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Medical Review Officer Guidance Manual for Federal Workplace Drug Testing Programs

Department of Health and Human Services
Substance Abuse and Mental Health Services Administration
Center for Substance Abuse Prevention
Division of Workplace Programs

Substance Abuse and Mental Health Services Administration
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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 using Urine (82 FR 7920) dated January 23, 2017 (effective October 1, 2017).

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).

This revision of the manual includes a reorganization of material in the manual. 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 Web site:

https://www.samhsa.gov/workplace

Previous versions of this manual are obsolete.

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CHAPTER 1
Introduction

This guidance is intended to assist Medical Review Officers (MROs) in carrying out their regulated responsibilities under the Mandatory Guidelines for Federal Workplace Drug Testing Programs using Urine (82 FR 7920). This guidance does not establish legally enforceable responsibilities, but may reference actions or responsibilities that are required under statutory or regulatory authorities. The use of the word "should" in this guidance means that something is suggested or recommended, but not necessarily required by law.

1.1 The Federal Drug Testing Program

Following the identification of heroin use by military personnel in Southeast Asia during the Vietnam era, then President Nixon and Secretary of Defense Melvin Laird (at the urging of Dr. Jerome Jaffee, the President's Drug Advisor) initiated drug tests on returning servicemen. Anyone who tested positive in Vietnam was required to undergo a brief rehabilitation treatment and have negative tests before returning to the United States. This approach of testing for heroin and rehabilitation was followed until 1982 when "worldwide" surveys indicated a high rate of drug abuse among service members. The Department of Defense extended testing to common street drugs such as marijuana, cocaine, phencyclidine, and amphetamines. Tests for marijuana and batch procedures for chain of custody and testing were developed and a number of analytical advances, such as use of gas chromatography/mass spectrometry, were applied to the testing.

Following the success of this program, recommendations from the President's Commission on Organized Crime and the Anti-Drug Abuse Act of 1986, President Reagan established testing for Federal Civil Service employees in safety and sensitive positions by Executive Order 12564 (1986)—an order that was soon followed by Public Law 100-71 (1987). The U.S. Department of Health and Human Services (HHS) was given administrative responsibility and funding to implement the program. Since that time the collection procedures, testing methods, and medical review processes have evolved and are well documented. The program currently resides in the Division of Workplace Programs (DWP) of the Substance Abuse and Mental Health Services Administration (SAMHSA).

DWP is responsible for providing oversight for the Federal Drug-Free Workplace Program aimed at deterring and detecting illicit use of drugs by workers in the federal workforce. DWP also administers the National Laboratory Certification Program (NLCP), the HHS accreditation program for laboratories to conduct forensic drug testing for federal agencies. Two

types of test facilities may become HHS-certified: laboratories that perform both initial and confirmatory testing and instrumented initial test facilities (IITFs) that perform initial testing.

In addition to administering the Federal Civil Service program, DWP provides—

- Assistance to organizations and businesses establishing drug-free workplace programs (including drug testing);
- Primary substance abuse prevention information for workplace health and wellness programs;
- Information on intervention, treatment, and recovery for employee assistance programs;
- Management of the contract that administers the NLCP program (currently with RTI International) to certify all laboratories that are permitted to test Federal Civil Service employees;
- Requirements for MROs for training and for the review and verification of federally mandated drug testing results; and
- Coordination with the Office of National Drug Control Policy on the President's National Drug Control Strategy.

The numbers of specimens tested at HHS-certified laboratories expanded when the U.S. Department of Transportation (DOT) required that workers in regulated industries be tested at HHS-certified laboratories. The DOT program is administered separately from the Federal Civil Service Program but coordinates program requirements with the DWP. This Medical Review Officer Guidance Manual (hereinafter, "the manual") does not apply to specimens collected and tested under the DOT program.

1.2 The Medical Review Officer (MRO)

An essential component of any drug testing program is a comprehensive final review of laboratory results, which includes review of appropriate documentation, as well as an interview with the donor of the specimen to discover whether or not an acceptable medical explanation exists for the laboratory result. A confirmed positive test result reported from a laboratory does not automatically identify an employee or job applicant as having misused drugs, nor does a laboratory result of invalid, substituted, or adulterated automatically identify a person as having tampered with a specimen. A physician with a detailed knowledge of possible legitimate medical explanations must determine drug test results in the context of all information including the test result and the donor interview. HHS requires the MRO to fulfill this important function. In the

remainder of this manual the term "illicit drug use" will be used to represent not only illegal drug use, but also unauthorized pharmaceutical drug use.

The HHS Mandatory Guidelines for Federal Workplace Drug Testing Programs (Mandatory Guidelines) define that an MRO must be a currently 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;
- The training necessary to serve as an MRO, specifically the following:
  - The collection procedures used to collect federal agency specimens;
  - The interpretation of test results reported by HHS-certified IITFs and laboratories (e.g., negative, negative/dilute, positive, adulterated, substituted, rejected for testing, and invalid);
  - The chain of custody, reporting, and recordkeeping requirements for federal agency specimens;
  - The HHS Mandatory Guidelines for Federal Workplace Drug Testing Programs (i.e., for all authorized specimen types);
  - The procedures for interpretation, review (e.g., donor interview for legitimate medical explanations, review of documentation provided by the donor to support a legitimate medical explanation), and reporting of results specified by any federal agency for which the individual may serve as an MRO; and
  - To continue serving as an MRO for federal agency specimens, the MRO must complete training on any revisions to the Mandatory Guidelines prior to the effective date of the changes.
- Satisfactorily passed an initial examination administered by a nationally recognized entity or a subspecialty board that has been approved by the Secretary to certify MROs; and
- At least every 5 years, completed requalification training on the above topics and satisfactorily passed a requalification examination administered by a nationally recognized entity or a subspecialty board that has been approved by the Secretary to certify MROs.

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 HHS-certified laboratory or IITF 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 HHS-certified laboratory or IITF that may be construed as a potential conflict of interest.

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

The MRO has the following responsibilities:

- Review all positive, adulterated, rejected for testing, invalid, and (for urine) substituted test results;

- Ensure that specimens reported as negative and (for urine) negative/dilute are properly reviewed and reported to the agency's designated representative. The MRO must review at least 5% of the negative results reported by staff to ensure the MRO staff are properly performing the review process. This review should include all specimens that required corrective action;

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

- Complete action on a report from an HHS-certified laboratory or (for urine) HHS-certified IITF by—

  - Reviewing the information on the MRO copy of the Federal Custody and Control Form (CCF) that was received from the collector and the report received from the HHS-certified laboratory or IITF;
  - Interviewing the donor when required (e.g., to verify the existence of prescribed medication that could explain the result and/or to collect evidence of the prescription and subsequent dispensing of that prescription);
  - Making a determination regarding the result; and
  - Reporting the verified result to the federal agency.

- Maintain all records for a minimum of 2 years while maintaining the confidentiality of the information. The MRO may discard hardcopy records 6 months after conversion to electronic records (with appropriate security);

- Conduct a medical evaluation of the donor or a review of the examining physician's findings and make a determination of "refusal to test" or "cancelled test" when a collector reports that the donor was unable to provide a urine specimen;

- Monitor the frequency of errors and notify responsible parties to take corrective action to prevent recurrence; and
- Review the results of federal agency blind samples and perform the initial investigation into discrepant results.
- Request additional testing (as allowed) to help in the determination of a final result for a donor specimen.

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. A glossary of terms used in this manual is found in Appendix A.

CHAPTER 2

The Federal Drug Testing Custody and Control Form

2.1 General Information

Federal agencies are required to use the Federal Custody and Control Form (CCF) approved by the Office of Management and Budget (OMB) for their agency workplace drug testing programs. Federal CCFs are available from a number of different sources (e.g., instrumented initial test facilities [IITFs], laboratories, collectors, consortia/third-party administrators, Medical Review Officers [MROs]).

OMB extended the use of the Federal CCF as of August 8, 2017. The Federal CCF may be used as follows:

- **Paper CCF.** A hardcopy form formatted in accordance with the OMB-approved form and signed using handwritten (i.e., "wet") signatures;
  - Option 1: a preprinted, five-part carbonless form; or
  - Option 2: a multiple-part CCF that is printed at the collection site prior to the collection. At a minimum, the collector prints Copy 1 and Copy 2 on carbonless paper for signatures.
- **Electronic CCF.** An electronic document used to record all CCF events from collection through reporting and signed using electronic signatures (e.g., collector and donor "digitized" signatures made using a signature pad); or
- **Combination Electronic/Paper CCF.** An electronic form used to document the collection process that is then printed and signed using handwritten (i.e., "wet") signatures. At a minimum, the collector prints Copy 1 and Copy 2 on carbonless paper for signatures.

A copy of the 2017 Federal CCF and guidance for its use are on the SAMHSA web site: https://www.samhsa.gov/workplace/drug-testing. OMB has granted an extension for using the 2014 Federal CCF (i.e., the CCF without the four new analytes – oxycodone, oxymorphone, hydrocodone, and hydromorphone) until June 30, 2018. As of July 1, 2018, the 2017 Federal CCF must be used for federal specimens, and the laboratory must treat the use of the 2014 Federal CCF as a correctable discrepancy. An example of the Test Facility Copy (1) and the MRO Copy (2) of the CCF are shown in Appendix B.

Employers are prohibited from using the Federal CCF for—

- Private-sector employee drug testing programs, other than testing conducted under the DOT or Nuclear Regulatory Commission (NRC) regulations;

- State workplace drug testing programs; or
- Department of Justice drug testing programs.

The use of an incorrect form for a federal agency specimen does not, in and of itself, constitute a reason for the test facility to reject the specimen for testing or for the MRO to cancel the test. For example, in rare cases, a collector may use a non-federal form or incorrect Federal CCF for a federal agency collection by mistake or as the only means to conduct a collection under unusual circumstances (e.g., post-accident test with insufficient time to obtain a Federal CCF). In these cases, the collector must submit a memorandum for the record (MFR) with the specimen, and the test facility must test and report the specimen. The form used and the collector's MFR should provide all information required on the Federal CCF.

If an IITF or a laboratory discovers the use of a non-federal or incorrect federal form, the test facility processes and tests the specimen but holds the report. The collector is notified to provide an MFR stating the reason the correct Federal CCF was not used for the federal agency collection. If the collector does not provide an MFR after at least 5 business days, the IITF or laboratory will report a "rejected for testing" result to the MRO who will cancel the test.

If an MRO discovers the use of a non-federal or an incorrect federal form, the collector is notified to provide an MFR with the reason for using the incorrect form. If the collector does not provide an MFR after at least 5 business days, the MRO will cancel the test.

The MRO must implement procedures and administrative, technical, and physical controls to ensure donor privacy by restricting access to donor information and drug test results recorded on hardcopy and electronic Federal CCFs, or entered into a computer system or database. Access to donor information and drug test results must be limited to those individuals requiring access to fulfill job duties. Such individuals must receive training to make them aware of their responsibilities for protecting the information. All drug testing service providers, including MROs, must maintain the confidentiality of Federal CCF information from the time the donor information is obtained through transmission/transport of the Federal CCF, specimen testing, reporting, and records handling (i.e., storage, retrieval, and final destruction). (See additional information in Chapter 6, Section 6.6, of this manual, including requirements for external service providers.)

2.2 Use of an Electronic Federal CCF

A federal agency may use the Federal CCF as an electronic document in its federal workplace drug testing program. An electronic Federal CCF (ECCF) must be the functional equivalent of a paper Federal CCF with respect to content, integrity, accuracy, and accessibility.

Before implementing a Federal ECCF, HHS-certified IITFs and laboratories must provide documentation on the ECCF system for HHS review and authorization for its use. The documentation will be submitted through the National Laboratory Certification Program (NLCP), and the ongoing review of records, procedures, and practices associated with the ECCF will be part of the NLCP inspection process.

The ECCF system provider and the federal agencies and drug testing service providers (e.g., collectors, test facilities, MROs) who use electronic or combination electronic and paper Federal CCFs must implement procedures and administrative, technical, and physical controls to ensure the confidentiality, integrity, and availability of electronic records, and to ensure that electronic signatures are the legally binding equivalent of traditional handwritten signatures. These procedures and controls include, but are not limited to, the following:

- System validation;
- The ability to generate accurate and complete copies of records in both human readable and electronic forms suitable for inspection, review, and copying upon request of authorized parties (e.g., the MRO, federal agency, or Substance Abuse and Mental Health Services Administration [SAMHSA]);
- Protecting records to enable accurate and ready retrieval throughout the records' retention period;
- Limiting system access to authorized individuals. Procedures must be in place for managing the user authentication system (e.g., assignment, review, revocation);
- Maintaining secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete records from the time of initiation of the Federal CCF (changes should be evident when reviewing the original record, and any electronic or paper copy of the original record); and
- Using authority checks to ensure that only authorized individuals use the system, sign a record electronically, access the operation or computer system input or output device, alter a record, or perform the operation at hand.

2.3 Federal CCF Content Requirements

The Federal CCF contains information for the test facility (i.e., on Copy 1) and information for the MRO (i.e., on Copy 2). The remaining copies, which are identical to the MRO copy, are for the employer, collection site, and donor.

A paper Federal CCF includes a legend (i.e., copy number and recipient name) at the bottom of each copy. A Federal ECCF is not required to have the legend at the bottom of Copy 2-5.

2.3.1 Test Facility Identification

At the top of the Federal CCF, the test facility must be identified by one of the following:

- A specific IITF or laboratory name and address;
- A list of addresses with checkboxes to allow the collector to check the box for the IITF or laboratory to which the specimen will be shipped; or
- A corporate name and telephone number (the collector will annotate the address of the IITF or laboratory to which the specimen will be shipped, or the test facility that receives the specimen for testing will annotate its address).

2.3.2 Bottle Labels/Seals

The tamper-evident specimen bottle labels/seals may be at the bottom of Copy 1 or may be separate from the form. There must be two labels/seals: one marked with the letter "A" to designate the primary specimen and the other marked with the letter "B" to designate the split specimen. Each label/seal must have the following:

- The same specimen identification (ID) number that is at the top of the Federal CCF;
- A place for the collector to annotate the date of the collection; and
- A place for the donor to initial the label/seal after it is placed on the specimen bottle.

2.3.3 Required Statements

Wording of required statements must be identical to that on the OMB-approved Federal CCF. The statements must be provided as follows:

- Instructions for Completing the Federal Drug Testing Custody and Control Form for Urine Specimen Collection for—
  - Paper Federal CCF: printed on the back of the donor copy (Copy 5); or

- Federal ECCF: provided to the donor as a separate page (e.g., hardcopy, onscreen, posted at the collection site).

- Display of the Public Burden Statement:
  - Paper Federal CCF: printed on the back of each copy (i.e., Copies 1 through 5); or
  - Federal ECCF: provided to CCF recipients as a separate page (i.e., with the electronically transmitted Federal CCF copies). The Public Burden Statement may be displayed onscreen or posted at the collection site for the donor and collector, and/or provided to the donor as a hardcopy.
- Privacy Act Statement (For Federal Employees Only):
  - Paper Federal CCF: printed on the back of the donor copy (Copy 5); or
  - Federal ECCF: provided to the donor as a separate page (e.g., hardcopy, onscreen, posted at the collection site).

2.4 Federal CCF Distribution

Employers, collectors, test facilities, and MROs are responsible for ensuring the security of data transmissions and limiting access to any data transmission, storage, and retrieval systems for Federal CCFs. (See Chapter 6, Section 6.6, of this manual for requirements for the use of third-party service providers.)

At the end of the collection, the collector distributes the CCF as described below.

2.4.1 Paper Federal CCF

- Copy 1 (Test Facility Copy) is signed by the collector and is shipped with the specimen package to the IITF or laboratory. This paper form is the specimen chain of custody.
- Copy 2 (MRO Copy) signed by the donor is sent to the MRO by one of the following methods:
  - The original is sent by courier or mail; or
  - A copy is sent via fax or provided electronically. The collector maintains the original Copy 2 in the collection site records.
- Copy 3 (Collector Copy) is maintained in the collection site records.
- Copy 4 (employer copy) is sent via fax, courier, or mail, or is provided electronically.
- Copy 5 (donor copy) is given to the donor or, if acceptable to the donor, may be provided electronically.

Note: CCF definitions are in Section 2.1 (General Information) of this chapter. The steps above apply to both paper CCFs and combination electronic and paper Federal CCFs. The collector will have at least two CCF pages (Copy 1 and Copy 2) for distribution (see Appendix B: Sample of CCF). When fewer than five parts are printed, the collector distributes copies of Copy 2 in lieu of separate CCF Copies 3-5.

2.4.2 Federal ECCF

- Copy 1 (test facility copy) is signed by the collector and is provided electronically to the IITF or laboratory. This electronic form is the specimen chain of custody. To facilitate linkage of the specimen package to the Federal ECCF sent to the test facility, the collector must either:
  - Include a printed copy of the Test Facility copy (i.e., Copy 1) of the Federal CCF with the specimen; or
  - Apply a label to the outside of the specimen package with the specimen ID number, test facility name, and contact information, and collection site name and contact information.
- Copy 2-5 is signed by the donor and is maintained as an electronic file by the collector/collection site and—
  - A copy is provided electronically to the MRO;
  - A copy is provided electronically to the employer; and
  - A copy is provided to the donor. This may be a printed copy or a copy that is electronically provided.

