

Note: This manual is essentially the same as the 1997 HHS Medical Review Officer (MRO) Manual except for changes related to the new Federal Custody and Control Form (CCF). The appendix has also been deleted since the new Federal Custody and Control Form is available as a separate file on the website.

## **Medical Review Officer Manual for Federal Agency Workplace Drug Testing Programs for use with the new Federal Drug Testing Custody and Control Form (OMB Number 0930-0158, Exp Date: June 30, 2003)**

This manual applies to federal agency drug testing programs that come under Executive Order 12564 and the Department of Health and Human Services (HHS) Mandatory Guidelines.

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### **Chapter 1. The Medical Review Officer (MRO)**

An essential part of the drug testing program is the final review of results as required by the Mandatory Guidelines for Federal Workplace Drug Testing Programs initially published in the Federal Register on April 11, 1988 (53 FR 11970-11989) and revised in the Federal Register on June 9, 1994 (59 FR 29908-29931). A positive laboratory test result does not automatically identify an employee or job applicant as an illegal drug user. An individual with a detailed knowledge of possible alternative medical explanations is essential in performing this final review of results. The Medical Review Officer (MRO) fulfills this important function.

An MRO is defined as a licensed physician who receives laboratory results, has knowledge of substance abuse disorders, and has appropriate medical training to interpret and evaluate an individual's positive test result together with his or her medical history and any other relevant biomedical information. Only individuals holding either a Doctor of Medicine (M.D.) or Doctor of Osteopathy (D.O.) degree may serve as MROs for federally regulated programs.

The MRO may be an employee or a contractor for the Federal agency; however, the MRO must not be an employee or agent of or have any financial interest in the laboratory for which the MRO is reviewing drug testing results. Additionally, the MRO must not derive any financial benefit by having an agency use a specific drug testing laboratory or have any agreement with the laboratory that may be construed as a potential conflict of interest. The purpose of this requirement is to prevent any arrangement between a laboratory and an MRO that would prevent the MRO from reporting a problem identified with a laboratory's test results or testing procedures.

The MRO has the following responsibilities:

1. Determine that the information on the Federal drug testing custody and control form (CCF) is forensically and scientifically supportable;
2. Interview the donor when required;
3. Make a determination regarding the test result;
4. Report the verified result to the Federal agency (employer); and
5. Maintain records and confidentiality of the information.

It is recommended that MROs maintain a Standard Operating Procedure manual to ensure consistency and improve overall quality of the review process and participate in continuing education activities.

From initial requirements that an MRO be a licensed physician with knowledge of substance abuse disorders, practical requirements have evolved regarding the availability of various training programs. These programs ensure that MROs are familiar with current regulations and receive the latest information on interpreting drug testing results. Although there is no regulatory requirement for formal certification at the present time, the training courses offered by the various professional organizations have served a very important role in providing continuing education programs.

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

American College of Occupational and Environmental Medicine (ACOEM)

1114 North Arlington Heights Road  
Arlington Heights, IL 60004  
(847) 818-1800

American Society of Addiction Medicine (ASAM)  
4601 North Park Avenue, Suite 101  
Chevy Chase, MD 20815  
(301) 656-3920

American Association of Medical Review Officers (AAMRO)  
17 Running Brook Court  
Durham, NC 27713  
(919) 489-5407

The listing of these organizations is not an endorsement by the Federal government nor is attendance at one of their courses a regulatory requirement.

## **Chapter 2. Federal Drug Testing Custody and Control Form**

For specimens collected under the Guidelines, an Office of Management and Budget (OMB) approved Federal Drug Testing Custody and Control Form (CCF) must be used to document the collection of a specimen at the collection site. The CCF is available from a number of different sources (e.g., laboratories, collectors, MROs).

A sample of the CCF (OMB No. 0930-0158, Exp. Date: 6/30/2003) is on the SAMHSA web site (<http://www.health.org/workpl.aspx>). All discussions throughout this revised manual refer to this version of the CCF form.

The CCF has five copies that are distributed as indicated:

- Copy 1. Laboratory Copy
- Copy 2. Medical Review Officer Copy
- Copy 3. Collector Copy
- Copy 4. Employer Copy
- Copy 5. Donor Copy

## **Chapter 3. The MRO Review Process**

### **A. Administrative Review of the CCF**

The MRO reviews the MRO Copy of the CCF, or if not available, a legible copy of any copy signed by the donor, which was received directly from the collection site. The MRO ensures that:

1. An OMB-approved CCF was used for the specimen collection.

2. There is a specimen ID number on the top of the form along with the name and address of the laboratory testing the specimen.
3. Step 1 has all the required information (i.e., employer name and address, MRO name, address and phone number, donor SSN or other ID number, reason for the test, tests to be performed, collection site information).
4. The collector marked one of the temperature boxes, one of the specimen collection boxes, and the observed collection (if it was an observed collection) in Step 2 on the CCF.
5. The collector provided his or her printed name, a signature, date and time for the collection, and a comment (if appropriate) on the "Remarks" line in Step 2 on the CCF. The collector also provided the specific name of the delivery service that was used to transfer the specimen to the laboratory.

Appears to be adulterated). The identification of these types of problems are for informational use by the laboratory and the MRO and, generally by themselves, are insote: The collector must use the "Remarks" line in Step 2 to identify any problem that may have occurred during the collection (e.g., donor refused to sign the donor statement on Copy 2 of the CCF, temperature of the specimen was outside the acceptable range and a second direct observed collection was conducted, why a specimen was not collected, why an observed collection was conducted, specimen apufficient to cancel the test).

6. Step 5 on the CCF gives the donor identifying information (i.e., printed name, signature, date signed, daytime phone number, business phone number, and date of birth).

The MRO reviews Copy 1 of the CCF that is received from the testing laboratory.

Note: A laboratory may transmit a result (negative or non-negative) to an MRO by either faxing the completed Copy 1 or transmitting a scanned image of the completed Copy 1 by computer. A fax or scanned image of a completed Copy 1 is sufficient, by itself, for reviewing a negative result. For **a non-negative** result, the laboratory must send a hard copy of a completed Copy 1 to the MRO before the MRO can report the result to the employer.

Copy 1 is similar to Copy 2, but has the following additional information:

1. An accession number, if assigned by the laboratory, appears on the top of Copy 1 along with the specimen ID number.
2. The accessioner at the laboratory completed Step 4 (i.e., the accessioner provided a printed name and signature, indicated whether the primary specimen bottle seal was or was not intact, and indicated to whom or where the specimen bottle was released).
3. Step 5a indicates the test result (i.e., the test result for a single specimen or the test result for the primary specimen (Bottle A) from a split specimen collection) and has the printed name and signature of the certifying scientist

and date signed. There may also be a comment on the "Remarks" line if the laboratory identified a problem with the specimen. The "Test Lab" line must also be completed if the test laboratory is different than the name appearing on the top of Copy 2.

Note: A comment on the "Remarks" line may identify either an administrative or a technical problem when the specimen was received or during the testing process (e.g., the seal on the primary specimen bottle was broken upon receipt, why the laboratory reported the specimen as adulterated or substituted, why the specimen was rejected for testing, why the laboratory reported an "Invalid Result"). The MRO must consider these comments when making a determination.

Note: Many laboratories also provide a separate computer generated report that gives much of the same information contained on Copy 1 of the CCF.

