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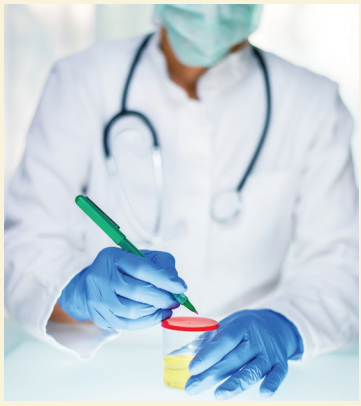
Medical Review Officer Guidance Manual for Federal Workplace Drug Testing Programs



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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Medical Review Officer Guidance Manual
for Federal Workplace Drug Testing Programs

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, the Department of Health and Human Services Mandatory Guidelines for Federal Workplace Drug Testing Programs using Urine (88 FR 70768) dated October 12, 2023 (effective February 1, 2024), and the Department of Health and Human Services Mandatory Guidelines for Federal Workplace Drug Testing Programs using Oral Fluid (88 FR 70814) dated October 12, 2023 (effective October 10, 2023).

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

https://www.samhsa.gov/workplace

Previous versions of this manual are obsolete.

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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 (88 FR 70768) and the Mandatory Guidelines for Federal Workplace Drug Testing Programs using Oral Fluid (88 FR 70814). For the purposes of this document, abbreviations "UrMG" and "OFMG" are used to refer to the guidelines using urine and oral fluid, respectively, and "Mandatory Guidelines" is used as the general term. 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 words "should" or "may" 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) in 1971 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 include marijuana. Tests for marijuana and batch procedures for chain of custody and testing were developed. Many of the "common industry standards" such as cutoff levels, isomer testing, and the need for two different analytical procedures for positive specimens were developed as well as the introduction of gas chromatography/mass spectrometry as the "Gold Standard" for confirmation 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 as well as comprehensive certification and inspections of certified laboratories 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 (urine and oral fluid); and instrumented initial test facilities (IITFs) that perform initial testing (urine only).

Subpart L, section 12.1, of the OFMG prohibits an IITF from testing oral fluid specimens for a Federal agency's workplace drug testing program. This decision was primarily due to the limited specimen volume of oral fluid collected from the donor.

In addition to administering the Federal Workplace Drug Testing Program DWP provides:

- Assistance to organizations and businesses establishing drug-free workplace programs (including drug testing);
- A Drug Free Workplace Helpline (800-967-5752) and a website at www.samhsa.gov/workplace;
- 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 and federally mandated 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, adulterated, or substituted 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.

1.2.1 MRO Requirements, Restrictions, Responsibilities

The 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, positive, adulterated, rejected for testing, invalid, substituted, and [for urine] negative/dilute);
  - The chain of custody, reporting, and recordkeeping requirements for Federal agency specimens;
  - The HHS Mandatory Guidelines for each authorized specimen type (urine and oral fluid); and
  - 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.

- 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;

- 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; and

- Certified MROs must complete training on any Mandatory Guidelines revisions including any changes to the drug and biomarker panels prior to their effective date, to continue serving as an MRO for Federal agency specimens.

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 substituted test results. (See also Table 4 - Medical Review Officer Actions for Primary (A) Specimen Reports; and Table 5 - Medical Review Officer Actions for Split (B) Specimen Reports)

- Ensure that specimens reported as negative and (for urine) negative/dilute are properly reviewed and reported to the agency's designated representative. Staff under the direct, personal supervision of the MRO may review and report negative and (for urine) negative/dilute test results 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 (for reason other than pH, creatinine, specific gravity, or nitrite reported as ≥200 mcg/mL and <500 mcg/mL using a nitrite confirmatory test) 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 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 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 two years while maintaining the confidentiality of the information. The MRO may discard hardcopy records six months after conversion to electronic records (with appropriate security);

- Conduct a medical examination of the donor or a review of the examining physician's findings and determine "refusal to test" or "cancelled test" when a collector reports that the donor was unable to provide a specimen and an alternate specimen (i.e., another authorized specimen type, urine, or oral fluid) was not collected;

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

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

- 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.

The UrMG (88 FR 70768, effective February 1, 2024) and OFMG (88 FR 70814, effective October 10, 2023) are on the SAMHSA website: www.samhsa.gov/workplace/resources.

1.2.2 Federal Agency Responsibilities for Designating an MRO

Before allowing an individual to serve as an MRO for the agency, a Federal agency must verify and document the following:

- that the individual satisfies all requirements in Section 1.2.1, including certification by an MRO certification organization that has been approved by the Secretary; and
- that the individual is not an employee, agent of, or have any financial interest in an HHS-certified laboratory that tests the agency's specimens.

The Federal agency must verify and document that each MRO reviewing and reporting results for the agency:

- completes training on any revisions to these Guidelines, including any changes to the drug and biomarker testing panels, prior to their effective date;
- at least every five years, maintains their certification by completing requalification training and passing a requalification examination; and
- provides biannual reports to the Secretary or designated HHS representative as required in Section 4.7.2.

The Federal agency must ensure that each MRO reports drug test results to the agency in accordance with Sections 4.7.1.

- Before allowing an MRO to report results electronically, the agency must obtain documentation from the MRO to confirm that the MRO and any external service providers ensure the confidentiality, integrity, and availability of the data and limit access to any data transmission, storage, and retrieval system.

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. The Federal CCF is available from a number of different sources (e.g., IITFs, laboratories, collectors, consortia/third-party administrators, and Medical Review Officers [MROs]).

The Federal CCF may be a paper (hardcopy) form or an electronic form (ECCF) which may be a digital form or a combination electronic and paper format, 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.
- **Digital CCF (ECCF).** An electronic document used to record all CCF events from collection through reporting and signed by the collector and donor using electronic signatures or "digitized" signatures (made using a signature pad); or
- **Combination Electronic/Paper CCF.** There are two types of combination electronic and paper ECCF systems:
  - Option 1. An electronic form is used to document the collection process, printed, and signed using handwritten (i.e., "wet") signatures. The donor signs in Step 5 of Copies 2-5 using a wet-signature and the collector signs in Step 4 of Copies 1-5 using a wet-signature.

    At a minimum, the collector prints Copy 1 and Copy 2 on carbonless paper for wet-signatures.
  - Option 2. An electronic form is used to document the collection process, signed using electronic signatures (e.g., collector and donor "digitized" signatures made using a signature pad), and the collector prints Copy 1 with his or her electronic signature. The printout of ECCF Copy 1 must be designated as the single authoritative copy of the ECCF.

A proof of the 2023 Federal CCF and guidance for its use are on the SAMHSA website: https://www.samhsa.gov/workplace/drug-testing. OMB approved the use of the

2023 Federal CCF as of May 1, 2023, for urine and oral fluid specimens. Examples of the Test Facility Copy (1) and the MRO Copy (2) of the Federal CCF are shown in Appendix B. (See Notes for Expired CCFs below.)

Employers are prohibited from using the Federal CCF for

- Private-sector employee drug testing, with the exception of transportation industry testing conducted under the DOT regulations;
- State workplace drug testing programs; or
- Department of Justice drug testing programs.

The use of a non-Federal CCF, an expired Federal CCF, or 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. All parties (collector, laboratory or IITF, MRO, employer) must take all practical action to correct a recoverable error so that the test is not cancelled. 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.

Notes for Expired CCFs:

- The 2023 Federal CCF is the same as the expired 2020 Federal CCF. Therefore, use of the 2020 Federal CCF is approved and no MFR is required.
- Use of an expired Federal CCF (2017 or earlier) with a urine specimen may be recoverable with a collector MFR. Expired (urine only) CCFs are not allowed for oral fluid specimens unless the collector includes the required oral fluid collection information at the time of collection.

If a laboratory or an IITF 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.

If the collector provides an MFR within at least 5 business days, the laboratory should send a copy of the MFR received from the collector to the MRO or include a comment on the Federal CCF and electronic report noting that an MFR was received. The lab can reanalyze the specimen using regulated procedures at the request of the MRO if the specimen is negative for all drugs or positive only for a regulated analyte (not if specimen is positive for non-regulated analyte). For reanalyzed specimens, the laboratory or IITF must send a corrected report with the test results obtained for the specimen.

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 urine and oral fluid Federal CCFs 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 specimen type, content, integrity, accuracy, and accessibility.

Before implementing a Federal ECCF, HHS-certified laboratories and IITFs 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. SAMHSA maintains the list of HHS-certified test facilities (laboratories and IITFs) approved to use an ECCF, with the ECCF

system(s) that each is authorized to use, on the SAMHSA website: www.samhsa.gov/workplace/resources.

The ECCF system provider and the Federal agencies and drug testing service providers (e.g., collectors, test facilities, MROs) who use digital 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 ("wet") signatures. These procedures and controls include, but are not limited to, the following:

- System validation on a lab-by-lab basis;
- 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 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), information for the MRO (i.e., on Copy 2), and information for the collection site (i.e., on Copy 3). The remaining copies, which are identical to the collection site copy, are for the employer 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 Specimen Labels/Seals

The tamper-evident specimen bottle/tube labels/seals may be at the bottom or the side 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 (A) specimen and the other marked with the letter "B" to designate the split (B) 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;
- A place for the donor to initial the label/seal after it is placed on the specimen bottle/tube;
- The label/seal must allow for placement without covering the specimen container expiry date for oral fluid; and
- The label/seal size must allow for observation of the specimen.

2.3.3 Required Statements

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

- Display of the Public Burden Statement:
  - Paper Federal CCF: printed on the back of Copies 1 - 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 on screen 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).

- Note: Instructions for Completing the Federal Drug Testing Custody and Control Form have been removed from the back of the Federal CCF form. SAMHSA instructions for completing the Federal CCF for urine and oral fluid are on the SAMHSA website: https://www.samhsa.gov/workplace/drug-testing.

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 CCFs 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 laboratory or the IITF. 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 a paper Federal CCF and a combination electronic and paper Federal ECCF. 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 Digital Federal ECCF

- Copy 1 (test facility copy) is signed by the collector and is provided electronically to the laboratory or the IITF. 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 electronically signed by the donor, maintained as an electronic file, and:
  - A copy is provided electronically to the MRO;
  - A copy is maintained in the collection site records;
  - A copy is provided electronically to the employer; and
  - A copy is provided to the donor. The donor may request a printed copy or a copy that is electronically provided.

Note: The Instructions for Completing the Federal Drug Testing Custody and Control Form for Specimen Collection have been removed from the back of the Federal CCF form. SAMHSA instructions for completing the Federal CCF for urine and oral fluid are on their website. See MRO Manual section 2.3.3.

2.5 Test Facility Report to MRO

When testing has been completed, the laboratory or IITF records the results for a primary specimen (Bottle/Tube A) on the Federal CCF Copy 1 by marking the appropriate result boxes and includes any additional comments concerning the specimen's testing or processing on the "Positive", "Remarks", and "Test Facility" lines. The original Federal CCF Copy 1 is retained in the specimen records at the test facility that reported the result. The laboratory or IITF 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 (for urine) 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 urine 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 urine 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 and ng/mL concentration recorded on the Positive line);
- Adulterated (with the adulterant or pH value recorded on the Remarks line); and
- Substituted (with the urine creatinine and urine specific gravity values recorded on the Remarks line).
- 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.

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 their metabolites, and are authorized to test each specimen for other Schedule I or II drugs as provided in the drug testing panel. SAMHSA will publish the drug test analytes and cutoffs (i.e., the "drug testing panel") for initial and confirmatory drug tests in the Federal Register each year. The authorized drug testing panels will also be available on the SAMHSA website at https://www.samhsa.gov/workplace. Appendix D lists the drug testing panel analytes (i.e., drugs and drug metabolites) and test cutoffs specified by the UrMG and OFMG. SAMHSA publishes a list of all HHS-certified laboratories, the specimen type(s) each laboratory is certified to test, and the ECCF approved laboratory list. The list is updated as needed. These drug testing resources are included on the SAMHSA website: www.samhsa.gov/workplace/resources/drug-testing

Testing for an drugs other than those in the drug testing panel 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) website, https://www.dea.gov.

- A Federal agency may routinely test its federal employees' workplace specimens for a drug or drug class not listed in the drug testing panel described 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 drugs other than those in the drug testing panel is justified or authorized as described above, the Federal agency or the MRO will arrange the additional testing at an HHS-certified laboratory. The MRO will contact the laboratory Responsible Person (RP) who in turn will notify HHS and the NLCP of the MRO request for additional testing. Alternatively, the Federal agency representative may notify HHS of the request directly. HHS will review the request for the additional test and provide a written acknowledgment to the RP to proceed with the test.

The NLCP 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 initial 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. 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) website at: https://www.dea.gov/drug-information/csa and a description is included in Appendix E.

3.1.2 Specimen Collection

Only specimen types authorized by Mandatory Guidelines for Federal Workplace Drug Testing Programs may be collected. The MRO must be familiar with the specimen collection procedures required by the Mandatory Guidelines. A Federal agency may collect urine and/or oral fluid for its workplace drug testing program.

For non-MRO determined refusals to test, the collector stops the collection, notifies the Federal agency by means (e.g., telephone, e-mail, or secure fax) that ensures that the notification is immediately received, documents the refusal to test including the reason on the Federal CCF, and (c) sends all copies of the Federal CCF to the Federal agency's designated representative.

3.1.2.1 Urine

The HHS Urine Specimen Collection Handbook (available at https://www.samhsa.gov/workplace/drug-testing) contains guidance for collectors to supplement the urine collection procedures required by the UrMG.

The collector shall instruct the donor to wash and dry the donor's hands prior to urination. After washing the donor's hands, the donor must remain in the presence of the collector and must not have access to any water fountain, faucet, soap dispenser, cleaning agent, or any other materials which could be used to adulterate or substitute the specimen. If the donor refuses to wash the donor's their hands when instructed by the collector, this is considered a non-MRO determined refusal to test.

The collector asks the donor to empty the donor's pockets and display the contents to ensure no items are present that could be used to adulterate or substitute the specimen. If an

item is present that appears to have been brought to the collection site with the intent to adulterate, substitute, or dilute the specimen (e.g., a commercial drug culture product or other item for which the donor has no reasonable explanation), this is a non-MRO determined refusal to test. If an item that could be used to adulterate, substitute, or dilute the specimen (e.g., common personal care products such as eyedrops, mouthwash, or hand sanitizer) appears to have been inadvertently brought to the collection site, the collector must secure the item and continue with the normal collection procedure. If the donor refuses to show the collector the items in their pockets, this is a non-MRO determined refusal to test.

The collector must inform the donor that, once the collection procedure has begun, the donor must remain at the collection site (i.e., in an area designated by the collector) until the collection is complete. This includes the wait period (i.e., up to 3 hours or until the donor has provided a sufficient urine specimen) if needed to provide a sufficient specimen. Failure to follow these instructions is a non-MRO determined refusal to test.

Each Federal agency urine specimen is collected as a split specimen. The collector prepares a split urine specimen by pouring the specimen from the collection container into two bottles, which are then designated as Bottle A (the primary (A) specimen) and Bottle B (the split (B) specimen).

The collection procedure begins when the collector will provide or the donor may select a specimen collection container that is clean, unused, wrapped/sealed in original packaging and compliant with Subpart G - Urine Specimen Collection Containers and Bottles. The specimen collection container package will be opened in view of the donor.

The collector, in the presence of the donor, pours the urine from the collection container into two specimen bottles to be labeled “A” and “B.” The collector pours at least 30 mL of urine into Bottle A and at least 15 mL into Bottle B, and caps each bottle.

The collector notes any unusual behavior or appearance of the donor on the Federal CCF. If the collector detects any conduct that clearly indicates an attempt to tamper with a specimen (e.g., substitute urine in plain view or an attempt to bring into the collection site an adulterant or urine substitute), this is a non-MRO determined refusal to test

The collector measures the temperature of the specimen within 4 minutes of receiving the specimen from the donor. The collector records on the Federal CCF whether or not the temperature is in the acceptable range of 32°-38°C/90°-100°F. If the temperature of the specimen is outside the range of 32°-38°C/90°-100°F, that is a reason to believe that the

donor may have adulterated or substituted the specimen. Another specimen must be collected under direct observation. The collector forwards both specimens (i.e., from the first and second collections) to an HHS certified laboratory for testing and records a comment on the Federal CCF for each specimen. If the donor fails to remain present through the completion of the collection or declines to have a direct observed collection to provide a second specimen as required, the collector stops the collection and reports the non-MRO determined refusal to test.

The collector inspects the specimen to determine if there is any sign indicating that the specimen may not be a valid urine specimen (e.g., unusual color, presence of foreign objects or material, unusual odor). The collector notes any unusual finding on the Federal CCF. A specimen suspected of not being a valid urine specimen must be forwarded to an HHS-certified laboratory for testing. When there is any reason to believe that a donor may have adulterated or substituted the specimen, another specimen must be obtained as soon as possible under direct observation. The collector must forward both specimens (i.e., from the first and second collections) to an HHS-certified laboratory for testing and record a comment on the Federal CCF for each specimen. The collector must determine the volume of urine in the specimen container. If the donor fails to remain present through the completion of the collection or declines to have a direct observed collection to provide a second specimen as required, this is a non-MRO determined refusal to test.

The collector must never combine urine collected from separate voids to create a specimen. If the volume is less than 45 mL, the collector discards the specimen and immediately collects a second specimen using the same procedures as for the first specimen. The collector may give the donor a reasonable amount of liquid to drink for this purpose (e.g., an 8 ounce glass of water every 30 minutes, but not to exceed a maximum of 40 ounces over a period of 3 hours or until the donor has provided a sufficient urine specimen). However, the donor is not required to drink any fluids during this waiting time. If the donor has not provided a sufficient specimen (i.e., at least 45 mL) within three hours of the first unsuccessful attempt to provide the specimen, the collector records the reason for not collecting a urine specimen on the Federal CCF, notifies the Federal agency's designated representative for authorization to collect an alternate specimen, and sends the appropriate copies of the Federal CCF to the MRO and to the Federal agency's designated representative. The Federal agency *may* choose to provide the collection site with a standard protocol to follow in lieu of requiring the collector to notify the agency's designated representative for authorization in each case. If an alternate specimen is authorized, the collector may begin the

collection procedure for the alternate specimen. If the donor fails to remain present through the completion of the collection, refuses to provide a second specimen as required or refuses to provide an alternate specimen as authorized, this is a non-MRO determined refusal to test.

3.1.2.2 Oral Fluid

The HHS Oral Fluid Specimen Collection Handbook (available at https://www.samhsa.gov/workplace/drug-testing) contains guidance for collectors to supplement the collection procedures required by the OFMG.

The collector shall instruct the donor to wash and dry the donor's hands under the collector's observation, and to keep their hands within view and avoid touching items or surfaces after handwashing. If the donor refuses to wash their hands when instructed by the collector, this is a non-MRO determined refusal to test.

If the collector will not keep the donor under direct observation from this point until the end of the collection, the collector asks the donor to empty the donor's pockets and display the contents to ensure no items are present that could be used to adulterate or substitute the specimen. If an item is present that appears to have been brought to the collection site with the intent to adulterate, substitute, or dilute the specimen (e.g., a commercial drug culture product or other item for which the donor has no reasonable explanation), this is a non-MRO determined refusal to test. If an item that could be used to adulterate, substitute, or dilute the specimen (e.g., common personal care products such as eyedrops, mouthwash, or hand sanitizer) appears to have been inadvertently brought to the collection site, the collector must secure the item and continue with the normal collection procedure. If the donor refuses to show the collector the items in their pockets, this is a non-MRO determined refusal to test.

The collector must inform the donor that, once the collection procedure has begun, the donor must remain at the collection site (i.e., in an area designated by the collector) until the collection is complete. This includes the wait period (i.e., up to 1 hour must be provided or until the donor has provided a sufficient oral fluid specimen) if need to provide a sufficient specimen. Failure to follow these instructions is a non-MRO determined refusal to test.

If the collector's inspection of the donor's oral cavity reveals any items that could impede or interfere with the collection of an oral fluid specimen (including abnormally colored saliva, candy, gum, food, tobacco), or the donor claims to have "dry mouth", the collector gives the donor water (e.g., up to 4 oz) to rinse their mouth. The donor may drink

the water. The collector must then wait 10 minutes before beginning the specimen collection. If the donor refuses to remove an item or refuses to rinse, this is a non-MRO determined refusal to test.

Each Federal agency oral fluid specimen is collected as a split specimen. Two specimens (Tube A [the primary (A) specimen], Tube B [the split (B) specimen]) are collected (1) concurrently or serially, and independently sealed in the presence of the donor; or (2) as a single specimen using a single collection device, subdivided into a primary Tube A specimen and a split Tube B specimen, and independently sealed in the presence of the donor. The second serial specimen collection must begin within two minutes after the completion of the first collection.

The collection procedure begins when the collector will provide or the donor may select the specimen collection device(s) that are clean, unused, wrapped/sealed in original packaging and compliant the Subpart G. The device(s) must be within the manufacturer's expiration date printed on the specimen tube(s). The specimen collection container package will be opened in view of the donor.

A volume of at least 1 mL of undiluted (neat) oral fluid is collected for the specimen designated as primary Tube A and a volume of at least 1 mL of undiluted (neat) oral fluid is collected for the specimen designated as split Tube B.

The collector notes any unusual behavior or appearance of the donor on the Federal CCF. If the collector detects any conduct that clearly indicates an attempt to tamper with a specimen (e.g., an attempt to prevent the device from collecting sufficient oral fluid; an attempt to bring into the collection site an adulterant or oral fluid substitute), this is a non-MRO determined refusal to test collector must report a non-MRO determined refusal to test.

The collector inspects the specimen to determine if there is any sign indicating that the specimen may not be a valid oral fluid specimen (e.g., unusual color, presence of foreign objects or material). The collector notes any unusual finding on the Federal CCF and takes action (e.g., recollection) to obtain an acceptable specimen. If the donor fails to remain present through the completion of the collection, fails to follow the instructions for the collection device, refuses to begin the collection process after a failure to collect the specimen, refuses to provide a split specimen as instructed by the collector, or refuses to provide an alternate specimen when directed to do so, this is a non-MRO determined refusal to test.

If the donor states that they could provide a specimen after drinking some fluids after they demonstrate their inability to provide a specimen after 15 minutes of using the collection device, there is insufficient volume or no oral fluid collected using the device, the collector gives the donor a drink (up to 8 ounces) and waits an additional 10 minutes before beginning the specimen collection. If the donor simply needs more time before attempting to provide an oral fluid specimen, the donor may choose not to drink any fluids during the 1 hour wait time. If the donor states that they are unable to provide an oral fluid specimen, the collector records the reason for not collecting an oral fluid specimen on the Federal CCF, notifies the Federal agency's designated representative for authorization to collect an alternate specimen, and sends the appropriate copies of the Federal CCF to the MRO and to the Federal agency's designated representative. The Federal agency *may* choose to provide the collection site with a standard protocol to follow in lieu of requiring the collector to notify the agency's designated representative for authorization in each case. If an alternate specimen is authorized, the collector may begin the collection procedure for the alternate. If the donor fails to remain present through the completion of the collection, refuses to provide a second specimen as required or refuses to provide an alternate specimen as authorized, this is a non-MRO determined refusal to test.

