Drug Testing in Urine, Oral Fluid, and Hair

Part 2: Analysis

2019

This is the second of a two-part Drug Testing Matters series on drug testing of urine, oral fluid, and hair. This part discusses the collection and testing of each matrix and provides a comparison of the use of these three matrices.

Urine has been the only approved matrix for federal workplace drug testing programs since 1988. However, in 2015, *proposed* Mandatory Guidelines were published that would allow the collection and testing of oral fluid specimens as part of a drug testing program upon the publication and implementation of Final Guidelines. Hair is also being considered as a potential workplace drug testing matrix to be used in the future. This article compares the collection, testing, and interpretation of results for urine, oral fluid, and hair; presents a review of urine testing; and serves as a brief introduction to oral fluid and hair testing.

Urine Drug and/or Drug Metabolite Testing

Urine has been tested in federal workplace drug testing programs for 30 years; therefore, methods for the collection and testing of urine are well established. This section serves as a brief review of urine testing. An employment-related urine drug test starts with the identification of the donor and collection of a urine specimen in a controlled environment and under chain of custody. In some cases, the donor must be observed while providing their urine specimen by an individual of the same gender as the donor. Urine temperature is used as one indication of the validity of the collected urine and is evaluated by the collector immediately after the donor provides the sample. The collected urine is then split into an "A" and a "B" Bottle, both of which are sealed, labeled, and transported to the testing laboratory. In the testing laboratory, both the A and B Bottles are received and accessioned. The laboratory tests the specimen in the A Bottle and stores the B Bottle with its seal intact.

The A Bottle is subjected to initial drug testing—typically using an immunoassay—and specimen validity testing (SVT). All specimens must be tested for creatinine, pH, and one or more oxidizing adulterants. Specific gravity must be tested when the creatinine result is outside specified limits.

The initial and confirmatory drug test cutoffs from the *2017 Mandatory Guidelines for Federal Workplace Drug Testing Programs* for urine testing are listed in Table 1.[1]

Table 1. Urine Drug Test Cutoffs from the 2017 Mandatory Guidelines.[1]

Initial test analyte	Initial test cutoff	Confirmatory test analyte	Confirmatory test cutoff concentration
Marijuana metabolite (11-nor-Δ^9-tetrahydrocannabinol-9-carboxylic acid [THCA])	50 ng/mL	THCA	15 ng/mL
Cocaine metabolite (Benzoylecgonine)	150 ng/mL	Benzoylecgonine	100 ng/mL
Codeine/Morphine	2,000 ng/mL	Codeine Morphine	2,000 ng/mL 2,000 ng/mL
Hydrocodone/Hydromorphone	300 ng/mL	Hydrocodone Hydromorphone	100 ng/mL 100 ng/mL
Oxycodone/Oxymorphone	100 ng/mL	Oxycodone Oxymorphone	100 ng/mL 100 ng/mL
6-Acetylmorphine (6-AM)	10 ng/mL	6-AM	10 ng/mL
Phencyclidine	25 ng/mL	Phencyclidine	25 ng/mL
Amphetamine/Methamphetamine	500 ng/mL	Amphetamine Methamphetamine	250 ng/mL 250 ng/mL
Methylenedioxymethamphetamine (MDMA)/ Methylenedioxyamphetamine (MDA)	500 ng/mL	MDMA MDA	250 ng/mL 250 ng/mL

Valid specimens with negative initial drug test results are reported as negative. If an initial drug test is positive or if any of the urine indices is out of range, further testing is performed on a fresh aliquot from the A Bottle. The Mandatory Guidelines specify SVT methods and the criteria for reporting specimens as dilute, adulterated, substituted, or invalid based on SVT results. A dilute result is only reported in conjunction with a positive or negative drug test.