Note: If Copy 1 and Copy 2 are complete, it would appear that the collector followed the required collection procedure and the laboratory correctly tested and reported the test result.

If the MRO finds that the laboratory made an administrative error on Copy 1 or failed to identify an administrative error made by the collector, the MRO must contact either the collector or the laboratory (whichever made the administrative error) to determine if the collector or the laboratory can provide a Memorandum For Record (MFR) to recover/correct the administrative error.

1. If the laboratory or the collector provides an MFR to recover/correct the administrative error, the MRO reports the verified result (i.e., whether the analytical test result was determined to be negative, positive, adulterated, substituted, or invalid result) to the employer and retains the MFR as part of the records associated with the testing of the specimen.
2. If the laboratory or the collector cannot provide an MFR to recover/correct the administrative error and the MRO believes that the administrative error has a significant impact on the validity of the entire collection and testing process, the MRO may make and report a "Test Canceled" determination. If the MRO believes the administrative error does not have a significant impact on the validity of the collection or testing process, the MRO may report the verified result (i.e., whether the analytical test was determined to be negative, positive, adulterated, substituted, or invalid result) and must describe the administrative error that could not be recovered/corrected.

Note: When an MRO reports a "Test Canceled" result because the MRO believes that the administrative error has had a significant impact on the validity of the collection and testing process, it is the employer's decision whether or not to immediately collect another urine specimen from the donor. Certain tests, such as, pre-employment, return to duty, require having a valid negative drug test result.

## **B. Technical Review of Single Specimen or Primary (Bottle A) Specimen Test Result**

Note: It is assumed that the copies of the CCF were complete and all the information was accurate, except in some cases when the laboratory reports a "Rejected for Testing" result.

A specimen is defined to be:

1. Dilute if the creatinine is  $< 20$  mg/dL and the specific gravity is  $< 1.003$ , unless the criteria for a substituted specimen are met.
2. Substituted (i.e., the specimen does not exhibit the clinical signs or characteristics associated with normal human urine) if the creatinine concentration is  $\leq 5$  mg/dL and the specific gravity is  $\leq 1.001$  or  $\geq 1.020$ .
3. Adulterated if the nitrite concentration is  $\geq 500$  g/mL.
4. Adulterated if the pH is  $\leq 3$  or  $\geq 11$ .
5. Adulterated if an exogenous substance (i.e., a substance which is not a normal constituent of urine) or an endogenous substance at a higher concentration than normal physiological concentration is present in the specimen.

When the laboratory reports a:

### **Negative Result**

The MRO makes a "Negative" determination, completes Step 6 on Copy 2 of the CCF, and reports the "Negative" result to the employer.

If a laboratory also marked the dilute box, the MRO verifies the test result as "Negative," marks the dilute box, and informs the employer that the next time the donor is selected for a drug test the employer may require the specimen to be collected under direct observation because the specimen was dilute.

Note: A comment indicating that the specimen was dilute does not affect the validity of a "Negative" test result.

### **Positive Result**

The MRO interviews the donor. If the donor is unable to provide a valid alternative medical explanation, a positive laboratory test result is determined as a "Positive" by the MRO. If the donor provides a valid alternative medical explanation, the MRO reports the test result as "Negative." The MRO completes Step 6 on Copy 2 of the CCF and reports the appropriate result to the employer.

If a laboratory also marks the dilute box, the MRO reports the verified test result (i.e., either "Positive" or "Negative"), marks the dilute box, and informs the employer that the

next time the donor is selected for a drug test the employer may require the specimen to be collected under direct observation because the specimen was dilute.

### **Rejected for Testing Result**

A laboratory will report a "Rejected For Testing" result and give the reason for rejecting the specimen when either of the following circumstances occur:

1. The specimen is not tested because a fatal flaw was identified when the specimen was accessioned (e.g., the specimen bottle seal was not intact upon receipt by the laboratory, the specimen ID number on the specimen bottle does not match the specimen ID number on the CCF, the specimen bottle contained insufficient volume, the specimen in Bottle A had a different appearance than the Bottle B specimen).
2. The specimen test result is not reported because the collection site was unable to provide a Memorandum for Record to correct/recover a flaw identified on the CCF or on the specimen bottle label/seal (e.g., the collector could not recall actually measuring the specimen temperature and had not checked the temperature box).

Note: If the collection site provides an MFR to correct/recover a flaw, the laboratory does not report a "Rejected for Testing" result but reports a "Negative" or "Positive" result as appropriate and a copy of the MFR is provided to the MRO when the test results are reported.

A "Rejected for Testing" result is determined by the MRO as a "Test Canceled" result. The MRO completes Step 6 on Copy 2 of the CCF and reports a "Test Canceled" result along with the reason for the cancellation to the employer. The MRO must also inform the employer that an immediate collection of another specimen is permitted, if the employer needs a "Negative" drug test result (e.g., pre-employment, return to duty, and follow-up tests require a "Negative" result).

### **Adulterated or Substituted Result**

Adulteration refers to a donor's attempt to externally add something to his or her urine specimen in an attempt to affect the drug test. There are several products sold through the internet and advertised in drug culture magazines for this intended purpose.

Substitution refers to a donor's attempt to replace his or her urine specimen with "clean" urine, synthetic urine, water, or other fluid during the collection procedure.

An "Adulterated" or "Substituted" result is determined by the MRO as a "Refusal to Test." The MRO completes Step 6 on Copy 2 of the CCF and reports a "Refusal to Test" result along with the reason to the employer.

Note: When a specimen is reported adulterated or substituted, the laboratory does not

report a "Positive" drug test result even though the laboratory may have conducted and completed the confirmatory test.

Note: When a specimen appears to have an interferant that prevents the detection of the drug/metabolite in the confirmatory test **and** there is significant reduction or no recovery of the internal standard even after multiple extraction attempts, the laboratory may consult with the MRO and send the specimen to another HHS certified laboratory that has the capability of conducting scientifically suitable validity tests to identify the interfering substance/adulterant. If this process does not identify the interferant, the second laboratory will report an "Invalid Result."

### **Invalid Result**

A laboratory will report an "Invalid Result" when either of the following circumstances occur:

1. The specimen is unsuitable for testing (e.g., physical appearance of the specimen is unacceptable and may affect the ability to analyze the specimen);
2. Valid initial drug test results cannot be obtained (e.g., a laboratory is unable to obtain a valid initial test result for each initial test and cannot specifically identify the cause); or
3. An unknown substance interferes with the confirmatory test.

The MRO must interview the donor to determine if the donor can provide any possible reason why the specimen could not be properly tested by the laboratory (e.g., medical illness, prescription medications, health food supplements).

Note: Tolectin® (Tolmetin - a non-steroidal anti-inflammatory medication), Flagyl® (metronidazole - an antifungal and antibacterial agent), and Cipro® (ciprofloxacin - an antibacterial agent) are the only known prescription medications that may interfere with some immunoassay tests.

If the donor is unable to give an explanation, provides a valid prescription for one of the above medications, or denies having tampered with the specimen, the MRO completes Step 6 on Copy 2 of the CCF, reports a "Test Canceled" result, and informs the employer that another specimen must be collected using a direct observed collection. The collection of a second specimen may possibly provide information needed to determine the reason why the first specimen was reported as "Invalid Result." If the second specimen collected using direct observation exhibits the same behavior as the first specimen, the MRO again reports the result for the second specimen as "Test Canceled" and recommends to the employer that no further action is required because the donor is either taking a valid prescription medication that interferes with the drug test or there is some unknown endogenous substance present in the donor's urine that prevents getting a valid drug test result.

