



NRL/MR/6170--03-8727

Selecting the Best Drug-Testing Procedures

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November 28, 2003

20040114 041

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. REPORT DATE (DD-MM-YYYY) November 28, 2003			2. REPORT TYPE Memorandum report		3. DATES COVERED (From - To)	
4. TITLE AND SUBTITLE Selecting the Best Drug-Testing Procedures					5a. CONTRACT NUMBER	
					5b. GRANT NUMBER	
					5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) David A. Kidwell					5d. PROJECT NUMBER 61-2203-A-2	
					5e. TASK NUMBER	
					5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Naval Research Laboratory, Code 6177 4555 Overlook Avenue, SW Washington, DC 20375-5320					8. PERFORMING ORGANIZATION REPORT NUMBER NRL/MR/6170-03-8727	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) Naval Surface Warfare Center DoD Counter-Narcoterrorism Technology Program Office 17320 Dahlgren Road Code B07, Bldg. 1460, Room 1212 Dahlgren, VA 22448-5150					10. SPONSOR / MONITOR'S ACRONYM(S)	
					11. SPONSOR / MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution is unlimited.						
13. SUPPLEMENTARY NOTES						
14. ABSTRACT This report discusses the advantages and limitations of the matrices of urine, saliva, hair, sweat, and skin swabs for monitoring of illicit drug use in a criminal justice environment. A three phase testing scheme is proposed employing all these matrices. The scheme recognizes the limitations of each matrix, keeping cost and inconvenience to a minimum, yet ensuring a drug-free clientele.						
15. SUBJECT TERMS Drugs of abuse; Urine testing; Hair testing; Saliva testing; Sweat testing						
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UL	18. NUMBER OF PAGES 20	19a. NAME OF RESPONSIBLE PERSON David A. Kidwell	
a. REPORT Unclassified	b. ABSTRACT Unclassified	c. THIS PAGE Unclassified			19b. TELEPHONE NUMBER (include area code) (202) 767-3575	

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Selecting the Best Drug-Testing Procedures*

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Introduction

Historically, drug-testing programs have relied on urinalysis as the gold standard for establishing illicit drug use. Due to the pharmacokinetics of most drugs and the normally applied immunoassay cut-off concentration, drug-testing programs generally require urine collection every 3-4 days to ensure a drug free clientele.^{1,2} The frequent and inconvenient testing required by urinalysis prompts development of alternative means to test for illicit drug use. The 3-4 day window after ingestion of drugs is termed the "window of detection". A typical excretion curve for the cocaine metabolite, benzoylecgonine, in urine is shown in Figure 1a for an individual who used cocaine for only a limited time. For comparison, the urine levels of benzoylecgonine for a consistent user of cocaine are shown in Figure 1b. For the chronic user of cocaine, the window of detection is anytime.

Lower cut-off concentrations extend the window of detection for any matrix at the expense of possible false positives from inadvertent environmental exposure, including such sources as gross external contamination (for example, living in areas where drugs had been used) and trace ingestion. Trace ingestion, considered to be 1-5% of a physiologically active dose (approximately 1-5 mg for cocaine), likely would not result in a noticeable physiological effect, but capable of producing a substantial urine positive. For example, in consuming Inca Tea, an individual ingests 2-3 mg of cocaine. This has been shown to cause positive urine results for 21-26 hr.³ Consuming larger amounts (25 mg) of cocaine produces positive urine results for up to 36 hr.⁴ Even at this dosage level, only a slight numbing of the mouth was observed during the consumption. For many criminal justice applications, environmental exposure is minimal. In these cases, one could extend the window of detection 25-50% for most drugs in urine by lowering the cut-off level.⁵

To ensure a drug-free population, one would need to test by urinalysis within this window of detection.⁶ Other matrices such as hair, sweat,⁷ skin swabs, and saliva have different windows of detection (see Figure 2).

* Manuscript approved September 30, 2003.

Figure 1 – Benzoyllecgonine levels in urine from two individuals in drug rehabilitation. The use amount is unknown but the occasional user is assumed to have used cocaine between Friday afternoon and Saturday morning. The window of detection would be 3 days at a 300 ng/mL cut-off level for benzoyllecgonine in urine and four days at 100 ng/mL. This could even be extended to five days at the limit of detection of the instrumental analysis. Note that the chronic user of cocaine reaches very high benzoyllecgonine levels in his urine compared to the occasional user. The window of detection for the chronic user would be anytime.