Note: The Instructions for Completing the Federal Drug Testing Custody and Control Form for Urine Specimen Collection are provided to the donor, either printed on the back of the donor's copy of the paper Federal CCF or provided as a separate page (e.g., hardcopy, onscreen, posted at the collection site).

2.5 Test Facility Report to MRO

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.

The test facility must fax, courier, mail, or electronically provide the completed Federal CCF (copy of Copy 1) to the MRO, with one exception. The test facility may report specimens as negative or negative-dilute using only a computer-generated electronic report, provided that

the report contains all required elements, to ensure that the test result is properly associated with the MRO copy (Copy 2) of the Federal CCF. (See Chapter 4, Sections 4.1.1 and 4.1.2 of this manual for the required elements.)

For all specimens forwarded by an IITF to a laboratory, the reporting laboratory must also send a copy of the completed IITF Supplemental CCF to the MRO. This chain of custody form documents the transfer of the specimen to the laboratory. The laboratory may fax, courier, mail, or electronically provide this form. An example form is provided as Appendix C of this manual.

For non-negative specimens, laboratories are required to report all results for the 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
Drug Testing

3.1 Federal Workplace Drug Testing Overview

3.1.1 Drugs

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

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

- 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 or post-accident 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 D 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 (DEA) Web site, https://www.dea.gov.

- A federal agency may routinely test its federal employees' workplace specimens for a drug or drug class other than those listed in Appendix D when the agency has been granted a waiver by the Secretary of the Department of Health and Human Services (HHS) to do so.

For any circumstance where testing for an additional drug is justified or authorized as described above, the federal agency must contact the MRO to arrange the additional testing at an HHS-certified laboratory. The MRO will contact the laboratory Responsible Person (RP) who in turn will notify the NLCP of the MRO request for additional testing. HHS will review the request for the additional test and provide a written acknowledgment to the RP to proceed with the test.

HHS maintains a list of HHS-certified laboratories that will test regulated specimens for one or more Schedule I or II drugs upon request from a federal agency. HHS provides the updated list to federal agencies upon request. The information includes the laboratory name, address, contact information, and the Schedule I or II drug(s). If an immunoassay test is not available for an additional Schedule I or II drug, the federal agency may request the laboratory analyze the drug by testing two separate aliquots of a specimen using the confirmatory analytical method.

3.1.2 Specimen Collection

The MRO must be 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 https://www.samhsa.gov/workplace/drug-testing) contains guidance for collectors to supplement the collection procedures required by the Mandatory Guidelines.

3.1.3 Security and Chain of Custody

The Mandatory Guidelines specify requirements for collection sites, instrumented initial test facilities (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.

Permanent sites used solely for specimen collection must be secured at all times. At facilities that are not dedicated specimen collection sites, access to the areas used for specimen collections must be restricted to authorized personnel only during the collection. Individual areas within an IITF or laboratory (e.g., receiving/accessioning area, testing areas, sample preparation area, and 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. Because 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 the action. 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 Federal CCF 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.

3.1.4 Specimen Validity

Specimen validity testing must be performed for each federal agency specimen. For urine specimens, 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 or 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).

3.1.5 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 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 and 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 D.

In most cases, 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 an administrative proceeding to defend an original positive, adulterated, or substituted result;
- When the MRO has requested analysis of the primary specimen (Bottle A) for adulteration 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. In this case, the MRO reports the failed to reconfirm result and the refusal to test, and gives the donor 72 hours to request that the first laboratory (i.e., that reported Bottle A) test the primary specimen (A) for the adulterant. If the second laboratory reported the split specimen (B) as substituted, the MRO reports the failed to reconfirm result and the refusal to test, and gives the donor 72 hours to request that the first laboratory review the specific gravity and creatinine results of the primary specimen (Bottle A);
- When HHS has directed the laboratory to reanalyze the specimen;
- When an initial test specimen is invalid due to a general oxidant or adulterant being present and the MRO would like to have confirmatory or additional testing completed; or
- When the specimen is confirmed positive for methamphetamine and the MRO elects to have D,L enantiomer testing performed.
- When additional test information on a positive result may be useful to the MRO in determining the final test result. One example is testing for metabolites such as norhydrocodone and noroxycodone which may be helpful to the MRO in determining a final test result when a prescription does not support the laboratory's reported results. Another example would be the use of a test for the presence of Δ^9-tetrahydrocannabivarin (THCV) to confirm the use of cannabis as opposed to pharmaceutical THC. This additional testing may only be performed on a case-by-case basis.

When the primary specimen (Bottle A) is reported as 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. If a donor does not ask to have the split specimen (Bottle B) tested, a federal agency may have the split specimen tested as part of a legal or an administrative proceeding to defend an original positive, adulterated, or substituted result.

3.2 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 testing procedures.

3.2.1 Initial Drug Tests

IITFs and laboratories are required to use either immunoassay or an alternate technology (e.g., spectrometry, spectroscopy) for initial drug tests. The method must be validated and accurate and reliable for testing of specimens for drugs or metabolites.[1]

Immunoassays are 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. For drug classes with multiple initial test analytes (such as opioids and amphetamines), the Mandatory Guidelines allow a single immunoassay test for the drug class or separate immunoassay tests. When one test is used, the test is calibrated with one analyte from the group identified as the target analyte. The cross-reactivity of the immunoassay to each of the other analytes in the group must be 80% or greater. Alternatively, the laboratory may use separate immunoassay tests for the analytes within the group.

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

An IITF or a laboratory may use a technology other than immunoassay to differentiate negative specimens from those requiring further testing. Technological advances have led to increased throughput and lower costs that enable the use of such methods in initial testing. For marijuana metabolites and cocaine metabolite initial tests using an alternate technology that is specific for the target analyte, the confirmatory test cutoff must be used (i.e., 15 ng/mL for THCA, 100 ng/mL for benzoylecgonine). For drug classes with multiple initial test analytes (such as opioids and amphetamines), one or all analytes from the group must be used to calibrate

the test, depending on the technology. For a specimen to be positive by the initial test, at least one analyte within the group must have a concentration equal to or greater than the initial test cutoff or, alternatively, the sum of the individual analyte concentrations must be equal to or greater than the initial test cutoff. Any specimen that is positive by the initial test must be subjected to a confirmatory test using the confirmatory test cutoff, which is applied to each individual analyte. In addition, for forensic defensibility, the confirmatory test is performed on a separate aliquot of the specimen.

3.2.2 Confirmatory Drug Tests

Laboratories are required to use a confirmatory drug test method that specifically identifies and quantifies 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 (MS). 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 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. Urine specimens must undergo a specimen preparation process (i.e., extraction) prior to GC/MS analysis and may require preparation prior to LC/MS/MS analysis. Tandem MS methods are also allowed and provide additional analytical benefits.

3.2.3 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 analyte. 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.

3.2.4 Split Specimen (Bottle B) Testing

A donor may request testing of the split specimen (Bottle B) at a second HHS-certified laboratory to reconfirm or refute a positive, adulterated, or substituted result reported for the specimen (Bottle A). The second laboratory tests the split specimen using only the confirmatory test(s) needed to reconfirm the primary specimen result(s). The laboratory performs drug tests at the laboratory's limit of detection (LOD) or limit of quantitation (LOQ)—not the HHS cutoffs. Split specimen reconfirmations for adulterated and substituted specimens are performed at the HHS cutoffs for primary specimens. The laboratory is required to inform the MRO of the level that is that laboratory's LOD/LOQ, but the reconfirmation report is issued as a qualitative "reconfirmed" or "failed to reconfirm" result only. Chapter 4, Section 4.5, 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 (laboratory B) 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 and the NLCP to decide whether to send the specimen to a third HHS-certified laboratory for additional confirmatory testing. For federal specimens, the MRO must submit a signed request to the split testing laboratory to have the additional testing done at a third laboratory. This is not required for DOT-regulated specimens. The third laboratory should use a confirmatory test method more similar to that used by the first laboratory (i.e., the laboratory that reported the primary specimen result).

3.3 IITF or Laboratory Reports

- For negative and negative/dilute results, the IITF or laboratory is allowed to report results using only 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).
- If the report is provided by electronic means, the electronic transmission must be secure (e.g., a Web portal in which the MRO can log into a password-protected site to download the scanned copy of the CCF or by encryption).

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.

3.4 Specimen and Records Storage

Laboratories are required to maintain the following specimens in a secure frozen storage area for at least 1 year after reporting:

- Drug positive specimens;
- Substituted specimens;
- Adulterated specimens;
- Invalid specimens;
- Split specimens (B Bottles) of the primary specimens (A Bottles) listed above; and
- 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. If a specimen is rejected due to a missing collector signature and no

MFR to provide the signature is received, the specimen will be held for at least 5 business days prior to reporting and then discarded.

Collection site records (e.g., collector copies of the Federal CCF) must be maintained for at least 2 years by the collector or collector employer. IITFs and laboratories must maintain records generated to support test results for a minimum of 2 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 6.4, Donor Rights to Information). The agency's request must be in writing and must specify the period of time for record retention. MROs must also maintain all drug test records for a minimum of 2 years. See Chapter 4, Section 6 for additional information.

Hardcopy records may be discarded 6 months after conversion to electronic records.

3.5 Oral Fluid Testing

(Space reserved)

CHAPTER 4

MRO Review and Reporting Procedures

The Medical Review Officer (MRO) must review all positive, adulterated, substituted, rejected for testing, 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 5% of the specimen results reported by MRO staff to ensure that staff is properly performing the review process. If a staff member reports a negative/dilute, the staff member or MRO must notify the agency of the need to immediately collect another specimen from the donor.

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;
- Documentation and recordkeeping;
- Reporting the drug test to the federal agency's designated representative;
- Confidentiality; and
- Discrepancies to cancel test.

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

4.1 Administrative Review of Documents

NOTE: The following Federal Custody and Control Form (CCF) description and instructions are for the MRO Copy (Copy 2) of the Federal CCF.

4.1.1 MRO Copy of the Federal CCF (Copy 2)

The collector is required to send the MRO copy of the Federal CCF (paper or electronic Copy 2) to the MRO within 24 hours, or 1 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 a paper Federal CCF was used and 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). If an electronic copy was used, the MRO must contact the collector to resend the MRO copy (Copy 2).

The MRO checks for the following items on Copy 2 of the Federal CCF (not all are essential to report a specimen).

- The correct Federal CCF approved by the Office of Management and Budget (OMB) was used to document the specimen collection.
- The Federal CCF contains the specimen identification (ID) number.
- Each test facility is identified by one of the following:
  - A specific instrumental initial test facility (IITF) or laboratory name and address at the top of the CCF;
  - A list of addresses with checkboxes 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).
- The Federal CCF was properly completed.
  - Step 1 contains—
    - Federal agency name and address and employer ID number (as appropriate);
    - MRO name, address (i.e., street address; not a Post Office Box number), telephone number, and fax number;
    - Donor's ID (e.g., social security number [SSN], employee ID number) or collector's remark in Step 2 if the donor refuses to provide the SSN or ID number);
    - Testing authority (i.e., Department of Health and Human Services [HHS], Nuclear Regulatory Commission [NRC], Department of Transportation [DOT] and the specific administration, or United States Coast Guard [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.

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

Certified IITFs and laboratories report drug test results to the MRO using a legible image or copy of the Federal CCF (Copy 1) and/or a computer-generated electronic report. The Federal CCF is used to report all positive, adulterated, substituted, invalid, and rejected specimens. The test facility may send a computer-generated electronic report in addition to the Federal CCF for these specimens. The test facility may send only a computer-generated electronic report for

negative and negative-dilute specimens. The MRO must have procedures in place to ensure the confidentiality of the reports (i.e., hardcopy and electronic).

The test facility may send reports by courier or mail or use various electronic means (e.g., teleprinter, fax, secure electronic transmission). Transmissions of the reports must ensure confidentiality and the results may not be reported verbally by telephone. IITFs, laboratories, and other service providers must ensure the confidentiality, integrity, and availability of the data and limit access to any data transmission, storage, and retrieval system. (See Chapter 6, Section 6.6, of this manual for requirements for the use of external service providers.)

The MRO checks for the following items on the CCFs (not all are essential to report a specimen):

- 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.
- 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 specimen (Bottle A) bottle seal condition upon receipt at the test facility.
  - Step 5a contains—
    - Primary specimen (Bottle A) test results;
    - Certifying technician's or certifying scientist's printed name;
    - Certifying technician's or certifying scientist's signature;
    - Date of result certification;
    - Comments on the Remarks line (as appropriate) as follows:
      - Quantitative test results;
      - Comments as required by HHS for specimens reported as adulterated, substituted, rejected for testing, invalid result, or dilute (see Table 3); and
      - Observations or explanatory comments recorded by IITF and/or laboratory staff concerning the specimen.
    - 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; and
- If a separate Split Specimen Report was sent, a reference to the separate laboratory report in the Reason line in Step 5b of the CCF.

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

– Laboratory name and address;
– MRO's name and fax number;
– Specimen ID number;
– Laboratory accession number;
– Donor's ID (SSN or employee ID number), if provided;
– RECONFIRMED result requires the following:
  - For RECONFIRMED drug results: the specific drug analyte(s) reconfirmed;
  - For RECONFIRMED ADULTERATED results: adulterated with the measurand(s) reconfirmed; and
  - For RECONFIRMED SUBSTITUTED: substituted with the creatinine and specific gravity values.
– FAILED TO RECONFIRM result requires the following:
  - 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; and
  - For FAILED TO RECONFIRM substituted results: NOT SUBSTITUTED.
– FAILED TO RECONFIRM drug results requires the following:
  - The specimen validity tests performed; and
  - 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, or invalid [with required comment]).
– Certification statement;
– Certifying scientist's signature, printed name, and certification date;

- Required comments/explanatory remarks for reconfirmed results; and
- Required comments/explanatory remarks for failed to reconfirm results.

- Memoranda for the record from the collector, IITF, or laboratory to address any correctable discrepancies identified (see Section 4.1.3, Federal CCF or Specimen Errors);

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

  - Test facility name and address;
  - Federal agency name;
  - MRO's name;
  - Specimen ID number;
  - Donor's ID from the Federal CCF (e.g., SSN, employee ID number);
  - Collector's name and telephone number;
  - Reason for test (if provided);
  - Date of collection;
  - Date received at IITF and/or laboratory;
  - Certifying technician's 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.

- 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).

4.1.3 Federal CCF or Specimen Errors

An IITF, a laboratory, or an MRO may identify errors made on a Federal CCF. An IITF or a laboratory may identify a problem with a specimen during processing. (See Section 4.1.5 for MRO actions in response to identified problems.) The various types of errors are outlined below:

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

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

b. The specimen bottle label/seal is missing, misapplied, broken, or shows evidence of tampering on the primary specimen (Bottle A) and the split specimen (Bottle B) cannot be redesignated as the primary specimen.

c. The collector's signature and printed name are omitted from the CCF.

d. 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.

e. The accessioner at the laboratory or the IITF failed to document the primary (A) specimen seal condition on the Federal CCF and the split specimen (Bottle B) cannot be redesignated as the primary specimen.

f. The specimen was received at the HHS-certified laboratory or IITF without a CCF.

g. The CCF was received at the HHS-certified laboratory or IITF without a specimen.

h. The collector performed two separate collections using one CCF.

i. The HHS-certified laboratory or IITF identified a flaw other than those above that prevents testing or affects the forensic defensibility of drug test and cannot be corrected.

2. *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) include the following:*

   a. The collector failed to sign the CCF (but the printed name is present). The laboratory must contact the collector to recover the signature. If the error is corrected, the test result is reported. If the signature is not recovered after at least 5 business days, the laboratory must report rejected for testing and indicate the reason on the Federal CCF.

   b. The collector used a non-federal form or an incorrect/expired Federal CCF (and the specimen was tested in accordance with Mandatory Guidelines requirements). The laboratory must contact the collector for an MFR to explain the use of the non-federal or incorrect/expired CCF and ensure that all required information is present. If the explanatory MFR is not obtained after at least 5 business days, the laboratory must report a rejected for testing result and indicate the reason on the Federal CCF.

   c. The IITF redesignated the primary specimen (Bottle A) and split specimen (Bottle B), but failed to include a comment on the Federal CCF. The laboratory must contact the IITF for an MFR to explain the redesignation. If the explanatory MFR is not obtained after at least 5 business days, the laboratory must report a rejected for testing result and indicate the reason on the Federal CCF.

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

    a. Incorrect IITF or laboratory name and address;

    b. Incomplete/incorrect/unreadable employer name or address;

    c. MRO name is missing;

    d. Incomplete/incorrect MRO address;

    e. Transposition of numbers in the donor's social security number or ID number;

    f. Missing/incorrect telephone or fax number;

    g. A "Reason for Test" box is not marked;

    h. A "Drug Tests to be Performed" box is not marked;

    i. The single or split "specimen collection" box is not marked;

    j. The "Observed" box is not marked for an observed collection;

    k. No collection site address; (When no collection information is on the CCF, the laboratory must process the specimen. If no MFR obtained after at least 5 days, the laboratory will report with comment e.g., "unable to recover missing information.")

    l. The collector's printed name is missing, but the collector's signature is properly recorded;

    m. The time of collection is not indicated;

    n. The date of collection is not indicated;

    o. Incorrect/missing name of delivery service;

    p. Donor's name included on the test facility copy of the CCF or on seal labels;

    q. Signature present without printed name (i.e., of collector, accessioner, certifying technician, or certifying scientist);

    r. The collector has changed or corrected information by crossing out the original information but did not date and initial the change.

    s. No temperature block mark and no explanatory comment in the Remarks line (see Section 4.1.4, Federal CCF Remarks).