### **C. Interview Donor**

For the situations described above that require the MRO to interview the donor, the MRO contact and interview with the donor must include the following steps:

1. The MRO or an assistant makes the initial contact with the donor as soon as possible after receiving the result from the laboratory. There are no specific regulatory time lines, but the first attempt to contact the donor is usually within 24 hours after receiving either the electronic transmission (if there is one) or the hard copy of the CCF (Copy 2) from the laboratory.
2. The MRO or an assistant makes a positive identification of the donor when the donor is actually contacted (e.g., asks the donor to provide his or her SSN).

Note: An assistant to the MRO may make the initial contact with the donor. This initial contact is useful since it is often time consuming to locate a donor, especially if the donor travels frequently or the donor's phone number is incorrect. The assistant's role must be limited to locating and making the initial contact with the donor. Once the donor is contacted and his or her identification is verified, the MRO must continue the interview.

3. The MRO tells the donor, before obtaining any information, that any confidential medical information provided by the donor during the review process may be disclosed to the employer.
4. The MRO informs the donor that the laboratory has reported either a "Positive" drug test result or an "Invalid Result."
5. The MRO asks the donor if there is any possible explanation for either result.

Note: If the donor voluntarily admits to illegal drug use consistent with the test results, the MRO must advise the donor that a verified "Positive" result will be reported to the employer.

Note: If the donor claims to have used a legally prescribed medication or the drug use was associated with a legitimate medical procedure, the MRO must require the donor to provide the appropriate documentation (e.g., medical record, doctor's report, copy of a prescription). The MRO must give the donor a deadline for submitting the medical information.

6. If a split specimen was collected and the Bottle A specimen was reported "Positive," the MRO informs the donor of the opportunity to request that the split specimen be tested. If the donor requests the split specimen to be tested, the MRO directs the laboratory to send Bottle B to another certified laboratory for confirmatory testing.
7. If the information submitted by the donor is or is not sufficient to support the legitimate medical use of a prescription medication that would cause the "Positive" test result for the drug reported by the laboratory, the MRO reports the result to the employer as a verified "Negative" or "Positive," respectively, and completes Step 6 on Copy 2 of the CCF.

Note: Ideally, the MRO is always able to contact the donor, obtain the appropriate information, and make a determination during or immediately after the interview. However, this is not always the case. Occasionally, the MRO is unable to contact the donor for various reasons (e.g., the donor has moved, no longer works for the employer, or was a job applicant and has moved).

The MRO may verify a positive test as "Positive" without having communicated directly with the donor (i.e., a non-contact determination) for the following reasons:

The donor expressly declines the opportunity to discuss the test result;

1. The MRO, after making all reasonable efforts, has not been able to contact the donor within 14 days of the date on which the MRO receives the "Positive" test result from the laboratory; or
2. The employer has contacted the donor and instructed the donor to contact the MRO, but the donor has not contacted the MRO within 5 days after being contacted by the employer.

The MRO must establish guidelines as to what constitutes a reasonable effort to contact the donor and must document all attempts that were made to contact the donor. When contacting the employer regarding the effort made to contact the donor, the MRO may not reveal the test result or any information about the drug test. The employer must confidentially direct the donor to contact the MRO within 5 days and must inform the MRO once the donor has been so instructed or if unable to contact the donor.

#### **D. Retest Request**

##### Single Specimen or Primary (Bottle A) Specimen

Before making a determination on a "Positive" test result, only the MRO is permitted to request a retest of a single specimen or the primary (Bottle A) specimen from a split specimen collection if there is any question regarding the accuracy or validity of the test result. The MRO's request must be based on a review of technical information (provided by the laboratory or donor) that makes the MRO believe that the result may be scientifically insufficient and, therefore, believes that a retest would be useful before making the determination.

Note: The MRO can request that the retesting of the original specimen be performed by the same laboratory or that an aliquot of the single specimen be sent for a retest to another certified laboratory. The Mandatory Guidelines are silent with respect to who chooses the second laboratory. The only requirement is that the second laboratory is certified by HHS whether it is chosen by the agency/employer, donor, MRO, or the first laboratory.

Note: It is unacceptable for an MRO to automatically request a retest on every specimen. There must be a sound justifiable scientific basis for each retest request.

Note: To ensure that a specimen is available if a retest is requested either by an MRO or by an official administrative or judicial proceeding, HHS requires laboratories to place all specimens confirmed positive in properly secured frozen storage for a minimum of one year. This is generally a sufficient amount of time to allow for a retest to occur; however, the time may be extended beyond one year by either the employer or an administrative/judicial official to allow completion of any litigation/arbitration that may be ongoing with the donor. If split specimens were collected, the laboratory keeps both specimen bottles frozen for one year. If Bottle B was sent to another laboratory for confirmatory testing, that laboratory retains Bottle B in frozen storage for one year.

The MRO must request the retest of a single specimen or the primary (Bottle A) specimen in writing (i.e., a memorandum or letter format). The written request may be mailed, faxed, or electronically sent to the laboratory where the specimen was tested and must contain the following information:

1. MRO name and address (use MRO letterhead);
2. Laboratory name and address (i.e., Laboratory A) where original analysis was performed;
3. Specimen I.D. Number (i.e., number on the Custody and Control Form);
4. Laboratory Accession Number (i.e., the number assigned by Laboratory A to the specimen when it was accessioned); and
5. Request confirmatory retest for the drug/metabolite reported by Laboratory A.

Note: If the retest is to be performed at a different certified laboratory (Laboratory B), the MRO also includes the name and address of this certified laboratory. Laboratory B may be selected by the MRO, the employer in its contract with the laboratory that tested the single specimen (Laboratory A), or by the donor.

Note: The result of a retest of a single specimen is reported by the laboratory using an appropriate laboratory report form to the MRO.

### Split (Bottle B) Specimen

After making the determination that the primary Bottle A specimen is "Positive," the MRO must inform the donor of his or her right to request an analysis of the split (Bottle B) specimen. The donor's request to have the split specimen tested must be made through the MRO. Although the time allowed for a retest request may vary, the donor is given a maximum of 72 hours to initiate the request. This will ensure that the analysis of the split specimen is performed in a timely manner.

The MRO must request the testing of the split (Bottle B) specimen in writing (i.e., a memorandum or letter format). The written request may be mailed, faxed, or electronically sent to the laboratory where the specimen was tested and must contain the following information:

1. MRO name and address (use MRO letterhead);
2. Laboratory name and address (i.e., Laboratory A) where analysis of the primary (Bottle A) specimen was performed;
3. Specimen I.D. Number (i.e., number on the Custody and Control Form);
4. Laboratory Accession Number (i.e., the number assigned by Laboratory A to the specimen when it was accessioned);
5. Request confirmatory test for drug/metabolite reported by Laboratory A; and
6. Name and address of the laboratory (i.e., Laboratory B) selected to test the Bottle B specimen.

Note: Laboratory B may be selected by the MRO, the employer in its contract with Laboratory A, or by the donor.

Note: Laboratory B will report the result for the split (Bottle B) specimen on Copy 1 of the CCF to the MRO. The MRO reports the result to the employer and the donor.