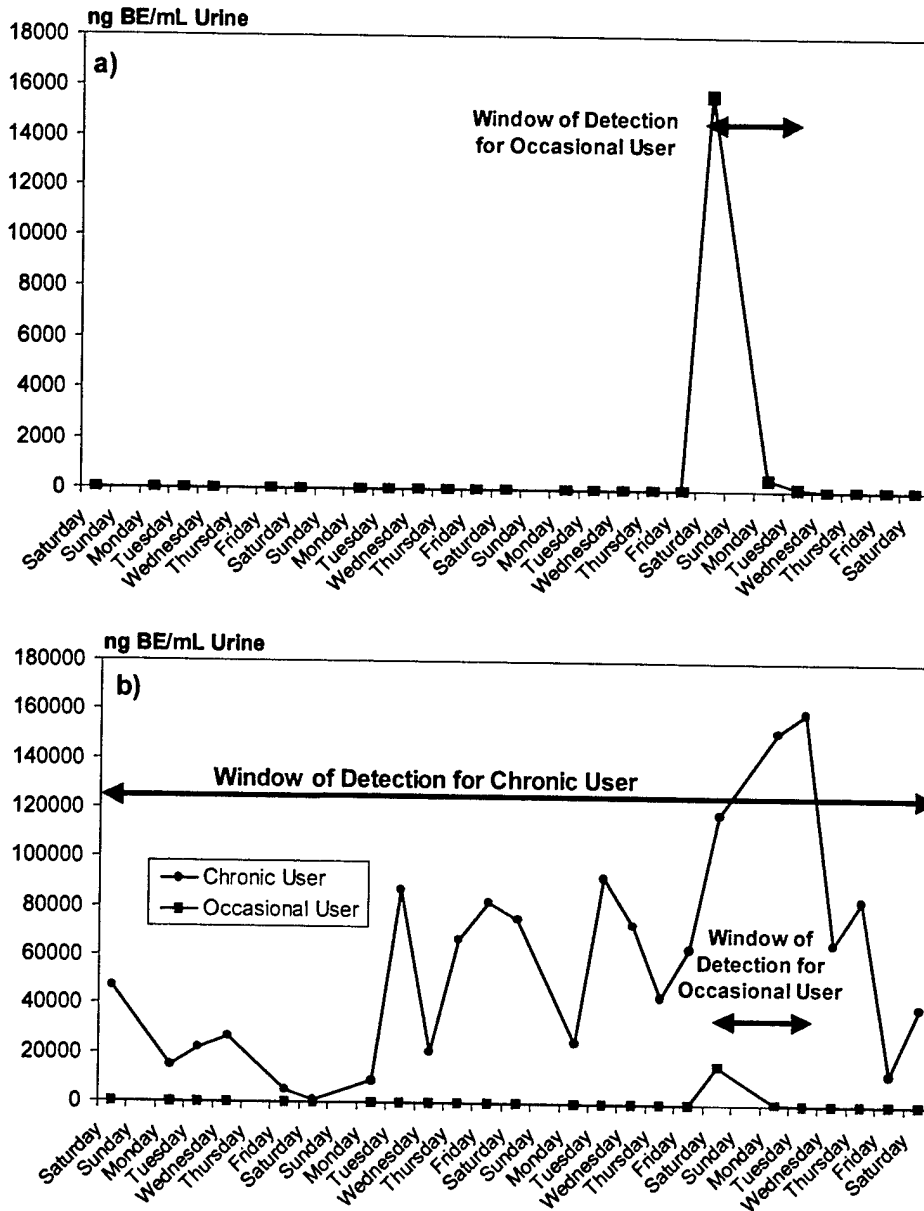
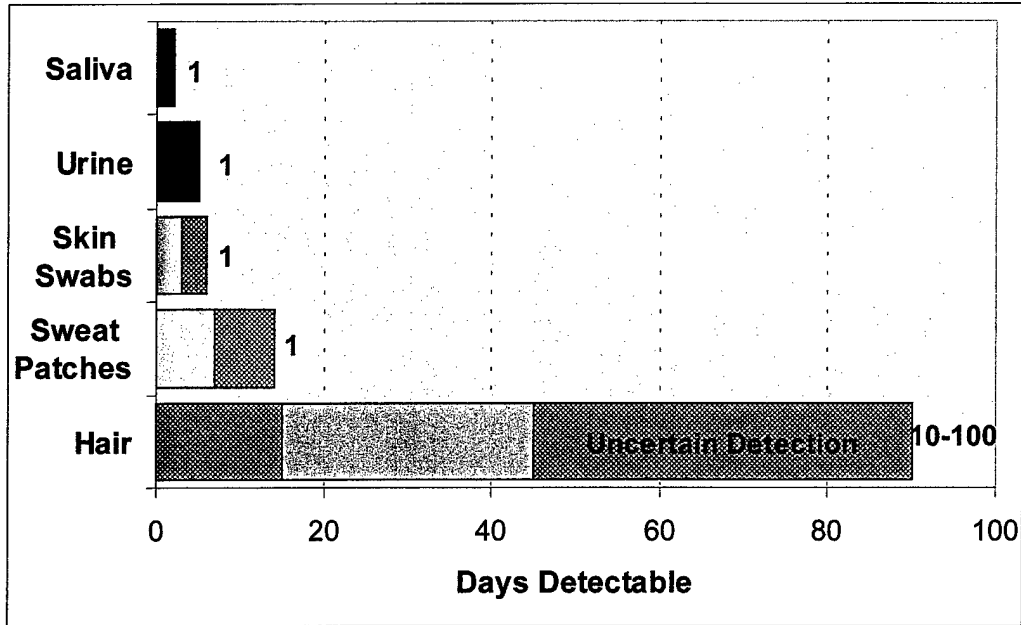