4. *Administrative errors that are judged by the MRO to have a significant impact on the forensic defensibility of the results and may require the MRO to cancel a test unless corrected by an MFR. Examples include, but are not limited to:*

    a. 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. The MRO must contact the collector for an explanatory MFR. If the MRO does not receive the MFR after waiting at least 5 business days, the test is cancelled.

    b. There is no certifying scientist signature on the CCF for a positive, adulterated, invalid, or (for urine) substituted specimen. The MRO must contact the certifying scientist for an explanatory MFR that the review was properly conducted. If the MRO does not receive the MFR after waiting at least 5 business days, the test is cancelled.

    c. The electronic report from the laboratory did not contain all required data elements for a drug positive, adulterated, invalid, or (for urine) substituted specimen. The MRO must contact the laboratory for a corrected report. If the MRO does not receive the MFR after waiting at least 5 business days, the test is cancelled.

5. *Report discrepancies may be identified by an IITF or a laboratory after a report has been sent to the MRO, or may be identified by an MRO during administrative review. The IITF or laboratory must reissue the report and/or send an MFR to document the correct information in the specimen records. Examples include:*

    a. Incorrect or outdated CCF information (e.g., account number);

    b. Data entry errors due to illegible or misread CCF information;

    c. Data review or transcription errors by the certifying technician or certifying scientist; or

    d. A discrepancy between the Federal CCF and electronic report.

4.1.4 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, or 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 line 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, the MRO either attempts to obtain an MFR or cancels the test.

4.1.5 Actions Based on Administrative Review

1. *When a fatal flaw is identified (as defined in Section 4.1.3a), the following may occur:*

    a. If an IITF or a 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.

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

    c. The MRO reports the cancellation and the reason to the federal agency, which then determines whether or not to immediately collect another urine specimen from the donor.

2. *When a correctable discrepancy (as defined in Section 4.1.3b) by the collector or IITF is identified by the IITF, the laboratory, or the MRO, the responsible party is notified to provide an MFR to address the error.*

    a. For a missing collector signature, the following may occur:

        - 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 5 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.

    b. For a regulated specimen submitted with a non-federal form or an incorrect/expired Federal CCF, the following may occur:

        - 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 nonregulated 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 5 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.

c. 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, the laboratory must proceed as follows:

- 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 5 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.

3. *When a significant administrative error is identified by the MRO (as defined in Section 4.1.3d), the MRO notifies the responsible party to provide an MFR to address the error. If the MFR is not provided within at least 5 business days after this notification, the MRO must cancel the test.*

4. *When a report discrepancy is identified (as defined in Section 4.1.3e), 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. A corrected report when the IITF or laboratory has changed specimen ID or result (e.g., corrected donor's 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 retransmission date on the report; or

b. An amended report when the IITF or laboratory has changed information other than the specimen ID or result (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.

5. *The MRO should 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 test results 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 an administrative review. The MRO should maintain a record of such errors. When the MRO identifies frequent errors (i.e., more than once a month) by an individual collector or staff member at an IITF or a 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; and

c. The MRO maintains the documentation of error notification and corrective action response in its records

6. *Procedure to change the Donor ID Number.*

The Donor ID Number (e.g., social security number or employee ID number) is recorded in Step 1 of the Federal CCF. If the MRO identifies a difference between the Donor ID Number on the Federal CCF and the number in the employer or MRO records (e.g., a transposition of numbers), the ID may be corrected. In such cases, the MRO may include a memorandum for the record (MFR) in their records for that drug test to explain the discrepancy. The MRO may also request that the laboratory change the Donor ID Number in the laboratory records to the different ID number by submitting an MFR to the laboratory. That MFR must include an explanation of the reason for the change. The CCF is not to be modified. The laboratory will provide a report or corrected report with the updated ID number and the reason for the change.

4.1.6 Use of the 2017 and 2014 Federal CCFs

The 2017 Federal CCF was implemented on October 1, 2017 (82 FR 11051). A sample of the 2017 Federal CCF is available for viewing on the OMB website: https://ww.reginfo.gov. OMB granted an extension for using the 2014 Federal CCF (i.e., the CCF without the four new analytes – oxycodone, oxymorphone, hydrocodone, and hydromorphone) until June 30, 2018. During this period, IITFs and laboratories must accept and process federal agency specimens received with the 2014 Federal CCF using their routine procedures. As of July 1, 2018, IITFs and laboratories must treat the use of the 2014 Federal CCF as a correctable discrepancy.

4.2 Donor Interview

The MRO must attempt to contact and interview the donor when the donor's specimen is reported by the laboratory as positive, adulterated, substituted, and/or invalid. The MRO should attempt to contact a donor promptly after receiving the report (usually within 24 hours). The MRO, or MRO staff, should make at least three attempts to contact a donor within a 72-hour period. MRO staff members are limited to conducting the initial contact with the donor in order to schedule the discussion between the MRO and the donor. Federal CCFs may include the following donor contact information: donor's daytime and evening telephone numbers (e.g., cell phone number, direct work telephone number, home telephone number); work e-mail address; and personal e-mail address. MROs should utilize all of the contact information made available in the Federal CCF. When contacting donors, MROs should also 1) communicate that the MRO is authorized to discuss the donor's drug test result under Section 13.5 of the Mandatory Guidelines, 2) provide notice to the donor to contact the MRO within specified timeframe, and 3) provide the donor with the MRO's contact information. For all attempts to contact a donor by phone, MROs should document the time, date, telephone number used, and whether a message was left for the donor. MROs should also document when a donor declines an opportunity to discuss drug testing results with the MRO.

If a donor does not contact the MRO within five business days of the first attempt, or otherwise expressly declines an opportunity to discuss a drug test result with the MRO, the MRO should follow the procedures for when a donor fails to provide a legitimate medical (or other) explanation for a drug test result. (For example, see sections 13.5(d) through (g) in the Urine Mandatory Guidelines.)

1. *The interview process occurs as follows:*
    a. The donor must be positively identified by the MRO or staff requesting that the donor provide identifying information (e.g., employee ID number, SSN) 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.)

    b. The MRO informs the donor, prior to obtaining any information, that medical information provided during the interview that affects medical qualification or safety may be disclosed to the federal agency.

    c. The MRO informs the donor of the laboratory test result(s).

    d. The MRO takes action based on the donor's response, as follows:

- If the donor admits illicit use of a drug consistent with the test results or admits that he/she tampered with the specimen, advise the donor that the test result will be reported to the federal agency.
- If the donor does not admit to illicit use of a drug or specimen tampering, ask the donor if there is any possible explanation for the test result(s):
    - If the donor provides a legitimate explanation (e.g., claims that a positive result was due to a prescribed medication, that the positive result was due to a drug administered by a health care professional, or that a medication may have interfered with the drug test), the donor must provide appropriate supporting documentation as determined by the MRO.
    - If the donor has no legitimate medical explanation for the result, advise the donor that the test result will be reported to the federal agency.

e. For positive, adulterated, or substituted results: Inform the donor that they 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 as described in Chapter 4, Section 4.4.

f. If the donor requests split specimen (Bottle B) testing, use the procedures described in Chapter 4, Section 4.4 (Split Specimen Tests) to direct the laboratory to send the split specimen to another certified laboratory for confirmatory testing.

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

h. The reporting of the primary specimen (A) bottle result occurs immediately after the MRO has reviewed the information contained on Copy 2, and Copy 1 of the Federal CCF (as described above) has completed the interview with the donor and received all documentation necessary for the result determination. The federal agency is notified of the result and whether the donor has chosen to have the split (B) bottle tested at a second laboratory.

2. 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 review for 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:

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

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

c. 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).

d. 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. For a pre-employment drug test, the collection is initiated at the time the donor receives or selects a specimen collection container. If the donor departs the collection site after this point, the collector reports a refusal to 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).

4.3 Handling of Multiple Results or Multiple Collections During the Same Testing Event

1. *The HHS-certified laboratory may report multiple results for a primary (A) specimen.*

   a. The MRO must report all verified positive, adulterated, substituted, or "refusal to test" results to the agency.

   b. If an invalid result was reported in conjunction with a positive, adulterated, or substituted result, do not report the verified invalid result to the federal agency at this time. The MRO reports the verified invalid result(s) for the primary (A) urine specimen only if the split specimen is tested and reported as a failure to reconfirm.

2. *In the event the MRO is aware that two (or more) specimens were collected from one donor during a single collection event and were submitted to the laboratory for testing, the MRO must reconcile the testing results as follows:*

   a. If both specimens were verified negative, report the result as negative (single report).

   b. If one specimen was verified negative and the other was not (i.e., the specimen was verified as negative/dilute or as positive, adulterated, substituted, and/or invalid), report only the verified result(s) other than negative.

   c. If both specimens were verified as positive, adulterated, and/or substituted, report all results. For example, if verified, report a positive and the refusal results to the federal agency.

   d. If one specimen has been verified and the HHS-certified laboratory has not reported the result(s) of the other specimen—

      - Report verified result(s) of positive, adulterated, or substituted immediately and do not wait to receive the result(s) of the other specimen; and

- Do not report a verified result of negative, negative/dilute, or invalid for the first specimen to the federal agency. Hold the report until results of both specimens have been received and verified.

e. When the HHS-certified laboratory reports an invalid result for one or both specimens, follow the procedures in Section 4.3.1 above.

4.4 Split Specimen Tests

Note: Donors are not authorized 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:

- The MRO must inform the donor that the donor has the opportunity to request testing of the split specimen (Bottle B) when the MRO informs the donor that the primary specimen (Bottle A) is being reported as positive, adulterated, or substituted to the federal agency. The donor has 72 hours from the time of his/her notification of the non-negative result to request the split specimen test. The MRO must document the donor's verbal request in the MRO records.

- 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:

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

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

- If the split specimen cannot be tested by another HHS-certified laboratory (e.g., insufficient volume, lost in transit, Bottle B not available, or no other certified laboratory tests for the specific adulterant)—

- The MRO reports to the federal agency 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; or
- If the test is cancelled because no other certified laboratory tests for the specific adulterant, the MRO notifies the appropriate regulatory office.

- If Laboratory B cannot complete testing (e.g., due to interference with the test method), but believes a measurand is present, the laboratory will consult the NLCP to identify another HHS-certified laboratory that may be able to perform the test(s) needed to reconfirm or refute the Bottle A results. Laboratory B will contact the MRO and provide information to assist the MRO in deciding whether to send the split specimen to a third laboratory (Laboratory C) and, if so, to select the HHS-certified laboratory to serve as Laboratory C. (If the split specimen cannot be tested by another HHS-certified laboratory, the MRO follows the procedures outlined above.)

- The split testing laboratory reports split specimen (Bottle B) test results to the MRO using a copy of Copy 1 of the Federal CCF. The laboratory may also provide a computer-generated electronic report and the laboratory's Split Specimen Report form. The laboratory's Split Specimen Report is required for specimens reported as failed to reconfirm to provide additional information (e.g., specimen validity test results). The laboratory may send reports by courier or mail, or use various electronic means (e.g., teleprinter, fax, secure electronic transmission). Transmissions of the reports must ensure confidentiality and the results must not be reported verbally by telephone. (See Chapter 6, Section 6.6, of this manual for requirements for the use of external service providers.)

- The MRO must take actions in response to the split testing laboratory's reported results as outlined in Table 5 (Reference: Section 14.6 of the Mandatory Guidelines).

- The MRO reports the result to the federal agency, but must not disclose the numerical values of drug test results to the agency. The MRO notifies the appropriate regulatory office of any failed to reconfirm test.

4.5 Interpretation and Result Verification

Chapter 7, Drug Information, provides information on the drugs specified in the HHS Mandatory Guidelines for testing in federal agency workplace programs, including the current Controlled Substances Act (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 Web site: https://www.samhsa.gov/workplace/drug-testing.

The MRO determines the drug test results based upon—

- The results reported by the test facility;
- The donor's explanation and supporting documentation; and
- The MRO's medical assessment of the donor's responses during the interview and physical signs during any face-to-face interview.

The MRO must report only verified results to the federal agency. The MRO must not inform the federal agency of a positive, adulterated, or substituted laboratory result if it has been verified as negative. The MRO must not disclose drug concentration results to the agency.

Table 4 describes MRO actions to be taken and required reports for primary specimen (Bottle A) results.

Table 5 describes MRO actions to be taken and required reports for split specimen (Bottle B) results.

4.5.1 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 D.

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 as the sole result for a specimen when a scientifically supportable negative test result cannot be established for the specimen due to an unidentified adulterant, an interfering substance, an abnormal physical characteristic, or an endogenous substance at an abnormal concentration (see Appendix D). When the term "invalid result" is reported in conjunction with a positive, adulterated, or substituted result (see Section 4.3 above), this is a separate result that does not refer to the drug(s)/drug metabolite(s) marked positive or to the tests supporting the adulterated or substituted result. The MRO should contact the laboratory if there is any confusion about the reported results.

When the MRO receives a sole 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). Exceptions to this rule are **specimens reported as invalid based on creatinine and specific gravity results, on pH, or on a confirmatory nitrite test concentration $\geq$ 200 and < 500 mcg/mL.** It is unlikely that testing by another certified laboratory would provide a different result when a specimen is reported as invalid for these reasons.

When reviewing a specimen that meets invalid criteria based on oxidant testing, the MRO should be aware of the oxidant testing performed on the specimen. (See Appendix D, Specimen Reporting Criteria, for the oxidant tests used by HHS-certified laboratories.) When an MRO chooses to send an invalid-oxidant specimen to another laboratory for additional testing, the specimen should be tested at an HHS-certified laboratory with initial and confirmatory oxidant tests that will identify multiple oxidants of interest (at a minimum: nitrite, chromium VI, and iodate). NLCP will provide assistance in identifying a laboratory that meets these criteria.

4.5.2 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 should 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.

4.5.3 Prescriptions

If the donor claims to have taken a prescribed medicine that contains either the drug reported positive or a substance that can metabolize to that drug, the donor should provide the medicine container with the appropriately labeled prescription (or the label from the container), a

copy of the medical record documenting the valid medical use of the drug during the time of the drug test, or other information acceptable to the MRO. There is an additional concern in the case of invalid results. Certain antibiotics and NSAIDs are known to cause immunoassay interferences. In those cases of potential interference, the verification of prescriptions or medical records should be completed in the same manner as a positive test result.

When reviewing the positive test result, the MRO will take all reasonable and necessary steps to verify the authenticity of all medical records and other medical information provided by the donor that may be relevant to the medication being prescribed. The MRO should use reasonable medical judgment to make the decision that the provided prescription was generated in response to the donor's current medical condition. Contact with the prescribing physician may be helpful for the MRO in coming to this decision if the donor has provided any consent that may be required. A prescription may be verified by means such as:

- Photos sent by text, e-mail, or fax showing enough angled shots of the bottle label that the MRO can verify the name of the donor on the label, prescription number, name of the drug, prescribing physician, date filled, number of pills in the prescription, number of refills, and the pharmacy name, address, and contact information.
- A verification call to the pharmacy (after the MRO has verbally obtained the information in the item above from the donor and documented it on the MRO record).
- A copy of a pharmacy printout showing the medication dispensing history.
- A signed statement from, or phone discussion with, the prescribing physician. In all cases, the MRO should verify that the contact was with the prescribing physician. For example, the MRO may request the DEA number or state license number. For additional security, the MRO may obtain the physician's telephone number from another source (e.g., online search) and call the individual to verify identity.

Under no circumstances can prescriptions be legally transferred from a different individual to a donor in the event the donor exhausts his or her own prescription medication, even if the other individual's medication is identical and prescribed for the same medical condition (Controlled Substances Act Revised 2010, Pharmacist's Manual, Section X—Dispensing Requirements—Required Information for Prescription Labels. https://www.deadiversion.usdoj.gov/pubs/manuals/pharm2/pharm_content.htm#10). "Federal Food and Drug Administration regulations require that the label of any drug listed as a "controlled substance" in Schedules II, III, or IV of the CSA must, when dispensed to or for a patient, contain the following warning: **"*CAUTION: Federal law prohibits the transfer of this drug to any person other than the patient for whom it was prescribed*."**

A donor's Schedule III, IV, or V prescription medication may be transferred between pharmacies for refill dispensing on a one-time basis only. However, Schedule II prescription medications are issued only once, do not have refills, and cannot be transferred between pharmacies (Title 21 Code of Federal Regulations, Part 1306.25—Transfer between pharmacies of prescription information for Schedules III, IV, and V controlled substances for refill purposes. https://www.deadiversion.usdoj.gov/21cfr/cfr/1306/1306_25.htm).

When determining whether a legitimate medical explanation exists for a positive test, the MRO may consider whether a medication was used during the time period for which it was legitimately prescribed. If a donor's use was not medically authorized, the specimen will be reported as positive. With respect to Schedule II medications, Schedule II drugs are substances that have high potential for abuse, which may lead to severe psychological or physical dependence, or adversely impact the cognitive functioning of the donor. An MRO's decision to contact a donor's employer under these circumstances is not required or authorized by this manual or the Mandatory Guidelines. Rather, an MRO's decision to contact an employer regarding safety issues related to a donor's valid prescription is subject to the MRO's voluntary choice and any obligations the MRO may have with the donor's employing agency. Additional information related to this issue is provided in Chapter 6, Section 6.3, Occupational and Public Safety.