## **E. Retest Result**

### Single Specimen or Primary (Bottle A) Specimen

If the retesting of the original specimen fails to reconfirm the original laboratory result, the MRO will report the result as "Negative" to the employer.

Note: Since this retest was performed because the MRO had concerns regarding the validity of the positive test result reported by the laboratory, the MRO cannot make a determination before the retest result is reported to the MRO by the laboratory.

Note: When a retest does not reconfirm the presence of a drug, the MRO must contact the appropriate regulatory office. The regulatory office will conduct an investigation to determine the reason for not reconfirming the presence of the drug and to ensure that appropriate corrective action is implemented.

### Split (Bottle B) Specimen

If the testing of the split (Bottle B) specimen reconfirms the presence of the drug/drug metabolite, the MRO verifies the result for the split (Bottle B) specimen as "Reconfirmed" on Copy 2 of the CCF.

If the testing of the split (Bottle B) specimen fails to reconfirm the result reported by the laboratory that tested the primary (Bottle A) specimen, the MRO verifies the result as "Failed to Reconfirm" along with the reason on Copy 2 of the CCF

Note: Since the "Positive" result for the primary (Bottle A) specimen had been reported to the employer by the MRO, the employer will be required to reverse any personnel action that may have been taken against the donor. Additionally, the donor reenters the group of individuals subject to random testing as if the test had not been conducted.

Note: The Federal agency must notify the appropriate regulatory office whenever a "Failed to Reconfirm" result has occurred on a split (Bottle B) specimen. The regulatory office will investigate the "Failed to Reconfirm" result and attempt to determine the reason for the inconsistent results. HHS will report its findings to the Federal agency including recommendations and/or actions taken to prevent the recurrence of the "Failed to Reconfirm" result.

There is a technical problem that occasionally occurs when Laboratory B retests an aliquot of a single specimen or tests a split (Bottle B) specimen that had been reported "Positive" by Laboratory A. Laboratory B is unable to reconfirm the presence of the drug or metabolite reported by Laboratory A because it uses a different analytical procedure and/or instrumentation. These differences occasionally prevent a Laboratory B from reconfirming the presence of a drug or metabolite because the analytical results do not satisfy all the criteria required to make a positive identification.

Note: If Laboratory B believes that the drug or metabolite is present in the aliquot of the single specimen or the split (Bottle B) specimen that was received from Laboratory A, but cannot reconfirm the presence of the drug or metabolite, Laboratory B, after consultation with the MRO, may send the aliquot of the single specimen or the split (Bottle B) specimen to Laboratory C for confirmatory testing. The MRO may also request Laboratory A to send another aliquot of the single specimen to Laboratory C if there is an insufficient quantity of urine remaining in the aliquot of the single specimen tested at Laboratory B. Laboratory C should be selected such that it uses a confirmation method more similar to that used by Laboratory A.

## **F. Report Verified Result to Employer**

The MRO may report all verified (negative and non-negative) results to the agency/employer by either faxing a completed Copy 2, transmitting a scanned image of a completed Copy 2, or faxing a separate report using a letter/memorandum format. A verified result may not be reported to the employer until the MRO has completed the review process. The MRO must send to the agency/employer a hard copy of either the completed Copy 2 or the separate letter/memorandum report for all non-negative results.

Note: If the MRO uses a letter or memorandum format, it must include, at a minimum, the following: donor name and/or SSN, specimen I.D. number from the CCF, the verified test result (if positive, list specific drug(s)), the MRO's printed name and signature, and the date the determination was made. The MRO may list results for several specimens on one memorandum or letter. The MRO report may include relevant comments provided by the collector and/or laboratory on the CCF as well as other information, such as, documentation of attempts to contact the donor or a statement of the donor's refusal to cooperate with the medical review process. The MRO may add any information provided by the donor (especially at the donor's request) to the verified result report. Such additional information must not, however, reveal specific confidential

medical information.

## **G. Full Documentation Package**

A donor or employer will occasionally request the testing laboratory to provide a complete package of analytical data, chain of custody records, and other administrative documents associated with the testing of a particular specimen. This package is generally referred to a "full documentation package"

The request must always be submitted to the laboratory through the MRO. A full documentation package must include copies of the batch test results that contain the test result for the donor's specimen, internal and external chain of custody documents for the batch of specimens that contain the donor's specimen, and any other relevant information pertaining to the testing of the donor's specimen.

Although each documentation package is different, it must contain all the information needed to determine if the test result reported by the laboratory is, in fact, scientifically and forensically supportable. The MRO is encouraged to contact the laboratory to discuss the information contained in the documentation package prior to sending it to the donor or employer. The MRO may find that additional information (e.g., a description of the laboratory's chain of custody procedures, a description of the laboratory's quality assurance program) would be helpful in reviewing the full documentation package.

## **H. Occupational and Public Safety**

Executive Order 12564 used the term "illegal drugs" to refer to any controlled substance that was included in Schedule I or II of the Controlled Substances Act. The Executive Order also stated that the term illegal drugs "does not mean the use of a controlled substance pursuant to a valid prescription or other uses authorized by law."

Note: The purpose of this policy is to ensure that a Workplace drug testing program does not intentionally identify an individual who is receiving legitimate medical care and, thereby, provides confidential medical information to an employer or anyone else.

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

If the side effects of a legitimately prescribed medication have a possible impact on the safety aspects of the work performed by a donor, the MRO must decide what must be done with the information. Although the Guidelines require an MRO to verify a drug test result as a negative result if the donor has legally taken a prescription medication, it is recommended that the MRO contact the prescribing physician to discuss the possible

impact that the medication may have on the safety aspects of the work performed by the donor. Additionally, some occupations have restrictions that prohibit an individual from taking specific medications which may, otherwise, be allowable for other occupations. In these instances, the MRO may inform the individual responsible for certifying that the donor is qualified to perform that job that the donor is taking a medication that is restricted for an individual in that occupation or that the medication may affect the individual's ability to perform a safety sensitive occupation.

## **I. State Initiatives and Laws**

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

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

Note: Medical Review Officers shall not accept a prescription or the verbal or written recommendation of a physician for a Schedule I substance as a legitimate medical explanation for the presence of a Schedule I drug or metabolite in a Federal employee/applicant specimen.

## **Chapter 4. Specific Drug Class Issues**

### **A. Amphetamines**

#### **1. Background**

Amphetamine and methamphetamine are substances regulated under the Controlled Substances Act (CSA, 21 U.S.C. § 801 et seq.), and implementing regulations as Schedule II stimulants (see 21 CFR § 1308.12(d)). Schedule II substances have legitimate medical uses, but also have a high potential for abuse. Both drugs have been used for treating attention deficit disorder in children, obesity, and narcolepsy.

Amphetamine and methamphetamine are central nervous system stimulants. A single therapeutic dose often enhances attention and performance, but exhaustion eventually occurs and performance deteriorates as the effects wear off. Frequently, repeated high-dose use produces lethargy, exhaustion, mental confusion, and paranoid thoughts.

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

Amphetamine and methamphetamine are usually taken orally as tablets or capsules. Abusers inject the drugs intravenously, sometimes take them by intranasal "snorting," and by smoking. Absorption from the gastrointestinal tract is good and they are distributed throughout the body.

## **2. Metabolism and Excretion**

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

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

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

Methamphetamine and amphetamine 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.

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

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

illegal use.