When a result is at or above the initial drug test cutoff, a fresh aliquot is tested by a confirmatory drug test method (e.g., gas chromatography-mass spectrometry [GC-MS], liquid chromatography-tandem mass spectrometry [LC-MS/MS]). The final negative or positive results are reported based on confirmatory testing, along with any applicable SVT results. The unopened B Bottle is held in reserve at the laboratory and can be sent to another laboratory for retesting at the donor's request if a positive, adulterated, or substituted result is obtained for the A Bottle.

Immunoassay

Immunoassays are the most commonly used initial drug and/or drug metabolite test in employment-related urine drug testing, and all require the interaction between an antibody directed against a given drug and a target drug that acts as an antigen.[2] The immunoassays utilized in forensic drug testing are listed in Table 2. Two of the most common drug testing immunoassays—enzyme multiplied immunoassay technique (EMIT) and cloned enzyme donor immunoassay (CEDIA)—also include a reporter enzyme in their commercial formulations. Another immunoassay, kinetic interaction of microparticles in solution (KIMS), measures the reduction of incident light passing through a reaction cell. This reduction occurs when an antibody comes into contact with its antigen (a drug and/or drug metabolite) coated on microparticles, leading to aggregation and, consequently, an increase in the reaction mixture's turbidity. Fluorescence polarization immunoassay (FPIA), which is often used only as a second immunoassay, reflects the increased polarizability of a small molecule bound by a much larger molecule, such as an antibody in an antigen-antibody complex.

Table 2. Common Homogeneous Urine Drug Testing Immunoassays.

Assay	Enzyme	Substrate	Co-factor	Positive result
EMIT	Glucose-6-phosphate dehydrogenase (G-6-PDH)	Glucose-6-phosphate	Nicotinamide adenine dinucleotide phosphate (NADPH)	Increase in absorbance at 340 nm (NADPH)
CEDIA	Galactosidase	2-Chlorophenol-galactoside	N/A	Increase in absorbance
KIMS	N/A	N/A	N/A	Decreased turbidity (absorbance)
FPIA	N/A	N/A	N/A	Decreased fluorescence polarization

All the above urine drug testing immunoassays require an antigen (drug or drug metabolite)-antibody reaction for analytical success. The antigen-antibody reaction is usually a robust process. However, for optimal results, an appropriate ionic strength and pH are required to ensure the best reaction. Extremes of pH or ionic strength may stop the reaction from proceeding. Furthermore, although water-soluble polymers such as polyethylene glycol (PEG) can be employed to help drive the antigen-antibody reaction to completion more quickly, the presence of a high-molecular-weight polymer can result in the formation of an inappropriate complex or even prevent complexation entirely. Both EMIT and CEDIA employ an enzyme to produce a marker of presumptive positivity. In general, enzyme reactions are more susceptible than antibodies to changes in pH or ionic strength and the addition of substances that may act as catalytic poisons (e.g., chelating agents that remove metals essential for enzyme activity).

Specimen Validity Testing (SVT)

Unfortunately, when urine drug testing is used for employment-related purposes, there is strong motivation to create the illusion that drug and/or drug metabolite results are negative with normal urine physiologic indices. Attempts to corrupt the results of the test can occur at numerous points in the collection process. Essentially, two primary methods are employed to defeat a drug test: 1) the adulteration of collected urine with various substances and 2) the substitution of a donor's urine with another substance. Table 3 summarizes the adulteration and substitution methods presented in the following text.

The adulteration or other manipulation of a urine specimen may affect the initial drug tests as described below. SVT is performed during initial testing to identify specimens where adulteration or substitution has occurred. Specimens can also be reported as invalid when a positive, negative, adulterated, or substituted result cannot be established for a drug or specimen validity test.[1] For example, a specimen with depressed immunoassay results is reported as invalid unless the laboratory confirms the presence of a specific adulterant in the specimen.

Table 3. Adulteration and Substitution.[3,4]

Attempt at defeating drug test	General class of substance used
Adulteration	Acids
	Bases
	Oxidants
	Cross-linking Agents
	Sequestering Agents
	Miscellaneous
Substitution	Water
	Salt Solutions
	Household Products
	Homegrown Formulations
	Commercial Substitution Products
	Miscellaneous

Some of the many substances that can be added to a urine specimen to attempt to defeat the initial test and the possible mechanisms by which they work are discussed below.