4.5.4 State Initiatives and Laws

State initiatives and laws, which make marijuana or marijuana preparations available to an individual, with or without a physician's 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 nonmedical 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 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.

4.5.5 Changing a Verified Test Result

The MRO may change a previously verified test result in the following situations:

- If an interview with the donor was not initially done and the donor presents information within 60 days of the verification to document that unavoidable circumstances (e.g., serious illness, injury) prevented contact with the MRO or federal agency. Under these circumstances, the MRO may change a test result if the donor presents a legitimate medical explanation for the confirmed test result;
- If information is received that was not available at the time of the original verification indicating an error was made by the laboratory; or
- If the MRO made an administrative error and reported the incorrect result.

4.6 Documentation and Recordkeeping

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

- Donors;
- Collectors;
- Federal agency representatives;
- IITF personnel; and
- Laboratory personnel.

The Mandatory Guidelines require MROs to retain drug test records for a minimum of 2 years from the date of collection. Hardcopy records may be discarded 6 months after conversion to electronic records. The MRO must ensure the confidentiality, integrity, and availability of the data and limit access to any data transmission, storage, and retrieval system. The MRO should have records management procedures to ensure proper disposition of records in accordance with the required retention schedule, and have a business discontinuance plan that ensures proper storage of records that have not reached the end of the retention period (e.g., maintain records or transfer to a secure archival location). (See additional information in Chapter 6, Section 6.6, of this manual, including requirements for external service providers.)

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

- Documentation to support a legitimate 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 private legal opinion.

4.7 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 using Copy 2 of the Federal CCF or a report using a letter/memorandum format. The MRO may send reports by courier or mail or use various electronic means (e.g., teleprinter, fax, secure electronic transmission). Reporting instructions are detailed in Tables 4 and 5. The reporting of the primary specimen (A) bottle result occurs immediately after the MRO has reviewed the information contained in Copy 1 and Copy 2 of the Federal CCF (as described above) and has completed the interview with the donor. The MRO notes in the report to the federal agency if the donor has chosen to have the split (B) bottle tested at a second laboratory.

The report must include the following:

- Donor's name and SSN or employee ID number;
- Specimen's 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.

The MRO must not disclose any numerical values of drug test results to the federal agency unless law or regulation requires that disclosure. Quantitative values are rarely useful because the level may be increasing or decreasing and the quantitative level will vary with the urine specimen concentration (dilution). The important factor is that the drug is present—interpretation of levels is unreliable and there is no such thing as a drug test that is a "little" positive.

4.8 Confidentiality

The Mandatory Guidelines require the MRO to—

- 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
- Maintain the confidentiality of the information received during the review process, including the following (see exceptions below):
  - Information related to the donor's medical condition;
  - Medications;
  - Medical diagnosis; and
  - Medical history.

Despite this general requirement to maintain the confidentiality of medical information, there may be certain circumstances in which an MRO is required to provide such information to other parties. In these instances, prior to the donor interview, the MRO should inform the donor of the circumstances in which disclosure of information may occur.

4.9 Discrepancies That May Require the MRO to Cancel a Test

The MRO must attempt to correct the following errors:

- A missing donor's signature on the MRO copy of the Federal CCF and the collector did not note that the donor refused to sign. The MRO must contact the collector to

obtain a statement that the donor refused to sign the MRO copy. If the collector cannot provide that statement after at least 5 business days following collection, the MRO must cancel the test.

- The certifying scientist failed to sign the laboratory copy of the Federal CCF for a specimen being reported drug positive, adulterated, invalid, or (for urine) substituted. The MRO must contact the certifying scientist to obtain a statement that he/she inadvertently forgot the signature on the laboratory report, but that the certification review was properly conducted. If the MRO does not obtain the statement from the certifying scientist after waiting at least 5 business days, the MRO must cancel the test.

- The electronic report provided by the HHS-certified laboratory or HHS-certified IITF as the sole report for a negative or negative-dilute specimen does not contain the required data elements to ensure that the test result is properly associated with the MRO copy (Copy 2) of the Federal CCF. (See Chapter 4, Section 4.1.2, for the list of required elements.) The MRO must contact the laboratory or the IITF to obtain a corrected electronic report. If the laboratory or IITF does not transmit a corrected copy after waiting at least 5 business days, the MRO must cancel the test.

CHAPTER 5

Interpretation of Results

5.1 Amphetamines

The Medical Review Officer (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.

The Department of Health and Human Services (HHS) instituted the following assay validation and reporting requirements that prevent the possibility of false positive methamphetamine results:

- 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.

- Certified laboratories are required to validate all assays prior to use with federal agency specimens. For amphetamine 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. In February 2013, the National Laboratory Certification Program (NLCP) added substituted phenethylamines to the performance testing (PT) program to ensure all certified laboratories were distinguishing those from the amphetamines.

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 quantification (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.

5.1.1 Enantiomers

An enantiomer in chemical terms is a drug that exists in two forms that are mirror images but are not superimposable. This is exemplified by the right and left hands of a person which are mirror images but not superimposable. Amphetamines are of particular interest as enantiomers because the D-methamphetamine has much greater activity than the L-methamphetamine and the most common confirmation methods do not distinguish the D- and L- forms. 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. Amphetamine confirmatory tests specifically identify amphetamine and methamphetamine if present, but do not distinguish between enantiomers (unless a chiral assay is employed as discussed below). Therefore, there is a possibility that a laboratory positive result could be reported for L-methamphetamine and/or L-amphetamine.

(Comment: Enantiomer test results aid in result interpretation.[2] Some laboratories perform enantiomer testing as part of their test protocol and include the results in the original report. If this is not the case, the MRO may request the completion of the chiral assay on individual specimens following the interview with the donor or may have a blanket request for all amphetamine/methamphetamine results. The latter may be a desirable action for the MRO to allow the MRO to initiate the interview with the donor with a definitive result in hand. In addition, there can be a significant time savings in the case of the blanket request—the testing laboratory can proceed directly to completing the test or sending the primary specimen for the additional testing for enantiomers. The number of amphetamines reported and requiring the chiral assay is relatively small and the MRO may obtain concurrence from the federal agency on the blanket request. Although few laboratories perform the D,L-amphetamine assay, HHS [NLCP] can provide a laboratory name for testing of the amphetamine enantiomers, as needed.)

Some laboratories may employ a chiral GC/MS or LC/MS/MS assay that distinguishes between the D- and L-enantiomers (isomers) and determines the relative percentages of each

enantiomer for both amphetamine and methamphetamine. 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 Bottle A 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 (e.g., when the MRO receives a methamphetamine positive result from a laboratory and the donor reports use of a nasal inhaler product within days prior to the test).

5.1.2 Prescription Drug Products

A number of drugs contain, or are metabolized to, amphetamine or methamphetamine. One example is selegiline (Eldepryl), a brain monoamine oxidase inhibitor used in the adjunctive treatment of Parkinson's disease and 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. Representative brand names that may produce a positive result for amphetamine or methamphetamine are benzphetamine, Adderall, Vyvanse, Desoxyn, Eldepryl, and Didrex. Note that benzphetamine metabolizes to D-methamphetamine and Eldepryl metabolizes to the L-enantiomer. Additional information is presented in Table 6. The use of enantiomeric analysis is useful in distinguishing methamphetamine abuse from prescription medications.

5.1.3 Non-prescription Drug Products

Some non-prescription products contain sympathomimetic amines that 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 over-the-counter (OTC) products (e.g., inhalers such as Vicks® VapoInhaler® as well as some generic brands) 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.

5.1.4 Designer Sympathomimetic Substances

A positive MDMA or MDA result is evidence of illegal drug use. There are no prescription or OTC medications that contain these designer sympathomimetics and there are no legal medical uses of the substances. These substances are differentiated from the amphetamines during testing and will not be misidentified as amphetamines using a confirmatory test as required by the Mandatory Guidelines. Generally, the designer sympathomimetics are considered detectable in urine for 2 to 3 days.

5.2 Cannabinoids

As of the publishing date of this manual, 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. An oral 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.

In previous years, marijuana was generally consumed by smoking cannabis of rather limited drug concentration. Over the past few decades, cannabis potencies have increased substantially and methods have been developed to provide highly concentrated exposures. A variety of cannabis preparations have become available for consumption by smoking, inhalation, oral ingestion, and other routes of administration.

A prescription medication that also produces positive tests for cannabinoids is dronabinol. The active ingredient of this product is THC and is available as Marinol® (Roxane Laboratories) in 2.5, 5, or 10 mg soft gelatin capsules for oral administration. When a donor claims to have a prescription for dronabinol, the MRO should allow the donor the opportunity to provide the supporting documentation. A valid prescription for dronabinol is a legitimate medical explanation for a positive THCA result. Marinol® is approved for the treatment of anorexia associated with weight loss in patients with AIDS, and for treating nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. The drug has psychoactive effects that may present safety issues, and patients prescribed Marinol® should be warned not to drive, operate complex machinery, or engage in hazardous activity. Nabilone (Cesamet®) is a synthetic cannabinoid. This drug is not, and does not metabolize to, THC or THCA, so will not produce a positive drug test. Therefore, the use of Nabilone is not an acceptable medical explanation for a positive confirmed drug test.

Compounds or substances that have not been approved by FDA cannot be used as a legitimate medical explanation. For example, Sativex® (GW Pharma Ltd, UK) is not currently FDA-approved. Sativex® contains THC and cannabidiol (CBD) and is proposed as treatment for symptom improvement in adult patients with moderate to severe spasticity. Use of Sativex ® may result in a positive drug test for THCA. Another example is Epidiolex® (GW Pharma Ltd, United Kingdom), a CBD-enriched product for the control of intractable epilepsy in children. Epidiolex is CBD only and does not contain THC. Therefore, this compound would not cause a positive drug test. A product named Charlotte's Web Oil is being advertised in Colorado for similar symptoms. That product appears to be a marijuana extract enriched with higher ratios of CBD to THC. The product might give a positive THCA test result. The DEA has reiterated their position on the extracts of marijuana such as CBD or Charlotte's Web Oil. CBD is currently being illegally produced and marketed in the United States in violation of the CSA and the Federal Food, Drug, and Cosmetic Act. Because this extract is a derivative of marijuana, it falls within the definition of marijuana under federal law and is listed as Schedule I.[3]

5.3 Cocaine

There is no prescription medication that contains cocaine; however, the medical community uses a solution containing 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. Other anesthetics do not produce positive test results. If cocaine is used, the licensed physician performing the procedure would document its use in the donor's medical record. The medical use must have occurred within 2 or 3 days prior to when the urine specimen was collected for a possibility of a positive result. Use at an earlier time may not cause a positive urine test.

5.4 Opioids

The federal drug testing program's goal regarding opioids is to detect the illicit use of morphine, codeine, heroin, oxycodone, oxymorphone, hydrocodone, and hydromorphone. For specimens that have been reported positive for one or more of these opioid analytes, an MRO may request quantitative information from the laboratory for any other opioid analytes (i.e., morphine, codeine, 6-acetylmorphine (6-AM), oxycodone, hydrocodone, oxymorphone, hydromorphone) that are present below the cutoff. 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 opioid analytes is reported as positive.

5.4.1 Morphine and Codeine

A donor who tests positive for one or more opioids may have legally used the drug(s) (see Chapter 7, Drug Information). The opioid drug class poses some unique challenges with regard to interpretation because a positive result may be from a legitimate source, including the following:

- Codeine or morphine may be present due to consumption of poppy seeds.
- A positive result for any of the opioid analytes (with the exception of 6-AM) may be from legitimate use of a drug product.
- 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.

The MRO must assess the laboratory result and the information from the donor to verify the drug test positive.

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

- 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 illicit use of any opium or opium derivative (e.g., morphine or codeine) listed in the Controlled Substances Act (CSA) Schedule I or II, the MRO verifies the result as positive; or
  - If there is no clinical evidence of illicit use, the MRO verifies the result as negative.
- When a laboratory reports a specimen as positive for codeine and/or morphine and the codeine and/or morphine result is greater than or equal to 15,000 ng/mL—
  - If the donor does not present a legitimate medical explanation for the presence of morphine or codeine (e.g., a valid prescription), the MRO verifies the result as positive. Consumption of food products is not a legitimate medical explanation for the donor having morphine or codeine at or above this concentration; or
  - 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.

5.4.2 Oxycodone, Hydrocodone, Oxymorphone, Hydromorphone

These semi-synthetic opioids are available as pharmaceutical narcotic analgesics and are generally taken orally; however, the presence of hydromorphone and oxymorphone in the urine may be due to the use of the pharmaceutical or due to metabolism of hydrocodone or oxycodone, respectively, by O-demethylation. Metabolism of morphine and codeine also has been shown to lead to formation of minor amounts of hydromorphone and hydrocodone, respectively, but these minor metabolites have only been observed where there were very high concentrations of the parent drug present. Due to individual metabolic differences, not all metabolites or parent drug may be present. The urinary pattern of excretion changes significantly on an individual basis due to variations in time of dosing, fluid intake, absorption, metabolism, and excretion. In addition, single-dose studies have been completed and have defined certain ratios and clearance times; however, higher doses by abusers and long-term use or abuse patterns may be quite different. These semi-synthetic opioids are not found in food products and are therefore subject to review as the only appropriate use is by prescription.

Oxycodone is a widely used and abused prescription drug in the United States. Interpretation of urine tests for oxycodone is complicated by its metabolism to oxymorphone, which is also available commercially and misused. A single administration of a low dose of oxycodone (20 mg) characterized the metabolism and disposition of oxycodone in human urine. Oxycodone appeared in the urine in about 2 hours and was generally found along with oxymorphone. Peak concentrations of oxycodone and metabolites occurred between 3 and 19 hours. The mean peak concentration of oxycodone was higher than that of the oxymorphone, but the oxycodone concentration declined more quickly than the concentration of oxymorphone. At a cutoff concentration of 50 ng/mL, detection times were approximately 30 hours for oxycodone and oxymorphone. Some final specimens at relatively low concentrations contained only oxymorphone.[4]

Like oxycodone, hydrocodone is widely used and abused in the United States. Interpretation of urine tests for hydrocodone is complicated by its metabolism to hydromorphone, which is also available commercially and misused. An investigation of a single, oral, immediate release, 20 mg dose of hydrocodone was completed using 12 healthy, drug-free adults. The hydrocodone was administered in a controlled clinical setting and urine specimens were collected at timed intervals for up to 52 hours. Hydrocodone appeared within 2 hours followed by the appearance of hydromorphone. Hydrocodone exhibited peak concentrations higher than the metabolite, hydromorphone, which was excreted extensively as a conjugate. At

the cutoff concentration of 50 ng/ml, detection times were around 28 hours for hydrocodone and 26 hours for hydromorphone.[5]

5.4.3 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/she had eaten poppy seeds around the time the urine was collected. HHS included additional criteria in the Mandatory Guidelines to distinguish between specimens testing positive due to opioids abuse and specimens testing positive due to poppy seeds. See 5.4.2 above.

5.4.4 6-Acetylmorphine Positive Specimens

When a laboratory reports a specimen as positive for the heroin metabolite (6-AM), it is proof of heroin use. There is no legitimate medical explanation for a 6-AM positive result. 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. 6-AM is metabolized to morphine, so morphine is generally present (i.e., at or above the program cutoff of 2000 ng/mL) in positive 6-AM specimens. There are reasons that morphine may not be present or is present below 2000 ng/mL in a positive 6-AM 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). There have been reports of these "atypical" specimens containing 6-AM without detectable morphine.

5.5 Phencyclidine

A positive phencyclidine (PCP) result is evidence of illegal drug use. There is no prescription or OTC medication that contains PCP, there is no legal medical use of PCP, and there is no other substance that can be misidentified as PCP using a confirmatory test as required by the Mandatory Guidelines. PCP is considered detectable in urine for several days to several weeks depending on the frequency of use.

5.6 Other Non-Negative Reports

5.6.1 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 the following:

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

A certifying technician at an instrumental initial test facility (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's response to a dilute specimen report depends on whether the drug test result is positive or negative. These MRO actions are shown in Table 4, Medical Review Officer Actions for Primary Specimen Reports (Bottle A).

5.6.2 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, the donor is given the opportunity to prove the ability to produce urine that meets substitution criteria as described below.

- If the donor claims to have personal characteristics such that his/her urine normally satisfies the substitution criteria—
  - The MRO requests that the donor demonstrate this by providing a urine specimen that is collected following routine procedures for direct observation.
  - The second specimen must meet the criteria for "substituted" and provide a reasonable basis to conclude that the donor's personal characteristics are a legitimate medical explanation.

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 donor must provide a copy of the medical record showing the creatinine and specific gravity values to support that claim.

5.6.3 Adulterated Specimens

The MRO is required to attempt to contact the donor to 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.

5.6.4 Invalid Specimens

The MRO is required to attempt to contact the donor to give the donor an opportunity to explain any reason for the invalid result (e.g., provide information on medications or a medical condition) for specimens invalid due to a possible adulterant or for specimens with an abnormal physical characteristic. The MRO is **NOT** required to contact the donor for specimens invalid due to discrepant creatinine/specific gravity values, for specimens invalid due to abnormal pH, or for specimens that contain nitrite ≥200 mcg/mL and <500 mcg/mL by a nitrite confirmatory test.