3.1.3 Security and Chain of Custody

The Mandatory Guidelines specify requirements for collection sites, laboratories, and IITFs to ensure the security and integrity of specimens and to maintain confidentiality of donor and drug test information. Collection sites, laboratories, and IITFs 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) must be 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 urine bottles or oral fluid tubes 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.

Laboratories and IITFs 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 urine 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

HHS-certified laboratories are authorized to test each specimen for one or more biomarkers as provided in the biomarker testing panel. All specimen validity tests must be validated by the HHS-certified laboratory and approved by the NLCP and SAMHSA. MROs can contact the NLCP or SAMHSA to identify tests and individual labs approved to conduct additional testing.

HHS-certified laboratories are authorized to perform tests for drugs other than those in the drug testing panel and/or specimen validity tests on a case-by-case basis as necessary to provide information that the MRO would use to report a verified drug test result (e.g., specimen validity tests [for oral fluid]; specimen validity tests or tetrahydrocannabivarin [for urine],). HHS-certified laboratories are not authorized to routinely test for drugs or biomarkers other than those included in the drug testing panel or the biomarker testing panel and/or specimen validity tests at the request of an MRO without prior authorization from the Secretary or designated HHS representative, with the exception of the determination of d, l stereoisomers of amphetamine and methamphetamine. Laboratories are allowed to perform

additional testing for d, l stereoisomers on a case-by-case basis based on MRO request or routinely based on positive initial or positive confirmatory test results.

SAMHSA will publish the drug and biomarker test analytes and cutoffs (i.e., the "drug testing panel" and "biomarker testing panel") for initial and confirmatory drug and biomarker tests in the Federal Register each year. The drug and biomarker testing panels will also be available on the Internet at https://www.samhsa.gov/workplace.

This drug testing panel will remain in effect until the effective date of a new drug testing panel published in the Federal Register.

3.1.4.1 Urine

Specimen validity testing must be performed for each Federal agency urine 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 20.0 mg/dL, and one or more tests for oxidizing adulterants must be performed.

HHS-certified laboratories are authorized to test each specimen for one or more biomarkers as provided in the biomarker testing panel.

Additional testing may be performed if a specimen exhibits abnormal characteristics (e.g., unusual odor or color, semi-solid characteristics), causes reactions or responses characteristic of an adulterant during initial or confirmatory drug tests (e.g., non-recovery of internal standard, unusual response), or contains an unidentified substance that interferes with the confirmatory analysis.

Specimen validity tests must be performed for the split specimen (Bottle B) when a laboratory fails to reconfirm a drug analyte reported positive in the primary specimen (Bottle A).

3.1.4.2 Oral Fluid

HHS-certified laboratories are authorized to test each specimen for one or more biomarkers as provided in the biomarker testing panel.

Federal agencies are authorized to test each specimen for one or more biomarkers as provided in the biomarker testing panel and, upon an MRO's request, to test an oral fluid specimen to determine specimen validity using, for example, a test for a specific adulterant.

Additional testing may be performed if a specimen exhibits abnormal characteristics (e.g., unusual odor, color, or semi-solid characteristics), causes reactions or responses characteristic of an adulterant during initial or confirmatory drug tests (e.g., non-recovery of internal standard, unusual response), or contains an unidentified substance that interferes with the confirmatory analysis.

3.1.5 Testing

3.1.5.1 Urine

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 and on the SAMHSA website: https://www.samhsa.gov/workplace. The two types of test facilities allowed under the UrMG are IITFs and laboratories.

IITFs perform only the initial screening test for a urine specimen, and are allowed to report urine specimens as negative, negative, and dilute, and rejected for testing. Dilute is defined as creatinine greater than 5.0 mg/dL but less than 20.0 mg/dL and the specific gravity is equal to or greater than 1.002 but less than 1.003. Federally regulated specimens with all other presumptive results (positive, adulterated, and substituted) reported by an IITF must be forwarded to an HHS-certified laboratory for further testing.

Laboratories perform all tests for a urine specimen (initial and confirmatory) and are the only facilities that may report specimens as positive, adulterated, substituted, invalid, and dilute. Certified laboratories report urine specimen as dilute when the creatinine is greater than 5.0 mg/dL and less than 20.0 mg/dL and the specific gravity is equal to or greater than 1.002 but less than 1.003; or the creatinine concentration is equal to or greater than 2.0 mg/dL, but less than 20.0 mg/dL and the specific gravity is greater than 1.0010 but less than 1.0030.

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 urine specimen prior to reporting the specimen as invalid. Urine 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 (A) 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 (A) specimen for adulteration because a second HHS-certified laboratory failed to reconfirm the drug(s) reported in the primary (A) specimen, and reported that the split (B) specimen 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 primary [A]) retest the primary specimen (A) for the adulterant. If the second laboratory reported the split (B) specimen 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:

  - For urine substitution based upon creatinine and specific gravity, review the specific gravity and creatinine results of the primary (A) specimen; or
  - For substitution based upon biomarker testing, test the primary (A) specimen using its confirmatory test for the biomarker.

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

The MRO may request additional/different testing of a primary specimen (Bottle A) or split (Bottle B) urine specimens under the following circumstances:

- The laboratory has notified the MRO that the initial or confirmatory test result is invalid due to a possible presence of an adulterant and the MRO would like to have additional/different testing completed.

- The specimen is confirmed positive for methamphetamine and the MRO elects to have d, l enantiomer testing performed. This testing may be performed on a case-by-case basis or, for primary (A) specimens, with a blanket request from the MRO.

- When additional test information on a positive result may be useful to the MRO in determining the final test result. For example, the MRO may request 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 Δ9-tetrahydrocannabivarin (THCV) to confirm the use of cannabis as opposed to pharmaceutical THC.

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 urine specimen tested as part of a legal or an administrative proceeding to defend an original positive, adulterated, or substituted result.

3.1.5.2 Oral Fluid

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 and on www.samhsa.gov/workplace. The only test facilities allowed under the OFMG are laboratories. *Only HHS-certified laboratories are authorized to test oral fluid specimens for Federal agency workplace drug testing programs.*

Oral fluid specimens are usually collected using a device, which may or may not contain a diluent. HHS-certified laboratories must process oral fluid specimens using validated procedures that are specifically for the collection device used to collect the specimen. The NLCP maintains a list of HHS-certified oral fluid laboratories and the device(s) that each laboratory tests.

Laboratories may report oral fluid specimens as negative, positive, adulterated, substituted and invalid.

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 an oral fluid specimen prior to reporting the specimen as invalid. Oral fluid specimen reporting criteria are in Appendix D.

In most cases, the MRO is not allowed to request retesting of a reported primary (A) specimen. Primary (A) 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 HHS has directed the laboratory to reanalyze the specimen; or
- When the MRO has requested analysis of the primary (A) specimen for adulteration or substitution because a second HHS-certified laboratory failed to reconfirm the drug(s) reported in the primary (A) specimen, and reported that the split (B) specimen was adulterated or substituted. 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 primary (A) specimen) retest the primary specimen (A) for the adulterant or substituted result.

The MRO may request additional/different testing of a primary (A) or split (B) oral fluid specimens under the following circumstances:

- The laboratory has notified the MRO that the initial or confirmatory test is invalid due to possible presence of an adulterant and the MRO would like to have additional/different testing completed.
- The specimen is confirmed positive for methamphetamine and the MRO elects to have d,l enantiomer testing performed. This testing may be performed on a case-by-case basis or, for primary specimens, with a blanket request from the MRO.
- When additional test information on a positive result may be useful to the MRO in determining the final test result. For example, the MRO may request additional specimen validity testing (e.g., tests for a biomarker and/or an adulterant) on a case-by-case basis.

When the primary (A) oral fluid specimen is reported as positive, adulterated, or substituted, the donor is given an opportunity to request testing of the split (B) specimen at a second HHS-certified laboratory. If a donor does not ask to have the split (B) oral fluid specimen tested, a Federal agency may have the split (B) oral fluid 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. HHS-certified laboratories are required to validate all methods prior to implementation to ensure that they are accurate and reliable for testing of Federal workplace drug testing specimens.[1]

3.2.1 Initial Drug Tests

Laboratories and IITFs are required to use either immunoassay or an alternate technology (e.g., spectrometry, spectroscopy) for initial drug tests.

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 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 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 UrMG and OFMG 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.

A laboratory or IITF 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 metabolite, cocaine metabolite, and heroin 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 urine Δ9- tetrahydrocannabinol-9- carboxylic acid [THCA], 100 ng/mL for urine benzoylecgonine, 2 ng/mL for oral fluid Δ9- tetrahydrocannabinol [THC], 2 ng/mL for oral fluid 6-acetylmorphine [6-AM]). For drug classes with multiple initial test analytes (such as codeine/morphine, hydrocodone/hydromorphone, oxycodone/ oxymorphone, methylenedioxymethamphetamine (MDMA)/methylenedioxyamphetamine (MDA), amphetamine/methamphetamine, and, for oral fluid only, cocaine/ benzoylecgonine), 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 UrMG and OFMG 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. 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 using multiple reaction monitoring (MRM) analysis are also allowed and provide additional analytical benefits.

3.2.3 Specimen Validity Tests

3.2.3.1 Urine

The UrMG specify test method requirements for some urine 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 or validate 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.

3.2.3.2 Oral Fluid

The OFMG specify that laboratories are authorized to test each specimen for one or more biomarkers as provided in the biomarker testing panel and, upon a Medical Review Officer's request, to test an oral fluid specimen to determine specimen validity using, for example, a test for a specific adulterant. Each invalid, adulterated or substituted specimen validity test result must be based on an initial specimen validity test on one aliquot and a

confirmatory specimen validity test on a second aliquot. The OFMG do not specify tests or test method requirements for oral fluid initial and confirmatory specimen validity testing if performed upon request by the Medical Review Officer. It is not possible to provide guidance on test methods for all substances that may be used to adulterate or validate an oral fluid specimen. As new adulterants are identified, laboratories are permitted to implement analysis for HHS-approved adulterants. There may be more than one acceptable test method for a particular analyte. All specimen validity tests must be scientifically and forensically supportable.

3.2.4 Split (B) Specimen Testing

The second HHS-certified laboratory must report the result to the MRO using the HHS-specified nomenclature published with the drug and biomarker testing panels.

3.2.4.1 Urine

A donor may request testing of the split (B) urine specimen at a second HHS-certified laboratory to reconfirm or refute a positive, adulterated, or substituted result reported for the primary (A) specimen. The second laboratory tests the split (B) specimen using only the confirmatory test(s) needed to reconfirm the primary (A) specimen result(s). The laboratory performs drug tests at the laboratory's limit of detection (LOD) or limit of quantification (LOQ)—not the HHS cutoffs. For substitution based on biomarker testing: The laboratory must test for the biomarker using its confirmatory test (i.e., using the confirmatory test analytes and cutoffs in the biomarker testing panel). Otherwise, split (B) specimen reconfirmations for adulterated and substituted specimens are performed at the HHS cutoffs for primary (A) specimens. For adulterants without a specified cutoff (e.g., glutaraldehyde, chromium [VI], pyridine, halogens [such as, chlorine from bleach, iodine], peroxidase, peroxide, other oxidizing agents), the laboratory must use its confirmatory specimen validity test at the laboratory's LOQ to reconfirm the presence of the adulterant. The laboratory is required to inform the MRO of the laboratory's LOD/LOQ, but the reconfirmation report is issued as a qualitative "reconfirmed" or "failed to reconfirm" result only. If the laboratory fails to reconfirm one or more drug analytes reported as positive in the primary (A) specimen, the laboratory performs specimen validity tests for the split (B) specimen.

If the split (B) specimen testing laboratory (laboratory B) believes that the analyte (i.e., drug, drug metabolite, adulterant) is present in the split (B) specimen but cannot reconfirm its presence, the laboratory must consult with the MRO and the NLCP to decide whether to send the split (B) specimen to a third HHS-certified laboratory for additional

confirmatory testing. For Federal specimens, the MRO must submit a signed request to the split (B) specimen testing laboratory to have the additional testing done at a third laboratory. This is not required for DOT-regulated urine 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 (A) specimen result).

3.2.4.2 Oral Fluid

A donor may request testing of the split (B) oral fluid specimen at a second HHS-certified laboratory to reconfirm or refute a positive or adulterated result reported for the primary (A) specimen. Prior to sending an oral fluid specimen or aliquot to another HHS-certified laboratory, the sending laboratory must ensure that the receiving laboratory has validated procedures for testing specimens using the specific collection device. If a laboratory receives a primary or split (B) specimen for additional testing and the laboratory does not have validated procedures for the additional test(s) using the same collection device, that laboratory must notify the sending laboratory and obtain MRO authorization to send the specimen to another HHS-certified laboratory that has validated procedures.

The second laboratory tests the split (B) specimen using only the confirmatory test(s) needed to reconfirm the primary (A) specimen result(s). The laboratory performs drug tests at the laboratory's limit of detection (LOD) or limit of quantification (LOQ)—not the HHS cutoffs. Split (B) specimen reconfirmations for adulterated specimens are performed at the laboratory's LOQ. When testing the split (B) specimen for substitution based on biomarker testing, the laboratory must test for the biomarker using its confirmatory test (i.e., using the confirmatory test analytes and cutoffs in the biomarker testing panel). The second HHS-certified laboratory may only conduct the confirmatory biomarker test(s) needed to reconfirm the substituted result reported by the first HHS-certified laboratory. 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. MRO Manual chapter 4, section 4.5, Interpretation and Result Verification, has additional information concerning testing of split (B) specimens. If the laboratory fails to reconfirm one or more drug analytes reported as positive in the primary (A) specimen, the laboratory may perform specimen validity test(s) for the split (B) specimen.

If the split (B) testing laboratory (laboratory B) believes that the analyte (i.e., drug, drug metabolite, adulterant) is present in the split (B) but cannot reconfirm its presence, the laboratory must consult with the MRO and the NLCP to decide whether to send the oral fluid

specimen to a third HHS-certified laboratory for additional confirmatory testing. The third laboratory must have validated confirmation methods that are specific to the specimen collection device. 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 oral fluid 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 (A) specimen result).

3.3 IITF or Laboratory Reports

An MRO may **not** request SVT values for a specimen that is reported only as negative or positive. For example, an MRO may not request creatinine results for a specimen that was reported as positive for codeine.

A dilute finding is reported as a CCF Step 5A checkbox and a Remarks comment only in conjunction with a negative or positive result. Laboratories must report the creatinine and specific gravity values supporting a dilute finding (i.e., negative-dilute, and positive-dilute).

Laboratories must report ALL "non-negative" test results for a specimen. For example, a laboratory MUST report a specimen substituted AND ALSO positive for a given drug metabolite if the criteria for both results have been met. Laboratories must report the numerical values of specimen validity test results that support an adulterated result (i.e., confirmatory adulterant test result, confirmatory pH test result), substituted result (i.e., confirmatory creatinine and specific gravity values), or invalid result (as appropriate).

- For negative and (for urine) negative/dilute results, the laboratory and IITF is allowed to report results using only a computer-generated report.
- For rejected for testing specimens, the laboratory or IITF must send a copy or a legible image of the test facility Federal CCF Copy 1 to the MRO. The laboratory or IITF is allowed to send a computer-generated report in addition to the Federal CCF.
- For positive, adulterated, invalid, and substituted results, the laboratory must send a copy or a legible image of the test facility 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 name and concentration recorded on the Positive line);
- Adulterated (with the adulterant or pH value recorded on the Remarks line);
- Substituted (with the biomarker value recorded on the Remarks line or [for urine only] 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).

Note: These are separate results. For example, "invalid result" does not refer to the drug(s)/drug metabolite(s) reported positive. The MRO should contact the laboratory if there is any confusion about the reported results.

- 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 Federal CCF Copy 1 or by encryption).
- An HHS-certified laboratory or IITF must report results using the HHS-specified nomenclature published with the drug and biomarker testing panels.

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 (B) specimens of the primary (A) specimens listed above; and
- Any split (B) specimens or primary (A) 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.

Laboratories and IITFs may discard negative, rejected, and (for urine) negative-dilute 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 two years by the collector or collector employer. IITFs and laboratories must maintain records generated to support test results for a minimum of two years. A Federal agency may request the test facility to maintain a copy of the documentation package for a urine 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 two years. See Chapter 4, Section 4.6 for additional information.

The MRO and external service providers must ensure the confidentiality, integrity, and availability of the data and limit access to any data transmission, storage, and retrieval system. Hardcopy records may be discarded six months after conversion to electronic records.

4. MRO Review and Reporting Procedures

The MRO must review all positive, adulterated, rejected for testing, invalid test, and substituted results before reporting the results, in a timely manner, to the Federal agency's designated representative. This applies even if the first test was cancelled and another specimen was collected from the donor due to the administrative problem (e.g., collector failed to provide an MFR when directed). Staff under the direct, personal supervision of the MRO may review and report negative and (for urine) 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 reports a negative/dilute result to the agency and directs the agency to immediately collect another specimen from the donor. Refer to Section 4.5.5 for changing a verified test result.

The MRO process consists of—

- Administrative review of documents;
- Interview with the donor (as required);
- Handling split (B) specimen 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 descriptions and instructions are for the MRO Copy (Copy 2) of the Federal CCF.

Note: The MRO should check to ensure that neither the donor nor collector has listed medications as part of their completion of Copy 2. This information would also appear on the client/employer Copy 4, which is not to be used to disclose medications or medical conditions. Since entries made on Copy 2 will not appear on the laboratory Copy 1, it is the MROs responsibility to notify the collection site to prevent future problems.

Note: All copies of the CCF are sent to the Federal agency's designated representative for non-MRO determined refusals to test. The MRO does not review these records.

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 Copy 2 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 2 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.
- Specimen collected is identified as either urine or oral fluid.
- Each test facility is identified by one of the following:
  - A specific laboratory or IITF name and address at the top of the Federal 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 (see also sections 6.5 and 6.6).

- Step 1 contains—
  - Federal agency name and address and employer ID number (as appropriate);
  - MRO name or MRO company 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 mode 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—
  - Specimen collected is either Urine or Oral fluid;
  - The collection was:
    - A split specimen;
    - A single-specimen collection; or
    - No specimen was collected and why (if applicable).

    Note: Split specimen collections are required for Federal agency specimens.
  - For urine:
    - The temperature of the urine specimen was, or was not, within the required temperature range;
    - 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.
  - For oral fluid:
    - The specimen collection split type:
      - ► Serial;
      - ► Concurrent; or
      - ► Subdivided.
    - Each collection device is within expiration date;
    - The specimen collection device volume indicator(s) observed; and

- Comments on the "Remarks" line (as appropriate) recording the collector's observations or explanatory comments concerning the donor, the specimen, or collection events.

Note: Split specimen collections are required for Federal agency specimens.

- Step 3 contains—
  - Collector's printed name;
  - Collector's signature;
  - Date and time of the collection; and
  - Specific name of the delivery service that specimen bottle(s)/tube(s) were released to for transfer the specimen to the test facility.
- Step 4 contains—
  - Donor's printed name;
  - Donor's signature;
  - Date signed;
  - Donor's email address;
  - 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 laboratories and IITFs 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 Copy 1 is used to report all positive, adulterated, invalid, rejected, and substituted specimens. The test facility may send a computer-generated electronic report in addition to the Federal CCF Copy 1 for these specimens. The test facility may send only a computer-generated electronic report for negative and (for urine) 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., fax, computer, 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 Federal CCF Copy 1 (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—
    - Laboratory or IITF accessioner's printed name;
    - Accessioner's signature;
    - Date of receipt;
    - Documentation of the primary (A) specimen (Bottle/Tube A) seal condition upon receipt at the test facility;
    - Documentation for Specimen Bottle(s)/Tube(s) Released to, and

      (for oral fluid) the expiration dates for each primary/single specimen collection device and the split specimen collection device.

      If the manufacturer puts the same expiration date on the outer package as that on the specimen tube(s) in the package, it is acceptable for the collector to record the outer package dates in Step 4 of the Federal CCF. The accessioner records the oral fluid collection device expiration date on the A specimen tube as the Primary/Single Specimen Device Expiration Date, and the expiration date on the B specimen tube as the Split Specimen Device Expiration Date. If the collector recorded the expiration dates in Step 4 of the Federal CCF, the accessioner verifies the recorded expiration dates versus those on the A and B specimen tubes. If an expiration date differs from that on the tube, the accessioner makes a single line through the incorrect date, records the date that is on the tube, and initials and dates the annotation. The accessioner must proactively document their verification of the expiration dates:
    - For a paper or combination electronic/paper Federal CCF Copy 1, the accessioner documents their verification in Step 4. On the Copy 1 form, the accession must initial each expiration date.
    - For an electronic (digital) Federal CCF Copy 1, the accessioner documents their verification electronically (i.e., on the ECCF or in the specimen record in the laboratory information system).
  - Step 5a contains—
    - Primary (A) specimen test results including confirmatory concentration (ng/mL) of each drug or drug metabolite reported for a Positive result;

- 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:
  - Comments as required by HHS for specimens reported as adulterated, rejected for testing, invalid result, substituted or (for urine) dilute (see Table 3); and
  - Observations or explanatory comments recorded by laboratory or IITF 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 (B) specimen (Bottle/Tube B) was tested, Step 5b contains—

- Name and address of the split testing laboratory;
- Results for the split (B) 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 is recorded in the Reason line in Step 5b of the Federal CCF Copy 1.

■ For a split (B) specimen, 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 biomarker or (for urine) the creatinine and specific gravity values.

– FAILED TO RECONFIRM result(s) require 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 urine) 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, invalid [with required comment], or substituted with confirmatory biomarker or creatinine and specific gravity values).
  - 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, laboratory, or IITF 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;
  - Federal 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

A laboratory, MRO, or IITF may identify errors made on a Federal CCF. A laboratory or IITF 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:

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

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

- For oral fluid, the primary (A) specimen was collected using an expired device (i.e., the device expiration date precedes the collection date) and the split (B specimen cannot be re-designated as the primary (A) specimen.

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

- For oral fluid, the collector failed to document observation of the volume indicator(s) at the time of collection for a collection device containing a diluent.

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

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

- In addition to documenting seal condition on the Federal CCF, the laboratory may require a proactive entry by the accessioner to document the seal condition by choosing either intact or not intact in the laboratory information management system (LIMS). It is not sufficient for the accessioner to make an entry only when the seal is not intact. To recover the accessioner's omission of the required seal condition information on the Federal CCF, the certifying technician/scientist may recover the omission with an MFR and must verify that the seal condition was proactively documented in the LIMS at the time of accessioning.