1. Acids. Strong acids, such as hydrochloric acid (swimming pool water acidifier), hydrofluoric acid (boiler descaler), and sulfuric acid (battery acid), are readily available as household products and/or commercial industrial products. The addition of strong acid to a collected urine specimen will lower its pH. If a sufficient amount of acid is added, the buffer necessary for an immunoassay antigen-antibody reaction can be broken; as a result, the antigen-antibody reaction will not occur or may proceed so slowly as to extend beyond the time window necessary to produce a proper result. Additionally, if an enzyme is involved in the immunoassay test, the pH will be outside the range required for enzyme function, giving rise to a non-reaction and a false negative drug and/or drug metabolite result. Antibodies and enzymes are both proteins. The addition of enough acid will cause protein denaturation, leading to a non-reaction and a false negative drug and/or drug metabolite result. However, if enough acid is added to defeat the drug test, the urine pH will be lowered substantially, which will be detected in the required pH test.
2. Bases. Caustics, such as sodium and potassium hydroxide (drain cleaner), are readily available as household and/or commercial products. Although bases act to raise urine pH rather than to lower it, their overall effects on a urine initial drug test are similar to those described above for acids. Again, the addition of enough base to defeat an initial drug test should be detected by the required pH test.
3. Oxidants. Perhaps the largest and most common category of urine drug test adulterants is oxidizing agents or oxidants. Numerous oxidants, such as hydrogen peroxide, hydrogen peroxide with the enzyme peroxidase, nitrites, nitrates, persulfates, dichromate salts, chromate salts, and pyridinium chlorochromate, have all been marketed as additives to destroy THCA, the major metabolite of THC, in urine. Numerous other powerful oxidizers, such as bleach and solid peroxides, are available both commercially and as household products.
4. Cross-linking agents. As stated above, antibodies and enzymes used in commercial immunoassay are proteins with unique three-dimensional structures. Cross-linking agents will disrupt this structure, preventing the protein from being active. Organic reagents such as glutaraldehyde contain two functional groups that allow binding to two places on the protein molecule, creating a bridge or cross-link that inactivates the enzyme or antibody. Whether because of cross-linking or another chemical phenomenon, the addition of substances such as glutaraldehyde to urine generally inhibits even the background reaction of an enzyme, leading to a negative reaction that may be below the rate observed for a negative urine and, thus, giving a false negative result.
5. Sequestering agents. Compounds such as detergents and the commercial eyecare product Visine® are known to be able to sequester small organic molecules such as THCA and keep them from being bound by the antibodies to THCA in an immunoassay. Soap and detergents may also denature proteins and cause a negative immunoassay result by disrupting the protein structure in much the same way as described above.

Some of the many substitution products that can be used in place of a donor's urine in an attempt to defeat urine drug testing are discussed below.

1. Water. This is probably the oldest substitution product. Water will produce a negative immunoassay test but will not produce a valid creatinine-specific gravity combination, resulting in a substituted report. Deionized and distilled water cannot be used as substitutes for urine as most immunoassay analyzers sense deionized and distilled water as air or "no sample." Before it can be used as a substitute for urine, water must be warmed to an acceptable temperature. Additionally, unlike authentic urine, water is colorless, although this issue can be remedied by adding a small amount of yellow food coloring.
2. Salt solutions. Although salt solutions such as normal saline can resolve analytical issues such as low specific gravity, they do not circumvent the problem that no creatinine will be found in the "urine specimen." Furthermore, just like water, salt solutions must be warmed to body temperature before use.
3. Household products. Numerous products such as sodas and sports drinks can provide the correct color to match urine, especially when diluted with water. However, substances such as diluted colored drinks may or may not contain creatinine or a substance that reacts like creatinine during testing. Additionally, these products do not contain other naturally occurring urine components such as uric acid and steroids common to both genders. Thus, common household products may or may not provide an acceptable substitute for urine, even if warmed properly prior to submission to a collector.
4. Homemade formulations. Numerous urine substitute formulations and recipes can be found on the internet. One product encountered by the author was simply undistilled vinegar, which had the proper color and contained a substance that reacted like creatinine in the Jaffé reaction (i.e., the common creatinine test method). To counter the pH discrepancy when pH testing was introduced at a later date, the donor added a small amount of baking soda to neutralize the pH. The donor, who was a cocaine user, was later apprehended when he bragged to his fellow employees about "how he beat the drug test."
5. Commercial substitution products. Several commercial manufacturers produce both synthetic and "clean" authentic urine. They also provide delivery methods that place a product at acceptable temperature in the specimen collection container. Early versions of synthetic urine lacked essential components such as uric acid. However, later versions have remedied earlier deficiencies using unknown procedures that provide uric acid.

