test value) mcg/mL	Nitrite ≥ 200 & < 500 mcg/mL on confirmatory test
	Oxidant Activity = (≥ 200 mcg/mL nitrite-equivalents, ≥ 50 mcg/mL Cr VI-equivalents, or ≥ halogen or other oxidant LOQ)[2]	Oxidant = nitrite, chromium VI, halogen, etc.
	Possible (characterize as Aldehyde or Surfactant) Activity[2]	
	Immunoassay Interference[2]	
	(Specify confirmatory drug test method) interference[2]	
	Abnormal Physical Characteristic - (Specify)[2]	
	Bottle A and Bottle B - Different Physical Appearance[2]	
Rejected	Fatal Flaw: Specimen ID number mismatch/missing	ID mismatch/missing on either Bottle A or B
	Fatal Flaw: No collector printed name & No signature	
	Fatal Flaw: Bottle A label/seal broken or shows evidence of tampering	If redesignation is not possible
	Fatal Flaw: Bottle A insufficient specimen volume	
	Fatal Flaw: Bottle A seal condition not marked on CCF by IITF	
	Uncorrected Flaw: Wrong CCF used[3]	Wait 5 business days before reporting flaw if not corrected
	Uncorrected Flaw: Collector signature not recovered	
	Uncorrected Flaw: A & B redesignation not documented by IITF	

[1] Remarks on CCF (Step 5a) & on elec. report for primary specimens; Remarks on Split Specimen Report & on elec. report for split specimens

[2] Lab shall contact the MRO to discuss the Invalid Result in accordance with the HHS Guidelines (73 Fed. Reg. 71858) section 11.19.g.

[3] Error identified before testing or after testing with regulated procedures: obtain collector MFR and report; reject after 5 days if no MFR. *See NLCP Manual (IITF Question E8g and Laboratory Question E9g) for further guidance.*

Table 5. MRO Actions for Primary Specimen Reports (Bottle A)

Reported Primary Specimen Result	MRO Action
Negative	Report the negative result.
Negative and Dilute	Report the negative result and direct the Federal agency to immediately collect another specimen from the donor.
Positive **or** **Positive and Dilute**	Contact the donor to determine if he/she has a valid medical explanation for the positive result. If the medical explanation for the positive result appears to be: a. Legitimate – Verify the result as negative and report a negative result to the agency. If the specimen was also reported as dilute, direct the Federal agency to immediately collect another specimen from the donor. *(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 duties in a safety sensitive occupation.)* b. Not legitimate – Report the positive drug result to the Federal agency. If the specimen was also reported as dilute, the MRO may choose not to report the dilute finding.
Substituted	Contact the donor to determine if he/she has a valid medical explanation for the substituted result. If the medical explanation for the substituted result appears to be: a. Legitimate – Report a negative result to the Federal agency. b. Not legitimate – Report a refusal to test (substituted) to the Federal agency.
Adulterated	Contact the donor to determine if he/she has a valid medical explanation for the adulterated result. *(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 prove adulteration. There is no valid medical explanation.)* - Report a refusal to test (adulterated) to the Federal agency.

Reported Primary Specimen Result	MRO Action
Invalid Result	*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 EXCEPT when the invalid result is based on creatinine and specific gravity, pH, or a confirmatory nitrite test result less than 500 mcg/mL.* For invalid result based on **pH between 9.0 and 9.5**: • Consider whether there is evidence of elapsed time and high temperature that could account for the result. Contact the collection site, IITF, and/or laboratory to discuss time and temperature issues. Contact the donor to determine if he/she has an explanation for the invalid result. • If the medical explanation is legitimate OR the time and temperature conditions appear to account for the pH between 9.0 and 9.5 for a first invalid result: o Report the test as canceled with the reason for the invalid result and inform the Federal agency that a recollection is **not** required because there is an acceptable explanation for the invalid result *unless* the Federal agency plan requires a negative drug test result based on the reason for testing (e.g., Federal agency applicant/pre-employment, return to duty, follow-up). • If the medical explanation is not legitimate OR the time and temperature conditions do <u>not</u> appear to account for the pH between 9.0 and 9.5: o 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. • If a specimen is recollected using direct observation and that specimen is also reported as invalid: see required MRO actions in items 3 and 4 in **Chapter 4, Section E, *Interpretation and Result Verification, Invalid Specimens*** of this Manual.
Multiple Reported Results	Follow the review procedures above as appropriate for each reported result and report **all** verified results.
Rejected for testing	Report the test as canceled along with the reason for the cancellation and direct the Federal agency to immediately collect another specimen from the donor.

Table 6. MRO Actions for Split Specimen Reports (Bottle B)

Reported Split Specimen 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	Contact the donor to determine if he/she has an explanation for the adulterated/substituted result. If the explanation for the adulterated/substituted result appears to be: • Legitimate - Report as failed to reconfirm (specify drug(s)) and cancel both tests. • Not legitimate – Give the donor 72 hours to request that Laboratory A tests Bottle A for the adulterant/substitution. 1. If Bottle A contains the adulterant/is substituted - Report as refusal to test with the reason (adulterant present/substituted) 2. 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) 3. If Bottle A does not reconfirm Bottle B results (i.e., does not contain the adulterant/is not substituted): • Cancel both tests, • 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.

[1] Laboratory B conducts specimen validity tests to determine whether the failure to reconfirm the drug(s) is because the split specimen is adulterated, substituted, or invalid.

Laboratory Split Specimen Result			MRO Action
Reconfirmed	**Failed to Reconfirm**	**Additional Testing Results[1]**	
	Drug(s)	Invalid	*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.* If the invalid result cannot be resolved: • Report as failed to reconfirm (specify drug(s)) with the reason for the invalid result, • Cancel both tests, 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.
	Drug(s)	Not adulterated Not substituted Not invalid	*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.* • 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.
	Adulterated		• Report as failed to reconfirm (specify adulterant), • Cancel both tests, and • Notify the appropriate regulatory office regarding the test results for the specimen.
	Substituted		• Report as failed to reconfirm (not substituted), • Cancel both tests, and • Notify the appropriate regulatory office regarding the test results for the specimen.

[1] Laboratory B conducts specimen validity tests to determine whether the failure to reconfirm the drug(s) is because the split specimen is adulterated, substituted, or invalid.

When Laboratory A reported **multiple results** (i.e., drug-positive, adulterated, substituted) for the primary specimen and Laboratory B **reconfirmed some but not all of the results** for the split 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 split 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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