For invalid results based on pH of 9.0 to 9.5, the MRO must consider if time and warm temperature could account for the result.[6] The MRO must contact the collection site, IITF, and/or laboratory to investigate the conditions of shipping and storage. The procedures to follow are described in Table 4.

The MRO must take the following actions for a specimen with an invalid result:

1. If the donor's explanation is medically legitimate OR if time and temperature conditions appear to account for pH in the 9.0–9.5 range, report the test as cancelled 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 below.

2. If the donor's explanation is not medically legitimate OR if time and temperature conditions do not appear to account for pH in the 9.0–9.5 range, report the test as cancelled with the reason for the invalid result and direct the federal agency to immediately collect another specimen using a direct observed collection procedure. If the specimen recollected under direct observation is valid, the result is reported in accord with Chapter 5 and Table 4 of this manual.

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 cancelled 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; or

b. A different reason than reported for the first specimen, **do not contact the donor**. Report the test as cancelled 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); or

   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 in the 9.0–9.5 range).

5. If needed under Item 4 above, arrange for a medical evaluation of the donor as follows:

   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.

   c. The MRO reports in writing to the federal agency as follows:

      – "**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 sign and symptom of drug use exist; or

- "**Test cancelled**" when the medical evaluation reveals clinical evidence of drug use. The MRO must inform the federal agency that the cancelled 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
    - Basis for determining that signs and symptoms of drug use exist.

The MRO must report a verified test result to an agency by faxing a completed MRO copy of the Federal CCF, transmitting a scanned image of the completed MRO copy of the Federal CCF, or faxing a separate report using a letter or memorandum format. If a report is sent electronically, the MRO must ensure the security of the transmission. In most cases, the federal agency will be expected to provide the medical examination to ensure the report is unbiased.

CHAPTER 6

Additional Medical Review Officer Responsibilities

6.1 Federal Agency Blind Samples

Federal agencies are required to have blind samples submitted with donor specimens to each instrumented initial test facility (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 (to a maximum of 400 blind samples with 75% negative, 15% positive for one or more drugs, and 10% either adulterated or substituted). 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 Medical Review Officer [MRO]).

The Mandatory Guidelines include requirements for blind samples as follows:

- 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 1.5–2 times the initial drug test cutoff (see Appendix D, Specimen Reporting Criteria).
- A blind sample that is positive must be validated by the supplier as to its content using appropriate initial and confirmatory tests.
- 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.
- A blind sample that is adulterated must be validated by the supplier using appropriate initial and confirmatory tests, and have the characteristics to clearly show that it is an adulterated sample at the time it is validated by the supplier.
- A blind sample that is substituted must be validated by the supplier using appropriate initial and confirmatory tests, and must have the characteristics to clearly show that it is a substituted sample at the time it is validated by the supplier.
- The supplier must provide information on the blind sample's content, validation, expected results, and stability to the collection site/collector sending the blind samples to the laboratory or IITF, and must provide the information upon request to the MRO, the federal agency for which the blind sample was submitted, and the Department of Health and Human Services (HHS).

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 Custody and Control Form (CCF) and to properly label the specimen bottle(s) containing the sample. Because there is no donor associated with a blind sample, the collector generates a fictitious social security number (SSN) or employee identification (ID) number and fictitious initials to write on the specimen bottle label/seal.

The collector or the federal agency that 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 may not have properly submitted the sample.

When an IITF or a 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:

- Contact the laboratory or IITF and attempt to determine if the laboratory or IITF made an error during the testing or reporting of the sample;
- Contact the supplier of the blind sample and attempt to determine if the supplier made a mistake when preparing the blind sample;
- 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; and
- Notify both HHS and the federal agency for which the blind sample was submitted (if there is no obvious reason for the inconsistent result).

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.

6.2 Insufficient Specimen

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 3 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, not to exceed a maximum of 40 ounces over 3 hours). 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 5 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 that MRO has the appropriate expertise.

If the laboratory reports insufficient volume, the MRO consults with the laboratory and the collection site to determine the reason for the insufficient volume. If the insufficient volume is due to leakage in transit or laboratory error (e.g., spill), the MRO may consider the basis for the test and contact the agency concerning the test. The MRO must inform the federal agency that the cancelled 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 is **NOT** required to contact the donor for specimens insufficient due to spillage or error. If the insufficient volume is due to a limited collection that was not noted, the MRO will implement the medical evaluation procedure.

The purpose of the evaluation is to determine whether the donor has an ascertainable physiological condition (e.g., urinary system dysfunction) or medical documentation existing prior to the collection attempt of a 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 the following:

- Destruction of the glomerular filtration system leading to renal failure;
- Unrepaired traumatic disruption of the urinary tract;
- Diagnosis of "social anxiety disorder" that has been medically documented and meets the DSM criteria.

Acute or temporary medical conditions such as cystitis, urethritis, or prostatitis may interfere temporarily but do not receive the same considerations as the conditions listed as examples. Unsupported assertions of "situational anxiety" or dehydration are not considered valid reasons and shall be regarded as a refusal to test.

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

- 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);
- The consequences of a refusal to take a drug test for the federal agency (see Chapter 4, Section 4.2, Refusal to Test); and
- That the examining physician must agree to submit a written statement and instructions for submitting the written statement to the MRO with a recommendation for the MRO's determination and the basis for the recommendation. (The statement must not include any detailed information on the donor's medical condition beyond that necessary to explain the recommendations.) The recommendation for the MRO determination must be one of the following:
  - 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 donor from providing a sufficient amount of urine. The MRO reports a refusal to test to the federal agency
  - That the donor's medical condition has or, with a high degree of probability, could have precluded the donor from providing a sufficient amount of urine, but is not a permanent or long-term disability. The MRO reports a test cancelled to the federal agency; or
  - That a permanent or long-term medical condition has or, with a high degree of probability, could have precluded the donor from providing urine, but is highly likely to prevent the employee from providing a sufficient amount of urine for a very long or indefinite period. In the case the result is needed for the agency, the MRO follows paragraph 6.2.1 below. Otherwise, the MRO reports a test cancelled to the federal agency.

In making a determination based on the medical evaluation, the MRO must consider and assess the recommendations made by the referral physician. The MRO reports in writing to the federal agency as follows:

- **Refusal to test** when the MRO determines that there is no adequate basis for determining a medical condition interfered with the collection; or
- **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.

6.2.1 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 may also consult 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:

- "**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 sign or symptom of drug use exists.

or

- "**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.

6.3 Occupational and Public Safety

Executive Order 12564 uses the term "illegal drugs" to refer to any controlled substance included in Schedule I or II of the Controlled Substances Act (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 incorrectly identify an individual who is receiving medical care as misusing drugs and, thereby, provide confidential medical information to an agency.

There is 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 an MRO is given information that indicates that a donor's use of a legitimately prescribed medication creates a safety risk (given the donor's job functions), the MRO may be faced with a decision about what to do with this information. The Mandatory Guidelines do not address this situation, and they do not require MROs to determine whether a valid prescription medication can be used safely while performing a donor's work functions. Therefore, before an MRO decides to discuss safety information related to a donor's valid prescription with the donor's agency, the MRO should consult (1) the terms of the service agreement with the agency, (2) any agency policies or rules that govern such circumstances, and/or (3) private legal counsel. In addition, if an MRO's service agreement with an agency does not address how to handle safety information related to a donor's valid prescription, the MRO should discuss this issue with the agency. Please be advised, however, that nothing in this section or manual is intended to reflect a SAMSHA or an HHS position regarding whether an MRO's disclosure of safety information that is obtained during the course of the drug testing process and conveyed to an agency, is legal or appropriate in any given circumstance. Also note that if an MRO does discuss safety-sensitive information with a donor's employer, the MRO cannot disclose drug testing numerical values in that discussion.

6.4 Donor Rights to Information

An individual who is the subject of a drug test may, upon written request through the MRO and the federal agency, have access to records relating to his/her drug test; any records relating to the results of any relevant certification, review, or revocation of certification proceedings; and a documentation package (at the donor's expense). 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:

- A cover sheet that provides a brief description of the drug testing procedures and specimen validity tests performed on the donor's specimen;
- A table of contents that lists, by page number, all documents and materials in the package;
- 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;
- A brief description of the initial drug tests and specimen validity test 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;
- 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;
- A copy of the résumé or curriculum vitae for the certifying technician or certifying scientist that certified the test result; and
- A copy of the résumé or curriculum vitae for each of the IITF's Responsible Technicians or each of the laboratory's Responsible Persons.

6.5 Protection of Personally Identifiable Information (PII)

Personally identifiable information (PII) is information that can be used to distinguish or trace an individual's identity alone or when combined with other personal identifying information that is linked or linkable to a specific individual. PII that may be on the Federal CCF includes the donor's SSN or employee ID number, name, date of birth, telephone numbers, and employment status. As the use of electronic means of communications in the MRO business increases, it is incumbent on the MRO and all persons with access to this information to ensure that all donor PII is protected.

All federal agencies and drug testing service providers (e.g., collectors, test facilities, MROs) must implement procedures and administrative, technical, and physical controls to ensure donor privacy by restricting access to PII and to drug test results on hardcopy and electronic Federal CCFs or drug test results entered in to a computer system or database. Access to donor PII and drug test results must be limited to those individuals requiring access to fulfill job duties. Such individuals must receive training to make them aware of their responsibilities for protecting the information. Confidentiality must be maintained from the time the donor's PII is obtained through transmission/transport of the Federal CCF, specimen testing, and records handling (i.e., storage, retrieval, and final destruction).

MROs are required to provide a written verification to each HHS-certified IITF and HHS-certified laboratory for which they review results that the devices used to receive reports are in a secure area. This verification must be provided annually. If the MRO obtains laboratory drug test reports electronically via either a laboratory-owned system or a laboratory-contracted external service provider (as described in Section 6.6), the MRO must provide a letter to the laboratory annually attesting to the security and confidentiality of the information (e.g., username, password) that allows access to the system. For example, many laboratories provide Web-based online access to results to allow the MRO (or designated employees) to log in to the portal and download results. To control and protect information, the MRO must ensure that the access information is carefully protected and is only known by key personnel and changed immediately upon the departure of any employee possessing the password.

6.6 External Service Providers

An external service provider (e.g., third party administrator, ECCF provider, software service provider, cloud service provider) may perform services on behalf of the MRO related to regulated drug testing. For example, an MRO, MRO employer, or MRO group (i.e., MRO organization with more than one MRO), may have a contractual agreement with an external service provider to provide administrative services and/or receive MRO copies of the Federal CCF from collectors and reports from HHS-certified laboratories and IITFs, provide these documents to the MRO, and store these and other MRO records.

MROs who use external service providers are strongly encouraged to enter into a binding written agreement/contract (i.e., between the MRO, the MRO's employer, or the MRO's group, and an authorized representative of the external service provider) that specifies responsibilities of the external service provider as they relate to regulated drug testing. Appendix F of this manual provides an MRO Verification Statement that specifies the priority elements that should be

addressed in an MRO agreement/contract with an external service provider. In addition, the MRO whose name appears on the Federal CCF as the MRO of record is responsible for ensuring that the external service provider complies with applicable requirements of the Mandatory Guidelines (e.g., Subparts M and N), unless the MRO's employer or group provides documentation that designates another MRO within its organization as responsible for the external service provider's compliance with the Guidelines.

To ensure that MROs are properly identified (on Federal CCFs), MROs, MRO employers, or MRO groups should provide federal agencies with documentation that designates a specific MRO to be listed in the agency's Federal CCFs. It is also recommended that this documentation be provided to a federal agency within seven business days following the execution of a binding agreement between the federal agency and the MRO (or the MRO's employer/group) for the provision of MRO services that are subject to the Mandatory Guidelines. MROs, MRO employers, and MRO groups that have an existing agreement with a federal agency to provide MRO services as of the effective date of this manual should provide the documentation described in this paragraph to the federal agency within 30 calendar days following the effective date of this manual if such documentation has not been provided previously.

MROs are also strongly encouraged to ensure their external service providers adhere to any specific federal agency requirements.

Section 4.6 of this manual addresses MRO documentation and recordkeeping, including the requirement for the MRO to retain drug test records for a minimum of 2 years from the date of collection. MROs using an external service provider to maintain their records must ensure that such records are discarded in accordance with the required retention schedule. MROs should also ensure that their external service providers have a business discontinuance plan that addresses records disposition. Records must be returned to the MRO or to another location/entity that has been agreed to by the MRO.

HHS-certified laboratories and IITFs are not allowed to report drug test results to entities other than the MRO of record (i.e., MRO whose name is listed on the Federal CCF) prior to obtaining an MRO Verification Statement (see Appendix F), or similar statement—from the MRO, MRO's employer, or MRO's group—that documents that an external service provider is authorized to receive and/or disseminate federally regulated drug testing information and records on the MRO's behalf.

CHAPTER 7
Drug Information

7.1 Drug Classes Subject to Regulated Testing

The Federal Government classifies controlled substances under five schedules in the Controlled Substances Act (CSA). The CSA is available on the Drug Enforcement Administration (DEA) Web site at: https://www.deadiversion.usdoj.gov/schedules/ and a description is included in Appendix E.

7.1.1 Amphetamines

a. Amphetamine and Methamphetamine

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

Tolerance can develop to the effects of amphetamine and methamphetamine. A typical therapeutic dose is 5 mg. Individuals who abuse these drugs are reported to inject up to 1 g in a single 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).

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 reabsorption and thus allowing more of it to be metabolized. In 24 hours, about 74% of a dose will be excreted unchanged if urine is acidic, while 1 to 2 % is excreted if urine is alkaline.

Pharmaceuticals and Use

A single therapeutic dose of amphetamine or methamphetamine can produce a positive urine test 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. 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 over-the-counter (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.[7]

Table 6 lists some substances known to metabolize to amphetamine and methamphetamine.

b. Methylenedioxymethamphetamine and Methylenedioxyamphetamine

Background

3,4-Methylenedioxymethamphetamine (MDMA, "Ecstasy," "Molly," "E," "XTC") and its major, active metabolite, 3,4-methylenedioxyamphetamine (MDA, EA-1299, "Love") are psychoactive amphetamines. Both MDMA and MDA are available as illicit parent drugs and are used at "rave" parties; these drugs may be used with other drugs or the same tablets may actually contain other drugs such as ephedrine, dextromethorphan, ketamine, caffeine, cocaine, methamphetamine, or even synthetic cathinones (bath salts).

MDMA and MDA are central nervous system stimulants and are used recreationally as hallucinogens with effects similar to those of mescaline and amphetamines. Both MDMA and MDA can exist as D- and L-enantiomers (see definition above under Amphetamine and Methamphetamine).

Routes of Administration

- MDMA—MDMA is taken orally, usually as a capsule or tablet. The popular term "Molly" (slang for "molecular") refers to the pure crystalline powder form of MDMA, usually sold in capsules. The drug's effects last approximately 3 to 6 hours, although it is not uncommon for users to take a second dose of the drug as the effects of the first dose begin to fade. It is commonly taken in combination with other drugs.

- 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.

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.

Pharmaceuticals and Use

MDMA and MDA in both enantiomeric forms are regulated as Schedule I drugs and are not available as pharmaceuticals.

7.1.2 Cannabinoids (Marijuana)

a. Background

Marijuana, *Cannabis sativa*, is controlled under Schedule I of the CSA and contains many cannabinoid substances. 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).[8]

Cannabinoids produce euphoria or a "high" and a sense of relaxation 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.

Current marijuana is much stronger than the plant of the 1960s. Plants that produce high concentrations of THC are not grown from seeds, but from cuttings of high producers to retain the genetic characteristics of the parent plant. As a result, concentrations of THC in current crops frequently exceed 10% and are often much higher. The growing plants are trimmed to remove excess undergrowth and stems and prevent loss of nutrients to enhance flowering. When the plants flower, the buds are manicured to remove large leaves and the trimmed buds are dried. The trimmings are saved and used to prepare various products. The buds are generally smoked and the dried resin beads can be used as "kief" or pressed into hash for storage and smoked or used in other ways. A relatively recent and dangerous procedure for getting high is using "Dabs." The THC is extracted from trimmings using a highly flammable solvent such as butane and then concentrated to make an amber-like material called "wax" that is very high in THC (60%–80%). The "wax" is volatilized by a propane flame and the person dabbing inhales as the THC is

volatilized in a "piece," pulling the smoke into the person's lungs. THC is also prepared and consumed in candy, baked goods, beverages, and other foods. The significance of the changes in growth and use of marijuana is that the THC concentration is increasing in the plants and users are now extracting and purifying the THC to enhance their hits.

Routes of Administration

- Marijuana—smoking, oral (i.e., eating), and inhalation through a hash pipe.
- Hashish—smoking (preferred) and oral (i.e., eating).
- Wax, shatter, dabs—inhaled or smoked (especially by e-cigarettes).

Cannabinoids are usually smoked or vaporized through a water pipe. Transpulmonary 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, gastrointestinal 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 THCA.