- The specimen was received at the HHS-certified laboratory or IITF without a Federal CCF.
- The specimen was collected using an unapproved ECCF system.
- The Federal CCF was received at the HHS-certified laboratory or IITF without a specimen.
- The collector performed two separate collections using one Federal CCF.
- 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.
- The specimen ID number on either the primary or split specimen bottle/tube label/seal is not unique.
- The collector used an expired collection device for the primary oral fluid specimen and Tube B cannot be redesignated as the primary (A) specimen.
- For oral fluid specimen collection devices with diluent, the collector did not document observation of the device volume indicator(s) at the time of collection. This is not a fatal flaw for undiluted (neat) oral fluid specimens.

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:

- The collector failed to sign the Federal CCF (but the printed name is present). The laboratory must hold the specimen and attempt to obtain a memorandum for the record to recover the collector's 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.
- 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 Federal 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.
- For an oral fluid specimen collected using a non-Federal or expired Federal CCF, the collector must document observation of the device volume indicator(s) on the Federal CCF or an MFR at the time of the collection and send the documentation to the laboratory with the specimen.

- 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.

- The specimen was received with Federal CCF Copy 2-5, the accessioner documents receipt on an internal chain of custody form and the specimen is placed on hold and is not tested. The laboratory must contact the collector to send the Federal CCF Copy 1 with collector wet signature along with an explanatory MFR. If the Federal CCF Copy 1 and the explanatory MFR are 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.

- The specimen was received with reprint ECCF without the collector's wet signature, the accessioner documents receipt on the ECCF received and the specimen is placed on hold and is not tested. The laboratory must contact the collector to send the ECCF with the collector's wet signature and printed name along with an explanatory MFR. If the ECCF and the explanatory MFR are 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.

- If the collector cannot provide the required documentation (e.g., no longer works at the collection site) for the errors described in the above paragraphs, the collection site supervisor may provide the documentation. For example, for an ECCF, the collection site supervisor may sign the authoritative copy (if available) OR a reprint of Copy 1 using their wet signature verifying that the collector who signed the Federal CCF performed the collection. The collection site supervisor must send the signed Copy 1 to the laboratory via courier/mail. Both the collector's electronic signature and printed name must be on Copy 1. The collection site supervisor may also send the required MFR to the laboratory.

- The laboratory must send a copy of the MFR received from the collector to correct the error of using the wrong CCF to the MRO or, alternatively, include a comment on the CCF and electronic report identifying the error and noting that an MFR was received. The specimen is rejected if an MFR is not obtained.

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

- Incorrect laboratory or IITF name and address;

- Incomplete/incorrect/unreadable employer name or address;

- When the Federal CCF does <u>not</u> include an MRO company name, the MRO name is missing or incorrect;

- Incomplete/incorrect MRO address;
- Transposition of numbers in the donor's social security number or ID number;
- Missing/incorrect telephone or fax number;
- A "Reason for Test" box is not marked;
- A "Drug Tests to be Performed" box is not marked;
- For oral fluid, the Oral Fluid" box is not marked (i.e., by the collector or laboratory)
- A box is not marked under Step 2, "Collection";
- For oral fluid, the box titled "Each Device Within Expiration Date?" is not marked
- The "Observed" box is not marked for an observed urine collection;
- No collection site address; (When no collection information is on the Federal CCF, the laboratory must process the specimen. If no MFR obtained after at least 5 days, the laboratory will report results with comment e.g., "unable to recover missing information.")
- The collector's printed name is missing, but the collector's signature is properly recorded;
- The time of collection is not indicated;
- The date of collection is not indicated;
- Incorrect/missing name of delivery service;
- Donor's name included on the test facility copy of the Federal CCF or on seal labels;
- Signature present without printed name (i.e., of collector, accessioner, certifying technician, or certifying scientist);
- The collector has changed or corrected information by crossing out the original information but did not date and initial the change.
- No urine specimen temperature block mark and no explanatory comment in the Remarks line (see Section 4.1.4, Federal CCF Remarks). The laboratory must contact the collector for an MFR to explain the omission. If, after at least 5 business days, the collector cannot provide a MFR to attest to the fact that the collector did measure the specimen temperature, the HHS certified laboratory or IITF may report the test result for the specimen but indicates that the collector could not provide a memorandum to recover the omission.

- Omitted/incorrect specimen type on Federal CCF – accessioner marks correct checkbox, and (if marked) lines through incorrect checkbox, initials and dates the edit.

- Incorrect Federal CCF or ECCF expiration date for oral fluid collection device – the accessioner makes a forensic edit to record the date that is on the tube (See Chapter 4, Section 4.1.2, Copy 1, step 4).

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:

- The donor's signature is missing on the MRO Copy 2 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.

- There is no certifying scientist signature on the Federal CCF for a positive, adulterated, invalid, or 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.

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

5. Report discrepancies may be identified by a laboratory or an IITF 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:

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

- Data entry errors due to illegible or misread Federal CCF information;

- Data review or transcription errors by the certifying technician or certifying scientist;

- A discrepancy between the Federal CCF and electronic report;

- The accessioner failed to identify an oral fluid collection incorrect expiration date and the device was not expired; or

- Test cancelled – the accessioner failed to identify an incorrect expiration date and the device was expired.

4.1.4 Federal CCF Remarks

Collectors are required to include comments on the Remarks line in Step 2 (the collector's section) of the Federal CCF to document any unusual donor behavior or incidents occurring during the collection. Laboratory and IITF 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), as well as explanatory reporting comments required by the program (e.g., the basis for reporting a specimen as adulterated, the basis for reporting a specimen as invalid, the reason for rejection, or [for urine] creatinine and specific gravity values supporting a substituted result, —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 4.1.3-1), the following may occur:

- If a laboratory or IITF 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 Federal CCF Copy 1 and any other report to the MRO.
- If the MRO receives a rejected for testing specimen report or identifies a fatal flaw during review, the MRO cancels the test.
- The MRO reports the cancellation and the reason to the Federal agency, which then determines whether or not to immediately collect another specimen for the same type (i.e., urine or oral fluid) from the donor.

2. When a correctable discrepancy (as defined in Sections 4.1.3-2 and 4.1.3-4) 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.

- 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.

- For a regulated specimen submitted with a non-Federal CCF or expired Federal CCF, the following may occur:
  - For an oral fluid specimen collected using a non-federal or expired Federal CCF, the collector must document observation of the device volume indicator(s) on the Federal CCF or an MFR at the time of the collection and send the information to the laboratory with the specimen. The laboratory will reject the specimen if the collector did not document observation of volume indicator(s) at the time of collection. This requirement applies to oral fluid specimens collected using a device with a diluent, not to neat oral fluid specimens.
  - The collector must provide the laboratory with an MFR explaining why the incorrect form was used and providing all information required on the Federal CCF.
- For a regulated specimen submitted with an incorrect Federal CCF, the following may occur:
  - If the laboratory received Copy 2-5 of the Federal CCF, the laboratory may not begin testing the specimen until it receives Copy 1 with the collector's wet signature and an MFR explaining the receipt of the incorrect copy.
  - The laboratory must either send a copy of the MFR to the MRO or include a comment on the CCF and electronic report identifying the error and noting that an MFR was received. The specimen is rejected if the signed Copy 1 and an MFR are not obtained.
- For a regulated specimen submitted with a non-Federal form, the following may occur:
  - If the collector provides an MFR and the specimen was tested in accordance with the UrMG or OFMG, 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 used for regulated specimens, the laboratory or IITF must follow guidance provided in the NLCP Manual for Urine Laboratories and the NLCP Manual for Oral Fluid Laboratories (Use of Non-Regulated CCF) for use of a non-regulated CCF for a regulated specimen and requests to upgrade a non-regulated specimen to a regulated test.

    If the specimen is negative for all drugs or positive only for a regulated analyte, the laboratory must reanalyze the specimen using regulated procedures after receiving a signed request from the MRO. For reanalyzed specimens, the laboratory or (for urine) IITF may send an MFR with the certification statement from the Federal CCF and the certifying scientist's signatures, name, and date.

The MRO reports the verified result to the Federal agency and maintains the MFR in the files for the specimen.

If the specimen is positive for a non-regulated analyte, the MRO is not allowed to request an upgrade to a regulated test. The laboratory must reject the request and not re-analyze the specimen. If a laboratory is unable to change a specimen from non-regulated to regulated, the laboratory must reject the specimen. 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 rejected tests and notifies the Federal agency of the cancelled test and the reason for cancellation.

Use of Non-Regulated ECCF:

For requests to change a non-regulated test collected with an ECCF to a regulated test using a combination electronic/paper CCF Option 1:

- If the ECCF system is the same as HHS-approved system, the specimen can be reported as regulated if the following required documents are obtained:
  - Laboratory MFR signed by the RP attesting that the ECCF system is same as the HHS-approved system; and
  - MFR from collector that explains the use of the incorrect form.
- If the ECCF system is not the same as HHS-approved system and specimen collection is not post-accident or reasonable suspicion/cause, it cannot be changed to regulated.
- If the ECCF system is not the same as HHS-approved system and specimen collection is post-accident or reasonable suspicion/cause, the laboratory must notify the NLCP and the Federal agency for guidance.
- For requests to change a non-regulated test collected with an ECCF to a regulated test using a combination electronic/paper CCF Option 2:
- If the ECCF system is the same as HHS-approved system and the authoritative copy was received with specimen, the specimen can be reported as regulated if the following required documents are obtained:
  - Laboratory MFR signed by the RP attesting that the ECCF system is same as the HHS-approved system; and
  - MFR from collector that explains the use of the incorrect form.
- If the ECCF system is the same as the HHS-approved system and the authoritative copy was not received with specimen, the specimen can be reported as regulated if the following required documents are obtained:
  - Laboratory MFR signed by the RP attesting that the ECCF system is same as the HHS-approved system;
  - MFR from collector that explains the use of the incorrect form and explains why the authoritative copy was not sent

Note: The laboratory must obtain Copy 1 of the CCF with the collector's wet signature prior to testing the specimen.

- If the ECCF system is not the same as HHS-approved system and specimen collection is not post-accident or reasonable suspicion/cause, the laboratory will not change it to regulated and will reject the specimen.

- If the ECCF system is not the same as HHS-approved system and specimen collection **is** post-accident or reasonable suspicion/cause, the laboratory will notify NLCP and the Federal agency for guidance.

  To change a regulated specimen (submitted using a Federal CCF) to a non-regulated test the laboratory must take actions as follows:

- If the laboratory has not performed any testing on the specimen, the laboratory must request an MFR from the collector (or collection site supervisor if the collector is not available) explaining the use of the incorrect form. Once the MFR is received, the laboratory will process the specimen using the laboratory's procedures for non-regulated specimens and report the specimen as a non-regulated drug test.

- If the laboratory has performed any testing on a specimen collected using the Federal CCF, the laboratory must report the specimen as a regulated specimen to the MRO. The laboratory must take action as follows:

  - The laboratory may "downgrade" specimens reported as Negative, Invalid Result, or Rejected for Testing to a non-regulated test upon receiving a signed request from the MRO.
  - For specimens reported to the MRO as Positive and/or Adulterated, the laboratory must take additional action as follows:
    - The laboratory must consult with the Federal agency,
    - The laboratory must provide the confirmed test result and the specimen identification number to the Federal agency, and
    - If the Federal agency determines that the test is non-regulated rather than a regulated test, the laboratory must include a statement regarding that determination in the specimen records.

- If the collector does not provide an MFR for the situations 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.

- For a regulated urine specimen received at an HHS-certified laboratory with redesignated primary (A) specimen (Bottle A) and split (B) 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 4.1.3-4), 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 4.1.3-5), the IITF or laboratory must reissue a report and/or provide an explanatory MFR, depending on the significance of the discrepant information. A reissued report will be either—

- A corrected report when the IITF or laboratory has changed specimen 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

- 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—

- The MRO notifies the responsible party of the errors;

- 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
- The MRO maintains the documentation of error notification and corrective action response in its records.
- If errors continue after MRO notification, the MRO reports the collector/collection site, IITF, or laboratory to the Federal agency and the NLCP.

4.1.5.1 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 Federal 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 an Expired Federal CCF

The 2023 Federal CCF was approved for use on May 1, 2023. Additional information is available at https://www.reginfo.gov/ (enter the OMB number 0930-0158 in the search area). A proof of the 2023 Federal CCF and Guidance for its use are available for viewing on the SAMHSA website: https://www.samhsa.gov/workplace. Because the 2023 Federal CCF is the same as the expired 2020 Federal CCF, use of the 2020 Federal CCF is approved. IITFs and laboratories must treat the use of the 2017 Federal CCF for urine specimens as a correctable discrepancy. The 2017 Federal CCF is not authorized for use with oral fluid specimens.

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 on 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 (f) in the UrMG and sections 13.5(c) through (e) in the OFMG.)

1. The interview process occurs as follows:

   - 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.)

   - 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.

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

   - 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.

- For positive, adulterated, or substituted results: Inform the donor that they may have the split (B) specimen 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 (B) specimen testing when the primary (A) specimen was reported as invalid as described in Chapter 4, Section 4.4.

- If the donor requests split (B) specimen 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.

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

- The reporting of the primary (A) specimen result occurs immediately after the MRO has reviewed the information contained on Copy 2 and Copy 1 of the Federal CCF (as described above) and 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 UrMG and OFMG 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 removal from Federal employment. An applicant's refusal to take a pre-employment test may result in non-selection for Federal employment. The MRO reports a "refusal to test" to the Federal agency in the following instances where:

- The donor refuses to participate at any point in the drug testing process, including:

- Fails to appear for any test within a reasonable time, as determined by the Federal agency, consistent with applicable agency regulations, after being directed to do so by the Federal agency;

- Fails to remain at the collection site until the collection process is complete;

- Fails to provide a specimen (e.g., urine, oral fluid, or another authorized specimen type) for any drug test required by the Mandatory Guidelines or Federal agency regulations;

- Fails to provide a sufficient amount of urine or oral fluid when directed, and it has been determined, through a required medical evaluation, that there was no legitimate medical explanation for the failure;

- Fails or declines to participate in an alternate specimen collection as directed by the Federal agency or collector;

- Fails to undergo a medical examination or evaluation, as directed by the MRO as part of the verification process. In the case of a Federal agency applicant/pre-employment drug test, the donor is deemed to have refused to test on this basis only if the Federal agency applicant/pre-employment test is conducted following a contingent offer of employment. If there was no contingent offer of employment, the MRO will cancel the test;

- Fails to cooperate with any part of the testing process (e.g., disrupt the collection process; fail to wash hands or rinse their mouth after being directed to do so by the collector; refuse to provide a split specimen);

- Brings materials to the collection site for the purpose of adulterating, substituting, or diluting the specimen;

- Attempts to adulterate, substitute, or (for urine) dilute the specimen;

- Admits to the collector or MRO that they have adulterated or substituted the specimen;

- Fails to permit the observation or monitoring of provision of a urine specimen in a direct observed or monitored urine collection; or

- Possesses or wears a prosthetic or other device that could be used to interfere with the urine collection process.

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

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 using a secure method (e.g., telephone, fax, email).

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.

See also Appendix Tables 4 and 5

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

- 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:

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

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

- 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.

- 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 the results of all specimens have been received and verified.

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

4.4 Split Specimen Tests

Note: Donors are not authorized to request split (B) specimen testing of primary (A) specimens reported as invalid. For a positive, adulterated, or substituted result reported on a primary (A) specimen, a donor may request through the MRO that the split (B) specimen be tested by a different (i.e., second) HHS-certified laboratory to verify the result reported by the first HHS-certified laboratory.

If a donor chooses not to have the split (B) specimen tested by a second HHS-certified laboratory, a Federal agency may have a split (B) specimen retested as part of a legal or administrative proceeding to defend an original positive, adulterated, or substituted result (see also Sections 3.1.5.1 and 3.1.5.2).

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 (B) specimen when the MRO informs the donor that the primary (A) specimen 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 (B) specimen test. The MRO must document the donor's verbal request in the MRO records.

- The MRO must request testing of the split (B) specimen in writing (i.e., a memorandum or letter format). For oral fluid split (B) specimen testing, the laboratory selection must be compatible with the split (B) specimen collection device type. The written request may be mailed, faxed, or electronically sent to the laboratory where the primary (A) specimen 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 (B) specimen.

- Laboratory B may be selected by the MRO, the Federal agency, or the donor. In most instances when split (B) specimen 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, split (B) specimen not available, or another certified laboratory to perform the test):

  - 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 using 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 primary (A) specimen 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. The MRO must submit a signed request to send the split specimen to a third laboratory. (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 (B) specimen 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 urine or oral fluid 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., fax, computer, 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 UrMG or Section 14.5 of the OFMG).

- 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.

- The MRO must report drug test results using the HHS-specified nomenclature published with the drug and biomarker testing panels.

4.5 Interpretation and Result Verification

Chapter 5, Drug Information and Interpretation of Results, provides information on the drugs authorized 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 urine and oral fluid 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 urine and oral fluid MRO Case Studies are available on the SAMHSA website: https://www.samhsa.gov/workplace/drug-testing.

The MRO determines the drug test results based upon—

- Specimen type (e.g., urine or oral fluid)
- 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 (A) specimen 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

Laboratory and IITF 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 laboratories and IITFs to report Federal agency specimen results. Only HHS-certified laboratories are authorized to test oral fluid specimens for Federal agency workplace drug testing program. These criteria are described in Appendix D.

After receiving a drug test report, the MRO should contact the laboratory and/or IITF 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 for a specimen when a scientifically supportable 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). A specimen is not reported as invalid result and negative. If an invalid result was 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 validity of the testing. The laboratory will only report specimens as positive, adulterated, or substituted based on scientifically supportable test results. The MRO should contact the laboratory if there is any confusion about the reported results. The MRO reports the verified positive, adulterated, and/or substituted results to the agency, but reports the verified invalid result(s) for the primary (A) specimen only if the split specimen is tested and reported as a failure to reconfirm.

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 urine specimens reported as invalid based on creatinine and specific gravity results, on pH, or on a confirmatory nitrite test concentration > 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 specific oxidants of interest (e.g., 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, invalid, or substituted 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, invalid, 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 nonsteroidal anti-inflammatory drugs (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 prescriptions, medical records, and other medical information provided by the donor that may be relevant to determining whether a legitimate medical explanation for the positive drug test exists. 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 VIII—Dispensing Requirements—Required Information for Prescription Labels. https://www.deadiversion.usdoj.gov/GDP/(DEA-DC-046R1)(EO-DEA154R1)_Pharmacist's_Manual_DEA.pdf). "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.dea.gov/drug-information/csa).

Executive Order (E.O.) 12564, section 3(a) requires the "head of each Executive agency" to "establish a program to test for the use of illegal drugs by employees in sensitive positions." In addition, E.O. 12564, Sec. 7(c) defines, "illegal drugs" as "a controlled substance included in Schedule I or II, . . . the possession of which is unlawful under Chapter 13 of that title. The term "illegal drugs" does not mean the use of a controlled substance pursuant to a valid prescription or other uses authorized by law." Accordingly, for purposes of the Federal Drug-free Workplace Program, "illegal drug" use is defined as the use of an unlawfully possessed drug under Federal law, and does not include situations that involve legal drug use. Accordingly, neither the Mandatory Guidelines (nor this Manual) sanction the reporting of a donor's legal drug use even when such use may raise safety concerns.

When determining whether a legitimate medical explanation exists for a positive test, the MRO should consider whether a medication was used during the time period for which it was legitimately prescribed, if such a time period is specified. If a donor possesses a valid prescription with no time limitations on the drug's use (even if the dispensed prescription is

past its expiration date), the donor's specimen should be reported as negative. If a donor does not possess a valid prescription that would supply a legitimate medical explanation for the positive drug test result, the specimen should be reported as positive.

Please note that an MRO's decision to contact a donor's employer for the purpose of addressing safety concerns associated with a donor's legal drug use is not required, sanctioned, or authorized by 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 independent and voluntary choice, and subject to 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. For purposes of the Federal Drug Free Workplace Program, Federal law pertaining to marijuana control supersedes State marijuana laws, and therefore, a physician's recommendation for marijuana use is not a legitimate medical explanation for a positive marijuana test.

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 2018 Agricultural Improvement Act (Farm Bill) removed hemp from the definition of marijuana within the Controlled Substances Act (CSA). In addition, the act defined that Δ9-tetrahydrocannabinol (THC) level in hemp-derived products must be no greater than 0.3 percent on a dry weight basis. Studies have shown that some cannabidiol (CBD) products' labeling does not accurately reflect their content and may contain trace amounts of THC despite claims of being "THC Free." Regardless of whether a CBD product was derived from hemp meeting the regulations in the Farm Bill, employees are not free from the risk of testing positive for THC metabolite if they use these products. As such, an

employee's drug test may be positive for the THC metabolite, Δ9-tetrahydrocannabinol-9-carobxylic acid (THCA), due to THC in the CBD product.[32]

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

- Note: Designated Agency Representatives (DER) (or Designated Program Coordinators [DPC]) are responsible for processing non-MRO determined situations (i.e., collection-based issues that may qualify as refusal to test). DERs and DPCs cannot change a MRO-verified report. DERs and DPCs follow agency-specific administrative guidance that may result in non-MRO determined test cancellations and refusals to test. See Section 3.1.2 for non-MRO determined action.

Only the MRO may change a previously a MRO-verified negative (or non-negative) test result, refusal to test or test cancellation 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 two years from the date of collection. Hardcopy records may be discarded six 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

4.7.1 Federal Agency Reports

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., fax, computer, secure electronic transmission). Reporting instructions are detailed in Tables 4 and 5. The reporting of the primary (A) specimen 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) specimen 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, laboratory, and/or IITF on the Federal CCF;
- Specimen type (e.g., urine or oral fluid)
- 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. Drug testing is a prevention and deterrent method that is often part of a comprehensive drug-free workplace program to detect the presence of illicit drugs, or certain prescription drugs. The important factor is if the drug and/or drug metabolite is present - quantitative drug values are rarely useful because the level may be increasing or decreasing and the numerical level will vary with the urine specimen concentration (dilution) or oral fluid concentration (partitioning).

The MRO must report drug test results using the HHS-specified nomenclature published with the drug and biomarker testing panels.

Note: Test results for specific federal agencies may require additional administrative reporting tasks. For example, the DOT Federal Motor Carriers Safety Administration (FMCSA) requires MROs to report DOT FMCSA Part 382 Violation drug test results to the FMCSA Drug & Alcohol Clearinghouse. Refer to agency specific requirements.