The purpose of this subsection is not to provide a complete review of urine adulteration and substitution but to demonstrate that numerous methods exist to suborn urine drug testing via adulteration and substitution. Such methods support supplementing urine drug testing with other test matrices.

Confirmatory Drug Testing

Numerous methods for analyzing drugs in urine have been published. These methods typically consist of a sample preparation technique, such as liquid/liquid or solid-phase extraction, followed by GC-MS or LC-MS/MS. Drugs and/or drug metabolites are concentrated in the urine; thus, their concentrations are higher and easier to detect than those in other matrices.

Strengths and Weaknesses

The overall strengths and weaknesses of urine drug and/or drug metabolite testing are presented below:

Strengths
1. Urine is generally available in large quantity.
2. Urine is typically accessible by non-invasive collection.
3. Drugs and their metabolites are usually concentrated up to 100-fold relative to whole blood, plasma, serum, or oral fluid (*vide infra*), facilitating analysis.
4. Urine testing provides a moderate "look-back" timeframe of hours to weeks, making this a good matrix for random, pre-employment, and post-accident testing.
5. A second or "split" sample is easily obtained.
6. The test matrix is stable.
7. Many established initial and confirmatory urine testing methods are available.
8. SVT can be achieved using a wide variety of analytes to detect adulteration or substitution attempts.
9. Proficiency testing programs are available.
Weaknesses
1. Positive urine drug test results usually cannot be used to determine an individual's level of impairment or intoxication.
2. An observed specimen collection requires a same-gender collector/witness.
3. Numerous devices and products exist to suborn a drug test by adulteration or substitution.

Oral Fluid Drug and Drug Metabolite Testing

One alternative to urine testing is oral fluid testing. The collection of oral fluid is easier than the collection of urine in some respects: a private area is not required for collection, and collection can potentially be done on-site, eliminating the need for the donor to travel to a collection site. Every oral fluid collection is observed by a trained collector, minimizing the chance for specimen manipulation and, thereby, reducing the need for SVT. However, the procedure for collecting a split specimen is more complicated than for urine. Currently, one split device exists for neat oral fluid, and one split "pad type" collection device is available.

As might be anticipated, the concentrations of drugs and their metabolites in oral fluid are considerably lower than those in urine. Although a direct comparison between urine and oral fluid is not possible (e.g., urine testing for marijuana use employs the metabolite THCA, while oral fluid testing uses the parent drug THC), levels in oral fluid are approximately 1.5–33% of those found in urine. For a more complete discussion of this aspect of oral fluid drug testing, please see Chapter 5 in Reference 5. The initial and confirmatory drug test cutoffs for oral fluid in the proposed *2015 Mandatory Guidelines for Federal Workplace Drug Testing Programs using Oral Fluid* are listed in Table 4.[6] Similar to urine testing, initial oral fluid drug testing may be performed using immunoassay or an "alternate" technology, such as LC-MS/MS. Confirmatory drug testing procedures typically require sample preparation and analysis methods similar to those used for urine.