Figure 2 – Window of detection of cocaine in various matrices. The hatched areas represent times where drug use may go undetected. The numbers after the bars represent the relative amounts of cocaine that needs to be used for it to be detectable. Although hair appears to have a wider window of detection, this is tempered by the larger amounts that must be consumed to generate a positive. Additionally, hair has two areas where drug detection is uncertain. This is discussed further in the section on hair analysis.



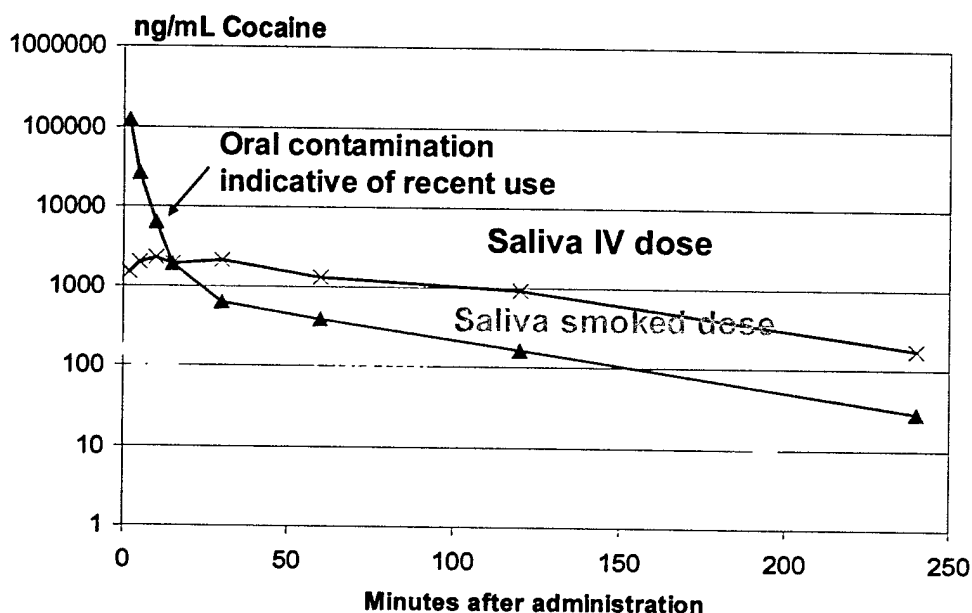
Besides the relatively short window of detection for urinalysis, urine is also susceptible to physiological dilution,⁸ adulteration or substitution to mask drug use. Because of this, urine is often collected under direct observation – a procedure that is inconvenient for both the client and the collector. Direct observation requires scheduling the client to come to a central location to donate the sample and having present probation officers of the same sex to observe the sample collection. For individuals under supervised release, frequent traveling to the probation office is inconvenient as these individuals often are poor and must take public transportation and need to be away from a job during this time. Additionally, urine cannot always be produced on demand so that delays in collection are inevitable, taking additional time from productive work. Although individuals in custody do not have the travel problem of those on supervised release, many probation officers do not like to observe urine collection or handle the specimens and an alternative monitoring system would be desirable. Due to these reasons, research in additional methods to detect and deter drug use is ongoing. Broadly, this research seeks to improve drug-use monitoring by: (1) making it more convenient to both those who administer drug testing programs and those who are subject to drug testing; (2) making drug testing less invasive/more dignified; and (3) extending the window of detection and lowering costs, while maintaining the high reliability currently associated with forensic urine drug testing as performed under the federal workplace drug testing guidelines.