4.7.2 Biannual Reports (Secretary or Designated HHS Representative)

An MRO must send to the Secretary or designated HHS representative a biannual report of Federal agency specimens that were reported as positive for a drug or drug metabolite by a laboratory and verified as negative by the MRO. The report must not include any personally identifiable information for the donor and must be submitted by mail, fax, or other secure electronic transmission method within 14 working days after the end of the biannual period (i.e., in January and July). The biannual report must contain the following information:

- Reporting period (inclusive dates);
- MRO name, company name, and address;
- Federal agency name; and
- For each laboratory-reported positive drug test result that was verified as negative by the MRO:
  - Specimen identification number;
  - Laboratory name and address;
  - Positive drug(s) or drug metabolite(s) verified as negative;
  - MRO reason for verifying the positive drug(s) or drug metabolite(s) as negative (e.g., a donor prescription [the MRO must specify the prescribed drug]);
  - All results reported to the Federal agency by the MRO for the specimen; and
  - Date of the MRO report to the Federal agency.

An MRO must provide copies of the drug test reports that the MRO has sent to a Federal agency when requested to do so by the Secretary.

If an MRO did not verify any positive laboratory results as negative during the reporting period, the MRO should file a report that states that the MRO has no reportable results during the applicable reporting period.

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 2 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 1 of the Federal CCF for a specimen being reported drug positive, adulterated, invalid, or 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 (for urine) negative-dilute specimen does not contain the required data elements to ensure that the test result is properly associated with the MRO 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.

5. Interpretation of Results and Drug Information

As described in the Federal Workplace Drug Testing Overview, MRO Manual section 3.1.1, Drugs, Federal agencies must test each urine specimen for marijuana metabolite, and cocaine metabolite (benzoylecgonine), while each oral fluid specimen must be tested for marijuana, cocaine, and cocaine metabolite (benzoylecgonine). Federal agencies are authorized to test each specimen for other Schedule I or II drugs as provided in the drug testing panel. SAMHSA will publish the drug test analytes and cutoffs (i.e., the "drug testing panel") for initial and confirmatory drug tests in the Federal Register each year. The drug testing panels will also be available on the SAMHSA website https://www.samhsa.gov/workplace. Appendix D lists the drug testing panel analytes (i.e., drugs and drug metabolites) and test cutoffs specified by the UrMG and OFMG.

Drug and/ or drug metabolite detection times are influenced by many pharmacological and chemical factors associated with the drug, dose, route of administration, frequency of drug use, biology of the individual, specimen type, and the sensitivity of the detection system. In general, detection times in oral fluid are somewhat shorter than observed for urine. In oral fluid, drugs of abuse are detected for 5 to 48 hours after use, whereas in urine, the detection time is 1.5 to 4 days or longer with chronic drug use.[2,3] Positivity rates for oral fluid reported for non-regulated workplace testing are the same as or higher than urine positivity rates. These rates demonstrate the equivalency of these specimen types in identifying drug use, despite differences in drug detection times.

Compared to urine, the composition of oral fluid is dynamic and varies with the rate of saliva production (flow rate). The pH of saliva is generally acidic, but may range from 6.0 to 7.8, depending upon the rate of saliva flow. As saliva flow increases, levels of bicarbonate increase, thus increasing pH.[4] Drugs enter oral fluid primarily by diffusion from blood and by deposition in the oral cavity from active drug use by oral, transmucosal, smoked, inhaled, and insufflated routes. The movement of drugs from blood (plasma) to oral fluid depends upon certain physicochemical properties of the drug including lipophilicity, degree of ionization, and the degree of drug binding with plasma proteins.[5] Lipid-soluble molecules pass through cell membranes more efficiently than those that are more water soluble (e.g., drug metabolites). Consequently, parent (unmetabolized) drug is frequently the predominant analyte identified in oral fluid. Biological membranes are not permeable to the drug fraction that is bound to plasma proteins or to drug that is in the ionized state; hence only free, non-

protein bound and non-ionized drug in plasma can diffuse into saliva. Consequently, oral fluid drug concentrations are closely related to the free, unbound drug in blood (plasma).

For drugs that are weak bases (e.g., cocaine, opioids, amphetamines, and phencyclidine), drug concentrations in oral fluid are frequently higher than plasma concentrations as a result of "ion trapping" due to oral fluid's higher acidity relative to plasma. Despite these restrictions, drug transfer from blood to oral fluid is a rapid process as demonstrated by consistent positive tests for drug in oral fluid two to five minutes following an intravenous injection of heroin or cocaine.[6,7] Deposition of drugs in oral fluid can also occur from external sources. For example, drugs in food sources (e.g., morphine in poppy seeds) are a potential source of contamination.[8] Drug residues can initially be deposited in high concentration in oral fluid during active drug administration by oral, transmucosal, smoked, inhaled, and insufflated routes.[6,7,9] Generally, deposited drug residues disappear rapidly because of inherent self-cleansing mechanisms of the oral cavity (e.g., saliva production and subsequent swallowing).

5.1 Amphetamines (AMP)

5.1.1 Amphetamine (AMP) and Methamphetamine (MAMP)

A positive test would be comprised of any or all analytes (amphetamine, methamphetamine) with a confirmed urine concentration equal to or greater than 250 ng/mL or a confirmed oral fluid concentration equal to or greater than 25 ng/mL.

Amphetamine and methamphetamine are available as prescription medications and a donor who tests positive for one or more amphetamines may have legally used the drug(s). However, there are no non-prescription or OTC medications that contain these sympathomimetics and these substances are differentiated from the amphetamines during testing and will not be misidentified as MDMA, MDA or other amphetamines using a confirmatory test as required by the Mandatory Guidelines.

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

The 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.

- Note: Effective February 1, 2024, laboratories are no longer required to quantitate at least 100 ng/mL amphetamine in a Federal agency or DOT-regulated urine specimen in order to report a positive methamphetamine result or to identify amphetamine above the LOD to report a split specimen as reconfirmed for methamphetamine. NRC will issue a Federal Register Notice with changes to their regulations if they remove this requirement.

Certified laboratories are required to validate all confirmatory assays (urine and oral fluid) 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.

5.1.1.1 Drug Testing

See Appendix D tables and below for urine and oral fluid reporting criteria.

For grouped analytes (i.e., two or more analytes that are in the same drug class and have the same initial test cutoff):

- Initial Test
  - 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.
- Confirmatory Test
  - Mass spectrometry: The test method must use an analytical method combining chromatographic separation and mass spectrometric identification (i.e., gas chromatography/mass spectrometry (GC-MS), liquid chromatography/mass

spectrometry (LC-MS), GC-MS/MS, LC-MS/MS] or equivalent. The test must be calibrated with each analyte from the group identified as the target analytes. Test method calibration must include at least one calibrator at the confirmatory cutoff.

(a) Urine

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Amphetamine/ Methamphetamine	500	Amphetamine Methamphetamine	250 250

(b) Oral Fluid

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Amphetamine/ Methamphetamine	50	Amphetamine Methamphetamine	25 25

When the MRO requests that a split specimen (Bottle/Tube 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 (e.g., urine 250 ng/mL, oral fluid 25 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.

- For urine, 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.

5.1.1.2 Enantiomer Drug Testing[10]

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.[10] *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 (A) 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 urine or oral fluid specimen container 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).

5.1.1.3 Background

Amphetamine and methamphetamine are substances regulated under the CSA as Schedule II sympathomimetic 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.

5.1.1.4 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).

Abusers may use in a variety of methods, including intravenous injection and smoking.

5.1.1.5 Metabolism and Excretion

(a) Urine

Nearly half of a methamphetamine dose is recovered from urine unchanged. A small percentage of methamphetamine is demethylated to amphetamine by the polymorphic cytochrome P450 enzyme CYP 2D6. 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 the genomic expression of the CYP2D6 gene and 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. Phenotype expression of the CYP2D6 depends upon the genome and may range from poor to ultra-rapid metabolizers. Generally, amphetamine and methamphetamine are considered detectable in urine for 2 to 3 days.

Note that detection of amphetamines in urine is affected by pH as acidic conditions enhance drug elimination.

(b) Oral Fluid

Amphetamine appears rapidly in oral fluid as unchanged amphetamine.[11] Methamphetamine and its metabolite, amphetamine, also appear rapidly in oral fluid with methamphetamine as the major constituent.[12,13] Both amphetamine and methamphetamine appearance in oral fluid are affected by pH. Amphetamine and methamphetamine detection in oral fluid is generally one day.[12]

5.1.1.6 Pharmaceuticals and Use

(a) Prescription Drug Products

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 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.[14]

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

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. Another example is benzphetamine (Didrex®). Benzphetamine is metabolized to d-methamphetamine and d-amphetamine. A d-isomer and l-isomer differentiation will reveal the presence of only l-methamphetamine and l-amphetamine after the ingestion of selegiline.

Examples of trade names of drugs that may produce a positive result for only amphetamine include Adderall® and Vyvanse®.

Examples of trade names of drugs that may produce a positive result for methamphetamine and/or amphetamine (metabolite of methamphetamine) include Desoxyn®, Eldepryl®* and Didrex®*. Additional information is presented in Table 6. The use of enantiomeric analysis is useful in distinguishing methamphetamine abuse from prescription medications.

*Note: Eldepryl® (selegiline) metabolizes to the l-enantiomer and Didrex® (benzphetamine) metabolizes to d-methamphetamine.

(b) 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) 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.

Note: donors reporting the use of nasal inhaler products is commonly referred to as the "Vicks defense" even though Vicks products no longer contain l-metamfetamine (l-methamphetamine).

5.1.2 Designer Sympathomimetic Substances (Methylenedioxymethamphetamine (MDMA) and Methylenedioxyamphetamine (MDA))

A positive test would be comprised of any or all analytes (MDMA, MDA) with a confirmed urine concentration equal to or greater than 250 ng/mL or a confirmed oral fluid concentration equal to or greater than 25 ng/mL.

A positive MDMA or MDA result is evidence of illegal drug use. There are no prescription, non-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 amphetamine, methamphetamine, or other amphetamines using a confirmatory test as required by the Mandatory Guidelines.

Certified laboratories are required to validate all confirmatory assays (urine and oral fluid) prior to use with Federal agency specimens. For MDMA and MDA confirmatory assays, each laboratory must document the assay's ability to identify and accurately quantitate MDMA and MDA in the presence of high levels of sympathomimetic amines and also demonstrate that these compounds are not misidentified as MDMA or MDA (i.e., by analyzing samples containing sympathomimetic amines without MDMA or MDA). 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 MDMA and MDA.

5.1.2.1 Drug Testing

See Appendix D tables and below for urine and oral fluid reporting criteria.

For grouped analytes (i.e., two or more analytes that are in the same drug class and have the same initial test cutoff):

- Initial Test
  - 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.
- Confirmatory Test
  - Mass spectrometry: The test method must use an analytical method combining chromatographic separation and mass spectrometric identification (i.e., gas chromatography/mass spectrometry (GC-MS), liquid chromatography/mass spectrometry (LC-MS), GC-MS/MS, LC-MS/MS] or equivalent. The test must be calibrated with each analyte from the group identified as the target analytes. Test method calibration must include at least one calibrator at the confirmatory cutoff.

(a) Urine

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
MDMA/MDA	500	MDMA MDA	250 250

(b) Oral Fluid

Initial Test Analyte	Initial Test Cutoff (ng/mL)	Confirmatory Test Analyte	Confirmatory Test Cutoff (ng/mL)
MDMA/MDA	50	MDMA	25
		MDA	25

When the MRO requests that a split specimen (Bottle/Tube B) be tested for MDA and/or MDMA, the second laboratory performs confirmatory testing for both MDA and MDMA 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 (e.g., urine 250 ng/mL, oral fluid 25 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 MDMA or MDA (at or above the laboratory's established LOD for the assay) in order to report MDMA or MDA as reconfirmed,
- An MRO may request the quantitative result of MDA or MDMA 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.

5.1.2.2 Background

3,4-Methylenedioxymethamphetamine (MDMA, "Ecstasy," "Molly," "E," "XTC") and its major, active metabolite, 3,4-methylenedioxyamphetamine (MDA, EA-1299, "Love") are psychoactive amphetamines regulated under the CSA as Schedule I hallucinogens. 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. MDMA also acts as an entactogen—a drug that can increase self-awareness and empathy.

MDMA and MDA 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. Illegal manufacture of MDMA and MDA is without regard to amounts of d-isomer or l-isomer. Certified laboratory urine and oral fluid drug testing do not distinguish between d-isomers and l-isomers of either MDMA or MDA.

5.1.2.3 Routes of Administration

- MDMA—oral (i.e., tablets or capsules).
- MDA—oral (i.e., tablets or capsules).

Abusers may use in a variety of methods, including intravenous injection and smoking.

5.1.2.4 Metabolism and Excretion

(a) Urine

MDMA is metabolized primarily by demethylation to form the active metabolite, MDA, and breaking the methylenedioxy bridge to form hydroxymethoxy- and dihydroxy-derivatives. Generally, MDMA or MDA is detectable in urine for 1 to 2 days.

(b) Oral Fluid

MDA appears rapidly in oral fluid as the unchanged drug MDA. MDMA and its active metabolite, MDA, also appear within hours in oral fluid with MDMA as the major constituent.[15] Limited studies have shown MDMA and MDA detectable in oral fluid for 71 and 47 hours, respectively, in oral fluid.[15]

5.1.2.5 Pharmaceuticals and Use

(a) Prescription Drug Products

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

(b) Non-prescription Drug Products

The popular term “Molly” (slang for “molecular”) refers to the pure crystalline powder form of MDMA, usually sold in capsules. A tablet contains approximately 100 mg, although street samples vary in dose and potency, and a typical oral dose is one to two tablets. 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. These effects 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. It is commonly taken in combination with other drugs.

5.2 Cannabinoids (THC)

5.2.1 THC and THCA

A positive test would be comprised of a confirmed marijuana metabolite Δ9-tetrahydrocannabinol-9-carboxylic acid (THCA) urine concentration equal to or greater than 15 ng/mL or a confirmed oral fluid Δ9-tetrahydrocannabinol (THC) concentration equal to or greater than 2 ng/mL

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.

Certified laboratories are required to validate all confirmatory assays (urine and oral fluid) prior to use with Federal agency specimens. For confirmatory assays, each laboratory must document the assay's ability to identify and accurately quantitate urine THCA and oral fluid THC. These experiments must be performed on at least an annual basis to verify the assay's continued performance.

5.2.1.1 Drug Testing

See Appendix D tables for urine and oral fluid reporting criteria.

For single analytes (i.e., one analyte that is in the drug class and a single initial test cutoff):

- Initial Test
  - 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.

    An initial test must be calibrated with the target analyte (i.e., Δ-9-

tetrahydrocannabinol-9-carboxylic acid [THCA] for urine and Δ-9-tetrahydrocannabinol [(THC] for oral fluid).

- 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.
- 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 urine THCA and 2 ng/mL for oral fluid THC).

■ Confirmatory Test

- Mass spectrometry: The test method must use an analytical method combining chromatographic separation and mass spectrometric identification (i.e., gas chromatography/mass spectrometry (GC-MS), liquid chromatography/mass spectrometry (LC-MS), GC-MS/MS, LC-MS/MS] or equivalent. The test must be calibrated with the analyte from the group identified as the target analyte. Test method calibration must include at least one calibrator at the confirmatory cutoff.

(a) Urine

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Marijuana (THCA)	50	THCA	15

(b) Oral Fluid

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Marijuana (THC)	4	THC	2

When the MRO requests that a split urine specimen (Bottle/Tube B) be tested for THCA or a split oral fluid specimen (Container B) for THC, the second laboratory performs (for urine) confirmatory testing for THCA or (for oral fluid) THC analyte 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 (e.g., urine THCA 15 ng/mL, oral fluid THC 2 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 urine THCA or (for oral fluid) THC (at or above the laboratory's established LOD for the assay) in order to report either urine THCA or oral fluid THC as reconfirmed.

5.2.1.2 Background

Marijuana, *Cannabis sativa*, is controlled under Schedule I of the CSA and contains many cannabinoid substances. The principal psychoactive agent in cannabinoids is Δ9-tetrahydrocannabinol (delta-9-tetrahydrocannabinol, commonly referred to as THC). Certified laboratories are required to use confirmatory testing that specifically identifies the major marijuana metabolite, Δ9-tetrahydrocannabinol-9-carboxylic acid (commonly referred to as THCA, Δ9-THCA or THC-COOH).[16]

Some cannabinoids produce euphoria or a "high" and a sense of relaxation that is commonly followed by drowsiness. The initial psychoactive effects of smoking marijuana 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.

5.2.1.3 Routes of Administration

- Dronabinol-oral (i.e., capsules and liquid solution).

- Marijuana—smoking, oral (i.e., eating), vaping, and inhalation through a hash pipe.

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

- Wax, shatter, dabs, extracts—inhaled, smoked, or vaping (especially by e-cigarettes).

Abusers may use in a variety of methods. 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 products. A variety of cannabis preparations have become available for consumption by smoking, inhalation, oral ingestion, and other routes of administration.

5.2.1.4 Metabolism and Excretion

Cannabinoids are usually smoked, vaped, 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 is also 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.

(a) Urine

Current urine 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.

(b) Oral Fluid

THC is reliably present in oral fluid immediately after smoked cannabis administration and remains detectable for 24–30 hours or longer. The major source of THC in oral fluid occurs from deposition in the mouth during smoking, vaping or oral use.[17] THC appears at its highest concentration in oral fluid immediately after smoking marijuana.[18-21] Initial high concentrations of THC in oral fluid decline rapidly within the first 30 minutes after use and thereafter decline over time in a manner similar to that observed for THC in plasma and serum.

5.2.1.5 Pharmaceuticals and Use

(a) Prescription Drug Products

(i) Pharmaceuticals

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 urine drug test result but not a positive THC oral fluid drug test result. Use of Marinol® does not produce a positive oral fluid THC result.[22,23] Marinol® is approved for treatment of anorexia associated with weight loss in patients with a confirmed diagnosis of acquired immune deficiency syndrome (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.

THC preparations from *Cannabis sativa* contain Δ9-THC and a number of closely related cannabinoids including Δ9-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; however, studies indicate that THCV is not present in all strains of cannabis and there is variability in the concentrations among strains of cannabis.[24-26] 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 interpretation of 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.

Epidiolex® (GW Pharma Ltd, United Kingdom) is an FDA-approved cannabidiol (CBD)-enriched product for the control of intractable epilepsy in children. Epidiolex is CBD and contains trace THC. Therefore, high daily doses of this compound have the potential to cause a positive 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 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 a product named Charlotte's

Web Oil that is being advertised in Colorado to treat similar symptoms. The product appears to be a marijuana extract enriched with higher ratios of CBD to THC. Use of this product might result in a positive THCA test. 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. [27]

(ii) 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.

(b) Non-prescription Drug Products

(i) Marijuana

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.

(ii) Passive Inhalation of Marijuana

Passive inhalation (i.e., an inadvertent exposure to marijuana) are frequent excuses for positive urine tests for THCA and positive oral fluid tests for THC; 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.[28] 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. In a similar study of passive inhalation and oral fluid THC, prolonged exposure to high levels of second-hand marijuana smoke may result in detectable levels of oral fluid THC but for only up to 3 hours after the individual willingly exposes themselves to extreme levels of second-hand marijuana smoke on a sustained basis and in an enclosed space.[29]

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 urine test or positive THC oral fluid test was due to passive inhalation, the MRO may not accept this as a legitimate explanation for a positive THCA (urine) or for a positive THC (oral fluid).

(iii) Hemp Products

The 2014 Agricultural Act legalized growing and cultivation of "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.[30] "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.

The 2018 Agricultural Improvement Act (Farm Bill), signed into law on 20 December 2018, removed hemp from the definition of marijuana within the Controlled Substances Act (CSA).[31] The Farm Bill states that the Δ9-tetrahydrocannabinol (THC) level in hemp-derived products must be no greater than 0.3 percent on a dry weight basis in order

to satisfy the revised definition of "hemp" provided in the Farm Bill. Studies have shown that some cannabidiol (CBD) products' labeling does not accurately reflect their content.

Cannabis based products containing a THC level greater than 0.3 percent on a dry weight basis do not fall under the Farm Bill's definition of hemp even if they are labeled as such. In one study, the amount of CBD in 69 percent of the 84 tested CBD products was inconsistent with that on the label, and some products contained unlabeled cannabinoids, including THC in amounts up to 6.4 mg/mL. As such, an employee's drug test may be positive for the THC metabolite, Δ9-tetrahydrocannabinol-9-carobxylic acid (THCA), due to THC in the CBD product.[32]

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.

(iv) Cannabinoid Isomers

The cannabinoid isomer Δ8-tetrahydrocannabinol (delta-8-tetrahydrocannabinol, commonly referred to as Δ8-THC) is a psychoactive cannabinoid agent that metabolizes to Δ8-tetrahydrocannabinol-9-carboxylic acid (commonly referred to as Δ8-THCA or Δ8-THC-COOH). The Δ8-THC and Δ8-THCA cannabinoid isomers cross-react with oral fluid and urine initial test immunoassays, respectively. Oral fluid specimens containing Δ8-THC and urine specimens containing Δ8-THCA could produce positive initial test results, even in the absence of Δ9-THC and Δ9-THCA. HHS-certified laboratories are required to successfully confirm and quantify oral fluid Δ9-THC and urine Δ9-THCA in the presence of Δ8-THC and Δ8-THCA, respectively.

Conversion of water-soluble CBD to Δ9-THC, using THC-free CBD products (an oil, a water-soluble CBD powder, and a water-soluble nano-emulsion formulation) incubated in synthetic gastric fluid, did not convert CBD to Δ8-THC. The nano-emulsion CBD formulation demonstrated <0.065% conversion and was the highest conversion to Δ9-THC observed. Resulting Δ9-THC concentrations would be less than "THC-free" or "<0.3% THC" levels in CBD products. Based upon a daily dose of 30 mg CBD, it is unlikely that gastric CBD conversion to Δ9-THC will produce a positive urinary drug test for Δ9-THC-COOH (50 ng/mL cutoff), but more extensive conversion *in vivo* and/or use of other products, cannot be ruled out.

The subject of cannabinoid isomers is rapidly evolving and may outpace the publication schedules for the MRO Manual. MROs should look for program updates as they become available from SAMHSA, the DOT, and MRO professional associations.

5.3 Cocaine (COC)[33]

5.3.1 Benzoylecgonine and Cocaine

A positive test would be comprised of a confirmed cocaine metabolite (benzoylecgonine) urine concentration equal to or greater than 100 ng/mL or a confirmed oral fluid concentration of any or all analytes (cocaine, benzoylecgonine) equal to or greater than 8 ng/mL.

There are no prescription, non-prescription or OTC medications that contain 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 are differentiated from cocaine and or benzoylecgonine during testing and will not be misidentified as either cocaine or benzoylecgonine using a confirmatory test as required by the Mandatory Guidelines.