Illegally manufactured amphetamine and methamphetamine often contain significant amounts of the *l*- isomer of each substance. This depends on the starting materials used by the clandestine laboratories.

The following prescription medications contain *d*-amphetamine or racemic *d,l*-amphetamine (i.e., equal amounts of *d*- and *l*-amphetamine):

Adderall®  
Benzedrine®  
Biphphetamine®  
Dexedrine®  
Durophet®  
Obetrol®

The following prescription medication contains *d*-methamphetamine:  
Desoxyn® (Gradumet®)

The following substances are known to metabolize to methamphetamine (and amphetamine):

Benzphetamine (Didrex®)  
Dimethylamphetamine  
Famprofazone  
Fencamine  
Furfenorex  
Selegiline (Deprenyl, Eldepryl®)

The following substances are known to metabolize to amphetamine:

Amphetaminil  
Clobenzorex (Dinintel®, Finedal®)  
Ethylamphetamine  
Fenethylamine (Captagon®)  
Fenproporex (Tegisec®)  
Mefenorex (Pondinil®)  
Mesocarb  
Prenylamine

Note: These lists are not all inclusive.

### **3. Interpreting Laboratory Result**

The donor provides the following response:

- a. Claims to have been taking a prescription medication.

(1) The MRO requests the donor to provide a copy of the prescription or the sample bottle with the appropriately labeled prescription.

Note: The prescription must be for a drug that contains either amphetamine, methamphetamine, or a substance that can metabolize to amphetamine or methamphetamine. If the prescription does not satisfy this requirement, the drug in the prescription provided by the donor is not a valid medical explanation for the positive amphetamine result and the "Positive" laboratory result is verified as a "POSITIVE."

Note: If the donor had completed taking the prescribed medication by the time he or she is contacted, the donor may no longer have the prescription bottle. When this occurs, the donor must provide a copy of the medical record that documents the valid medical use of the drug during the time of the drug test. There may be a need to contact the prescribing physician or the pharmacist who filled the prescription to verify the information provided by the donor.

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

Note: Selegiline is a brain monoamine oxidase inhibitor used in the adjunctive treatment of Parkinson's disease and for depression. Selegiline is metabolized to *l*-methamphetamine and *l*-amphetamine. A *d*- and *l*- isomer differentiation will reveal the presence of only *l*-methamphetamine and *l*-amphetamine after the ingestion of Selegiline.

(2) If this alternative medical explanation is substantiated for a specimen containing only *l*-methamphetamine/*l*-amphetamine, the MRO must verify and report the result as a "Negative."

b. Claims to have used a Vicks Inhaler®.

(1) Since the Vicks Inhaler® contains *l*-methamphetamine, there is a possibility that a laboratory positive result could be reported for *l*-methamphetamine and/or *l*-amphetamine.

(2) The MRO may request the laboratory to perform a *d*-, *l*- isomer differentiation.

Note: Although one would expect to see 100% *l*-methamphetamine following Vicks Inhaler® use, there may be a trace amount of *d*- isomer present because a very slight amount of *d*-methamphetamine may be present as a contaminant in the Vicks Inhaler® and a contaminant of the analytical procedure.

(3) After the laboratory conducts the isomer differentiation, if there is greater than

80% *l*-methamphetamine, the results are considered to be consistent with Vicks Inhaler® use and the result is verified as a "Negative."

Note: This is a very conservative interpretation.

(4) If there is more than 20% *d*-methamphetamine present, the results indicate the use of some source other than the inhaler and the result is verified as a "Positive."

c. Claims to have used other over-the-counter medications.

(1) The MRO would verify the laboratory result as a "Positive."

Note: There are no over-the-counter medications, other than the Vicks Inhaler®, that contain either *d*- or *l*- methamphetamine or amphetamine. Although we know that some sympathomimetic amines can test positive on an immunoassay test, they will not be reported positive by the laboratory after conducting the confirmatory test; the confirmatory GC/MS test is specific for methamphetamine and amphetamine.

The NLCP requires that a specimen reported as a "Positive" for methamphetamine only (i.e., above the confirmatory test level of 500 ng/mL), it must also contain amphetamine (which is a metabolite of methamphetamine) at a concentration equal to or greater than 200 ng/mL. The amphetamine will not be reported as "Positive" by the laboratory unless its concentration exceeds the 500 ng/mL confirmatory test level. In the case of a report stating only a methamphetamine positive, the MRO may contact the laboratory to verbally confirm that amphetamine was present between 200 and 500 ng/mL.

d. Admits or denies using any substance illegally. The MRO verifies the result as a "Positive" for amphetamine and/or methamphetamine.

## **B. Cocaine**

### **1. Background**

Cocaine is an alkaloid from the coca plant, *Erythroxylon coca*. It usually is obtained as cocaine HCl, but those who smoke the drug prepare the "freebase" or "crack" form, chemically removing the HCl. This form better survives the high temperatures involved in smoking.

Cocaine is widely used in the United States, and unlike most other drugs, its prevalence of abuse continues to expand.

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

Cocaine abusers, even if they do not use the drug at work, often report vocational impairment due to exhaustion; they use the drug until late at night. Among chronic users, exhaustion, lethargy, and mental depression appear, and the stimulant effect may seem progressively weaker. But the drug is highly reinforcing; repeated experiences with it tend to drive further episodes of self-administration. After repeated exposures, many patients say that although the drug no longer produces much of a "high," they are unable to abstain.

Short-term tolerance (tachyphylaxis) develops when several doses of cocaine are administered over a brief period. Reports of weaker "highs" with repeated use also suggest tolerance. However, animal studies show "reverse tolerance," with certain behavioral effects becoming stronger upon repeated administration. So the question of tolerance to cocaine remains an area for further research. Patients withdrawing from cocaine experience moderate lethargy and drowsiness, severe headaches, hyperphagia, vivid dreams, and some mental depression. These symptoms usually abate within a few days to a few weeks.

Cocaine usually is taken by one of three routes: intranasal "snorting" is the most common; its "freebase" or "crack" form of the drug is smoked, utilizing the pulmonary route; and intravenous injections.

## **2. Metabolism and Excretion**

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

## **3. Interpreting Laboratory Result**

The donor provides the following response:

- a. Claims to have used a prescription medication or was given cocaine during a medical or dental procedure.

Note: 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. Cocaine is structurally unique and does not resemble any of the other topical anesthetics, such as Novocain®, Xylocaine® (lidocaine), benzocaine, etc. Although these compounds have analgesic properties, there is no structural similarity to cocaine or its metabolite (benzoylecgonine).

(1) Request the donor to provide a copy of the medical record that documents the recent use of cocaine as a topical anesthetic.

(2) If this alternative medical explanation is substantiated, the MRO must verify and report the result as a "Negative."

Note: Keep in mind that the medical use must have occurred within 2 to 3 days prior to when the urine specimen was collected. Use at an earlier time will not cause a positive urine test.

b. Claims passive inhalation of crack cocaine.

(1) Allow the donor to describe the circumstances pertaining to how and when the passive exposure occurred.

(2) Passive inhalation is not an alternative medical explanation for the presence of benzoylecgonine in the donor's urine.

Note: A comprehensive study conducted at NIDA's Addiction Research Center (E.J. Cone, D. Yousefnejad, M.J. Hillsgrove, B. Holicky, and W.D. Darwin. Passive Inhalation of Cocaine. J.Anal.Toxicol. 19:399-411(1995)) has demonstrated that individuals passively exposed to "crack" smoke did not produce a urine positive for cocaine using the established testing levels.