Table 4. Proposed Oral Fluid Cutoffs from the 2015 Proposed Mandatory Guidelines

Initial test analyte	Initial test cutoff (ng/mL)	Confirmatory test analyte	Confirmatory test cutoff concentration (ng/mL)
Marijuana (THC)	4	THC	2
Cocaine/ Benzoylecgonine	15	Cocaine Benzoylecgonine	8 8
Codeine/ Morphine	30	Codeine Morphine	15 15
Hydrocodone/ Hydromorphone	30	Hydrocodone Hydromorphone	15 15
Oxycodone/ Oxymorphone	30	Oxycodone Oxymorphone	15 15
6-AM	3	6-AM	2
Phencyclidine	3	Phencyclidine	2
Amphetamine/ Methamphetamine	25	Amphetamine Methamphetamine	15 15
MDMA/MDA	25	MDMA MDA	15 15

Strengths and Weaknesses

The overall strengths and weaknesses of oral fluid drug and/or drug metabolite testing are presented below:

Strengths
1. Oral fluid is the preferred specimen type for many donors.
2. Collection is easy, minimally invasive, and rapid.
3. Oral fluid testing detects recent drug use when tested at standard cutoffs.
4. Because oral fluid drug testing often uses the active parent drug as the target analyte while urine drug testing generally targets a metabolite, oral fluid drug test results may, in some cases, be linked to clinical symptomatology and/or whether an individual was under the influence at the time of an accident or incident. Therefore, oral fluid is a good choice of matrix for post-accident and reasonable suspicion/cause testing.
5. Testing oral fluid may allow the therapeutic interpretation of drug concentrations.
6. Proficiency testing programs are available.
7. Oral fluid minimizes the need for SVT, except as described in Chapter 6 of Reference 5.

Weaknesses	
1.	Because of the pathways by which drug is incorporated into and eliminated from oral fluid and the half-life of a parent drug relative to its metabolites, the time window for oral fluid drug testing to identify the use of a drug is shorter than for urine or hair.
2.	Oral fluid testing is not ideal for pre-employment testing.
3.	The collection of a second "split" sample is not as straightforward as it is for urine.
4.	Unless neat oral fluid is used, a collection device is needed that is more expensive than those used for urine or hair.
5.	The actual quantitative value obtained may be subject to more variation than those obtained from blood, blood products, and urine.

Hair Drug and Drug Metabolite Testing

Another possible alternative to urine testing is hair testing. The collection of hair is relatively straightforward and minimally invasive. However, some donors may express concern about having a portion of their hair cut, and other donors may not have enough head hair to collect. Collectors must be trained to identify synthetic hair and weaves of donor hair with hair from another source.

Drugs and their metabolites in hair are found at much lower concentrations than in other matrices and must be analyzed using techniques that are extremely sensitive (e.g., radioimmunoassay for initial testing and LC-MS/MS or GC-MS/MS for confirmatory testing). Proposed initial and confirmatory drug test cutoffs for hair testing were published in 2004 and are listed in Table 5.[7] At the time this article was written, the technical requirements for hair testing were still being discussed.

Hair is different from the other matrices an analytical toxicologist performing workplace drug testing routinely works with, as hair is solid rather than liquid. However, this solid matrix can be converted easily into a more usable liquid form by breaking down the keratin (protein) with an enzyme mixture such as Proteinase K. Additionally, hair is probably the easiest matrix to store and shows the best long-term stability when compared to urine and oral fluid. Indeed, most hair samples are stored at room temperature in something as simple as a paper envelope.

Table 5. Proposed Hair Testing Cutoffs from the 2004 Guidelines

Initial test cutoff concentration	
Target	**Concentration (pg/mg)**
Marijuana metabolites	1
Cocaine metabolites	500
Opiate metabolites*	200
Phencyclidine	300
Amphetamines	500
MDMA	500
Confirmatory test cutoff concentration	
Target	**Concentration (pg/mg)**
Marijuana metabolite	0.05
Cocaine:	
Cocaine	500
Cocaine metabolites	50
Opiates:	
Morphine	200
Codeine	200
6-AM	200
Phencyclidine	300
Amphetamines:	
Amphetamine	300
Methamphetamine	300
MDMA	300
MDA	300

* Laboratories are permitted to initial test all specimens for 6-AM using a 200-pg/mg cutoff.