Certified laboratories are required to validate all confirmatory assays (urine and oral fluid) prior to use with Federal agency specimens. For confirmatory assays, each laboratory must document the assay's ability to identify and accurately quantitate urine benzoylecgonine and oral fluid benzoylecgonine and cocaine. These experiments must be performed on at least an annual basis to verify the assay's continued performance.

5.3.1.1 Drug Testing

See Appendix D tables for urine and oral fluid reporting criteria.

For single and grouped analytes (i.e., one analyte in the drug class; or two or more analytes that are in the same drug class and have the same initial test cutoff):

- Initial Test
  - 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.

- The confirmatory test cutoff must be used for an alternate technology initial test that is specific for the target analyte (i.e., 100 ng/mL for urine benzoylecgonine).

- Confirmatory Test

  - Mass spectrometry: The test method must use an analytical method combining chromatographic separation and mass spectrometric identification (i.e., gas chromatography/mass spectrometry (GC-MS), liquid chromatography/mass spectrometry (LC-MS), GC-MS/MS, LC-MS/MS] or equivalent. The test must be calibrated with each analyte from the group identified as the target analyte. Test method calibration must include at least one calibrator at the confirmatory cutoff.

(a) Urine

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Cocaine metabolite (Benzoylecgonine)	150	Benzoylecgonine	100

(b) Oral Fluid

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Cocaine/Benzoylecgonine	15	Cocaine Benzoylecgonine	8 8

When the MRO requests that a split urine specimen (Bottle/Tube B) be tested for the cocaine metabolite, benzoylecgonine, or a split oral fluid specimen (Container B) for cocaine and/or benzoylecgonine, the second laboratory performs confirmatory testing for (for urine) benzoylecgonine or (for oral fluid) cocaine and/or benzoylecgonine 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(s) (e.g., urine benzoylecgonine 100 ng/mL, oral fluid cocaine 8 ng/mL and/or benzoylecgonine 8 ng/mL single or combination) 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 urine benzoylecgonine or (for oral fluid) cocaine and/or benzoylecgonine (at or above the laboratory's established LOD for the assay) in order to report either urine benzoylecgonine or oral fluid cocaine and/or benzoylecgonine as reconfirmed.

5.3.1.2 Background

Cocaine, an alkaloid from the coca plant, is regulated under the CSA as Schedule II stimulant. Cocaine is usually sold as cocaine hydrochloride—a fine, white crystalline powder. Cocaine is rapidly metabolized to its major metabolite, benzoylecgonine. It is a widely used drug of abuse. The Federal Workplace Drug Testing Program requires analysis for the cocaine metabolite benzoylecgonine in urine specimens. Cocaine has only a limited legal use in the United States as a topical anesthetic in ear, nose, and throat surgery.

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.[34]

5.3.1.3 Routes of Administration

- Cocaine— oral, intravenous injection, smoking, and intranasal (i.e., snorting, inhalation).

- Abusers may use in a variety of methods, including intravenous injection and smoking. Smoking the "free base" or "crack" form of the drug has become the predominate route.

5.3.1.4 Metabolism and Excretions

(a) Urine

Cocaine is rapidly and extensively metabolized by liver and plasma enzymes to its major metabolite, benzoylecgonine.[35] 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. Benzoylecgonine can usually be detected in urine for 2 to 3 days after a single dose.

(b) Oral Fluid

Cocaine appears in oral fluid within minutes after use following intravenous, nasal and smoked administration.[6] Cocaine is rapidly metabolized to benzoylecgonine that also is excreted in oral fluid. At different times after use, cocaine and benzoylecgonine may be present singly or in combination in oral fluid. Generally, cocaine and or benzoylecgonine are detectable in oral fluid for 1 to 2 days.[9]

5.3.1.5 Pharmaceuticals and Use

(a) Prescription Drug Products

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.

(b) Non-prescription Drug Products

"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.

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.[36] 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 decocainized 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.

5.4 Opioids[37] (OPI)

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.

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).

The opioids have agonist or partial agonist activity at the opioid receptor and may or may not have structural similarity to the principal opium alkaloids. The use of opioids is a major illicit drug problem around the world, considering the impact on public health and public order.[38] 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.[39]

Effective October 1, 2017, HHS revised the Mandatory Guidelines to include the semisynthetic 6-keto opioids oxycodone, oxymorphone, hydrocodone, and hydromorphone as analytes, in addition to codeine and morphine. 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.

The Federal Workplace 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 results below the cutoff for any of the other opioid analytes tested. 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 positive urine test for codeine and or morphine would be comprised of a confirmed concentration equal to or greater than 2000 ng/mL codeine or 4000 ng/mL morphine. A positive oral fluid test for codeine and or morphine would be comprised of a confirmed concentration equal to or greater than 15 ng/mL codeine or 15 ng/mL morphine All of these drugs are available as prescription medications and a donor who tests positive for one or more opioids may have legally used the drug(s). These opioids are differentiated during testing and will not be misidentified using a confirmatory test as required by the Mandatory Guidelines.

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

For urine specimens, the confirmatory cutoffs for codeine and morphine (i.e., 2000 and 4000 ng/mL, respectively) are above concentrations seen in urine after consumption of poppy seed food products.

For oral fluid specimens positive for codeine and/or morphine, HHS included additional criteria in the OFMG as follows:

- When a laboratory reports codeine and/or morphine positive with a quantitative result less than 150 ng/mL (i.e., 10 times the confirmatory test cutoff):
  - The MRO reports the result as negative when the donor <u>does not admit</u> to unauthorized use of the drugs that caused the positive result(s).
  - The MRO shall report the result as positive when the donor <u>admits</u> unauthorized use of the drug(s) that caused the positive result.
- When a laboratory reports codeine and/or morphine positive with a quantitative result equal to or greater than 150 ng/mL:
  - The MRO must report the result as negative when the donor provides a legitimate medical explanation (e.g., valid prescription) for the positive result(s).
  - The MRO shall report the result as positive when the donor is unable to provide a legitimate medical explanation.

Note: Consumption of food products is not a legitimate medical explanation for the donor having morphine or codeine at or above this concentration.

Certified laboratories are required to validate all confirmatory assays (urine and oral fluid) prior to use with Federal agency specimens. For opioid confirmatory assays, each laboratory must document the assay's ability to identify and accurately quantitate 6-acetylmorphine, codeine, hydrocodone, hydromorphone, morphine, oxycodone, and oxymorphone in the presence of opioid metabolites (e.g., norcodeine, norhydrocodone, norhydromorphone, noroxycodone, noroxymorphone) and also demonstrate that these compounds are not misidentified as 6-acetylmorphine, codeine, hydrocodone, hydromorphone, morphine, oxycodone, and oxymorphone. These experiments must be performed on at least an annual basis to verify the assay's continued performance.

5.4.1.1 Drug Testing

See Appendix D tables and below for urine and oral fluid reporting criteria.

For grouped analytes (i.e., two or more analytes that are in the same drug class and have the same initial test cutoff):

- Initial Test
  - 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.
- Confirmatory Test
  - Mass spectrometry: The test method must use an analytical method combining chromatographic separation and mass spectrometric identification (i.e., gas chromatography/mass spectrometry (GC-MS), liquid chromatography/mass spectrometry (LC-MS), GC-MS/MS, LC-MS/MS] or equivalent. The test must be calibrated with each analyte from the group identified as the target analyte. Test method calibration must include at least one calibrator at the confirmatory cutoff.

(a) Urine

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Codeine/Morphine	2000	Codeine Morphine	2000 4000

(b) Oral Fluid

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Codeine/Morphine	30	Codeine Morphine	15 15

When the MRO requests that a split specimen (Bottle B) be tested for codeine and/or morphine, the second laboratory performs confirmatory testing for both codeine and morphine 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 (e.g., urine 2000 ng/mL codeine and 4000 ng/mL morphine, oral fluid 15 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 morphine or codeine (at or above the laboratory's established LOD for the assay) in order to report morphine and/or codeine as reconfirmed,

- An MRO may request the quantitative result of morphine or codeine 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.

5.4.1.2 Background

Morphine is the most abundant naturally occurring opiate and is representative of the opioid class of drugs. Morphine is regulated under the CSA as Schedule II opiate. Morphine is commonly used for its potent analgesic properties.

Codeine is regulated under the CSA as Schedule II opiate. Codeine is commonly used as an analgesic, antitussive, and antidiarrheal agent. 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.

5.4.1.3 Routes of Administration

- Morphine— oral (i.e., tablets), rectal, intravenous injection, smoking, and intranasal (i.e., snorting).
- Codeine— oral (i.e., tablets and liquid solution) and intravenous injection.
- Heroin—intravenous injection, intranasal (i.e., snorting), and smoking.
- Poppy seeds-oral (i.e., food, tea).

Abusers may use in a variety of methods, including intravenous injection and smoking.

5.4.1.4 Metabolism and Excretion

(a) Urine

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

diglucuronide). Generally, 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., hydrocodone, norcodeine, normorphine, morphine-3-ethereal sulfate, morphine-3,6-diglucuronide.)

(b) Oral Fluid

Morphine is rapidly absorbed, appears in oral fluid following use of morphine, heroin and poppy seeds.[7,40] Morphine detected in oral fluid following ingestion of poppy seeds indicated that morphine was positive for a shorter interval of 1-2 hours.[8] Single dose studies of codeine demonstrated codeine is detected in oral fluid within an hour but morphine was not detected.[41]

5.4.1.5 Pharmaceuticals and Use

(a) Pharmaceutical Drug Products

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.

Examples of morphine trade names include Roxanol®, MS Contin®, Roxanol-T®, Kadian®, Duramorph®, Embeda®, MorphaBond®, Avinza®, Arymo ER®, Astramorph PF®, Oramorph SR®, Infumorph®, and RMS®. Embeda® is a combination of morphine and naltrexone.

Examples of codeine combination product trade names include Fioricet®, Colrex®, Tylenol with Codeine #3®, Tylenol with Codeine #4®, Phenflu CDX®, Maxiflu CD®, Rolatuss®, Fiorinal with Codeine III®, Fiortal with Codeine®, SOMA Compound with Codeine®, Empirin with Codeine®, Ambenyl®, Dimetane DC®, Notuss-NX®, and Promethazine VC with Codeine®.

(b) Non-Pharmaceutical Drug Products

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 cutoff for urine morphine and codeine at 2000 ng/mL and confirmatory cutoffs at 4,000 ng/mL and 2,000 ng/mL, respectively.

Note: Heroin contaminated with acetylcodeine may produce positive test results for morphine, and codeine in addition to 6-acetylmorphine.

5.4.2 Oxycodone, Hydrocodone, Oxymorphone, Hydromorphone

A positive test for hydrocodone, hydromorphone, oxycodone, or oxymorphone would be comprised of any or all analytes with a confirmed urine concentration equal to or greater than 100 ng/mL or a confirmed oral fluid concentration equal to or greater than 15 ng/mL.

All of these drugs are available as prescription medications and a donor who tests positive for one or more opioids may have legally used the drug(s). There are no non-prescription or OTC medication that contain these opioids. These opioids are differentiated during testing and will not be misidentified using a confirmatory test as required by the Mandatory Guidelines.

Certified laboratories are required to validate all confirmatory assays (urine and oral fluid) prior to use with Federal agency specimens. For opioid confirmatory assays, each laboratory must document the assay's ability to identify and accurately quantitate 6-acetylmorphine, codeine, hydrocodone, hydromorphone, morphine, oxycodone, and oxymorphone in the presence of opioid metabolites (e.g., norcodeine, norhydrocodone, norhydromorphone, noroxycodone, noroxymorphone) and also demonstrate that these compounds are not misidentified as 6-acetylmorphine, codeine, hydrocodone, hydromorphone, morphine, oxycodone, and oxymorphone. These experiments must be performed on at least an annual basis to verify the assay's continued performance.

5.4.2.1 Drug Testing

See Appendix D tables and below for urine and oral fluid reporting criteria.

For grouped analytes (i.e., two or more analytes that are in the same drug class and have the same initial test cutoff):

- Initial Test
  - 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.

- Confirmatory Test
  - Mass spectrometry: The test method must use an analytical method combining chromatographic separation and mass spectrometric identification (i.e., gas chromatography/mass spectrometry (GC-MS), liquid chromatography/mass spectrometry (LC-MS), GC-MS/MS, LC-MS/MS] or equivalent. The test must be calibrated with each analyte from the group identified as the target analyte. Test method calibration must include at least one calibrator at the confirmatory cutoff.

(a) Urine

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Hydrocodone/Hydromorphone	300	Hydrocodone Hydromorphone	100 100
Oxycodone/Oxymorphone	100	Oxycodone Oxymorphone	100 100

(b) Oral Fluid

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Hydrocodone/Hydromorphone	30	Hydrocodone Hydromorphone	15 15
Oxycodone/Oxymorphone	30	Oxycodone Oxymorphone	15 15

When the MRO requests that a split specimen (Bottle B) be tested for hydrocodone, hydromorphone, oxycodone, or oxymorphone, the second laboratory performs confirmatory testing for hydrocodone, hydromorphone, oxycodone, or oxymorphone and 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 (e.g., urine 100 ng/mL, oral fluid 15 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 hydrocodone, hydromorphone, oxycodone, or oxymorphone (at or above the laboratory's established LOD for the assay) in order to report for hydrocodone, hydromorphone, oxycodone, or oxymorphone as reconfirmed.

5.4.2.2 Background

Hydrocodone and oxycodone are widely used and abused in the United States. Hydrocodone, hydromorphone, oxycodone, and oxymorphone are regulated under CSA as Schedule II opiates.

Hydrocodone is a 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 is a 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 O-demethylation.

Oxycodone is available 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 has approximately 10 times the potency of morphine for analgesia.

5.4.2.3 Routes of Administration

- Hydrocodone—oral (i.e., tablet, capsule, liquid, or extended-release tablet or liquid).
- Hydromorphone—oral (i.e., tablet or extended-release tablet), rectal, and intravenous injection.
- Oxycodone—oral (i.e., liquid, tablet, capsule, and extended-release tablet).
- Oxymorphone—oral (i.e., tablet or extended-release tablet).

Abusers may use in a variety of methods, including intravenous injection and smoking.

5.4.2.4 Metabolism and Excretion

(a) Urine

Note: Hydrocodone has been reported to be a minor metabolite of codeine and hydromorphone has been reported to be a minor metabolite of morphine.[41-43]

Hydrocodone is metabolized to norhydrocodone, hydromorphone, and minor metabolites such as hydrocodol and hydromorphol. There is little conjugation of 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. 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. Using 100 ng/mL as the cutoff, the study shows that hydrocodone and hydromorphone may be detectable in urine for one day.[44]

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. A metabolite of oxycodone, oxymorphone, is a potent narcotic analgesic while another metabolite, noroxycodone, is not active. Additional metabolites are noroxymorphone and the minor metabolites as noroxycodols and oxycodols. 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. Using 100 ng/mL as the cutoff, the study shows that oxycodone and oxymorphone are generally detectable in urine for one day.[45]

(b) Oral Fluid

Both oxycodone and oxymorphone have been reported to be readily detectable in oral fluid specimens collected from pain patients.[46,47] Oxycodone is metabolized in relatively minor amounts to oxymorphone.[48] Oxymorphone is a potent analgesic used for pain relief orally and parenterally, and is primarily metabolized by conjugation.[49] Hydromorphone appears rapidly in oral fluid following intravenous administration.[50]

A single administration of a 2 low doses of immediate-release hydrocodone/acetaminophen (10/325 mg) characterized the metabolism and disposition of hydrocodone in human oral fluid. Hydrocodone appeared in the oral fluid within 15 minutes. The metabolite norhydrocodone appeared 0.25-1 hours post dosing. Hydromorphone was not detected. Peak concentrations of hydrocodone occurred between 0.3 and 4 hours; the norhydrocodone between 1 and 8 hours. The mean peak concentration of hydrocodone was higher than that of the norhydrocodone, but the hydrocodone concentration declined more quickly than the concentration of noroxycodone. At a cutoff concentration of 1 ng/mL, detection times were approximately 30 hours for hydrocodone and 18 hours for norhydrocodone. Using 15 ng/mL as a cutoff, the study shows that hydrocodone is generally detectable in oral fluid for less than one day.[51]

A single administration of a low dose of controlled-release oxycodone (20 mg) characterized the metabolism and disposition of oxycodone in human oral fluid. Oxycodone appeared in the oral fluid in 15-30 minutes. The metabolite noroxycodone appeared 1.5-5 hours post dosing. Oxymorphone was frequently not detected. Peak concentrations of oxycodone and metabolites occurred between 2.5 and 8 hours. The mean peak concentration of oxycodone was higher than that of the noroxycodone, but the oxycodone concentration declined more quickly than the concentration of noroxycodone. At a cutoff concentration of 1 ng/mL, detection times were approximately 34 hours for oxycodone and noroxycodone. Using 15 ng/mL as a cutoff, the study shows that oxycodone is generally detectable in oral fluid for one day.[52]

5.4.2.5 Pharmaceuticals and Use

(a) Prescription Drug Products

Many pharmaceuticals containing opioids are available by prescription. MROs should have access to references with up-to-date information on such products.

Examples of hydrocodone trade names include Vicodin®, Lortab®, Anexsia®, Dolorex Forte®, Donatussin®, Drocon-CS®, Endacof XP®, Histussin D®, Hycet®, Hydrocet®, Liquicet®, Lorcet®, Lorcet Plus®, Lortab Elixir®, Maxidone®, Norco®, Polygesic®, Stagesic®, Vicodin®, Vicoprofen®, Xodol®, Zydone®, and Zohydro®

Examples hydromorphone trade names include Dilaudid®, Exalgo®, and Hydromorph Contin®.

Examples of oxycodone trade names include Percocet®, Percodan®, Oxycontin®, Combunox®, Dazidox®, Endocet®, Endocodone®, Endodan®, ETH-Oxydose®, Lynox®, Magnacet®, Narvox®, Oxycontin®, Oxyfast®, OxyIR®, Percocet®, Percodan®, Percolone®, Primlev®, Perloxx®, Roxicet®, Roxicodone®, Roxiprin®, Taxadone®, Tylox®, and Xolox®.

Examples of oxymorphone trade names include Opana® and Numorphan®.

(b) Non-prescription Drug Products

There are no non-prescription drug products with hydrocodone, hydromorphone, oxycodone, or oxymorphone.

5.4.3 Poppy Seeds

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 opiates initial testing at 2000 ng/mL and confirmatory cutoffs for morphine and codeine at 4000 ng/mL and 2000 ng/mL, respectively. 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.

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 5.5.1 above.

5.4.4 6-Acetylmorphine (6-AM)

A positive test would be comprised of a confirmed urine 6-AM concentration equal to or greater than 10 ng/mL or a confirmed oral fluid 6-AM concentration equal to or greater than 2 ng/mL.

A positive 6-AM result is evidence of illegal drug use. There are no prescription, non-prescription or OTC medications that contain heroin and there are no legal medical uses of heroin. 6-AM is differentiated from the opioids drugs during testing and will not be misidentified using a confirmatory test as required by the Mandatory Guidelines.

Certified laboratories are required to validate all confirmatory assays (urine and oral fluid) prior to use with Federal agency specimens. For opioid confirmatory assays, each laboratory must document the assay's ability to identify and accurately quantitate 6-AM in the presence of high levels of opioids and opioid metabolites and also demonstrate that these compounds are not misidentified as 6-AM (i.e., by analyzing samples containing opioids and opioid metabolites without 6-AM). These experiments must be performed on at least an annual basis to verify the assay's continued performance. The National Laboratory Certification Program (NLCP) includes opioids and opioid metabolites in the performance testing (PT) program to ensure all certified laboratories are distinguishing those from the 6-AM.

5.4.4.1 Drug Testing

See Appendix D tables and below for urine and oral fluid reporting criteria.

For single analytes (i.e., one analyte that is in the drug class and a single initial test cutoff):

- Initial Test

- 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.
- The confirmatory test cutoff must be used for an alternate technology initial test that is specific for the target analyte (i.e., 2 ng/mL for oral fluid 6-AM).

■ Confirmatory Test

- Mass spectrometry: The test method must use an analytical method combining chromatographic separation and mass spectrometric identification (i.e., gas chromatography/mass spectrometry (GC-MS), liquid chromatography/mass spectrometry (LC-MS), GC-MS/MS, LC-MS/MS] or equivalent. The test must be calibrated with the analyte from the group identified as the target analyte. Test method calibration must include at least one calibrator at the confirmatory cutoff.

(a) Urine

Initial Test Analyte	Initial Test Cutoff (ng/mL)	Confirmatory Test Analyte	Confirmatory Test Cutoff (ng/mL)
6-Acetylmorphine	10	6-Acetylmorphine	10

(b) Oral Fluid

Initial Test Analyte	Initial Test Cutoff (ng/mL)	Confirmatory Test Analyte	Confirmatory Test Cutoff (ng/mL)
6-Acetylmorphine	4	6-Acetylmorphine	2

When the MRO requests that a split specimen (Bottle/Tube B) be tested for 6-AM, the second laboratory performs confirmatory testing for 6-AM and 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 (e.g., urine 10 ng/mL, oral fluid 2 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 6-AM (at or above the laboratory's established LOD for the assay) in order to report 6-AM as reconfirmed.

5.4.4.2 Background

Heroin (diacetylmorphine), a semisynthetic opioid, is regulated under the CSA as Schedule II opium derivative. Heroin is 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).

5.4.4.3 Routes of Administration

- Heroin—intravenous injection, smoking, and intranasal (i.e., snorting).
- Abusers may use in a variety of methods, including intravenous injection and smoking.

5.4.4.4 Metabolism and Excretion

(a) Urine

Heroin is not easily detected in urine and, therefore, usage is determined by detection of its metabolite 6-acetylmorphine (6-AM). There is no legitimate medical explanation for a 6-AM positive result. Heroin itself is rarely detected in urine. Heroin (diacetylmorphine) is deacetylated to its primary metabolite, 6-acetylmorphine (6-AM), within minutes of administration. 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. Generally, 6-AM is most likely to be detected within the first 24 hours post-administration because of heroin's rapid metabolism to morphine.

Note: 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. Therefore, heroin itself is not detected in urine and 6-AM is rarely detected.

Note: Heroin contaminated with acetylcodeine may produce positive test results for morphine, and codeine in addition to 6-acetylmorphine.

(b) Oral Fluid

Heroin (diacetylmorphine) is deacetylated to its primary metabolite, 6-AM, within minutes of administration. 6-AM appears in oral fluid within minutes following smoked or injected heroin administration.[7] Generally, 6-AM detection in oral fluid is one day or less.

5.4.4.5 Pharmaceuticals and Use

(a) Prescription Drug Products

Heroin is regulated by the CSA as a Schedule I drug and is not available as a pharmaceutical product.

(b) Non-Prescription Drug Products

There are no non-prescription products that contain heroin.

Note: Heroin contaminated with acetylcodeine may produce positive test results for morphine, and codeine in addition to 6-acetylmorphine.