(3) MRO verifies and reports the result as a "Positive."

c. Claims to be ingesting "Health Inca Tea."

Note: In the early 1980s, health food stores were selling a tea under the tradename "Health Inca Tea." When it was discovered that this tea contained decocanized coca leaves with detectable amounts of cocaine present, the U. S. Food and Drug Administration banned the importation of this tea into the United States. Therefore, any tea being sold using the name "Health Inca Tea" should not contain any cocaine.

(1) Allow the donor to explain where and when the tea was purchased.

(2) Drinking "Health Inca Tea" is not an alternative medical explanation for the presence of benzoylecgonine in the donor's urine.

(3) MRO verifies and reports the result as a "Positive."

d. Admits or denies using cocaine. The MRO verifies the result as a "Positive" for cocaine.

## C. Marijuana

## **1. Background**

Marijuana comes from the hemp plant, *Cannabis sativa*. The principal psychoactive agent in marijuana is delta-9-tetrahydrocannabinol (THC).

Marijuana produces a pleasant euphoria or "high," commonly followed by drowsiness. Intoxication temporarily impairs concentration, learning, and perceptual-motor skills. Thus, for at least 4-6 hours after a dose of marijuana, employees probably function with reduced abilities. Preliminary studies suggest that performance is impaired long after the acute subjective effects have ended. Experienced pilots in a flight simulator were impaired for at least 24 hours after a dose, long after the subjective "high" had disappeared. Functional impairments are less well understood in cases of prolonged, heavy marijuana use, because although THC accumulates in the body, behavioral and physiological tolerance also develops.

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

## **2. Metabolism and Excretion**

Marijuana is usually smoked; transpulmonary absorption rapidly gets psychoactive drugs to the brain. Since the drug also is absorbed from the gastrointestinal tract, although much more slowly, marijuana sometimes is eaten. THC leaves the bloodstream and is distributed into different parts of the body where it is metabolized, excreted, or stored. The THC that is stored in fatty tissue gradually reenters the blood stream at very low levels, permitting metabolism and eventual excretion. THC is metabolized extensively in the liver and the major metabolite is 11-nor-tetrahydrocannabinol -9-carboxylic acid (delta-9 THCA).

The immunoassay procedures detect multiple metabolites of marijuana, while the GC/MS procedure specifically identifies and quantitates the delta-9 THCA metabolite. To be reported positive, a specimen must screen positive at or above the 50 ng/mL cutoff and have a concentration of the delta-9 THCA that is equal to or greater than the 15 ng/mL confirmatory cutoff level. Considering these cutoffs, a person with no marijuana experience who smokes a single marijuana cigarette may be positive for 1-3 days. But with repeated smoking, THC accumulates in fatty tissue; so frequent, chronic smokers slowly release THC over a longer time and may continue to produce detectable levels below the cutoff values for longer periods of time (depending upon the assay cutoff).

## **3. Interpreting Laboratory Result**

The donor provides the following response:

- a. Claims to have used a prescription or over-the-counter medication.

Note: Dronabinol is chemically synthesized delta-9- tetrahydrocannabinol (THC). It is available under the trade name Marinol® in 2.5, 5, or 10 mg soft gelatin capsules for oral administration. Marinol® may be used for stimulating appetite and preventing weight loss in patients with a confirmed diagnosis of AIDS and treating nausea and vomiting associated with cancer chemotherapy. Additionally, a few individuals have been permitted by a court order to use THC for the management of glaucoma. Patients that are prescribed Marinol® should be warned not to drive, operate complex machinery, or engage in hazardous activity.

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

(1) Request the donor to provide a copy of the medical record or court order that would document the legal use of Marinol® or marijuana.

(2) If this alternative medical explanation is substantiated, the MRO must verify and report the result as a "Negative."

- b. Claims passive inhalation or unknowing ingestion.

Note: Passive inhalation, unknowing ingestion (i.e., an inadvertent exposure to marijuana), or eating hemp seeds is frequently claimed as the basis for a positive urine test. Passive inhalation of marijuana smoke does occur and can result in detectable levels of THC and its metabolites in urine. Clinical studies have shown, however, that it is highly unlikely that a nonsmoking individual could unknowingly inhale sufficient smoke by passive inhalation to result in a high enough drug concentration in urine for detection at the cutoff levels used in the Federal program. Similarly, it is extremely difficult to achieve detectable levels through unknowing ingestion of hemp plant material (such as, leaves, stems) or eating food products containing hemp seeds. The studies also show that any measurable peak concentration in urine occurs within several hours after the exposure.

(1) Allow the donor to describe the circumstances pertaining to how and when the passive exposure, unknowing ingestion, or eating hemp seeds occurred.

(2) Generally, the circumstances will not approximate what would be needed to explain the presence of THC in the donor's urine.

(3) MRO verifies and reports the result as a "Positive."

Note: Additionally, none of the reasons mentioned in b1 above constitute an alternative medical explanation.

- c. Admits or denies using marijuana. The MRO verifies the result as a "Positive" for cannabinoids.

## **D. Opiates**

### **1. Background**

Opioids are a large class of analgesic drugs, the effects of which are stereospecifically antagonized by naloxone. Opiates refer to natural products derived from the juice of the opium poppy (loosely applied to morphine derivatives). The opium poppy flower is the source of the natural opiate prototype alkaloid, morphine. The opium poppy is also the source of the naturally occurring alkaloid codeine; codeine is also synthesized chemically for inclusion in medications available through prescription and over-the-counter. Heroin (or diacetylmorphine) is a semisynthetic opiate obtained by reacting natural morphine with acetic acid. Heroin has no legitimate medical uses in the United States and is only available illegally (DEA Schedule I).

Opioid intoxication may cause miosis, a dull facies, confusion or mental dullness, slurring of speech, drowsiness, partial ptosis, or "nodding" (the head drooping toward the chest and then bobbing up).

Tolerance develops to opioid effects, and abusers escalate doses when possible. Physical dependence results in a moderate, nonlethal, "flu"-like abstinence syndrome with nausea, diarrhea, coryza, occasional vomiting, weakness, malaise, "gooseflesh," and mydriasis. All opiates are physically and psychologically addictive, and produce withdrawal symptoms that differ in type and severity. Flu-like symptoms are common during opiate withdrawal, e.g., watery eyes, nausea and vomiting, muscle cramps, and loss of appetite.

Heroin and morphine are usually injected, but may be smoked as opium once was, or "snorted" (insufflated) onto the nasal mucosa.

Cognitive and psychomotor performance can be impaired by opiates, although the duration and extent of impairment depend on the type of opiate, the dose, and the experience and drug history of the user. Ingestion of low to moderate amounts produces a short-lived feeling of euphoria followed by a state of physical and mental relaxation that persists for several hours.

The following prescription medications contain morphine:

Astramorph PF®

Duramorph®

MSIR®

MS Contin Tablets®

Roxanol®

The following prescription medications contain codeine:

Actifed with Codeine Cough Syrup®

Codimal PH® Syrup

Dimetane-DC Cough Syrup®

Emprin with Codeine®

Fiorinal with Codeine®

Phenaphen with Codeine®

Robitussin A-C®

Triaminic Expectorant with Codeine®

Tylenol with Codeine(#1, 2, 3, or 4)®

Tussar-2®

Note: The above lists are only a representative sample of the prescription medications that contain codeine or morphine.