This paper outlines the advantages and limitations of each of the matrices shown in Figure 2. In addition, several novel testing programs are proposed that marry most of the matrices into a comprehensive system. These programs recognize the limitations of each matrix, keeping cost and inconvenience to a minimum, yet ensure a drug-free clientele.

Saliva

Saliva is excreted constantly from the blood supply and drug levels in saliva parallel those in blood. Because the blood levels of most drugs fall very rapidly (and so their effects), saliva is a short-term monitor of drug use. In contrast, urine has a concentrating effect on drugs and the levels found have little bearing to the state of intoxication. An example can be seen in Figure 3 for individuals that have been administered cocaine under controlled conditions. Since saliva has a short window of detection for most drugs, it is best employed for fitness for duty testing or driving under the influence investigations, where some link with performance and drug levels is desired. Alternatively, frequent, random saliva testing may be employed as a prescreen for testing by other matrices.⁹ Due to the self-cleansing nature of saliva, environmental contamination is almost non-existent.¹⁰

Figure 3 - Persistence of cocaine in saliva. Note that the Y-scale is logarithmic. The very high levels of drugs found in saliva from the smoked cocaine are indicative of oral contamination. This occurs with any smoked drug and generally clears within 10-20 minutes. After this time, the saliva levels parallel that found in blood plasma. Data from:¹¹



Saliva is generally collected with an absorbent media placed in the subject's mouth for a few minutes.¹² Saliva is easily obtained under observation at almost any time.¹³ A number of collection and testing devices are commercially available. The choice of saliva collection system should be considered if the results would be used for punitive sanctions. In this case, confirmation of any positive results by two independent tests should be required. For forensic testing, collection of sufficient sample is necessary (approximately 1 mL) for confirmation in a laboratory environment.

Sweat Monitoring with the Patch

A human body transpires about two quarts of water per day over the entire skin area. This is greatly increased during exercise or in warm climates. When an individual ingests a drug, some of the drug is excreted in sweat. Generally, sweat collection devices sandwich an absorbent pad between the skin and an outer membrane using a tamper-evident adhesive backing on the membrane. Careful preparation of the skin prior to application of the patch helps reduce the possibility of bacterial growth and previous skin contamination. Newer, non-occlusive membranes allow water vapor to pass through the membrane, which increases comfort for the wearer and allows longer-term wear.

Sudormed, Inc. has married the non-occlusive membrane with a collection pad to produce a sweat collection patch marketed by PharmChem, Inc. as the PharmChek™ Drugs of Abuse Patch (referred throughout the text as the sweat patch or patch). The patch is a Band-Aid® like device that an individual wears on the arm or upper back. The patch contains a paper pad, which traps any drugs or metabolites that are passed through the skin, and a polyurethane covering, which is claimed to protect the collection pad from external contamination and to allow water vapor to escape (permitting long-term wear). After the proscribed time period of wear, the patch is removed and sent to PharmChem for analysis. Another patch may be applied at the same time as removal to continue drug testing.

External, continuous monitors, such as the PharmChem sweat patch, offer substantial advantages over frequent urine testing, such as convenience and cost.¹⁴ Continual sampling of an individual's sweat for up to 14 days¹⁵ (the maximum patch wear period) using the sweat patch creates a wider time window for detecting drug use, with the potential to trap and accumulate drugs and their metabolites excreted in sweat. The patch has found wide application in the criminal justice system due to perceived advantages including user friendliness, non-invasiveness, easily observed placement and removal of the sweat patch, detectable adulteration attempts, long drug-use detection interval, and potential to identify unique metabolites. Additionally, the presence of the patch is a deterrent to drug use because it continually reminds the individual that he/she is undergoing drug testing.^{16,17}