5.5 Phencyclidine (PCP)[53]

5.5.1 Phencyclidine

A positive test would be comprised of a confirmed urine phencyclidine concentration equal to or greater than 25 ng/mL or a confirmed oral fluid phencyclidine concentration equal to or greater than 10 ng/mL.

A positive phencyclidine result is evidence of illegal drug use. There are no prescription, non-prescription or OTC medications that contain phencyclidine and there is no legal medical use of phencyclidine. There are no other substances that can be misidentified as phencyclidine using a confirmatory test as required by the Mandatory Guidelines.

Certified laboratories are required to validate all confirmatory assays (urine and oral fluid) prior to use with Federal agency specimens. For phencyclidine confirmatory assays, each laboratory must document the assay's ability to identify and accurately quantitate phencyclidine. These experiments must be performed on at least an annual basis to verify the assay's continued performance.

5.5.1.1 Drug Testing

See Appendix D tables and below for urine and oral fluid reporting criteria.

For single analytes (i.e., one analyte that is in the drug class and a single initial test cutoff):

- Initial Test
  - 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: 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.
- Confirmatory Test
  - Mass spectrometry: The test method must use an analytical method combining chromatographic separation and mass spectrometric identification (i.e., gas chromatography/mass spectrometry (GC-MS), liquid chromatography/mass spectrometry (LC-MS), GC-MS/MS, LC-MS/MS] or equivalent. The test must be calibrated with phencyclidine. Test method calibration must include at least one calibrator at the confirmatory cutoff.

(a) Urine

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Phencyclidine	25	Phencyclidine	25

(b) Oral Fluid

Initial Test Analyte	**Initial Test Cutoff (ng/mL)**	**Confirmatory Test Analyte**	**Confirmatory Test Cutoff (ng/mL)**
Phencyclidine	10	Phencyclidine	10

When the MRO requests that a split specimen (Bottle B) be tested for phencyclidine, the second laboratory performs confirmatory testing for phencyclidine analyte 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 (e.g., urine 25 ng/mL, oral fluid 10 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 phencyclidine (at or above the laboratory's established LOD for the assay) in order to report phencyclidine as reconfirmed,

5.5.1.2 Background

Phencyclidine, an arylcyclohexylamine, is regulated under the CSA as a Schedule II depressant.[54] Phencyclidine was first synthesized in the 1950s as a general anesthetic (Sernyl®). Street names include Angel Dust, Crystal, Killer Weed, Supergrass, and Rocket Fuel. Phencyclidine synthesis is relatively simple for clandestine laboratories. Phencyclidine's use as a human anesthetic was discontinued because it produced psychotic reactions (i.e., "emergence delirium"), but the drug remains in use as a veterinary tranquilizing agent.

Phencyclidine has a variety of effects on the central nervous system. Intoxication begins several minutes after ingestion and usually lasts 8 hours or more. Phencyclidine 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 phencyclidine 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.[55]

5.5.1.3 Routes of Administration

- Phencyclidine— oral (i.e., tablets, capsules), intravenous injection, smoking (preferred), and intranasal (i.e., snorting).

- Abusers may use in a variety of methods, including intravenous injection and smoking.

5.5.1.4 Metabolism and Excretion

(a) Urine

Phencyclidine is well absorbed by any route and is excreted unchanged and as conjugates of hydroxylated phencyclidine. About 4% to 19% of the phencyclidine dose is excreted in the urine as unchanged drug. Phencyclidine is a weak base that concentrates in

acidic solutions in the body. Because of gastric acidity, phencyclidine repeatedly re-enters the stomach from plasma and is reabsorbed into plasma from the basic medium of the intestine. Generally, phencyclidine is considered detectable in urine for several days to several weeks depending on the frequency of use.

(b) Oral Fluid

Phencyclidine has been measured in oral fluid following different routes of administration.[56,57] Phencyclidine detection in oral fluid is at least one day.

5.5.1.5 Pharmaceuticals and Use

(a) Prescription Drug Products

Phencyclidine is regulated as a Schedule II drug and is not available as a pharmaceutical.

(b) Non-prescription Drug Products

There are no non-prescription medications that contains this drug.

5.6 Other Non-Negative Reports

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.

5.6.1 Dilute Specimens

MRO actions are shown in Table 4, Medical Review Officer Actions for Primary (A) Specimen Reports.

5.6.1.1 Urine

This section on dilution/substitution deals only with urine specimens. A dilute finding may be reported in conjunction with a positive or negative urine 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.
- Medical conditions such as pituitary disorders (syndrome of inappropriate antidiuretic hormone secretion [SIADH]), diabetes, pregnancy, etc.

A certifying technician at an IITF may report a urine specimen as dilute in conjunction with a negative drug test only when the creatinine test result is greater than 5.0 mg/dL but less than or equal to 20.0 mg/dL and the specific gravity is equal to or greater than 1.002 but less than 1.003.

When creatinine is less than or equal to 5.0 mg/dL, the IITF must send the specimen to an HHS-certified laboratory for testing. Certified laboratories certified laboratory report urine specimen as dilute when the creatinine is greater than 5.0 mg/dL and less than 20.0 mg/dL and the specific gravity is equal to or greater than 1.002 but less than 1.003; or the creatinine concentration is equal to or greater than 2.0 mg/dL but less than 20.0 mg/dL and the specific gravity is greater than 1.0010 but less than 1.0030.

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

The MRO's response to a dilute urine specimen report depends on whether the drug test result is verified as positive or negative (see section 5.6.4.2 of this manual). MRO actions are shown in Table 4, Medical Review Officer Actions for Primary (A) Specimen Reports.

5.6.2 Substituted Urine Specimens

MRO actions are shown in Table 4, Medical Review Officer Actions for Primary (A) Specimen Reports.

5.6.2.1 Background

The HHS criteria for identifying substituted urine specimens are based on the physiological ranges for creatinine concentration and specific gravity value of normal human urine. Laboratories and IITFs are required to measure the creatinine concentration in all regulated urine specimens, and to test specific gravity for specimens with creatinine concentration less than 20.0 mg/dL. There are established program cutoffs for identifying invalid and 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 20.0 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.

5.6.2.2 MRO Actions

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 Urine Specimens

MRO actions are shown in Table 4, Medical Review Officer Actions for Primary (A) Specimen Reports.

5.6.3.1 Background

"Adulterated" is the term used for a specimen that has been altered by the donor in an attempt to defeat the drug test. The goal is to affect the ability of the test facility to properly test the specimen for drugs and/or to destroy any drug or drug metabolite that may be present in the specimen. Many substances can be used to adulterate a urine specimen in vitro, including common household products, commercial chemicals, and commercial products developed specifically for drug test specimen adulteration. 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 immunoassay initial drug test is more sensitive to adulterants than the required confirmatory drug test

method. Currently, gas chromatography /mass spectrometry (GC-MS) assays for marijuana metabolite (THCA) and opioids appear to be affected by adulterants more than GC-MS assays for other drugs.

When an IITF is unable to obtain a valid initial urine drug test result or when the IITF urine drug or specimen validity tests indicate a possible unidentified adulterant, the IITF sends the urine 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 urine 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 (A) Specimen Reports, concerning specimens reported as invalid based on pH in the greater than or equal to 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 six months of age.
- **Occupational exposure.** Workers in explosives and pharmaceuticals manufacturing may be exposed to nitrates.
- **Medications.** Organic nitrate and nitro compound drugs (e.g., used for angina, congestive heart failure, ulcers) metabolize to inorganic nitrite ion. Inorganic nitrite/nitrate salts have limited medical uses (e.g., used for cyanide poisoning).
- **Endogenous production.** The enzyme nitric oxide synthase (NOS) catalyzes the endogenous formation of nitric oxide radical, which oxidizes to nitrite and nitrate. This may result in normal human urine containing a small amount of nitrate with an extremely small ratio of nitrite.
- **Pathological conditions.** Some infectious and inflammatory conditions (e.g., sepsis, asthma, rheumatoid arthritis, tuberculosis, inflammatory bowel disease, Alzheimer's disease, multiple sclerosis) induce another enzyme (i.e., inducible NOS) that catalyzes the formation of nitric oxide radical.
- **Medical treatments.** Some medical treatments (e.g., Interleukin-2 in cancer treatment) can induce NOS and result in nitrite in the urine.
- **Urinary tract infections.** Some urinary tract infections are caused by bacteria that, if present in large numbers, may reduce nitrate to nitrite by microbial action.

Because low levels of nitrite may be present in human urine due to the reasons listed above, HHS set a cutoff level 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.

5.6.3.2 MRO Actions

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 or oral fluid specimen to meet the criteria for an adulterated result under the HHS Mandatory Guidelines.

5.6.4 Invalid Specimens

MRO actions are shown in Table 4, Medical Review Officer Actions for Primary (A) Specimen Reports.

5.6.4.1 Background

(a) Urine

"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 urine 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 urine report for reason other than pH, creatinine, specific gravity, or nitrite reported as ≥200 mcg/mL and <500 mcg/mL by a nitrite confirmatory test. A primary (A) specimen 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 urine specimen reported as invalid for pH, creatinine, specific gravity, or nitrite reported as ≥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.) If a specimen exhibits abnormal characteristics (e.g., unusual odor or color), causes reactions or responses characteristic of an adulterant during initial or confirmatory drug tests (e.g., non-recovery of internal standard, unusual response), or contains an unidentified substance that interferes with the confirmatory analysis, then additional testing may be performed.

An HHS-certified laboratory reports a primary (A) urine specimen as an invalid result when:

- Interference
  - Interference occurs on the initial drug tests on two separate aliquots (i.e., valid initial drug test results cannot be obtained);
  - Interference with the drug confirmatory assay occurs on two separate aliquots of the specimen and the laboratory is unable to identify the interfering substance;

- The physical appearance of the specimen (e.g., viscosity) is such that testing the specimen may damage the laboratory's instruments;
- The specimen has been tested and the appearances of the primary (A) and the split (B) specimens (e.g., color) are clearly different;
- A urine specimen reported as invalid for creatinine < 2.0 mg/dL and specific gravity acceptable (e.g., > 1.0010 and < 1.0200);
- A urine specimen reported as invalid for creatinine > 2.0 mg/dL and specific gravity < 1.0010;
- A urine specimen reported as invalid for pH greater than or equal to 4.0 and < 4.5 or pH greater than or equal to 9.0 and < 11.0;
- A urine specimen reported as invalid for nitrite greater than or equal to 200 mcg/mL and < 500 mcg/mL;
- A urine specimen reported as invalid for oxidant activity (e.g., greater than or equal to 200 mcg/mL nitrite equivalents, greater than or equal to 50 mcg/mL Chromium VI equivalents, or > halogen or other oxidant LOQ); or
- A urine specimen reported as possible aldehyde or surfactant activity.

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 urine 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.

(b) Oral Fluid

"Invalid" refers to a result reported by a laboratory for an oral fluid 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 oral fluid drug test result. HHS-certified laboratories are required to contact the MRO to discuss an invalid oral fluid report. A Medical Review Officer may request to test an oral fluid specimen for a specific

adulterant. A primary (A) oral fluid specimen 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. The Mandatory Guidelines do not specify the analytical methods to be used by HHS-certified laboratories for these additional 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.) If a specimen exhibits abnormal characteristics (e.g., unusual odor, color, or semi-solid characteristics), causes reactions or responses characteristic of an adulterant during initial or confirmatory drug tests (e.g., non-recovery of internal standard, unusual response), or contains an unidentified substance that interferes with the confirmatory analysis, then additional testing may be performed.

An HHS-certified laboratory reports a primary (A) oral fluid specimen as an invalid result when:

- Interference with testing
  - Interference occurs on the initial drug tests on two separate aliquots (i.e., valid initial drug test results cannot be obtained);
  - Interference with the confirmatory drug test occurs on two separate aliquots of the specimen and the laboratory is unable to identify the interfering substance;
- The physical appearance of the specimen (e.g., viscosity) is such that testing the specimen may damage the laboratory's instruments;
- The specimen has been tested and the appearances of the primary (A) and the split (B) specimens (e.g., color) are clearly different; or
- A specimen validity test on two separate aliquots of the specimen is not valid for testing.

The OFMG do not require routine specimen validity testing for oral fluid testing. The MRO must request biomarker testing for oral fluid.

Invalid oral fluid 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 5.6.4.2, and Tables 4 and 5.

5.6.4.2 MRO Actions

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 urine or oral fluid invalid specimens due to a possible adulterant or for specimens with an abnormal physical characteristic.

Prior to reporting a urine or oral fluid 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 (for urine) 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.

If a urine or oral fluid invalid result was reported in conjunction with a positive, adulterated, or substituted result, the MRO does not report the verified invalid result to the Federal agency at this time. The MRO takes action for the verified invalid result(s) for the primary (A) specimen only when:

- The MRO verifies the positive, adulterated, or substituted result as negative based on a legitimate medical explanation or (for oral fluid) codeine and/or morphine concentrations less than 150 ng/mL; or

- The split (B) specimen is tested and reported as a failure to reconfirm the positive, adulterated, or substituted result reported for the primary (A) specimen.

When the laboratory reports an invalid result for the primary (A) specimen, the MRO must contact the donor to determine if there is a legitimate explanation for the invalid result.

> Note: The MRO is NOT required to contact the donor for urine specimens invalid due to discrepant creatinine/specific gravity values, for urine specimens invalid due to abnormal pH, or for urine specimens that contain nitrite ≥200 mcg/mL and <500 mcg/mL by a nitrite confirmatory test.

In the case of a urine invalid result based upon of 9.0 to 9.5, when the donor has no other medical explanation for the pH in this range, the MRO must consider there is evidence of elapsed time and high temperature that could account for the pH value.[58] The MRO may contact the collection site, IITF, and/or laboratory to discuss time and temperature issues (e.g., time lapsed from collection to receipt at the testing facility, likely temperature conditions between the time of collection and transportation to the testing facility, specimen storage conditions). See Table 4.

Urine and Oral Fluid review and reporting – see also Table 4

- If the donor provides a legitimate explanation (e.g., a prescription medicine) or (for urine) if the MRO determines that time and temperature account for the pH in the 9.0 to 9.5 pH range, the MRO reports a test cancelled result with the reason for the invalid result and informs the Federal agency that a recollection is not required because there is a legitimate explanation 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.

- If the donor is unable to provide a legitimate explanation or (for urine) if the MRO determines that time and temperature fail to account for the pH in the 9.0 to 9.5 range, the MRO reports a test cancelled result with the reason for the invalid result and directs the Federal agency to immediately collect another specimen from the donor using (for urine) a direct observed collection.

- If the specimen collected (direct observation for urine) provides a valid result, the MRO reports the result in accord with Chapter 5 and Table 4 of this manual.

- If the specimen collected (direct observation for urine) provides an invalid result, the MRO reports this as a test cancelled and recommends that the agency collect another authorized specimen type (e.g., urine or oral fluid).

  If the Federal agency does not authorize collection of another specimen type, the MRO consults with the agency to arrange for a clinical evaluation to determine whether there is a legitimate medical reason for the invalid result. The Federal agency immediately directs the donor to obtain, within five days, an 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 perform this evaluation if the MRO has appropriate expertise. See Insufficient Specimen section 6.2 of this manual for medical evaluation.

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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 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). Approximately 75% of the blind urine samples submitted each year by an agency must be negative, 15% must be positive for one or more drugs, and 10% must be either adulterated or substituted. Approximately 75% of the blind oral fluid samples submitted each year by an agency must be negative and 25% must be positive for one or more drugs. 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 UrMG and OFMG include requirements for blind samples as follows:

- Urine:
  - A blind sample that is positive must be prepared at a concentration 1.5–2 times the initial drug test cutoff for one or more of the SAMHSA drug test panel drugs or metabolites(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).

- Oral Fluid:
  - The blind quality must be in the same specimen collection device as used by the agency and laboratory.
  - A blind sample that is positive must be prepared at a concentration 1.5–2 times the initial drug test cutoff for one or more of the SAMHSA drug test panel drugs or metabolites (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.
  - The supplier must provide information on the blind sample's date of manufacture, content, validation, expected results, expiration date, and validated stability to the collection site/collector sending the blind samples to the laboratory, 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 should be sent to the collection site in the collection device utilized by the laboratory and in addition, oral fluid should be accompanied by the expiration date for the sample as well as instructions for storage of the oral fluid blind sample before shipment. 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)/tube(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/tube label/seal. The collection site should ensure that the oral fluid blind sample will be received by the laboratory at least 5 days before the expiration of the sample.

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 and (for oral fluid) whether the sample was tested within the stability period for the 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 another specimen type (e.g., urine or oral fluid) was collected as authorized by the Federal agency, the MRO reviews and reports the test result in accordance with the Mandatory Guidelines for Federal Workplace Drug Testing Programs using the alternate specimen.

6.2.1 Urine

If the laboratory reports insufficient urine volume, the MRO consults with the laboratory and the collection site to determine the reason for the insufficient urine volume. If the insufficient urine 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 urine specimens insufficient due to spillage or error. If the insufficient urine volume is due to a limited collection that was not noted, the MRO will implement the medical evaluation procedure.

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 or donor claims that they have a medical condition, the MRO must reconcile the testing results. When another specimen type (e.g., oral fluid) was collected as authorized by the Federal agency, the MRO reviews and reports the test result in accordance with the Mandatory Guidelines for Federal Workplace Drug Testing Programs using the alternate specimen. When the Federal agency did not authorize the collection of an alternate specimen, the MRO consults with the Federal agency. The Federal agency immediately directs 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 perform this evaluation if the MRO has appropriate expertise.

The purpose of the evaluation is to determine whether the donor has an ascertainable physiological condition that, with a high degree of probability, could have prevented him or her from providing a sufficient amount of urine during the collection. This does not include unsupported assertions of "situational anxiety" or dehydration. Permanent or long-term medical conditions are those physiological (e.g., urinary system dysfunction), anatomic, or psychological abnormalities documented as being present prior to the attempted collection, and considered not amenable to correction or cure for an extended period of time. 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. For urine drug testing, 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.

As the MRO, if another physician will perform the evaluation, you must provide the other physician with the following information and instructions:

- 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 a sufficient urine or oral fluid as required for the test and an alternate specimen was not collected) ; and

- The consequences of a refusal to take a drug test for the Federal agency (see Chapter4, 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.)

As the MRO, if another physician performed the evaluation, you must consider and assess the referral physician's recommendations in making your determination. You must make one of the following determinations and report it to the Federal agency in writing:

- 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 employee from providing a sufficient amount of urine and is highly likely to prevent the employee from providing a sufficient amount of urine for a very long or indefinite period of time. As the MRO, you must follow the requirements of UrMG Section 13.7 as appropriate. If Section 13.7 is not applicable, you report a test cancelled result to the Federal agency and recommend that the agency authorize collection of an alternate specimen type (e.g., oral fluid) for any subsequent drug tests for the donor; or

- 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.

When a Federal agency receives a report from the MRO indicating that a test is cancelled, the agency takes no further action with respect to the donor. When a test is canceled and the MRO recommends collection of an alternate specimen type (e.g., oral fluid), the agency takes no further action with respect to the donor other than designating collection of an alternate specimen type (i.e., using Mandatory Guidelines for that specimen type) for any subsequent collections, in accordance with the Federal agency plan. The donor remains in the random testing pool.

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.

6.2.1.1 Permanent or Long-Term Medical Condition and Required Negative Test

Additional actions are required when the Federal agency does not authorize collection of an alternate specimen (e.g., urine or oral fluid), the MRO determines that a donor has a permanent or long-term medical condition that would likely prevent provision of a sufficient urine specimen for an extended or indefinite time, and the reason for the drug test was:

- Federal agency applicant/pre-employment; or
- 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 the determination that a permanent or long-term medical condition exists, making provision of a sufficient urine specimen impossible;
- The basis for determining that no signs and symptoms of drug use exist; and
- Recommend that the agency authorize collection of an alternate specimen type (e.g., oral fluid) for any subsequent collections.
- "**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) and any further medical examinations of the donor:
- The reason for the determination that a permanent or long-term medical condition exists, making provision of a sufficient urine specimen impossible;
- The reason for determining that signs and symptoms of drug use exist; and
- The Federal agency is not authorized to allow the donor to begin or resume official functions because a negative test is required.

6.2.2 Oral Fluid

The laboratory may test oral fluid specimens that are collected on or before the collection device expiration date (see also section 4.1.1). If the laboratory reports insufficient oral fluid volume, the MRO consults with the laboratory and the collection site to determine the reason for the insufficient oral fluid volume. If the insufficient oral fluid 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 oral fluid specimens insufficient due to spillage or error. If the insufficient oral fluid volume is due to a limited collection that was not noted, the MRO will implement the medical evaluation procedure.

When a donor is unable to provide an oral fluid specimen or the donor claims that they have a medical condition that prevents opening their mouth for inspection, the Federal agency may authorize the collection of an alternate specimen (e.g., urine). When the collector reports that the donor did not provide a sufficient amount of oral fluid for a drug test, the MRO must reconcile the testing results. When another specimen type (e.g., urine) was collected as authorized by the Federal agency, the MRO reviews and reports the test result in accordance with the Mandatory Guidelines for Federal Workplace Drug Testing Programs using the alternate specimen. When the Federal agency did not authorize the collection of an alternate specimen, the MRO consults with the Federal agency. The Federal agency immediately directs the donor to obtain, **within five days**, a medical evaluation from a licensed physician, acceptable to the MRO, who has expertise in the medical issues raised by the donor's failure to provide a specimen. The MRO may perform this evaluation if the MRO has appropriate expertise.

The purpose of the evaluation is to determine whether the donor has an ascertainable physiological condition 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 oral fluid during the collection. A medical condition includes an ascertainable physiological condition. Permanent or long-term medical conditions are those physiological, anatomic, or psychological abnormalities documented as being present prior to the attempted collection, and considered not amenable to correction or cure for an extended period of time.

As the MRO, if another physician will perform the evaluation, you must provide the other physician with the following information and instructions:

- The circumstances necessitating the medical evaluation (i.e., that the donor was required to provide oral fluid for a federally regulated drug test but was unable to provide at least 1 mL of neat oral fluid as required for the test and an alternate specimen was not collected);
- The consequences of a refusal to take a drug test for the Federal agency (see Chapter4, 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.)

As the MRO, if another physician performed the evaluation, you must consider and assess the referral physician's recommendations in making your determination. You must make one of the following determinations and report it to the Federal agency in writing:

- 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 oral fluid, 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 employee from providing a sufficient amount of oral fluid and is highly likely to prevent the employee from providing a sufficient amount of urine for a very long or indefinite period of time. As the MRO, you must follow the requirements of UrMG Section 13.7 as appropriate. If Section 13.7 is not applicable, you report a test cancelled result to the Federal agency and recommend that the agency authorize collection of an alternate specimen type (e.g., urine) for any subsequent drug tests for the donor; or

- 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 oral fluid. The MRO reports a refusal to test to the Federal agency.