Because environmental contamination, such as dust from coring seized cocaine blocks or smoke from vaporized heroin, is a major issue when only the parent substance is tested, washing hair prior to analysis appears to be a necessary analytical step. However, washing procedures have not been standardized at this time. Testing hair for unique drug metabolites in addition to the parent substance may remove doubt about whether the substance in hair is the result of actual drug use or environmental contamination. Please see Reference 8 for a more in-depth discussion of testing hair for metabolites vs. parent substance.

At first examination, hair would appear to require no SVT. However, synthetic hair can be intermixed with authentic donor hair, a donor may have a weave (i.e., donor hair woven with another individual's hair), and processes such as bleaching and dyeing may cause hair breakdown, including increased porosity. Thus, SVT may apply to hair samples submitted for drug and drug metabolite testing. However, at the time this article was written, SVT methods had not been standardized.

Strengths and Weaknesses

The overall strengths and weaknesses of hair drug and/or drug metabolite testing are presented below:

	Strengths
1.	Collection is easy and minimally invasive.
2.	Hair testing detects the long-term intake of drugs and alcohol when standard cutoffs are used.
3.	Hair offers a maximal "look-back" time, generally providing information about a donor's use of drugs in the weeks to months prior to the drug test. Thus, hair is a good matrix for pre-employment testing.
4.	Using hair minimizes the need for SVT except as described above.
5.	The collection of a split sample is easy.
	Weaknesses
1.	Unless unique metabolite testing or extensive washing is performed, the detection of a parent drug in or on hair could be attributable to environmental contamination rather than actual drug use.
2.	Hair testing is not useful for post-accident or reasonable suspicion/cause testing.
3.	The actual quantitative value obtained is subject to more variation than those obtained from oral fluid and urine.
4.	Proficiency testing programs are not as well established as those for urine and oral fluid.
5.	The analytical methodology is complex and cannot be performed by many testing laboratories.

Overall Conclusions

For drug testing, each of these matrices (urine, oral fluid, and hair) has strengths and weaknesses that make their potential utility strongly dependent on the reason for testing. The strengths and weaknesses of each test matrix are compared below, with an emphasis on forensic testing.

Collection

Urine is easily collected under chain of custody in large amounts, but adulteration or substitution may be introduced at numerous points in the process, especially if a standard collection procedure (e.g., that specified in Reference 6) is not followed. An "A" sample and a split "B" sample are easily obtained. Hair also is easy to collect under chain of custody, and there are few opportunities for substitution to be introduced and almost no opportunities for adulteration, except by changing the nature of the specimen via bleaching and dyeing prior to specimen collection. For most oral fluid collections, an oral fluid collection device is required, which makes oral fluid collection more expensive than urine or hair collection. However, if a good oral fluid collection protocol is followed, the chance of adulteration or substitution is essentially non-existent. Additionally, obtaining an "A" sample and a split "B" sample is possible but slightly more difficult than for urine or hair.

Analysis

Methods for the initial, specimen validity, and confirmatory testing of urine are well established. Of the three matrices discussed in this brief report, urine contains the highest and most easily analyzed levels of drugs and drug metabolites. Methods for the analysis of oral fluid and hair also are well established. However, compared to those in urine, the levels of drug and/or drug metabolite are lower in oral fluid and even lower in hair. In hair, parent drugs may be present because of the actual use of the drug and/or environmental contamination; thus, unique metabolite testing is highly desirable. Sample preparation techniques vary depending on the type of matrix tested and can range from simple "dilute-and-shoot" to extractions to time-consuming digestion of hair.