The following nonprescription products contain opium (i.e., morphine):

Amogel PG®

Diabismul®

Donnagel-PG®

Infantol Pink®

Kaodene with Paregoric®

Quiagel PG®

Paregoric

The following nonprescription product contains codeine:

Kaodene with Codeine®

Note: Each listed nonprescription product is used as an antidiarrheal. They are generally available over-the-counter; however, nonprescription sale is prohibited in some states. Paregoric alone is a Schedule III prescription drug, but in combination with other substances is a Schedule V over-the-counter product.

The following substance metabolizes to morphine:

Heroin

## **2. Metabolism and Excretion**

Heroin (diacetylmorphine) is rapidly deacetylated to 6-acetylmorphine (6-AM; also called 6-monoacetylmorphine, 6-MAM), and, therefore, heroin itself is rarely ever detected in the urine. Heroin's characteristic metabolite, 6-AM, is rapidly deacetylated to morphine, and will likely not be detected in most urine specimens of heroin users. Since codeine is a naturally occurring alkaloid in the same opium poppy juice that is the source of morphine used as the starting material for heroin synthesis, codeine may be found in the urine of heroin users.

Morphine is rapidly absorbed and excreted as unchanged morphine and as conjugated

glucuronides (i.e., morphine-3-glucuronide, morphine-6-glucuronide). The primary metabolite is morphine-3-glucuronide. Morphine and its metabolites can be detected in urine up to about 4 days after its use.

Codeine (methylnorphine) is also rapidly absorbed and is excreted as unchanged codeine, morphine, and glucuronide conjugates.

Since the body metabolizes codeine to morphine, both substances (i.e., codeine and morphine) may occur in the urine following the use of codeine. Recently ingested codeine explains the presence of both drugs in the urine specimen (i.e., parent drug codeine and morphine metabolite). After the ingestion of a legitimate medical preparation containing codeine, there comes a time when parent codeine has been completely excreted or metabolized to morphine, so that morphine only is detected in the urine.

Ingestion of morphine in any form will never account for the presence of codeine in the urine (codeine is not a metabolite of morphine).

Note: There are a number of synthetic or semisynthetic analgesics available including, but not limited to, alphaprodine (Nisentil®), hydromorphone (Dilaudid®), oxymorphone (Numorphan®), hydrocodone (Hycodan®), dihydrocodeine (Paracodin®), oxycodone (Percodan®), propoxyphene (Darvon®), methadone (Dolophine®), meperidine (Demerol®), fentanyl (Sublimaze®), pentazocine (Talwin®), and buprenorphine (Buprenex®). These drugs do not metabolize to either codeine, morphine, or 6-acetylmorphine. When a donor presents a prescription for a narcotic analgesic, the MRO must verify that it does not contain codeine or morphine and, therefore, cannot metabolize to codeine, morphine, or 6-acetylmorphine.

### **3. Interpreting Laboratory Result**

The opiate drug class poses some unique challenges with regard to interpreting a positive test result. A positive for codeine or morphine may be a result of a donor having taken a prescription medication that contains codeine or morphine or a donor consuming normal dietary amounts of poppy seeds. In addition, for the opiate drug class, there is a requirement to document clinical evidence of illegal use.

Note: Before an MRO verifies a confirmed positive result for opiates, he or she shall determine that there is clinical evidence - in addition to the urine test - of illegal use of any opium, opiate, or opium derivative. The main issue is the MRO must substantiate that there is "clinical evidence of illegal use" of an opiate substance before a positive result reported by a laboratory can be verified as a "Positive." Clinical evidence of illegal use may include, but is not limited to: a donor admits taking a prescription medication containing codeine or morphine that was prescribed to another individual; recent needle marks; or behavioral and psychological signs of acute opiate intoxication or withdrawal. If "clinical evidence of illegal use" is not present, the MRO must verify the "Positive" result reported by the laboratory as a "Negative" result to the employer.

Note: The 6-acetylmorphine metabolite comes only from heroin; therefore, its presence confirms the illegal use of heroin. When the presence of 6-AM is confirmed, there is no requirement for clinical evidence.

Note: For a positive morphine or codeine test result, an MRO may have a blanket written request on file at the laboratory to routinely receive the quantitative values associated with a positive codeine and morphine result. The MRO also may request quantitative information on the presence of codeine below the cutoff for specimens which have been reported positive for morphine only. This information may be helpful to the MRO in assessing the medical explanation provided by the donor.

Note: Quantitative test results may not be requested by the MRO from the testing laboratory on a routine basis for the other drug categories, but may be requested on a case-by-case basis.

The donor provides the following response:

- a. Admits taking morphine or codeine illegally or using heroin. The MRO verifies the result as a "Positive" for the drug reported by the laboratory.
- b. Claims to have taken a prescription medication.

The MRO requests the donor to provide a copy of the prescription or the medication with the appropriately labeled prescription.

Even if no valid medical explanation is provided by the donor, the MRO must verify and report the result as "Negative" unless there is clinical evidence of the abuse or illegal use of opiate drugs.

Note: The presence of 6-acetylmorphine (6-AM) confirms the illegal use of heroin and, therefore, it is not necessary to verify clinical evidence of illegal use.

Note: The MRO must verify as "Negative" any codeine or morphine test result for which the donor has taken a legally prescribed codeine or morphine medication.

Note: Occasionally, a donor will reveal information regarding the use of a narcotic analgesic (that does not contain codeine or morphine) believing that this medication was the reason for the positive codeine or morphine. Assuming that it was a legally prescribed medication, this confidential medical information cannot be provided to the employer and is not an explanation for the positive codeine or morphine. Since the use of a narcotic analgesic may have a possible effect on the ability of the donor to perform a specific task (such as, driving a vehicle), it may be appropriate to discuss the use of the medication with the prescribing physician. See Section G in Chapter 4 regarding the reporting of this information.

- c. Claims to have eaten foods that contain poppy seeds.

One reason for the requirement for clinical evidence of abuse or illegal use in opiate testing is that eating a normal dietary amount of poppy seeds can cause a urine specimen to test positive for morphine and codeine (i.e., they contain trace amounts of morphine with or without codeine). In many instances, a donor will not know that poppy seeds can cause a positive test or that he or she had eaten poppy seeds at the time the urine was collected. The concentration of morphine can be substantial, with usually very low concentrations or no detectable codeine. Unless clinical evidence of abuse or illegal use of opiates is verified, the MRO must verify and report the result as a "Negative."

## **E. Phencyclidine**

### **1. Background**

Phencyclidine (PCP), an arylcyclohexylamine, was first synthesized in the 1950's as a general anesthetic. Street names include Angel Dust, Crystal, Killer Weed, Supergrass, and Rocket Fuel. PCP's synthesis is relatively simple for clandestine laboratories. Phencyclidine's use as a human anesthetic was discontinued because it produced psychotic reactions ("emergence delirium"), and its more prolonged use as a veterinary tranquilizing agent also has stopped. PCP is currently a DEA Schedule II controlled substance, has no current therapeutic role, and all uses are illegal. The preferred route of ingestion is smoking, but it may be eaten, snorted, or injected intravenously.

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

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.