When a Federal agency receives a report from the MRO indicating that a test is cancelled, the agency takes no further action with respect to the donor. When a test is canceled and the MRO recommends collection of an alternate specimen type (e.g., urine), the agency takes no further action with respect to the donor other than designating collection of an alternate specimen type (i.e., using the Mandatory Guidelines for that specimen type) for any subsequent collections, in accordance with the Federal agency plan. The donor remains in the random testing pool.

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.

6.2.2.1 Permanent or Long-Term Medical Condition and Required Negative Test

Additional actions are required when the Federal agency does not authorize collection of an alternate specimen (e.g., urine), the MRO determines that a donor has a permanent or long-term medical condition that would likely prevent provision of a sufficient oral fluid specimen for an extended or indefinite time, and the reason for the drug test was:

- Federal agency applicant/pre-employment; or
- 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 the determination that a permanent or long-term medical condition exists, making provision of a sufficient oral fluid specimen impossible;
    - The basis for determining that no signs and symptoms of drug use exist; and
    - The recommendation that the agency authorize collection of an alternate specimen type (e.g., urine) for any subsequent collections.
- "**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) and any further medical examinations of the donor:
    - The reason for the determination that a permanent or long-term medical condition exists, making provision of a sufficient oral fluid specimen impossible; and
    - The reason 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 (i.e., legal drug use) 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 in the context of a donor's legal drug use is legal or appropriate in any given circumstance because this issue is outside the scope of the Mandatory Guidelines.

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 laboratory and/or an IITF 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 laboratory or IITF;
- 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 laboratory's Responsible Persons or each of the IITF's Responsible Persons/Technicians.

6.5 Protection of Personally Identifiable Information (PII)

PII is information that can be used to distinguish or trace an individual's identity alone or when combined with other personally identifiable 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. All Federal agencies and service providers involved in the Federal Workplace Drug Testing Program (e.g., clients, laboratories, collectors, employers, external service providers, and MROs) are responsible for maintaining the confidentiality of drug testing information and safeguarding the donor's PII on the Federal CCF. 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 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 into a computer system or database. It is not acceptable for service providers to use Federal CCF forms with incorrect or outdated MRO information (e.g., MRO name/organization, address, fax number). It is incumbent upon the laboratory or IITF to be proactive and take steps to prevent the use of outdated information which may lead to a violation of donor PII. Clients and collectors should edit incorrect information and provide correct information printed on CCF forms.

SAMHSA has determined that the name of the MRO is not an essential element on the Federal CCF. The MRO may be a sole practitioner or an MRO company with more than one practitioner (i.e., group/organization). Effective November 17, 2022, when the Federal CCF includes the name of an MRO company, laboratories will no longer be required to take action when the Federal CCF does not include the name of an MRO or when the MRO name is different on the CCF and electronic report.

Laboratories must continue to take action for a missing or incorrect MRO name when an MRO company name is not present and for other discrepant information (e.g., MRO company name, address, contact information). Laboratories must address the discrepant information by verifying the information in the laboratory computer system, ensuring the collector has the correct information, and providing new CCFs with correct information to the client.

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

urine or oral fluid 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 laboratory and HHS-certified IITF 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 or MRO company 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 or MRO company related to regulated drug testing. For example, an MRO, MRO employer, or MRO group, 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 or MRO company 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 or MRO companies are properly identified (on Federal CCFs), MROs, MRO employers, or MRO groups should provide Federal agencies with documentation that designates the name of a specific MRO or the MRO company name 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 UrMG and OFMG. 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 two 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 or MRO company 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.

APPENDIX A: GLOSSARY

The following definitions are primarily excerpted from the HHS Mandatory Guidelines for Federal Workplace Drug Testing Programs using Urine (UrMG, Effective February 1, 2024) and the HHS Mandatory Guidelines for Federal Workplace Drug Testing Programs using Oral Fluid (OFMG, Effective October 10, 2023), 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 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 a normal constituent (e.g., nitrite in urine).

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.

Biomarker Testing Panel. The panel published in the Federal Register that includes the biomarkers authorized for testing, with analytes and cutoffs for initial and confirmatory biomarker tests, as described under OFMG/UrMG Section 3.4.

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 the specimen has been 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 UrMG and OFMG).

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 an HHS-certified IITF.

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

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.

Collection Device. A product that is used to collect an oral fluid specimen and may include a buffer or diluent.

Collection Container. A receptacle used to collect a donor's drug test 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 an initial 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, drug metabolite, or biomarker concentration) used as the decision point to determine a result (e.g., negative; positive; adulterated; invalid; or 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.

Drug Testing Panel. The panel published in the Federal Register that includes the drugs authorized for testing, with analytes and cutoffs for initial and confirmatory drug tests, as described under Section 3.4 of the UrMG and OFMG.

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 HHS-certified IITF). It may be a paper

(hardcopy), electronic (digital), 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 adulterated, invalid, substituted, or (for urine) dilute.

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 established criteria (i.e., in Section 3.9 of the UrMG and Section 3.8 of the OFMG) 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 (LOD). 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, oral fluid collection device) 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 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.

Non-Medical Use of a Drug. The use of a prescription drug, whether obtained by prescription or otherwise, other than in the manner or for the time period prescribed, or by a person for whom the drug was not prescribed.

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 donor's (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 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 confirmatory test cutoff.

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 HHS-certified IITF when no tests are performed on a specimen because of a fatal flaw or an unrecovered correctable error (see Sections 4.1.3-1 and 4.1.3-2 of this MRO Guidance Manual).

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.

Secretary. The Secretary of the U.S. Department of Health and Human Services.

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.

Split Specimen Collection (for Oral Fluid). A collection in which two specimens [primary (A) and split (B)] are collected, concurrently or serially, and independently sealed in the presence of the donor; or a collection in which a single specimen is collected using a single collection device and is subdivided 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 specimen, as evidenced by the absence of a biomarker or a biomarker concentration inconsistent with that established for a human specimen, as indicated in the biomarker testing panel, or (for urine) creatinine and specific gravity values that are outside the physiologically producible ranges of human urine, in accordance with the criteria to report a urine specimen as substituted in UrMG Section 3.7.

Undiluted (neat) oral fluid. An oral fluid specimen to which no other solid or liquid has been added. For example, see OFMG Section 2.4: a collection device that uses a diluent (or other component, process, or method that modifies the volume of the testable specimen) must collect at least 1 mL of undiluted (neat) oral fluid.

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

FEDERAL DRUG TESTING CUSTODY AND CONTROL FORM

SPECIMEN ID NO. 0000001 ACCESSION NO.

OMB No. 0930-0158

STEP 1: COMPLETED BY COLLECTOR OR EMPLOYER REPRESENTATIVE

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

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

C. Donor SSN, Employee I.D., or CDL State and 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 Contact Info: Phone _____

Fax _____

Other _____

STEP 2: COMPLETED BY COLLECTOR (make remarks when appropriate). ☐ **URINE** ☐ **ORAL FLUID**

COLLECTION: ☐ Split ☐ Single ☐ None Provided, Enter Remark.

URINE: Collector reads urine temperature within 4 minutes. Temperature between 90º and 100º F? ☐ Yes ☐ No, Enter Remark ☐ Observed, Enter Remark

ORAL FLUID: Split Type: ☐ Serial ☐ Concurrent ☐ Subdivided Each Device Within Expiration Date? ☐ Yes ☐ No ☐ Volume Indicator(s) Observed

REMARKS:

STEP 3: Collector affixes seal(s) to bottle(s)/tube(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

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

SPECIMEN BOTTLE(S)/TUBE(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 Seal Intact ☐ YES ☐ NO If NO, Enter remark in Step 5A.

SPECIMEN BOTTLE(S)/TUBE(S) RELEASED TO:

Primary/Single Specimen Device Expiration Date: ____/____/____ **(Mo/Day/Yr)**

Split Specimen Device Expiration Date: ____/____/____ **(Mo/Day/Yr)**

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

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

☐ DILUTE

☐ **POSITIVE** for: _____
Analyte(s) in ng/mL

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 A

/ /
Date (Mo/Day/Yr)

_____
Donor's Initials

PLACE OVER CAP

0000001
SPECIMEN B

/ /
Date (Mo/Day/Yr)

_____
Donor's Initials

PLACE OVER CAP

COPY 1 - TEST FACILITY COPY

PRESS HARD - YOU ARE MAKING MULTIPLE COPIES

Version C 6May2020

80308

FEDERAL DRUG TESTING CUSTODY AND CONTROL FORM

SPECIMEN ID NO. 0000001 ACCESSION NO.

OMB No. 0930-0158

STEP 1: COMPLETED BY COLLECTOR OR EMPLOYER REPRESENTATIVE

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

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

C. Donor SSN, Employee I.D., or CDL State and 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 Contact Info: Phone _____

Fax _____

Other _____

STEP 2: COMPLETED BY COLLECTOR (make remarks when appropriate). ☐ **URINE** ☐ **ORAL FLUID**

COLLECTION: ☐ Split ☐ Single ☐ None Provided, Enter Remark.

URINE: Collector reads urine temperature within 4 minutes. Temperature between 90º and 100º F? ☐ Yes ☐ No, Enter Remark ☐ Observed, Enter Remark

ORAL FLUID: Split Type: ☐ Serial ☐ Concurrent ☐ Subdivided Each Device Within Expiration Date? ☐ Yes ☐ No ☐ Volume Indicator(s) Observed

REMARKS:

STEP 3: Collector affixes seal(s) to bottle(s)/tube(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

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

SPECIMEN BOTTLE(S)/TUBE(S) RELEASED TO:

_____
Name of Delivery Service

STEP 5: COMPLETED BY DONOR

I certify that I provided my specimen to the collector; that I have not adulterated it in any manner; each specimen bottle/tube 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/tube is correct.

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

Email address: _____ 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 ☐ **URINE** ☐ **ORAL FLUID**

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:
EXAMPLE IITF SUPPLEMENTAL CCF

Specimen I.D. #:_____

IITF Accession #:_____

IITF Name: _____ NLCP IITF No._____

IITF address: _____ ☐ Bottle A and Bottle B included

_____ ☐ CCF Copy 1 included

_____

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

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

Laboratory Remarks: _____
_____
_____

Date	Specimen Released by	Specimen Received by	Purpose

APPENDIX D:
URINE SPECIMEN DRUG TESTING PANEL AND REPORTING CRITERIA

This drug testing panel will remain in effect until the effective date of a new drug testing panel published in the Federal Register:

Initial Test Analyte	Initial Test Cutoff [1] (ng/mL)	Confirmatory Test Analyte	Confirmatory Test Cutoff (ng/mL)
Marijuana metabolite (THCA)[2]	50 [3]	THCA	15
Cocaine metabolite (Benzoylecgonine) (BZE)	150 [3]	Benzoylecgonine	100
Codeine/Morphine (COD/MOR)	2000	Codeine Morphine	2000 4000
Hydrocodone/Hydromorphone (HYC/HYM)	300	Hydrocodone Hydromorphone	100 100
Oxycodone/Oxymorphone (OXYC/OXYM)	100	Oxycodone Oxymorphone	100 100
6-Acetylmorphine (6-AM)	10	6-Acetylmorphine	10
Phencyclidine (PCP)	25	Phencyclidine	25
Amphetamine/Methamphetamine (AMP/MAMP)	500	Amphetamine Methamphetamine	250 250
MDMA[4]/MDA[5]	500	MDMA MDA	250 250

[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)

Drug Analyte Terminology and Abbreviations for Electronic Reports (Urine)

THCA	Marijuana metabolites[1]
BZE	Cocaine metabolite[2]
COD/MOR	Codeine/Morphine
HYC/HYM	Hydrocodone/Hydromorphone
OXYC/OXYM	Oxycodone/Oxymorphone
6-AM	6-Acetylmorphine
PCP	Phencyclidine
AMP/MAMP	Amphetamine/Methamphetamine
MDMA/ MDA	Methylenedioxymethamphetamine/ Methylenedioxyamphetamine

1 "THCA" or "delta-9-tetrahydrocannabinol-9-carboxylic acid" for the confirmatory analyte

2 "BZE" or "Benzoylecgonine" for the confirmatory analyte

NOTES:

The electronic report should clearly indicate whether the laboratory uses a single or multiple immunoassays for grouped analytes (e.g., one test for amphetamine, methamphetamine, MDMA, and MDA, or one test for amphetamine/methamphetamine and a separate test for MDMA/MDA). For grouped initial test analytes (e.g., hydrocodone and hydromorphone), it is not acceptable to only list the target analyte for the assay (i.e., hydrocodone).

The drug testing panel will include drugs authorized for testing in Federal Workplace Drug Testing Programs, with the required test analytes and cutoffs;

The biomarker testing panel will include biomarkers authorized for testing in Federal Workplace Drug Testing Programs, with the required test analytes and cutoffs; and

HHS-certified IITFs, HHS-certified laboratories, and Medical Review Officers must use the nomenclature (i.e., analyte names and abbreviations) published in the Federal Register with the drug and biomarker testing panels to report Federal workplace drug test results.

Negative

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

- All initial test 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. Validity test results are not reportable for valid specimens.

Positive

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

- The specimen's initial test 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.

- Note: Specimen validity test results may or may not be in the acceptable range. Validity test results are not reportable for valid specimens.

Dilute

An IITF or laboratory will report a urine specimen as dilute in conjunction with a negative drug test when—

- The creatinine concentration is greater than 5.0 mg/dL but less than 20.0 mg/dL;

And

- The specific gravity is greater than or equal to 1.002 but less than 1.003.

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 2.0 mg/dL but less than 20.0 mg/dL;

And

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

Substituted

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

- The creatinine concentration is less than 2.0 mg/dL;

And

- The specific gravity is less than or equal to 1.0010 or greater than or equal to 1.0200.

- or

- A biomarker is not detected or is present at a concentration inconsistent with that established for human urine for both the initial (first) test and the confirmatory (second) test on two separate aliquots (i.e., using the test analytes and cutoffs listed in the biomarker testing panel).

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 or equal to or greater than 11.0.

- Nitrite is present equal to or greater than 500 mcg/mL for both initial test (nitrite colorimetric or general oxidant colorimetric) and a different confirmatory test (e.g., multiwavelength spectrophotometry, ion chromatography, capillary electrophoresis).

- Chromium (VI) is present equal to greater than 50 mcg/mL for initial test (either general oxidant colorimetric or chromium (VI) colorimetric) and equal to or greater than the LOQ for a different confirmatory test (e.g., multi-wavelength spectrophotometry, ion chromatography, atomic absorption spectrophotometry, capillary electrophoresis, inductively coupled plasma-mass spectrometry).

- A halogen (e.g., chlorine from bleach, iodine, fluorine) is present for initial test (either general oxidant colorimetric [equal to or greater than 200 mcg/mL nitrite-equivalent cutoff or equal to or greater than 50 mcg/mL chromium (VI)-equivalent cutoff] or equal to or greater than the LOQ for a halogen colorimetric) and equal to or greater than the LOQ for a different confirmatory test (e.g., multi-wavelength spectrophotometry, ion chromatography, inductively coupled plasma-mass spectrometry).

- Glutaraldehyde is present for initial test (either aldehyde or characteristic immunoassay response on one or more drug immunoassay initial tests) and is equal to or greater than the LOQ for a different confirmatory test (e.g., GC-MS).

- Pyridine (pyridinium chlorochromate) is present for initial test (either general oxidant colorimetric [equal to or greater than 200 mcg/mL nitrite-equivalent cutoff or equal to or greater than 50 mcg/mL chromium (VI)-equivalent cutoff] or equal to or greater than 50 mcg/mL chromium (VI)-colorimetric) and equal to or greater than the LOQ for a different confirmatory test (e.g., GC-MS).

- Surfactant is present equal to or greater than 100 mcg/mL for both initial test (surfactant colorimetric using dodecylbenzene sulfonate-equivalent cutoff) and for a different confirmatory test (e.g., multi-wavelength spectrophotometry using dodecylbenzene sulfonate-equivalent cutoff).

- The presence of any other adulterant not specified above is verified using an initial test on the first aliquot and a different confirmatory test on the second aliquot.

- 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 2.0 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 2.0 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 (A) Specimen Reports, 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 (e.g., multi-wavelength spectrophotometry, ion chromatography, capillary electrophoresis).

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., chlorine from 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 initial test 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 initial test drug test occurs on two separate aliquots (i.e., valid initial test drug test results cannot be obtained).

   Note*:* Some substances may interfere with some initial test tests. Cross-reactivity information is included in package inserts provided by the immunoassay reagent manufacturer. Laboratories are required to contact the MRO prior to reporting a specimen as invalid based on initial test 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. A specimen validity test (i.e., other than the tests listed above) on two separate aliquots of the specimen indicates that the specimen is not valid for testing.

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

- 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.

Oral Fluid SPECIMEN Drug Testing Panel AND REPORTING CRITERIA

This drug testing panel will remain in effect until the effective date of a new drug testing panel published in the Federal Register:

Initial Test Analyte	Initial Test Cutoff [1] (ng/mL)	Confirmatory Test Analyte	Confirmatory Test Cutoff (ng/mL)
Marijuana (THC)[2]	4 [3]	THC	2
Cocaine/Benzoylecgonine (COC/BZE)	15	Cocaine Benzoylecgonine	8 8
Codeine/Morphine (COD/MOR)	30	Codeine Morphine	15 15
Hydrocodone/Hydromorphone (HYC/HYM)	30	Hydrocodone Hydromorphone	15 15
Oxycodone/Oxymorphone (OXYC/OXYM)	30	Oxycodone Oxymorphone	15 15
6-Acetylmorphine (6-AM)	4 [3]	6-Acetylmorphine	2
Phencyclidine (PCP)	10	Phencyclidine	10
Amphetamine/Methamphetamine (AMP/MAMP)	50	Amphetamine Methamphetamine	25 25
MDMA[4]/MDA[5]	50	MDMA MDA	25 25

[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 (THC).

[3]Alternate technology (THC and 6-AM): The confirmatory test cutoff must be used for an alternate technology initial test that is specific for the target analyte (i.e., 2 ng/mL for THC, 2 ng/mL for 6-AM).

[4]Methylenedioxymethamphetamine (MDMA)

[5]Methylenedioxyamphetamine (MDA)

Drug Analyte Terminology and Abbreviations for Electronic Reports (Oral Fluid)

THC	Marijuana[1]
COC/BZE	Cocaine/Cocaine metabolite
COD/MOR	Codeine/Morphine
HYC/HYM	Hydrocodone/Hydromorphone
OXYC/OXYM	Oxycodone/Oxymorphone
6-AM	6-Acetylmorphine
PCP	Phencyclidine
AMP/MAMP	Amphetamine/Methamphetamine
MDMA/MDA	Methylenedioxymethamphetamine/

[1] "THC" or "delta-9-tetrahydrocannabinol" for the confirmatory analyte

NOTES: The electronic report should clearly indicate whether the laboratory uses a single or multiple immunoassays for grouped analytes (e.g., one test for amphetamine, methamphetamine, MDMA, and MDA, or one test for amphetamine/methamphetamine and a separate test for MDMA/MDA). For grouped initial test analytes (e.g., hydrocodone and hydromorphone), it is not acceptable to only list the target analyte for the assay (i.e., hydrocodone).

The drug testing panel will include drugs authorized for testing in Federal Workplace Drug Testing Programs, with the required test analytes and cutoffs;

The biomarker testing panel will include biomarkers authorized for testing in Federal Workplace Drug Testing Programs, with the required test analytes and cutoffs; and

HHS-certified IITFs, HHS-certified laboratories, and Medical Review Officers must use the nomenclature (i.e., analyte names and abbreviations) published in the Federal Register with the drug and biomarker testing panels to report Federal workplace drug test results.

Negative

A laboratory will report an oral fluid specimen as negative when the specimen has valid negative results at any point in the testing process and when—

- All initial test results are below the initial test cutoffs; or
- Confirmatory test results are below the confirmatory test cutoffs;

And

- If performed, specimen validity test results are in the acceptable range. Validity test results are not reportable for valid specimens.

Positive

A laboratory will report an oral fluid specimen as positive for a drug/drug metabolite when—

- The specimen's initial test 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.

Substituted Result

A laboratory will report an oral fluid specimen as substituted when a biomarker is not detected or is present at a concentration inconsistent with that established for human oral fluid for both the initial (first) test and the confirmatory (second) test on two separate aliquots (i.e., using the test analytes and cutoffs listed in the biomarker testing panel).

Adulterated Result

A laboratory will report an oral fluid specimen as adulterated result when the presence of an adulterant is verified using an initial test on a first aliquot and a different confirmatory test on a second aliquot.

Invalid Result

A laboratory will report an invalid result for an oral fluid specimen when results meet one of the following criteria:

- Interference with the initial drug test occurs on two separate aliquots (i.e., valid initial drug test results cannot be obtained);
- Interference with the confirmatory drug test occurs on two separate aliquots and the laboratory is unable to identify the interfering substance; or
- A specimen validity test on two separate aliquots of the specimen indicates that the specimen is not valid for testing.

A laboratory will report an invalid result for an oral fluid specimen when the laboratory identifies an abnormal physical characteristic and-

- The physical appearance of the specimen (e.g., viscosity) is such that testing the specimen may damage the laboratory's instruments; or
- The specimen has been tested and the appearances of the Tubes A and B are clearly different (note the laboratory tests the A Tube).

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) website (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 company/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 for: □ urine specimens □ oral fluid specimens

☐ 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*)

TABLES

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.

Note: 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).
Enzyme Immunoassay (EIA)	Albumin, Immunoglobulin G (IgG) concentration	An immunoassay based on competition for antibody binding sites between measurand in the specimen and measured labeled with an enzyme. Enzyme activity decreases when drug binds to the antibody. Measurand concentration in the specimen is measured by the change in enzyme activity.
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.
Microplate Enzyme-Linked Immunosorbent Assay	Albumin	A competitive binding enzyme immunoassay using measurand-specific antibodies that are immobilized in the wells of a microplate.
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 3a. Required Comments for IITF and Laboratory Specimen Reports - Urine

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 = (confirmatory test value) mcg/mL	≥ 500 mcg/mL nitrite
	Surfactant Present; dodecylbenzene sulfonate = (confirmatory test value) mcg/mL	≥ 100 mcg/mL dodecylbenzene sulfonate
	Chromium (VI) = (confirmatory test value) mcg/mL	adulterant ≥ LOQ
	(Specify Halogen) = (confirmatory test value)	
	Glutaraldehyde = (confirmatory test value) mcg/mL	
	Pyridine = (confirmatory test value) mcg/mL	
	(Specify Adulterant) Present = (confirmatory test value)	
Substituted	Creatinine = (confirmatory test value) mg/dL & SpGr = (confirmatory test value)	
	(Specify biomarker) = confirmatory 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 = (confirmatory 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 initial drug test method) Interference[2]	Drug analyte(s) must not be included on reports for invalid results based on assay interference
	(Specify confirmatory drug test method) 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 electronic report for primary specimens; Remarks on CCF/Split Specimen Report & on electronic 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 UrMG (88 Fed. Reg. 70768) section 11.19.g.