There are several issues with the sweat patch in its application of monitoring individuals related to wearability. First, some individuals may become sensitized to the adhesive in the patch and develop an allergic reaction. In our laboratory studies, one individual did develop such an allergy and was precluded from further evaluation of the patch.¹⁸ Second, the patch must remain on an individual during the proscribed period and not show signs of tampering. The adhesive is designed to adhere tightly but not readhere once removed. Anything that disrupts this adhesion will cause the patch to show such signs of "tampering". This is necessary because an individual could adulterate the patch if access to the interior collection pad was allowed. In our laboratory tests, adhesive failures were observed, especially on individuals undergoing heavy exercise.¹⁹ Additional failures were noted in field trials of the patch.²⁰ Thus, adhesive failures should not be interpreted as intentional adulteration of the patch and grounds for disciplinary action.

The biggest concern with the patch is the reliability of the results. Two features that would appear to increase the sweat patch's reliability are: 1) the skin is "cleansed" before application of the patch, potentially removing previously deposited drugs and 2) the patch appears to protect the skin from contamination by the external environment after being applied. However, we have shown that these perceptions are not always true and environmental contamination can result in

false positives.^{19,21} Based on previous laboratory experiments, two sources of contamination can occur. First, drug contamination on the external patch membrane cause what we have termed "Contamination From WithOut" (CFWO). In tests of CFWO, we observed rapid diffusion of drugs through the membrane and into the moistened interior of the patch (within minutes), resulting in patch drug amounts above the suggested manufacturer's cutoff concentration for determining a positive. Proof of patch penetration by other molecules further substantiates our findings. For example, certain dyes, with molecular weights (molecular weight influencing diffusion) that exceed those of most illicit drugs, penetrate the patch membrane. In the uncharged state, they readily diffuse through the patch membrane and deposit in the patch test pad when the interior pad is moist.^{19,21} Other researchers^{22,23} failed to observe these phenomena because dye penetration does not occur when the interior pad is dry.

The second source of contamination, Contamination from WithIn (CFWI), results from the presence of drugs on the skin before application of the patch. CFWI can occur from at least two sources: (1) an individual's own previous drug use and (2) being "around drugs" unrelated to intentional use by the individual in question.²⁴ Drugs persist on skin even though the skin is "cleaned" before the patch is applied and are difficult to remove. We have shown that, after an initial application of only 10 µg of drugs to the skin (1/1000 to 1/10,000 of a dose), six days of regular hygiene followed by "cleaning" with isopropanol wipes (as recommended by the manufacturer) does not prevent positive patch results.^{19,21}

Either source of contamination appears to occur in the real world. We followed the drug use patterns of individuals in cocaine rehabilitation by daily urine testing and patches.²⁰ In three individuals with no indication of cocaine use, false positives occurred at a 7% rate using the manufacturer's cut-off level for the patch. Although increasing the patch cut-off to 75 ng cocaine/patch would curtail the incidence of false positives in this limited population, any amount could be introduced from the external environment so that a simple cut-off level would be insufficient to define use vs. exposure.

Sweat Monitoring with Skin Swabs

Drugs readily bind to the skin and are difficult to remove by normal hygiene. Drugs on the skin may come from two sources: (1) through ingestion of a drug and having it excreted in sweat, and (2) through contact with a drug either from handling during use or contact with the environment. The cationic drugs, cocaine, amphetamines, and heroin, the drugs will remain on the skin and be removable for 3-5 days.²⁵ Binding of drugs to the skin suggests an alternative to the patch under circumstances where the individual undergoing drug testing is unlikely to come into contact with drugs or where knowledge of such contact would be useful intelligence information. Although external contamination would be less likely inside the prison system, in many prison systems, who is coming into contact with drugs is useful information. Additionally, a positive finding with a denial of drug use would trigger an investigation of the living and work areas of the inmate. Perhaps the cellmate of the inmate was the actual drug user or the inmate was selling drugs. A positive drug swab could be useful to target drug searches to where the use is most likely.

For monitoring with skin swabs, an individual is marked with a unique label such as a number, letter, figure, or combination of the above using a dye. The dyes may be visible under normal lighting to reinforce that the individual is being monitored, or may be visible only under UV light. The dye would have a similar binding to the skin as drugs, yet provide a visual indication of its presence. During normal hygiene, the individual could wash the marked area but just not scrub

hard enough to remove the dye at a rapid rate. Any part of the body could be marked, but areas most suitable for marking would be the upper arms, shoulders, and upper back. Periodically, during the line at lunch, for example, the area would be examined for the presence of the marker. If still present, then that individual need not take a drug test. If absent, then the individual would be subjected to immediate urinalysis. Once a week, the marked area would be swabbed, removing the dye and any drugs present. A rapid test could be performed on the swab and any positives investigated. Another area would then be selected for marking.