Specimen Validity Testing (SVT)

Numerous effective specimen validity test protocols exist for urine collected under chain of custody. However, as urine substitution products and their introduction into a collection process become more sophisticated, issues surrounding urine substitution may become more complex and difficult to overcome. SVT for oral fluid does exist; however, SVT is likely less important for the forensic testing of oral fluid than that of urine because all properly conducted oral fluid collections are witnessed. Additionally, SVT may be minimal for hair testing, as most attempts to substitute the hair can be identified by the collector. Porosity will likely have implications for the washing step in the analytical cascade and the interpretation of results.

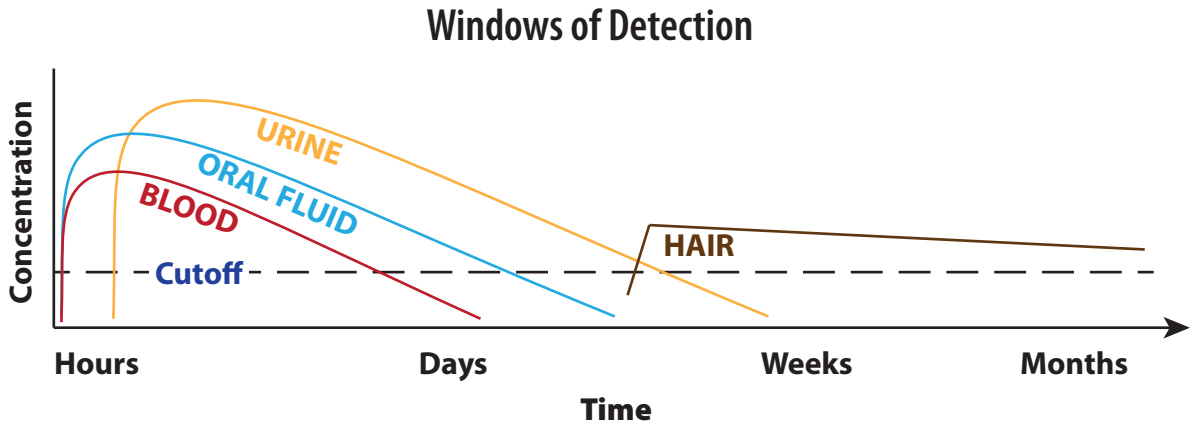

Figure 1. "Look-back" Timeframes for Urine, Oral Fluid, and Hair Compared to Blood (Cone EJ, personal communication, December 2016).

As shown in Figure 1, hair provides the longest "look-back," while oral fluid offers the shortest and is most similar to blood. The reason for testing must be considered when selecting the matrix that will provide the most useful information. For example, a hair test result would not provide information about drugs in a donor's system at the time of an accident. Therefore, hair would not be an ideal matrix for a post-accident test.

Stability and Storage

Drug may be lost even from urine specimens frozen at -20ºC or lower, although this phenomenon depends strongly on the drug and/or drug metabolite in question. Using higher storage temperatures generally results in much less recoverable drug and/or drug metabolite than freezing over the same timeframe. However, the recovery of drug and/or drug metabolite from urine at various temperatures is well established. Conversely, the recovery of drug and/or drug metabolite from oral fluid specimens is highly dependent on the collection system and the drug and/or metabolite for which testing is performed. Freezing may not be a viable option to extend the stability of drugs and drug metabolites in oral fluid. In contrast, as mentioned above, the long-term storage of hair is relatively easy and convenient.

Summary

Overall, the choice of a specimen type (urine, oral fluid, or hair) depends on the end user's expectations. To examine use within a short timeframe (e.g., reasonable suspicion/cause or post-accident tests), oral fluid would appear to be the specimen of choice, especially if any correlation between the quantitative level of a drug and clinical symptomatology is desirable. If the end user wants to know if an individual has ever used a given drug, hair is the specimen of choice, even with the limitations imposed by environmental contamination. Finally, urine is usually a good choice for pre-employment testing, despite the moderate to high potential for adulteration and substitution. The burden of the increased analytical capability that may be required for oral fluid and hair testing falls onto the testing laboratory, which must decide whether to add additional matrices, such as oral fluid or hair, to their test menu.

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