### **2. Metabolism and Excretion**

PCP is well absorbed by any route and is excreted as unchanged PCP and as conjugates of hydroxylated PCP. About 10 percent of the PCP dose is excreted in the urine as the parent compound. PCP is a weak base which concentrates in acidic solutions in the body. Because of gastric acidity, PCP repeatedly reenters the stomach from plasma, later returning into plasma from the basic medium of the intestine.

Generally, PCP is considered detectable in urine for several days to several weeks

depending on the frequency of use.

### **3. Interpreting Laboratory Result**

The donor provides the following response:

- a. Admits or denies using PCP. The MRO verifies the result as "Positive" for PCP.
- b. Claims to have taken a prescription or over-the-counter medication. The MRO verifies the result as "Positive" for PCP. There are no prescription or over-the-counter medications that contain PCP, legal medical uses of PCP, or any other substances that can be misidentified as PCP using gas chromatography/mass spectrometry.

## **Chapter 5. Documentation and Recordkeeping**

### **A. Recordkeeping**

Accurate recordkeeping is essential in documenting all aspects of the MRO review process. All communications, written or oral (including, but not limited to, those with donors, employer representatives, laboratory personnel, and collectors) must be appropriately documented.

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

Note: This two-year recommendation agrees with the requirement that each laboratory must retain records associated with the testing of a specimen for a minimum of 2 years.

No regulatory requirements exist requiring MROs to use a specific procedure to review drug tests; however, using a standard procedure is likely to ensure that each MRO review is complete and thorough. The use of a simple checklist will ensure that certain activities are always documented.

Documentation must normally include such things as copies of prescriptions or labels on prescription bottles, or notes that a prescription was verified at a pharmacy or by the treating physician. Any letters or notes received from an employee, relative, or physician providing treatment must be retained in the file.

Finally, MRO records must be separated from other medical and personnel records kept on an individual. For example, some physicians may also serve as a primary care provider and retain medical records related to that function.

### **B. Confidentiality**

The Guidelines require the MRO to report the final result of the drug test to an employer

in a manner designed to ensure the confidentiality of the information. The MRO also has a responsibility to maintain the confidentiality of the information received during the review process, including information related to the donor's medical condition, medications, medical diagnosis, and medical history. This role is particularly important with respect to confirmed "Positive" drug test results, and especially for those that may be verified by the MRO as "Negative" due to an alternative legitimate medical explanation.

Despite this general requirement to maintain the confidentiality of medical information, there are certain circumstances in which the MRO may provide such information to other parties. In these instances, the MRO must inform the donor, prior to the medical interview, that disclosure of information learned as part of the medical review process may occur if, in the judgment of the MRO, the information suggests there is a significant safety hazard associated with the information or there is a medical disqualification of the donor under an applicable regulation.

Note: Such information may also be released under other circumstances specified by Federal agency regulations.

Even when the MRO releases otherwise confidential information due to such concerns, the MRO must attempt to release as little specific information as possible and release such information only to parties with a clear need-to-know. Such parties include physicians responsible for medical certification of the donor, Federal agency officials as required by regulation, or designated employer representatives.

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

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

## **Chapter 6. Additional MRO Responsibilities**

### **A. Blind Quality Control Samples**

Federal agencies and most employers regulated by DOT are required to have blind quality control samples submitted with the donor specimens. Blind quality control

samples are helpful in determining if the entire testing process (i.e., from the collection of the specimen until a result is reported by the MRO) satisfies all requirements.

The blind quality control samples must be certified by immunoassay and GC/MS and have stability data which verifies their performance over time. The requirement to have certification data ensures that the blind quality control samples purchased from different sources are acceptable.

Generally, the employer will request the collector to purchase the blind samples or may provide them to the collector. In either case, the collector must submit each quality control sample as if it were a donor specimen. This requires completing a CCF and properly labeling a specimen bottle. Since there is no donor associated with a quality control sample, the collector must generate a fictitious social security number or employee identification number and fictitious initials to be written on the specimen bottle label/seal. On Copy 2 of the CCF (MRO copy), the collector must indicate that the specimen is a "Quality Control Sample" where a donor would normally print his or her name. In addition, the collector or the employer, whichever purchased the blind samples, must forward that information to the MRO. This will allow the MRO to determine if the laboratory reported the correct result.

Note: An incorrect result reported by the laboratory does not automatically indicate that the laboratory made an analytical error. For example, there could have been a problem with the stability and/or concentration of the quality control sample or the collector did not properly submit the sample.

If the laboratory reports a result different from the one expected based on information provided by the manufacturer of the blind sample, the MRO must contact the laboratory to determine if there is an obvious reason why the laboratory did not report the expected result. If there is no obvious reason, the MRO may request the laboratory to retest the specimen or have an aliquot sent to another certified laboratory for confirmatory testing. If the retest result confirms the original result reported by the laboratory, it is most likely that an error occurred at the collection site or there was a problem with the quality control sample as purchased. If the retest result does not confirm the original result, the laboratory likely made an error.

Note: A false negative result (i.e., the laboratory reports a negative on a blind sample when a positive result was expected) is a concern, but must not be considered serious unless it occurs frequently and the MRO would not be expected to request the laboratory to retest the blind sample. However, a false positive (i.e., the laboratory reports a positive on a blind sample when a negative result is expected) is serious and

must be investigated.

If the retest result has confirmed that a false positive was reported by the laboratory on a blind quality control sample, the MRO must contact the employer. The MRO must then contact the appropriate regulatory office who will conduct an investigation in an attempt to determine the exact cause of the false positive. When the specific cause is identified, appropriate corrective will be taken. The regulatory office will share the findings with the MRO.

## **B. Shy Bladder**

Occasionally, a donor is unable to provide a specimen upon arrival at the collection site because he or she either urinated recently or has a "shy bladder." Generally, the term "shy bladder" refers to an individual who is unable to provide a sufficient specimen either upon demand or when someone is nearby during the attempted urination.

If it is believed that an individual has a "shy bladder," the employer must arrange to have the donor evaluated, as soon as practical after the attempted collection, by a licensed physician (e.g., the MRO, a physician acceptable to the employer, the employer's occupational health physician) to determine whether the donor's inability to provide a specimen is genuine or constitutes a refusal to provide a specimen.

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

Unsupported assertions of "situational anxiety" or dehydration are not considered valid reasons for a donor's failure to provide an adequate amount of urine when sufficient time has elapsed and fluid volume has been ingested and shall be regarded as a refusal to take a test.

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

### **C. Testing for an Additional Drug**

HHS certified laboratories may only test regulated specimens for amphetamines, marijuana, cocaine, opiates, and phencyclidine. However, testing for an additional drug may occur for the following reasons:

1. There is reasonable suspicion/cause or a post accident incident for which testing for another drug listed in Schedule I or II of the Controlled Substances Act is justified; or
2. A Federal agency was granted a waiver by the Secretary of HHS to routinely test its employees for another drug or drug class.

For any circumstance where testing for an additional drug is justified or authorized, the collector marks the "Other" box in Step 1 on the CCF and specifies the name of the drug(s) to be tested. There must also be a memorandum from the Federal agency attached to the CCF explaining why the specimen is being tested for the additional drug. Otherwise, the laboratory must not test for that additional drug.

Since the MRO will be reviewing a test result that is not a normal part of the Federal Workplace Drug Testing Program, the MRO may want to obtain a full documentation package from the laboratory to assess the forensic and scientific acceptability of the test result.