Although as outlined above, an individual would undergo testing every week, a less frequent test routine could be implemented as a cost saving measure. In this situation, the swab would still be taken every 5-7 days, since that is the lifetime of the dye and drugs on the skin, and a new marker applied. However, the swab would only be tested on a random basis.

Hair Testing

In Figure 2, hair analysis is depicted as having the longest window of detection of any matrix for cocaine. This is tempered by the larger amount of drug that must be ingested before it is detectable by hair analysis. Additionally, there are two areas where hair analysis is uncertain. These will be discussed in the next section. There still remain three unanswered questions that limit hair testing. (1) Can environmental exposure be distinguished from use; (2) Does all hair behave the same; and (3) How much drug is necessary to reach a given cut-off level? Each of these topics is discussed below.

Mechanism of Drug Incorporation and Environmental Exposure

The original concept in using hair testing for determining drug use was that hair was in contact with the bloodstream as it grew and could sequester drugs in the hair matrix. As the hair grew out of the scalp, the concentrations of drugs present in the hair would reflect that present in the blood during the formation (Figure 4a).²⁶ Because hair grows at a relatively constant rate of about 1 cm/month, it would reflect a timeline of drug use in both time and amount. Once incorporated, the drugs remain in the hair, so a 3 cm portion of hair would reflect a 3-month drug usage history. Furthermore, it was thought that hair protects itself from contamination by the external environment.

Further research showed that this model was oversimplified and that molecules can be incorporated into hair from a number of sources including sweat (Figure 4b).²⁷ Drugs may be present in the sweat of an individual from use of the drugs as well as from contact of the individual with external sources of the substances. External contamination may then form a solution with the sweat from the individual and produce a positive hair sample indistinguishable from that of a true user. This latter source of drugs in sweat raises the most concern for misidentifying an individual as a drug user by mere contact with drugs in the environment.²⁸ In fact, we showed that young children living with mothers in drug rehabilitation have an average concentration of cocaine in their hair similar to their cocaine-using mothers.²⁴ From evidence of skin swabs, environmental exposure rather than intentional ingestion is the most likely explanation for the hair positives.

Figure 4a - Original model for drugs binding to hair.

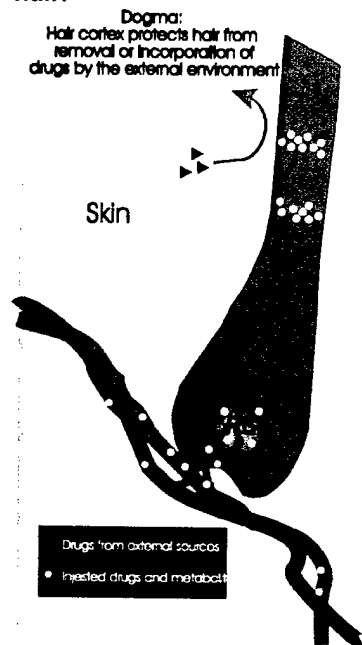
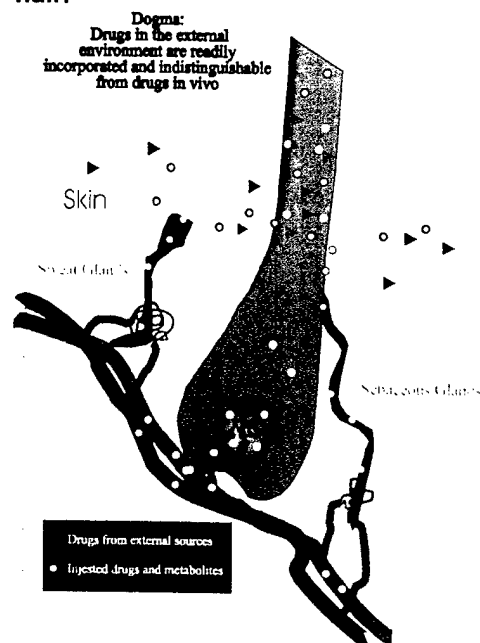


Figure 4b - Current model of sources of drugs in hair.