Current immunoassay procedures have significant cross reactivity to many marijuana compounds and metabolites that are excreted in urine, while the confirmatory test specifically identifies and quantifies the single metabolite THCA. The THCA metabolite that is confirmed has been found to account for approximately 30% of the urine immunoassay response—the explanation for the difference in the initial test cutoff of 50 ng/mL and the confirmatory cutoff of 15 ng/mL. 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 THCA that is equal to or greater than the 15 ng/mL confirmatory cutoff. Infrequent marijuana use may cause positive initial test results for 1 to 5 days. Chronic smokers slowly release THCA over a longer time and may continue to produce detectable levels of THCA for longer than 5 days.

Pharmaceuticals and Other Use

Dronabinol is available as Marinol® (Roxane Laboratories) in 2.5 mg, 5 mg, or 10 mg soft gelatin capsules for oral administration. When a donor claims to have a prescription for dronabinol, the MRO should allow the donor the opportunity to provide the supporting documentation. A valid prescription for dronabinol is a legitimate medical explanation for a

positive THCA result. Marinol® may be used for stimulating appetite and preventing weight loss in patients with a confirmed diagnosis of AIDS and for treating nausea and vomiting associated with cancer chemotherapy. The drug has psychoactive effects that may present safety issues and patients prescribed Marinol® should be warned not to drive, operate complex machinery, or engage in hazardous activity. THC preparations from *Cannabis sativa* contain Δ^9-THC and a number of closely related cannabinoids including Δ^9-tetrahydrocannabivarin (THCV). Marinol® is produced by a synthetic process that leads primarily to THC but with no THCV. As a result, THCV testing may distinguish between dronabinol use and cannabis use, or may identify an individual who uses cannabis in addition to prescribed dronabinol;[9] however, studies indicate that THCV is not present in all strains of cannabis[10] and there is variability in the concentrations among strains of cannabis.[11] As a result, the MRO must carefully consider the case if a THCA positive result is presented along with the results of a THCV assay. If the analytical results show the presence of THCV, the result may be useful to confirm the use of cannabis; however, if the THCV assay does not show the presence, the information has little use in a decision on the drug testing result.

Nabilone (Cesamet®) is a synthetic cannabinoid. This drug does not metabolize to THC or THCA, so would not produce a positive drug test. Therefore, the use of Nabilone is not an acceptable medical explanation for a positive confirmed drug test.

Compounds or substances that have not been approved by FDA cannot be used as a legitimate medical explanation. For example, Sativex® (GW Pharma Ltd, UK) contains 2.7 mg THC and 2.5 mg cannabidiol (CBD) per dose. Sativex® is indicated as treatment for symptom improvement in adult patients with moderate to severe spasticity and due to multiple sclerosis (MS) who have not responded adequately to other medications and who respond to Sativex® in an initial trial. Sativex® is a mixture of cannabinoids and may result in a positive THCA test. Another example is Epidiolex® (GW Pharma Ltd, UK), a medication to control intractable epilepsy in children. Epidiolex® is CBD and, according to GW Pharma, does not contain THC. Therefore, this compound would not cause a positive drug test.

b. Medical 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.

Passive Inhalation of Marijuana

Passive inhalation (i.e., an inadvertent exposure to marijuana) are frequent excuses for positive urine tests for THCA; however, it remains SAMHSA's position that passive exposure to a drug (e.g., second-hand marijuana smoke) is not a legitimate medical explanation for a positive marijuana test result under the Mandatory Guidelines. The basis for this position is that scientific studies have shown that there is very little possibility that a donor can test positive for the confirmatory analyte THCA in the urine as the result of passive exposure.[12] Prolonged exposure to high levels of second-hand marijuana smoke may result in detectable levels of THCA in the urine if the individual willingly exposes themselves to extreme levels of second-hand marijuana smoke on a sustained basis and in an enclosed space. Federal agencies may consider willful and sustained exposure to extreme levels of second-hand marijuana smoke as a form of active marijuana use even though the route of administration is through second-hand smoke.

When a donor claims that his/her positive THCA test was due to passive inhalation, the MRO may not accept this as a legitimate explanation for a positive THCA test result.

Hemp Products

"Industrial hemp" (marijuana with a THC content of 0.3 percent or less) for agricultural research purposes where permitted under state law; however, the Act does not permit the production of non-FDA-approved drug products made from cannabis.[13] "Non-consumable" hemp items (e.g., clothing, industrial solvents, and animal feed mixtures) are considered noncontrolled 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 may not accept such explanations as a legitimate explanation for a positive THCA test result.

7.1.3 Cocaine[14]

a. 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.[15]

Routes of Administration

- Intranasal (i.e., snorting, inhalation).
- Smoking the "free base" or "crack" form of the drug has become the predominate route.
- Intravenous injection.
- Oral ingestion.

Metabolism and Excretion

Cocaine is rapidly and extensively metabolized by liver and plasma enzymes to its major metabolite, benzoylecgonine.[16] Benzoylecgonine can usually be detected in urine for 2 to 3 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.

b. Pharmaceuticals and Other Use

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 no more than 2 or 3 days prior to when the urine specimen was collected. Use at an earlier time may not cause a positive urine test. Other potential explanations for a cocaine result include the following:

- **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 test for cocaine using the HHS cutoffs for initial and confirmatory testing. When a donor claims that the 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 (FDA) 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 the positive benzoylecgonine test was due to drinking a beverage with coca leaves as an ingredient, the MRO should allow the donor to explain where and when the tea was purchased. Drinking "Health Inca Tea" or other beverage purporting to contain coca leaves is not an acceptable alternative explanation for the presence of benzoylecgonine in the donor's urine.

7.1.4 Opioids[17]

a. Background

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 terms "opiates" and "opioids" are defined in the glossary in Appendix A. For this

manual, the term “opioids” is used to represent morphine, codeine, heroin, hydrocodone, hydromorphone, oxycodone, and oxymorphone.

The opioids have agonist or partial agonist activity at the opioid receptor and may or may not have structural similarity to the principle opium alkaloids. The use of opioids is a major illicit drug problem around the world, considering the impact on public health and public order.[18] In the United States, the problem of diverted pharmaceutical opioids is reaching crisis proportions. About one-sixth of the people aged 12 and older who started drug use in 2010 began with abuse of prescription painkillers from various sources.[19] In 15 states, the number of deaths from prescription medications now exceeds the number of traffic fatalities.[20]

Morphine is the most abundant naturally occurring opiate and is representative 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 is commonly used in analgesic, antitussive, and antidiarrheal agents. Codeine was first isolated in 1832 and is an opioid analgesic with weak affinity for the mu opioid receptor. In its pure form, codeine is considered a Schedule II compound but is classified as a Schedule III compound when combined with other weak analgesics (such as acetaminophen) and as Schedule V when in liquid cough suppressant preparations. Its analgesic potency is approximately 10% that of morphine. Codeine is produced commercially by 3-0-methylation of morphine. Codeine is most often dispensed based on a physician’s valid prescription: however, codeine may be available in certain preparations (e.g., liquid antitussive) without a prescription at the pharmacy counter in certain local jurisdictions throughout the United States, depending on state laws. If codeine is obtained legitimately through a pharmacy under those circumstances, the pharmacy will create and retain a record that can be verified by the MRO. In the absence of verification for the record of sale of the codeine preparation from the pharmacy, the MRO must report the result as positive.

Heroin (diacetylmorphine) is a semisynthetic opioid 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 metabolite 6-acetylmorphine (6-AM).

Hydrocodone (Vicodin®, Lortab®) is a Schedule II semisynthetic opioid derived from codeine and is indicated for moderate to moderately severe pain as well as symptomatic relief of a nonproductive cough. It is a very commonly prescribed opioid. Hydrocodone, like codeine, has

weak binding to the mu opioid receptor and acts as a pro-drug metabolizing to hydromorphone, which has significantly stronger mu opioid receptor binding activity.

Hydromorphone (Dilaudid®) is a Schedule II semisynthetic opioid that acts as an agonist on the mu opioid receptor with 7 to 10 times the potency of morphine. Hydromorphone is also a metabolite of hydrocodone via 0-demethylation.

Oxycodone (Percocet®, Percodan®, Oxycontin®) is a Schedule II semisynthetic opioid in pure form or in combination with acetaminophen or aspirin. Oxycodone has high oral bioavailability with a structure similar to hydrocodone with an added hydroxyl group on the number 14 carbon atom.

Oxymorphone (Opana®) is a Schedule II semisynthetic opioid and is a metabolite of oxycodone via phase I metabolism. The drug has approximately 10 times the potency of morphine for analgesia.

Cognitive and psychomotor performance can be impaired by opioids, although the duration and extent of impairment depend on the type of opioid, 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, confusion or mental dullness, slurring of speech, drowsiness, or nodding—the head drooping toward the chest and then bobbing up ("on the nod").

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 opioids are physically and psychologically addictive and produce withdrawal symptoms that differ in type and severity. Flu-like symptoms are common during opioid 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.
- Hydrocodone—tablet, capsule, liquid, or extended-release tablet or liquid for oral use.

- Hydromorphone—tablet or extended-release tablet for oral use, injection, or rectal.
- Oxycodone—liquid, tablet, capsule, and extended-release tablet for oral use.
- Oxymorphone—tablet or extended-release tablet for oral use.

The methods listed above represent the pharmaceutical preparations. Abusers may use in a variety of methods, including smoking.

Metabolism and Excretion

Morphine is rapidly absorbed and excreted as unchanged morphine, morphine-3-glucuronide (primary metabolite) and morphine-6-glucuronide conjugates, and 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), and minor metabolites (e.g., norcodeine, normorphine, morphine-3-ethereal sulfate, morphine-3,6-diglucuronide.)

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 not detected in urine and 6-AM is rarely detected.

Hydrocodone is metabolized to norhydrocodone, hydromorphone, and minor metabolites of hydrocodol and hydromorphol. There is little conjugation of the hydrocodone; however, a significant percentage of the hydromorphone is conjugated and excreted as the glucuronide conjugate.

The predominant excretion product of hydromorphone is the glucuronide conjugate. Hydromorphol is a very minor metabolite. Hydromorphone-3-glucuronide appears to have significant pharmacological activity.

Oxymorphone is extensively metabolized and is excreted as a glucuronide conjugate and as a 6-oxymorphol glucuronide conjugate.

Oxycodone is metabolized by N- and O- demethylation, 6 keto reduction and conjugation. One metabolite, oxymorphone, is a potent narcotic analgesic while noroxycodone is

not active. Additional metabolites are noroxymorphone and the minor metabolites as noroxycodols and oxycodols.

b. Additional Issues Regarding Opioids

Poppy seeds may be a significant dietary source of morphine and/or codeine. To alleviate this problem and to distinguish between heroin and legitimate morphine/codeine use, HHS has set the initial testing and confirmatory cutoffs for morphine and codeine at 2000 ng/mL. 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.

Effective October 1, 2017, HHS revised the Mandatory Guidelines to include the semisynthetic opioids oxycodone, oxymorphone, hydrocodone, and hydromorphone as analytes.[21]

Opioids included in the drug testing panel confirm correctly and independently of other synthetic opioids. Examples of pharmaceuticals that do not metabolize to the opioids above include, but are not limited to the following:

- Propoxyphene;
- Methadone;
- Meperidine;
- Fentanyl;
- Pentazocine;
- Buprenorphine; and
- Tramadol.

Many pharmaceuticals containing opioids are available by prescription, although codeine may be obtained over the counter in some cases. 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 opioids is found in Chapter 4, Section 4.5, Interpretation and Result Verification.

7.1.5 Phencyclidine (PCP)[22]

a. Background

Phencyclidine (PCP), an arylcyclohexylamine, was first synthesized in the 1950s 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. PCP'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.[23]

PCP has a variety of effects on the central nervous system. Intoxication begins several minutes after ingestion and usually lasts 8 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.[24]

Routes of Administration

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

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% of the PCP dose is excreted in the urine as unchanged drug. PCP is a weak base that concentrates in acidic solutions in the body. Because of gastric acidity, PCP repeatedly re-enters the stomach from plasma and is reabsorbed 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.

b. Pharmaceuticals and Use

A positive 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.

7.2 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. At this time, oral fluid specimens are expected to be more difficult to adulterate than urine specimens. As a result, this section on adulteration deals only with urine specimens. 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. Therefore, adulterants are 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, provided 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, gas chromatography (GC)/mass spectrometry (MS) assays for marijuana metabolite (THCA) and opioids appear to be affected by adulterants more than GC/MS assays for other drugs.

When an instrumented initial test facility (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 D 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 4.0) 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 the pH to be within the invalid range (i.e., greater than or equal to 9 and less than 11.0). Note: See Table 4, Medical Review Officer Actions for Primary Specimen Reports (Bottle A), concerning specimens reported as invalid based on pH in the 9.0 to 9.5 range.

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 runoff 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 6 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 greater than or equal to 500 mcg/mL for adulteration and 200 mcg/mL as an invalid result. 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 quantification (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 that 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 "anti-bubbles" 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. None of the halogens can be found in nature in their elemental forms. 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) that 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 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.

7.3 Dilution/Substitution

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 D describes Specimen Reporting Criteria from the Mandatory Guidelines.

A donor may attempt to decrease the concentration of drugs or drug metabolites that may be present in his/her urine by dilution. Dilution may occur in vivo, by consumption of 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.

- Biomarker analysis may be used to determine if commercially prepared material is being used to substitute for the authentic urine specimen; however, the reporting of the specimen will be as an invalid specimen.

7.4 Invalid Specimens

"Invalid" refers to a result reported by a laboratory for a urine specimen that contains an unidentified adulterant or interfering substance, has an abnormal physical characteristic, has an endogenous substance at an abnormal concentration that prevents the laboratory from completing testing or obtaining a valid drug test result, or the concentration of a biomarker is not consistent with that established for human urine. HHS-certified laboratories are required to contact the MRO to discuss an invalid report for reason other than pH, creatinine, specific gravity, or nitrite reported as $\geq$200 mcg/mL and <500 mcg/mL by a nitrite confirmatory test. A primary specimen (Bottle A) reported as invalid for a test may be sent out for additional testing if the HHS-certified laboratory and the MRO conclude that additional testing may provide a definitive result for that specimen. A specimen reported as invalid for pH, creatinine, specific gravity, or nitrite reported as $\geq$200 mcg/mL and <500 mcg/mL by a nitrite confirmatory test may not be sent out for additional testing. The HHS Guidelines specify the analytical methods to be used by HHS-certified laboratories for these tests and there are no definitive test methods to

apply to these specimens to provide a definitive result. (Note that additional testing should only be considered in the absence of a confirmed positive, adulterated, or substituted result and only if additional or different testing may lead to a definitive positive, negative, or adulterated drug test result.)

Biomarker analysis may be used to determine if a commercially prepared material is being used to substitute for the authentic urine specimen. Recent products entering the market and intended as substitute specimens have included creatinine and other biological materials (such as uric acid) to defeat the laboratory biomarker assays. A certified laboratory may complete analyses for biomarkers to attempt to detect the use of substitution to defeat the drug testing process. An HHS-certified laboratory reports a primary (A) specimen as an invalid result when the specimen is not consistent with human urine based on laboratory specimen validity testing (e.g., for a biomarker). **Invalid results are reported by the laboratory to the MRO as described in Appendix D and Table 3. The MRO then reports as described in Chapter 5, Section 5.6.**

APPENDIX A:
GLOSSARY

The following definitions are primarily excerpted from the HHS Mandatory Guidelines for Federal Workplace Drug Testing Programs (Effective October 1, 2017), but may include additional definitions.

Accessioner. The individual who signs the Federal Custody and Control Form at the time of specimen receipt at the HHS-certified laboratory or (for urine) the HHS-certified IITF.

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 portion of a specimen used for testing.

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 fulfill 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 fulfill these obligations.

Alternate Technology Initial Drug Test. An initial drug test using technology other than immunoassay to differentiate negative specimens from those requiring further testing.

Batch. A number of specimens or aliquots handled concurrently as a group.

Biomarker. An endogenous substance used to validate a biological specimen.

Blind Sample. A sample submitted to an HHS-certified test facility for quality assurance purposes, with a fictitious identifier, so that the test facility cannot distinguish it from a donor specimen.

Calibrator. A sample of known content and analyte concentration prepared in the appropriate matrix used to define expected outcomes of a testing procedure. The test result of the calibrator is verified to be within established limits prior to use.

Cancelled Test. The result reported by the MRO to the federal agency when a specimen has been reported to the MRO as an invalid result (and the donor has no legitimate explanation) or rejected for testing, when a split specimen fails to reconfirm, or when the MRO determines that a fatal flaw or unrecovered correctable flaw exists in the forensic records (as described in Sections 15.1 and 15.2 of the Mandatory Guidelines for Federal Workplace Drug Testing Programs using Urine).

Carryover. The effect that occurs when a sample result (e.g., drug concentration) is affected by a preceding sample during the preparation or analysis of a sample.

Certifying Scientist (CS). The individual responsible for verifying the chain of custody and scientific reliability of a 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, rejected for testing, and (for urine) negative/dilute results reported by an HHS-certified laboratory or (for urine) an HHS-certified IITF.

Chain of Custody Documents. Forms used to document the control and security of the specimen and all aliquots. The documents may account for an individual specimen, aliquot, or batch of specimens/aliquots and must include the name and signature of each individual who handled the specimen(s) or aliquot(s) and the date and purpose of the handling.

Chain of Custody Procedures. Procedures that document the integrity of each specimen or aliquot from the point of collection to final disposition.

Collection Container. A receptacle used to collect a urine specimen.