[3] See NLCP Manual for further guidance: IITF Checklist Question E9 and Laboratory Question E10m, CCF Decision Trees

Table 3a. Required Comments for IITF and Laboratory Specimen Reports - Urine (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)	
	Fatal Flaw: Specimen collected using an unapproved ECCF system	
	Fatal Flaw: Specimen ID number on bottle label/seal is not unique3	Incorrect label/seal for either the A or B specimen
	Uncorrected Flaw: Wrong CCF used3 (Specify: Expired/Non-regulated CCF; CCF Copy 2-5; ECCF Reprint without collector wet signature; ECCF Reprint without collector explanation)	Wait at least 5 business days before reporting if flaw not corrected
	Uncorrected Flaw: Collector signature not recovered	
	Uncorrected Flaw: A & B redesignation not documented by IITF	

[1] Remarks on CCF (Step 5a) & on electronic report for primary specimens; Remarks on CCF/Split Specimen Report & on electronic 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 UrMG (88 Fed. Reg. 70768) section 11.19.g.
[3] See NLCP Manual for further guidance: IITF Checklist Question E9 and Laboratory Question E10m, CCF Decision Trees

Table 3b. Required Comments for Laboratory Specimen Reports - Oral Fluid

Test Result	Required Comment[1]	Note
Positive	(Specify drug analyte) = confirmatory test quantitative result	
Adulterated	(Specify Adulterant) Present = confirmatory test value	
Substituted	(Specify biomarker) = confirmatory test value	
Invalid Result	(Specify initial drug test method) Interference[2]	Drug analyte(s) must not be included on reports for invalid results based on assay interference
	(Specify confirmatory drug test method) Interference[2]	
	Abnormal Physical Characteristic - (Specify)[2]	
	Tube A and Tube B - Different Physical Appearance[2]	
	(Specify measurand) = confirmatory test value	Examples: albumin, IgG
Rejected for Testing	Fatal Flaw: Specimen ID number (Specify: mismatch; missing)	ID mismatch/missing on CCF and/or either Tube 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: Tube A label/seal (Specify: missing; misapplied; broken; shows evidence of tampering)	If redesignation is not possible
	Fatal Flaw: Tube A seal condition not marked on CCF	
	Fatal Flaw: Tube A insufficient specimen volume (Specify reason and indicate collector error *when applicable*)	
	Fatal Flaw: Expired device used for Tube A collection	
	Fatal Flaw: Tube A device expiration date cannot be determined	Cannot verify device expiration date on Tube A and redesignation is not possible
	Fatal Flaw: Device volume indicator(s) not observed	This fatal flaw applies to specimens with a diluent (i.e., not a fatal flaw for neat oral fluid specimens)
	Fatal Flaw: Specimen collected using an unapproved ECCF system	
	Fatal Flaw: Specimen ID number on tube label/seal is not unique[3]	Incorrect label/seal for either the A or B specimen
	Fatal Flaw: (Specify: Urine or Non-regulated CCF used)	
	Uncorrected Flaw: Wrong CCF used[3] (Specify: CCF Copy 2-5; ECCF Reprint without collector wet signature; ECCF Reprint without collector explanation)	Wait at least 5 business days before reporting if flaw not corrected
	Uncorrected Flaw: Collector signature not recovered	Wait at least 5 business days before reporting if flaw not corrected

[1] Remarks on CCF (Step 5a) & on electronic report for primary specimens; Remarks on CCF/Split Specimen Report & on electronic report for split specimens. Labs 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 OFMG (88 Fed. Reg. 70814) section 11.17.f.
[3] See NLCP Manual for further guidance: Laboratory Question E11k, E-11o, CCF Decision Trees

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

Reported Primary (A) Specimen Result	Medical Review Officer (MRO) Action	Guideline[1] UrMG 13.5 OFMG 13.5
Negative	Report the negative result.	Ur – a OF – a
Negative and Dilute (for urine)	Report the negative result and direct the Federal agency to immediately collect another specimen from the donor. If the recollected specimen provides a negative or negative/dilute result, the MRO reports a negative result to the agency, with no further action required. If the recollected specimen provides a result other than negative, follow the appropriate procedures below.	Ur – b OF – N/A
Positive **or** **(for urine) Positive and Dilute**	*If the laboratory reports an invalid result in conjunction with a positive, adulterated, or substituted result, see **Invalid Results** guidance below.* Report all verified positive and/or refusal to test results to the Federal agency. Contact the donor to determine if he/she has a valid medical explanation for the positive result. • If the donor admits unauthorized use of the drug(s) that caused the positive result, the MRO reports the test result as positive to the agency. The MRO must document the donor's admission of unauthorized drug use in the MRO records and in the MRO's report to the Federal agency. • If the donor provides documentation (e.g., a valid prescription) to support a legitimate medical explanation for the positive result, report the test result as negative to the agency. • For a verified negative test result, if (for urine) the laboratory also reports the specimen is dilute, report a negative/dilute result to the agency and direct the Federal agency to immediately collect another specimen from the donor. For recollected specimens, refer to verification actions that are appropriate for the test result(s). Additional notes: ▪ *Passive exposure to a drug (e.g., exposure to marijuana smoke) is not a legitimate medical explanation for a positive drug test result.* ▪ *Ingestion of food products containing a drug (e.g., products containing marijuana) is not a legitimate medical explanation for a positive drug test.* ▪ *Ingestion of food products containing a drug (poppy seeds containing codeine and/or morphine) is not a legitimate medical explanation for a positive urine drug test result. See exception for positive oral fluid codeine and/or morphine results below.* ▪ *A physician's authorization or medical recommendation for a Schedule 1 controlled substance is not a legitimate medical explanation for a positive drug test result.*	Ur – c, d OF – b, c

(continued)

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

Reported Primary (A) Specimen Result	Medical Review Officer (MRO) Action	Guideline[1] UrMG 13.5 OFMG 13.5
	▪ *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.* If the donor is unable to provide a legitimate medical explanation for the positive urine result, the MRO reports the positive result to the agency. ▪ If the laboratory also reports that a urine specimen is dilute, the MRO may choose not to report the dilute result. If the donor is unable to provide a legitimate medical explanation for the positive oral fluid result, the MRO reports a positive result to the agency for all drugs except codeine and/or morphine as follows: ▪ For oral fluid codeine and morphine less than 150 ng/mL, the MRO must report the result as negative to the agency unless the donor admits unauthorized use of the drug(s) that cause the positive result. For oral fluid codeine and/or morphine equal to or greater than 150 ng/mL and no legitimate medical explanation, the MRO shall report a positive result to the agency. *Consumption of food products must not be considered a legitimate medical explanation for the donor having oral fluid morphine or codeine at or above this concentration.*	
Substituted	*If the laboratory reports an invalid result in conjunction with a positive, adulterated, or substituted result, see **Invalid Results** guidance below.* Contact the donor to determine if he/she has a valid medical explanation for the substituted result. If the donor provides a legitimate medical explanation for the substituted result, report a negative result to the Federal agency. If the donor is unable to provide a legitimate explanation, report a "refusal to test" (substituted) to the Federal agency.	Ur – e OF – d
Adulterated	*If the laboratory reports an invalid result in conjunction with a positive, adulterated, or substituted result, see **Invalid Results** guidance below.* Contact the donor to determine if he/she has a valid medical explanation for the adulterated result. If the donor provides a legitimate medical explanation for the adulterated result, report a negative result to the Federal agency. If the donor is unable to provide a legitimate explanation, report a "refusal to test" (adulterated) to the Federal agency.	Ur – e OF – d

(continued)

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

Reported Primary (A) Specimen Result	Medical Review Officer (MRO) Action	Guideline[1] UrMG 13.5 OFMG 13.5
Invalid Result	*If the laboratory reports an invalid result 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 takes action for the verified invalid result(s) for the primary (A) specimen only when:* • *the MRO verifies the positive, adulterated, or substituted results as negative based upon a legitimate medical explanation, or for oral fluid codeine and/or morphine concentrations less than 150 ng/mL, or* • *the split B specimen is tested and reported as a failure to reconfirm the positive, adulterated, or substituted 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 (for urine) 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.* Contact the donor to determine if he/she has a legitimate medical explanation for the invalid result. For urine pH results in the 9.0 to 9.5 invalid range, MROs may contact the collection site, laboratory, or IITF to discuss time and temperature issues (e.g., time elapsed from collection to receipt at the testing facility, likely temperature conditions between the time of the collection and transportation to the testing facility, specimen storage conditions). If the donor provides documentation (e.g., a valid prescription) or the MRO determines that time and temperature account for a urine pH in the 9.0 to 9.5 range to support a legitimate medical explanation for the invalid result, report a test cancelled result with the reason for the invalid result and inform the Federal agency that a recollection is not required because there is a legitimate explanation for the invalid result. *Exception note: a Federal agency plan may require a negative drug test result based on the reason for testing (e.g., Federal agency applicant/pre-employment, return to duty, follow-up).* If the donor is unable to provide a legitimate explanation or the MRO determines that time and temperature fail to account for the urine pH in the 9.0—9.5 range, report a test cancelled result with the reason for the invalid result and direct the Federal agency to immediately collect another specimen from the donor using a direct observed collection. If the second specimen collected provides an invalid result, report this specimen as test cancelled and recommend that the agency collect another authorized specimen type (e.g., oral fluid or urine). If the Federal agency does not authorize collection of another specimen type, the MRO consults with the agency to arrange a clinical evaluation to determine whether there is a legitimate medical reason for the invalid result. See also required MRO actions in the MRO Manual Chapter 5.6.4, items 3 and 4 for invalid specimens.	Ur – c, d, f, g OF – b, c, e

(continued)

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

Reported Primary (A) Specimen Result	Medical Review Officer (MRO) Action	Guideline[1] UrMG 13.5 OFMG 13.5
Multiple Reported Results	*If the laboratory reports an invalid result in conjunction with a positive, adulterated, or substituted result, see **Invalid Results** guidance above.* When the laboratory reports multiple results for the primary (A) specimen, follow the preceding verification procedures as appropriate for each reported result. Report all verified positive and/or "refusal to test" results to the Federal agency. When two separate specimens are collected during the same testing event and sent to the laboratory or IITF for testing (e.g., the collector sent a urine specimen out of temperature range and the subsequently collected specimen—urine or another authorized specimen type), report **all** verified positive and/or "refusal to test" results to the Federal agency and: ▪ If both specimens were verified negative, report the result as negative. ▪ If one specimen was verified negative and the other was not (i.e., the specimen was verified as positive, adulterated, invalid, substituted or [for urine] negative/dilute.), report only the verified result(s) other than negative. – For example, if you verified one specimen as negative and the other as a refusal to test because the specimen was substituted, report only the refusal to the Federal agency. ▪ If both specimens were verified as positive, adulterated, and/or substituted, report all results. – For example, if you verified one specimen as positive and the other as a refusal to test because the specimen was adulterated, report the positive and the refusal results to the Federal agency. ▪ If one specimen has been verified and the laboratory has not reported the result(s) of the other specimen: – Immediately report verified result(s) of positive, adulterated, or substituted and do not wait to receive the result(s) of the other specimen. – Do not report a verified result of negative, invalid or (for urine) negative/dilute for the first specimen to the Federal agency. Hold the report until results of both specimens have been received and verified. Do not report invalid results for the primary (A) specimen unless the split (B) specimen is tested and reported as a failure to reconfirm.	Ur – c, d-f, g OF – b, c-f

(continued)

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

Reported Primary (A) Specimen Result	Medical Review Officer (MRO) Action	Guideline[1] UrMG 13.5 OFMG 13.5
Rejected for Testing	When the laboratory or IITF reports a rejected for testing result for the primary (A) specimen, report a test cancelled result and recommend that the Federal agency collect another specimen of the same type (i.e., urine or oral fluid) from the donor.	Ur – h OF – f

1 Ur - Mandatory Guidelines for Federal Workplace Drug Testing Programs, section 13.5; OF - Mandatory Guidelines for Federal Workplace Drug Testing Programs— Oral Fluid, section 13.5

When Laboratory A reports **multiple results** (i.e., drug positive, adulterated, substituted) for the primary (A) specimen and Laboratory B **reconfirms some** (**but not all**) **of the results** for the split (B) specimen, the MRO takes the following action(s):

- Report to the agency 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 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 (A) specimen;
  - Whether Laboratory B found the split specimen to be adulterated, invalid, or substituted when performing specimen validity testing after failing to reconfirm a drug; or
  - 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.

For adulterated and substituted results, donor actions may impact actions the MRO takes after receiving the split (B) specimen result from the second laboratory (Laboratory B):

- If the donor provides a legitimate medical explanation for an adulterated and/or a substituted result or if the primary specimen was only reported as adulterated and/or substituted (but not positive for any drugs):
  - Report to the agency as failed to reconfirm result (specify drug[s]); and
  - Cancel both tests.
- If there is no legitimate medical explanation:
  - Report to the agency as "refusal to test" (specify adulterant and/or substituted);
  - Give the donor 72 hours to request that Laboratory A:
    - for adulterated, request that Laboratory A retest the primary (A) specimen for the adulterant;
    - for substituted based on biomarker testing, request that Laboratory A test the primary (A) specimen using its confirmatory test for the biomarker; or
    - for substituted based upon urine creatinine and specific gravity, review the creatinine and specific gravity results for the primary (A) specimen.
  - When the donor requests that Laboratory A retest the primary (A) specimen for the adulterant or biomarker or that Laboratory A review the urine creatinine and specific gravity results for the primary (A) specimen:
    - If Laboratory A reconfirms the adulterant, biomarker and/or (for urine) the review of Laboratory A original primary (A) specimen results for creatinine and specific gravity confirms the specimen was substituted:
      - Report to the agency as "refusal to test" (specify adulterant or substituted).
    - If Laboratory A fails to reconfirm the adulterant, biomarker and/or (for urine) the review of Laboratory A original primary (A) specimen results for creatinine and specific gravity fails to confirm the specimen was substituted:
      - Cancel both tests;
      - Direct the agency to immediately collect another specimen using a direct observation collection procedure; and
      - Notify the appropriate drug-free workplace regulatory office regarding the failed to reconfirm and cancelled test.

Subject to donor request for original specimen (A) retest and review actions described for adulterated and substituted results (above), the following are examples of MRO actions for combinations of reconfirmed results, failed to reconfirm results for drug(s), adulteration, invalid, and substituted.

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

Reported Split Specimen Result			Medical Review Officer (MRO) Action[2,3,4]	Guideline[5] UrMG 14.6 OFMG 14.6
Reconfirmed	**Failed to Reconfirm**	**Additional Testing Results[1]**		
Drug(s)			▪ Report to the agency a reconfirmed result (specify drug[s]).	Ur – a OF – a
Adulterated			▪ Report to the agency a reconfirmed result (adulterated [specify adulterant]).	Ur – a OF – a
Substituted			▪ Report to the agency a reconfirmed result (substituted).	Ur – a OF – a
	Drug(s)	Adulterated	▪ If the donor provides a legitimate medical explanation, report to the agency a failed to reconfirm result (specify drugs[s]) and cancel both tests. ▪ If there is no legitimate medical explanation, report to the agency a failed to reconfirm result (specify drugs[s]) and a "refusal to test" (specify drug[s] and that adulterant is present. ▪ (see above for donor request for Lab A primary (A) specimen retest)	Ur – b OF - b
	Drug(s)	Substituted	▪ If the donor provides a legitimate medical explanation, report to the agency a failed to reconfirm result (specify drugs[s]) and cancel both tests. ▪ If there is no legitimate medical explanation, report a failed to reconfirm (specifying the drug[s]) and a refusal to test (substituted) to the agency. ▪ (see above for donor request for Lab A primary (A) specimen retest)	Ur – c OF - c
	Drug(s)	Not adulterated or Not substituted	▪ Report to the agency a failed to reconfirm result (specify drug[s]); ▪ Cancel both tests; ▪ Notify the HHS office responsible for coordination of the drug-free workplace program	Ur – d OF - d
	Drug(s)	Invalid	If the invalid result cannot be resolved— ▪ Report a failed to reconfirm result (specify drug[s]) and give the reason for the invalid result; ▪ Cancel both tests; ▪ Direct the Federal agency to immediately collect another specimen. If this was a urine test, direct the Federal agency to immediately collect another specimen using a direct observed collection procedure; and ▪ Notify the HHS office responsible for coordination of the drug-free workplace program.	Ur – e OF – e

(continued)

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

Reported Split Specimen Result			Medical Review Officer (MRO) Action[2,3,4]	Guideline[5] UrMG 14.6 OFMG 14.6
Reconfirmed	**Failed to Reconfirm**	**Additional Testing Results[1]**		
Drug(s)	Drug(s)	Adulterated	▪ Report to the agency a reconfirmed result (specify drug[s]) and a failed to reconfirm result (specify drug[s]); ▪ Tell the agency it may take action based on the reconfirmed drug(s) although Laboratory B failed to reconfirm one or more drugs and found that the specimen was adulterated; and ▪ Notify the HHS office responsible for coordination of the drug-free workplace program	Ur – f OF – f
Drug(s)	Drug(s)	Substituted	▪ Report to the agency a reconfirmed result (specify drug[s]) and a failed to reconfirm result (specify drug[s]); ▪ Tell the agency it may take action based on the reconfirmed drug(s) although Laboratory B failed to reconfirm one or more drugs and found that the specimen was substituted; and ▪ Notify the appropriate drug-free workplace regulatory office regarding the test results for the specimen.	Ur – g OF – g
Drug(s)	Drug(s)	Not Adulterated Not Substituted	▪ Report to the agency a reconfirmed result (specify drug[s]) and a failed to reconfirm result (specify drug[s]); ▪ Tell the agency it may take action based on the reconfirmed drug(s) although Laboratory B failed to reconfirm one or more drugs; and ▪ Notify the appropriate drug-free workplace regulatory office regarding the test results for the specimen.	Ur – h OF – h
Drug(s)	Drug(s)	Invalid	If the invalid result cannot be resolved— ▪ Report to the agency a reconfirmed result (specify drug[s]) and a failed to reconfirm result (specify drug[s]); ▪ Tell the agency it may take action based on the reconfirmed drug(s) although Laboratory B failed to reconfirm one or more drugs and reported an invalid result; and ▪ Notify the appropriate drug-free workplace regulatory office regarding the test results for the specimen.	Ur – i OF – i
	Adulterated or Substituted		▪ Report to the agency a failed to reconfirm result (not adulterated: specify adulterant [pH for urine] or not substituted); ▪ Cancel both tests; and ▪ Notify the appropriate drug-free workplace regulatory office regarding the test results for the specimen.	Ur – j OF – j

(continued)

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

Reported Split Specimen Result			Medical Review Officer (MRO) Action[2,3,4]	Guideline[5] UrMG 14.6 OFMG 14.6
Reconfirmed	**Failed to Reconfirm**	**Additional Testing Results[1]**		
	Adulterated or Substituted	Invalid	▪ Report to the agency a failed to reconfirm result (not adulterated: specify adulterant [pH for urine] or not substituted, and the reason for the invalid result); ▪ Cancel both tests; and ▪ Direct the Federal agency to immediately collect another specimen. If this was a urine test, direct the Federal agency to immediately collect another specimen using a direct observed collection procedure; and ▪ Notify the appropriate drug-free workplace regulatory office regarding the test results for the specimen.	Ur – k OF – k
Adulterated or Substituted (urine)	Drug(s)		▪ Report to the agency a reconfirmed result (adulterated or substituted) and a failed to reconfirm result (specify drug[s] and ▪ Tell the agency it may take action based on the reconfirmed result (adulterated or substituted) although Laboratory B failed to reconfirm the drug(s) result.	Ur – l OF – l
	Drug(s) Adulterated or Substituted		▪ Report to the agency a failed to reconfirm result (specify drug[s] and not adulterated: specify adulterant [pH for urine] or not substituted); ▪ Cancel both tests; and ▪ Notify the appropriate drug-free workplace regulatory office regarding the test results for the specimen.	Ur – m OF – m
Drug(s) Adulterated	Drug(s)		▪ Report to the agency a reconfirmed result (specify drug[s] and adulterated) and a failed to reconfirm result (specify drug[s]); and ▪ Tell the agency it may take action based on the reconfirmed drug(s) and reconfirmed adulterated result although Laboratory B failed to reconfirm one or more drugs.	Ur – n OF – n
Drug(s)	Drug(s) Adulterated		▪ Report to the agency a reconfirmed result (specify drug[s]) and a failed to reconfirm result (specify drug[s] and not adulterated: specifying the adulterant [pH for urine]); ▪ Tell the agency it may take action based on the reconfirmed result (specify drug[s] although Laboratory B failed to reconfirm one or more drugs and failed to reconfirm the adulterated result.	Ur – o OF – o

(continued)

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

Reported Split Specimen Result			Medical Review Officer (MRO) Action2,3,4	Guideline[5] UrMG 14.6 OFMG 14.6
Reconfirmed	**Failed to Reconfirm**	**Additional Testing Results[1]**		
	Adulterated and Substituted		▪ Report to the agency a failed to reconfirm result not adulterated specifying the adulterant [pH for urine] and not substituted); ▪ Cancel both tests; and ▪ Notify the appropriate drug-free workplace regulatory office regarding the test results for the specimen.	Ur – p OF – p
Substituted	Adulterated		▪ Report to the agency a reconfirmed result (substituted) and a failed to reconfirm result (not adulterated: specifying the adulterant [pH for urine]); and ▪ Tell the agency it may take action based on the reconfirmed result (substituted) although Laboratory B failed to reconfirm the adulterated result.	Ur – q OF – q
Adulterated	Substituted		▪ Report to the agency a reconfirmed result (adulterated) and a failed to reconfirm result (not substituted); and ▪ Tell the agency it may take action based on the reconfirmed result (adulterated) although Laboratory B failed to reconfirm the substituted result.	Ur – r OF – r

[1] For urine: 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.

[2] See additional MRO actions (in chart above) if 1) the donor provides a legitimate medical explanation for adulterated and/or substituted results or 2) requests Laboratory A to retest (adulterant) or review original results (substituted) for the original primary (A) specimen.

[3] Prior to reporting a failed to reconfirm result 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.

[4] Prior to reporting a failed to reconfirm and invalid result to the MRO, the laboratory must contact the MRO to decide whether testing at a third laboratory would be useful.

[5] Ur - Mandatory Guidelines for Federal Workplace Drug Testing Programs, section 14.6; OF - Mandatory Guidelines for Federal Workplace Drug Testing Programs— Oral/Fluid, section 14.6

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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