Collection Site. The location where specimens are collected.

Collector. A person trained to instruct and assist a donor in providing a specimen.

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

Confirmatory Specimen Validity Test. A second test performed on a separate aliquot of a 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 analytical value (e.g., drug or drug metabolite concentration) used as the decision point to determine a result (e.g., negative; positive; adulterated; invalid; or, for urine, substituted) or the need for further testing.

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.

External Service Provider. An independent entity that performs services related to federal workplace drug testing on behalf of a federal agency; a collector/collection site; an HHS-certified laboratory; a Medical Review Officer (MRO); or, for urine, an HHS-certified Instrumented Initial Test Facility (IITF).

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

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 and chain of custody of a specimen from the time the specimen is collected until it is received by the test facility (i.e., HHS-certified laboratory or, for urine, HHS-certified IITF). It may be a paper (hardcopy), electronic, or combination electronic and paper format (hybrid). The form may also be used to report the test result to the Medical Review Officer.

Gender Identity. Gender identity means an individual's internal sense of being male or female, which may be different from an individual's sex assigned at birth.

HHS. The Department of Health and Human Services.

Initial Drug Test. An analysis used to differentiate negative specimens from those requiring further testing.

Initial Specimen Validity Test. The first analysis used to determine if a specimen is invalid, adulterated, or (for urine) diluted or substituted.

Instrumented Initial Test Facility (IITF). A permanent location where (for urine) 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 Section 3.9 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 drug testing, reporting of results, and recordkeeping are performed under the supervision of a Responsible Person.

Limit of Detection. The lowest concentration at which the analyte (e.g., drug or drug metabolite) can be identified.

Limit of Quantification (LOQ). For quantitative assays, the lowest concentration at which the identity and concentration of the analyte (e.g., drug or drug metabolite) can be accurately established.

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

Measurand. A physical quantity, property, or condition that is measured. In MRO use, this refers to a laboratory test result that is more general than analyte and that includes other characteristics, such as specific gravity and pH.

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

Monitor. The person assigned to monitor collection of the specimen for a 'monitored' collection according to UrMG section 8.12. The monitor's gender must be the same as the donor's (which is based on the donor's gender identity), unless the monitor is a medical professional. The monitor is not required to be a trained collector.

Monitored Collection. Collection procedure used when a monitored collection is required by UrMG Section 8.11. Same as a routine collection except the monitor provides visual privacy while being alert for signs of tampering. The monitor listens at the door of a restroom with no stall or enters a stall restroom with the donor, but must stay outside the individual stall. The monitor must not touch or handle the collection container, unless the monitor is also serving as the collector, and must not watch the donor urinate into the collection container.

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

Observed Collection. Collection procedure used when a direct observed collection is required by UrMG Section 8.9. Same as a routine collection except the observer is in the restroom or stall and watches the urine pass from the body of the donor to the collection container. The observer maintains visual contact with the specimen until the donor hands the container to the collector. The collection container cannot be handled by the observer unless the observer is also serving as the collector.

Observer. The person assigned to observe the collection of the specimen for a 'direct observed' collection according to UrMG section 8.10. The observer's gender must be the same as the donors (which is based on the donor's gender identity). The observer is not required to be a trained collector, but must be trained as an observer.

> **Note**: HHS has revised Sections 4.4(b), 8.1(b), and 8.10 of the UrMG to allow the donor to be observed by a person whose gender matches the donor's gender, which is determined by the donor's gender identity (defined above and in UrMG Section 1.5). The donor's gender identity may be the same as or different from the donor's sex assigned at birth.
>
> Before an observer is selected, the collector informs the donor that the gender of the observer will match the donor's gender, which is determined by the donor's gender identity. The collector then selects the observer to conduct the observation:
>
> - The collector asks the donor to identify the donor's gender on the Federal CCF and initial it.
> - The donor will then be provided an observer whose gender matches the donor's gender.
> - The collector documents the observer's name and gender on the Federal CCF.

Opiates. The term used to describe naturally occurring substances known as alkaloids derived from the opium poppy plant (e.g., codeine; morphine; and heroin, which is produced by the acetylation of morphine) that bind to specific receptors in the central nervous system and have analgesic as well as narcotic effects.

Opioids. A term that has expanded in scope over time and is used broadly to describe various compounds that bind to specific receptors in the central nervous system and have analgesic as well as narcotic effects. The broadly used term "opioids" includes naturally occurring alkaloid compounds known as opiates (e.g., codeine, morphine, and heroin); semi-synthetic compounds (e.g., hydrocodone, hydromorphone, methadone, oxycodone, and oxymorphone); and synthetic compounds (e.g., fentanyl). Opioids may or may not have structural similarity to the opium alkaloids.

Oral Fluid Specimen. An oral fluid specimen is collected from the donor's oral cavity and is a combination of physiological fluids produced primarily by the salivary glands.

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 a laboratory or (for urine) to an IITF 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 confirmation cutoff concentration.

Reconfirmed. The result reported for a split (B) specimen when the second HHS-certified laboratory corroborates the original result reported for the primary (A) specimen.

Rejected for Testing. The result reported by an HHS-certified laboratory or (for urine) HHS-certified IITF when no tests are performed on a specimen because of a fatal flaw or an unrecovered correctable error (see Sections 15.1 and 15.2 of the Mandatory Guidelines for Federal Workplace Drug Testing Programs).

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

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

Sample. A performance testing sample, calibrator, or control used during testing; or a representative portion of a donor's specimen.

Specimen. Fluid or material collected from a donor at the collection site for the purpose of a drug test.

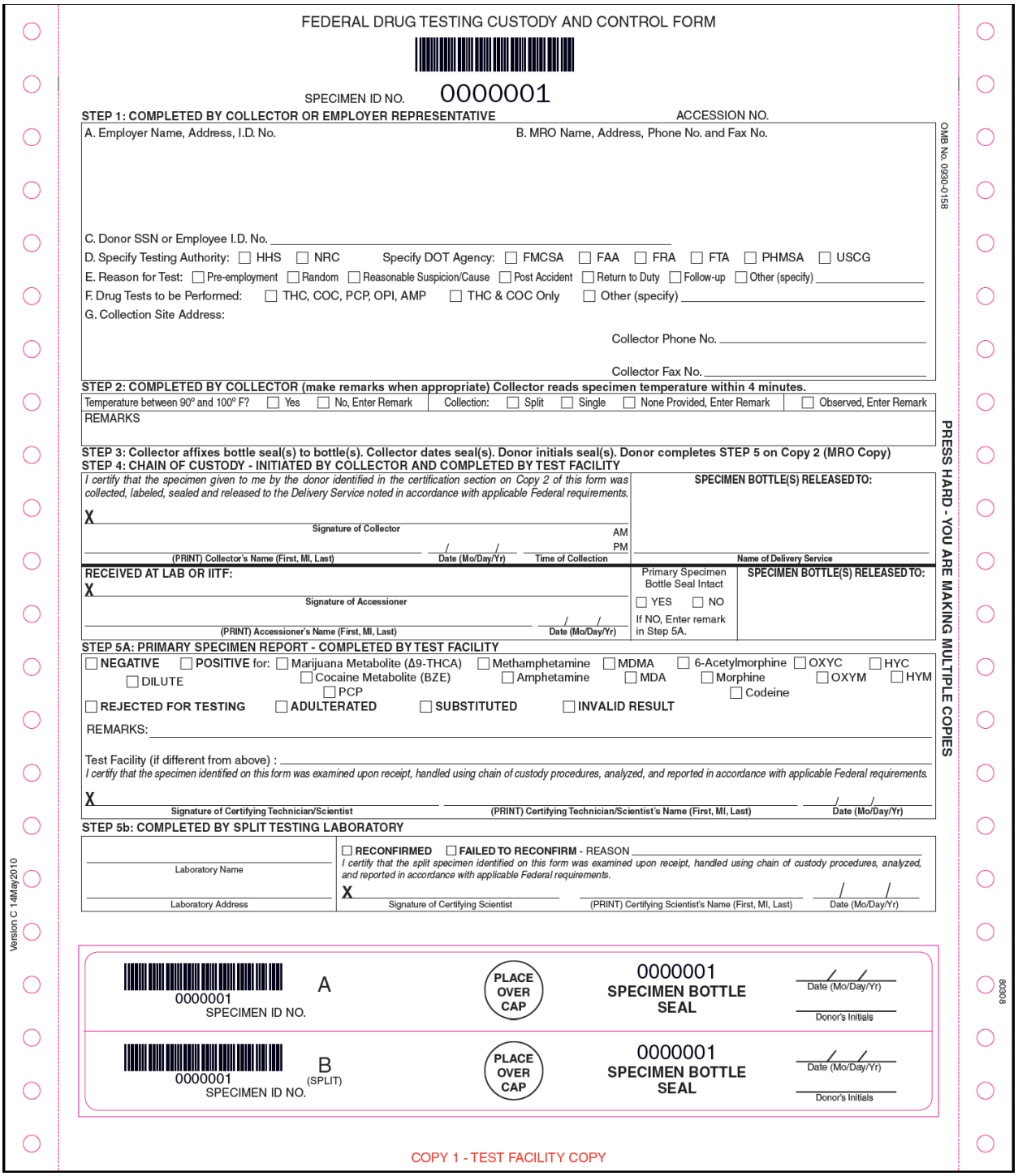
Split Specimen Collection (for Urine). A collection in which the specimen collected is divided into a primary (A) specimen and a split (B) specimen, which are independently sealed in the presence of the donor.

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 B:
SAMPLE OF CCF—TEST FACILITY COPY (1) AND MRO COPY (2)

(Note reduced size)



FEDERAL DRUG TESTING CUSTODY AND CONTROL FORM

SPECIMEN ID NO. 0000001

OMB No. 0930-0158

STEP 1: COMPLETED BY COLLECTOR OR EMPLOYER REPRESENTATIVE ACCESSION NO.

A. Employer Name, Address, I.D. No. B. MRO Name, Address, Phone No. and Fax No.

C. Donor SSN or Employee I.D. No. _____

D. Specify Testing Authority: ☐ HHS ☐ NRC Specify DOT Agency: ☐ FMCSA ☐ FAA ☐ FRA ☐ FTA ☐ PHMSA ☐ USCG

E. Reason for Test: ☐ Pre-employment ☐ Random ☐ Reasonable Suspicion/Cause ☐ Post Accident ☐ Return to Duty ☐ Follow-up ☐ Other (specify) _____

F. Drug Tests to be Performed: ☐ THC, COC, PCP, OPI, AMP ☐ THC & COC Only ☐ Other (specify) _____

G. Collection Site Address:

Collector Phone No. _____

Collector Fax No. _____

STEP 2: COMPLETED BY COLLECTOR (make remarks when appropriate) Collector reads specimen temperature within 4 minutes.

Temperature between 90° and 100° F? ☐ Yes ☐ No, Enter Remark | Collection: ☐ Split ☐ Single ☐ None Provided, Enter Remark | ☐ Observed, Enter Remark

REMARKS

STEP 3: Collector affixes bottle seal(s) to bottle(s). Collector dates seal(s). Donor initials seal(s). Donor completes STEP 5 on Copy 2 (MRO Copy)

STEP 4: CHAIN OF CUSTODY - INITIATED BY COLLECTOR AND COMPLETED BY TEST FACILITY

I certify that the specimen given to me by the donor identified in the certification section on Copy 2 of this form was collected, labeled, sealed and released to the Delivery Service noted in accordance with applicable Federal requirements.

X _____ Signature of Collector

(PRINT) Collector's Name (First, MI, Last) | Date (Mo/Day/Yr) | Time of Collection AM PM

SPECIMEN BOTTLE(S) RELEASED TO:

Name of Delivery Service

RECEIVED AT LAB OR IITF:

X _____ Signature of Accessioner

(PRINT) Accessioner's Name (First, MI, Last) | Date (Mo/Day/Yr)

Primary Specimen Bottle Seal Intact ☐ YES ☐ NO If NO, Enter remark in Step 5A.

SPECIMEN BOTTLE(S) RELEASED TO:

STEP 5A: PRIMARY SPECIMEN REPORT - COMPLETED BY TEST FACILITY

☐ **NEGATIVE** ☐ **POSITIVE** for: ☐ Marijuana Metabolite (Δ9-THCA) ☐ Methamphetamine ☐ MDMA ☐ 6-Acetylmorphine ☐ OXYC ☐ HYC ☐ DILUTE ☐ Cocaine Metabolite (BZE) ☐ Amphetamine ☐ MDA ☐ Morphine ☐ OXYM ☐ HYM ☐ PCP ☐ Codeine

☐ **REJECTED FOR TESTING** ☐ **ADULTERATED** ☐ **SUBSTITUTED** ☐ **INVALID RESULT**

REMARKS: _____

Test Facility (if different from above) : _____

I certify that the specimen identified on this form was examined upon receipt, handled using chain of custody procedures, analyzed, and reported in accordance with applicable Federal requirements.

X _____ Signature of Certifying Technician/Scientist | (PRINT) Certifying Technician/Scientist's Name (First, MI, Last) | Date (Mo/Day/Yr)

STEP 5b: COMPLETED BY SPLIT TESTING LABORATORY

Laboratory Name

Laboratory Address

☐ **RECONFIRMED** ☐ **FAILED TO RECONFIRM** - REASON _____

I certify that the split specimen identified on this form was examined upon receipt, handled using chain of custody procedures, analyzed, and reported in accordance with applicable Federal requirements.

X _____ Signature of Certifying Scientist | (PRINT) Certifying Scientist's Name (First, MI, Last) | Date (Mo/Day/Yr)

0000001 SPECIMEN ID NO. A | PLACE OVER CAP | 0000001 SPECIMEN BOTTLE SEAL | Date (Mo/Day/Yr) Donor's Initials

0000001 SPECIMEN ID NO. B (SPLIT) | PLACE OVER CAP | 0000001 SPECIMEN BOTTLE SEAL | Date (Mo/Day/Yr) Donor's Initials

COPY 1 - TEST FACILITY COPY

PRESS HARD - YOU ARE MAKING MULTIPLE COPIES

Version C 14May2010

80308

FEDERAL DRUG TESTING CUSTODY AND CONTROL FORM

SPECIMEN ID NO. 0000001

STEP 1: COMPLETED BY COLLECTOR OR EMPLOYER REPRESENTATIVE ACCESSION NO.

A. Employer Name, Address, I.D. No.

B. MRO Name, Address, Phone No. and Fax No.

OMB No. 0930-0158

C. Donor SSN or Employee I.D. No. _____

D. Specify Testing Authority: ☐ HHS ☐ NRC Specify DOT Agency: ☐ FMCSA ☐ FAA ☐ FRA ☐ FTA ☐ PHMSA ☐ USCG

E. Reason for Test: ☐ Pre-employment ☐ Random ☐ Reasonable Suspicion/Cause ☐ Post Accident ☐ Return to Duty ☐ Follow-up ☐ Other (specify) _____

F. Drug Tests to be Performed: ☐ THC, COC, PCP, OPI, AMP ☐ THC & COC Only ☐ Other (specify) _____

G. Collection Site Address:

Collector Phone No. _____

Collector Fax No. _____

STEP 2: COMPLETED BY COLLECTOR (make remarks when appropriate) Collector reads specimen temperature within 4 minutes.

Temperature between 90° and 100° F? ☐ Yes ☐ No, Enter Remark	Collection: ☐ Split ☐ Single ☐ None Provided, Enter Remark	☐ Observed, Enter Remark

REMARKS

STEP 3: Collector affixes bottle seal(s) to bottle(s). Collector dates seal(s). Donor initials seal(s). Donor completes STEP 5 on Copy 2 (MRO Copy)

STEP 4: CHAIN OF CUSTODY - INITIATED BY COLLECTOR AND COMPLETED BY TEST FACILITY

I certify that the specimen given to me by the donor identified in the certification section on Copy 2 of this form was collected, labeled, sealed and released to the Delivery Service noted in accordance with applicable Federal requirements.

SPECIMEN BOTTLE(S) RELEASED TO:

X _____
Signature of Collector

_____ (PRINT) Collector's Name (First, MI, Last)

_____/_____/_____ Date (Mo/Day/Yr)

_____ AM PM Time of Collection

_____ Name of Delivery Service

STEP 5: COMPLETED BY DONOR

I certify that I provided my urine specimen to the collector; that I have not adulterated it in any manner; each specimen bottle used was sealed with a tamper-evident seal in my presence; and that the information provided on this form and on the label affixed to each specimen bottle is correct.

X _____ Signature of Donor _____ (PRINT) Donor's Name (First, MI, Last) _____/_____/_____ Date (Mo/Day/Yr)

Daytime Phone No. (_____) _____ Evening Phone No. (_____) _____ Date of Birth _____/_____/_____ (Mo/Day/Yr)

After the Medical Review Officer receives the test results for the specimen identified by this form, he/she may contact you to ask about prescriptions and over-the-counter medications you may have taken. Therefore, you may want to make a list of those medications for your own records. THIS LIST IS NOT NECESSARY. If you choose to make a list, do so either on a separate piece of paper or on the back of your copy (Copy 5). – DO NOT PROVIDE THIS INFORMATION ON THE BACK OF ANY OTHER COPY OF THE FORM. TAKE COPY 5 WITH YOU.

STEP 6: COMPLETED BY MEDICAL REVIEW OFFICER - PRIMARY SPECIMEN

In accordance with applicable Federal requirements, my verification is:

☐ **NEGATIVE** ☐ **POSITIVE** for: _____
☐ DILUTE

☐ **REFUSAL TO TEST** because – check reason(s) below: ☐ **TEST CANCELLED**
☐ ADULTERATED (adulterant/reason): _____
☐ SUBSTITUTED
☐ OTHER: _____

REMARKS: _____

X _____ Signature of Medical Review Officer _____ (PRINT) Medical Review Officer's Name (First, MI, Last) _____/_____/_____ Date (Mo/Day/Yr)

STEP 7: COMPLETED BY MEDICAL REVIEW OFFICER - SPLIT SPECIMEN

In accordance with applicable Federal requirements, my verification for the split specimen (if tested) is:

☐ **RECONFIRMED** for: _____ ☐ **TEST CANCELLED**

☐ **FAILED TO RECONFIRM** for: _____

REMARKS: _____

X _____ Signature of Medical Review Officer _____ (PRINT) Medical Review Officer's Name (First, MI, Last) _____/_____/_____ Date (Mo/Day/Yr)

COPY 2 - MEDICAL REVIEW OFFICER COPY

APPENDIX C:
SAMPLE IITF SUPPLEMENTAL CCF

Specimen ID:_____

IITF Accession #: _____

IITF Name: _____**NLCP IITF #:** _____

IITF Address: _____

_____

_____

☐ **Bottle A and Bottle B included**
☐ **CCF Copy 1 included**

<table>
<tr><td colspan="3">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.</td></tr>
<tr><td colspan="2"></td><td rowspan="3">SPECIMEN BOTTLES RELEASED TO:

_____
Name of Delivery Service</td></tr>
<tr><td colspan="2">Signature of Certifying Technician</td></tr>
<tr><td></td><td>/ /</td></tr>
<tr><td>(Print) Certifying Technician Name (First, M I, Last)</td><td>Date (Mo/Day/Yr)</td><td></td></tr>
<tr><td colspan="3">RECEIVED AT LABORATORY</td></tr>
<tr><td colspan="2"></td><td rowspan="4">BOTTLE A SEAL INTACT

YES ☐
NO ☐

If NO, enter remark below</td></tr>
<tr><td colspan="2">Signature of Accessioner</td></tr>
<tr><td></td><td></td></tr>
<tr><td>(Print) Accessioner Name (First, M I, Last)</td><td>Date (Mo/Day/Yr)</td></tr>
</table>

Laboratory Remarks: _____

_____

Date	Specimen Released by	Specimen Received by	Purpose

APPENDIX D:
SPECIMEN REPORTING CRITERIA

Initial Test Analyte	**Initial Test Cutoff [1]**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff Concentration**
Marijuana metabolites (THCA)[2]	50 ng/mL[3]	THCA	15 ng/mL
Cocaine metabolite (Benzoylecgonine)	150 ng/mL[3]	Benzoylecgonine	100 ng/mL
Codeine/ Morphine	2000 ng/mL	Codeine Morphine	2000 ng/mL 2000 ng/mL
Hydrocodone/ Hydromorphone	300 ng/mL	Hydrocodone Hydromorphone	100 ng/mL 100 ng/mL
Oxycodone/ Oxymorphone	100 ng/mL	Oxycodone Oxymorphone	100 ng/mL 100 ng/mL
6-Acetylmorphine	10 ng/mL	6-Acetylmorphine	10 ng/mL
Phencyclidine	25 ng/mL	Phencyclidine	25 ng/mL
Amphetamine/ Methamphetamine	500 ng/mL	Amphetamine Methamphetamine	250 ng/mL 250 ng/mL
MDMA[4]/MDA[5]	500 ng/mL	MDMA MDA	250 ng/mL 250 ng/mL

[1]For grouped analytes (i.e., two or more analytes that are in the same drug class and have the same initial test cutoff):
Immunoassay: The test must be calibrated with one analyte from the group identified as the target analyte. The cross-reactivity of the immunoassay to the other analyte(s) within

the group must be 80 percent or greater; if not, separate immunoassays must be used for the analytes within the group. **Alternate technology:** Either one analyte or all analytes from the group must be used for calibration, depending on the technology. At least one analyte within the group must have a concentration equal to or greater than the initial test cutoff or, alternatively, the sum of the analytes present (i.e., equal to or greater than the laboratory's validated limit of quantification) must be equal to or greater than the initial test cutoff.
[2]An immunoassay must be calibrated with the target analyte, Δ-9-tetrahydrocannabinol-9-carboxylic acid (THCA).
[3]**Alternate technology (THCA and benzoylecgonine):** The confirmatory test cutoff must be used for an alternate technology initial test that is specific for the target analyte (i.e., 15 ng/mL for THCA, 100 ng/mL for benzoylecgonine).
[4]Methylenedioxymethamphetamine (MDMA)
[5]Methylenedioxyamphetamine (MDA)

Negative

An instrumented initial test facility (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 and when—

- All immunoassay results are below the initial test cutoffs;

Or

- Confirmatory test results are below the confirmatory test cutoffs;

And

- Specimen validity test results are 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 is 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) is 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 4.0.
- The pH is greater than or equal to 11.0.
- The nitrite confirmatory test result is greater than or equal to 500 mcg/mL.
- Chromium (VI) is present at greater than or equal to 50 mcg/mL in the initial test and greater than or equal to the LOQ for the confirmation method.
- A halogen (e.g., bleach [chlorine], iodine, fluorine) is present using a general oxidant test and a specific halogen is equal to or greater than the LOQ for confirmation.
- Glutaraldehyde is detected by an initial testing and is equal to or greater than the LOQ for confirmation.
- Pyridine (pyridinium chlorochromate) is present using a general oxidant test and pyridine is equal to or greater than the LOQ for confirmation.
- 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).
- 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.

    a. 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 of the initial and confirmatory specific gravity tests.
    b. 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 of the initial and confirmatory creatinine tests.

2. The pH is outside the acceptable range.

    a. The pH result is greater than or equal to 4.0 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.

    b. 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 4, Medical Review Officer Actions for Primary Specimen Reports (Bottle A), concerning specimens reported as invalid based on pH of 9.0 to 9.5.

3. Nitrite is present, but below the program cutoff for adulteration.

    a. Nitrite is greater than or equal to 200 mcg/mL using a nitrite colorimetric test for both the initial and confirmatory tests.

    b. 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.

    c. 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, fluorine) 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 Medical Review Officer (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.

11. The concentration of a biomarker is not consistent with that established for human urine.

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 appearances of Bottles A and B are 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 a Department of Health and Human Services [HHS]–certified laboratory to perform the testing; or
- The MRO does not authorize the laboratory to send the specimen for additional/different specimen validity testing.

APPENDIX E:
DRUG SCHEDULE 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 Drug Enforcement Administration (DEA) Web site (https://www.dea.gov).

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.

APPENDIX F:
MRO VERIFICATION STATEMENT FOR EXTERNAL SERVICE PROVIDER

I, the undersigned, have *or* My employer/MRO group, [*NAME*], has a binding agreement with an external service provider, [*NAME*], to perform the following (*check all that apply*):

- ☐ Receive MRO copies of the Federal CCF from collectors
- ☐ Receive laboratory/IITF reports of drug test results (i.e., Federal CCFs, electronic reports)
- ☐ Manage MRO data (e.g., donor contact information, donor interview documentation, statistical reports, billing and invoicing)
- ☐ Store MRO records related to federal/federally regulated drug tests
- ☐ Provide MRO reports of federal/federally regulated drug tests to the federal agency/employer
- ☐ Provide and manage a Federal ECCF system (i.e., as a third party ECCF system provider)
- ☐ Other (describe): _____

The agreement specifies [*NAME of external service provider*]'s responsibilities as an external service provider for federally regulated drug testing and requires compliance with all applicable Subparts of the United States Department of Health and Human Services (HHS) Mandatory Guidelines for Federal Workplace Drug Testing Programs including, but not limited to, restrictions and conditions with respect to regulated specimen and drug test information and records.

I have verified that the agreement/contract requires compliance with the following priority elements:

1. Limiting access to regulated specimen information
2. Implementing appropriate safeguards to prevent unauthorized use or disclosure of the information
3. Reporting any use or disclosure of regulated specimen information not addressed in the agreement, including incidents that constitute data breaches
4. Disclosing information to HHS that is related to regulated specimens and drug tests
5. Arranging for disposition of regulated specimen data (i.e., disposal in accordance with specified record retention periods; transfer to the MRO or to another location/entity, if agreed to by the MRO, upon termination of the agreement/contract)
6. Notifying me prior to allowing any of the external service provider's subcontractors to have access to regulated specimen and drug test information
7. Ensuring that the external service provider's subcontractors agree to the same restrictions and conditions that apply to the external service provider with respect to regulated specimen and drug test information

I hereby authorize [*NAME of external service provider*] to receive and/or disseminate federally regulated drug testing information and records on my behalf and in accordance with our binding agreement.

I certify that the statements and information presented above are true and correct as of this date.

Medical Review Officer (MRO) DATE
(*signature and printed name*)

Table 1. Immunoassay Tests

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 when drug binds to the antibody. Drug concentration in the specimen is measured by the change in enzyme activity.
Kinetic Interaction of Microparticles in Solution	KIMS	An immunoassay based on the principle of the kinetic interaction of microparticles in a solution. Drug content of the specimen is directly proportional to inhibition of 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. 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 retains its polarized characteristics. 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 that are immobilized in the wells of a microplate.

Other types of immunoassays to detect drugs and/or metabolites exist and may be used to test federal agency specimens. The Medical Review Officer (MRO) may contact the Instrumented Initial Test Facility (IITF) or laboratory as needed for information on the immunoassay method used for the initial drug test, if not listed above.

Table 2. Examples of 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. Elemental atoms absorb ultraviolet or visible light at a specific wavelength and make transitions to higher electronic energy levels. The adulterant concentration is determined from the amount of absorption at the specific wavelength.
Capillary Electrophoresis (CE)	Adulterant concentration (e.g., nitrite, chromium VI)	An electrophoretic separation technique using a small-bore, fused silica capillary tube. This separation technique 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, which allows them to be separated.
Characteristic Immunoassay (IA) Drug Test Responses	Adulterant concentration (e.g., glutaraldehyde)	Characteristic responses are exhibited by some IA tests in the presence of adulterants. This enables laboratories to develop criteria for initial drug test data that help identify a specific adulterant. If the IA response is validated by a laboratory for a specific adulterant, the laboratory may accept the abnormal 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 the tested material with that of a standard solution. In a colorimetric test, reagents are added to a sample and a reaction occurs, producing color. Because the intensity of the color is related to the concentration of the measurand, the measurand is determined by visually measuring the color or electronically measuring the intensity of light at selected wavelengths (i.e., spectrophotometry). This process is also used in some IA detection processes (e.g., ELISA).
Gas Chromatography/ Mass Spectrometry (GC/MS)	Adulterant concentration (e.g., glutaraldehyde, pyridine)	GC is a technique for separating and analyzing mixtures of chemical substances in their gas or vapor phase. GC/MS is a combined technique coupling an MS instrument with a GC instrument. Urine specimens must undergo a specimen preparation process (i.e., extraction) prior to GC/MS analysis. After the GC has separated the measurands in a specimen, the specimen enters the MS, which may be used to identify and quantify the separated measurands. The MS creates charged particles (ions) and separates the ions according to their mass-to-charge (m/z) ratios. The ions form unique mass spectra, which are used to identify measurands.
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 while the measurand remains in solution.

(continued)

Table 2. Examples of Specimen Validity Tests (continued)

Method	Measurand	Description
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 RF-induced plasma in the form of a solution, vapor, or solid. The temperature of the plasma may exceed 6000°C. The high thermal energy and electron-rich environment of the ICP results in the conversion of most atoms into ions. An MS is used to detect ions at different masses, allowing signals of individual isotopes of an element to be identified.
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 interactions with the resin. Its greatest utility in the federal program is for analysis of anions for which there are no other rapid analytical methods. It is also commonly used for the analysis of cations and the separation of larger molecules 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 confirmatory pH tests.
Refractometry	Urine specific gravity	The required test method for specific gravity analyses. A refractometer is used to determine the amount of solute (i.e., urinary total solids) in the urine by measuring the index of refraction. For program purposes, the refractive index is a measure of how much light is bent (refracted) by the urine sample being analyzed. The instrument manufacturer applies a formula to convert from refractive indices to the urine specific gravity values displayed by the refractometer. Laboratories and IITFs may use refractometers accurate to at least three decimal places to determine whether an initial specific gravity test is needed. 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.

NOTE: HHS = Department of Health and Human Services; IITFs = instrumented initial test facilities; RF = radiofrequency.

Table 3. 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 < 4.0 or ≥ 11.0 (within the range of controls in the batch)
	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 ≥ 4.0 & < 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.
	(Specify confirmatory drug test method) interference[2]	Drug analyte(s) must not be included on reports for invalid results based on assay interference
	Immunoassay Interference[2]	
	Possible (characterize as Aldehyde or Surfactant) Activity[2]	
	Abnormal Physical Characteristic - (Specify)[2]	
	Bottle A and Bottle B - Different Physical Appearance[2]	

[1] Remarks on CCF (Step 5a) & on elec. report for primary specimens; Remarks on CCF/Split Specimen Report & on elec. report for split specimens. Labs and IITFs may add explanatory comments in addition to these required comments.

[2] Lab shall contact the MRO to discuss the Invalid Result in accordance with the HHS Guidelines (82 Fed. Reg. 7920) section 11.19.g.

[3] See NLCP Manual for further guidance.

NOTE: CCF = Custody and Control Form; HHS = Department of Health and Human Services; ID = identification; IITF = instrumented initial test facility; LOQ = limit of quantitation; MFR = Memorandum for the record; MRO = Medical Review Officer; NLCP = National Laboratory Certification Program; SpGr = specific gravity.

Table 3. Required Comments for IITF and Laboratory Reports (continued)

Test Result	Required Comment[1]	Note
Rejected for Testing	Fatal Flaw: Specimen ID number (Specify: mismatch; missing)	ID mismatch/missing on CCF and/or either Bottle A or B
	Fatal Flaw: No collector printed name & No signature	
	Fatal Flaw: No CCF	
	Fatal Flaw: No specimen submitted with CCF	
	Fatal Flaw: Two separate collections performed using one CCF	
	Fatal Flaw: (Specify: flaw that prevents testing or affects forensic defensibility of the drug test and cannot be corrected)	
	Fatal Flaw: Bottle A label/seal (Specify: missing; misapplied; broken; shows evidence of tampering)	If redesignation is not possible
	Fatal Flaw: Bottle A seal condition not marked on CCF	
	Fatal Flaw: Bottle A insufficient specimen volume (Specify reason and indicate collector error *when applicable*)	
	Uncorrected Flaw: Wrong CCF used[3] (Specify: Expired/Non-Federal CCF; CCF Copy 2-5; ECCF Reprint without collector wet signature; ECCF Reprint without collector explanation)	Wait at least 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 CCF/Split Specimen Report & on elec. report for split specimens. Labs and IITFs may add explanatory comments in addition to these required comments.

[2] Lab shall contact the MRO to discuss the Invalid Result in accordance with the HHS Guidelines (82 Fed. Reg. 7920) section 11.19.g.

[3] See NLCP Manual for further guidance.

NOTE: CCF = Custody and Control Form; HHS = Department of Health and Human Services; ID = identification; IITF = instrumented initial test facility; LOQ = limit of quantitation; MFR = Memorandum for the record; MRO = Medical Review Officer; NLCP = National Laboratory Certification Program; SpGr = specific gravity.

Table 4. Medical Review Officer Actions for Primary Specimen Reports (Bottle A)

Reported Primary Specimen Result	Medical Review Officer (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.
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 greater than or equal to 200 mcg/mL and less than 500 mcg/mL.* For an invalid result based on pH in the 9.0 to 9.5 range— ▪ 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 pH is in the 9.0 to 9.5 range as a possible result of time and temperature for a first invalid result— – Report the test as cancelled 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).

(continued)

Table 4. Medical Review Officer Actions for Primary Specimen Reports (Bottle A) (continued)

Reported Primary Specimen Result	Medical Review Officer (MRO) Action
	▪ If the medical explanation is not legitimate AND the pH is not in the 9.0 to 9.5 range due to time and temperature— – Report the test as cancelled 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 5, Section 5.6.4, Invalid Specimens**, of this manual.
Multiple Reported Results	Follow the review procedures above as appropriate for each reported result and report **all** verified positive and/or "refusal to test" results. Do not report invalid results for the primary specimen unless the split specimen is tested and reported as a failure to reconfirm.
Rejected for Testing	Report the test as cancelled along with the reason for the cancellation and direct the federal agency to immediately collect another specimen from the donor.

Table 5. Medical Review Officer Actions for Split Specimen Reports (Bottle B)

Reported Split Specimen Result			Medical Review Officer (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 test 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.

Table 5. Medical Review Officer Actions for Split Specimen Reports (Bottle B) (continued)

Laboratory Split Specimen Result			Medical Review Officer (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; and ▪ 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 reports **multiple results** (i.e., drug positive, adulterated, substituted) for the primary specimen and Laboratory B **reconfirms 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; and
  - 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.

NOTE: SVT = specimen validity testing.

Table 6. Some Substances That Metabolize to Amphetamine and Methamphetamine

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

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