The presence of drug metabolites in the hair is not definitive evidence that the drugs passed through the human body. External contamination must still be considered even with metabolites present because most street drugs contain these metabolites as impurities. Additionally, in well-controlled studies where non-drug using individuals have intentionally contaminated their hair with drugs, the drugs can still be observed months later.^{29,30} Moreover, "metabolites" were observed to start forming in the hair as the drugs were exposed to the environment and degrade. The metabolite pattern in these externally exposed individuals was identical to that found in drug users.

The areas of uncertain detection in Figure 2 for hair analysis arise from the mechanism of incorporation. The first area, nearest to the point of ingestion, is uncertain because the contribution from the sweat of the drug user varies. In many controlled studies, some drugs have appeared in the hair of some participants hours after ingesting the drug. This rapid appearance of drug is consistent with the accepted mechanism shown in Figure 4b. However, individuals do not all sweat at the same rate so that drugs do not appear consistently across participants. After the initial rapid appearance of drug, frequently another bolus appears 7-21 days later. This would be the contribution from incorporation during the hair formation stage and would be consistent with the approximately 14-day time it takes hair to grow from the scalp. However, for reasons unknown, not all participants show this second bolus.

Although it would be nice to consider hair as a rigid rod, it is actually quite porous. This is obvious to anyone who has ever dyed his/her hair. The dye penetrates quickly but is removed slowly over weeks to months through normal hygiene. This is the source for the second area of uncertain detection shown in Figure 2 for hair analysis. Normal hygiene has been shown to remove approximately 30% of the incorporated drug during a 3-month period. If this removal reduces the

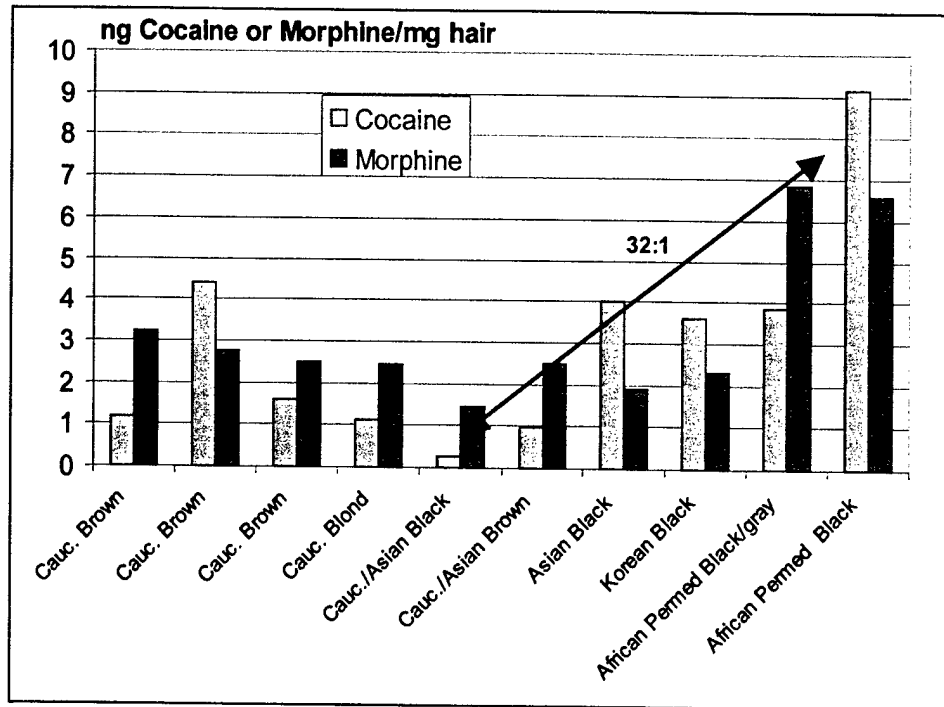
drug level to below the cut-off, then a negative hair test would result. Additionally, this process can be accelerated by prolonged washing of the hair or prolonged wetting of the hair, swimming being an example.

Finally, uncertain detection results from dilution of the positive hair with negative hair. If the drug were in bands, which does not frequently happen in controlled dose studies, and the user stopped using drugs, then the positive hair band would be diluted with negative hair. For research purposes, the hair is often sectioned into lengths representative of monthly intervals and each section is tested separately. For cost reasons, this is often not done with commercial hair testing. Instead a fixed length of hair, corresponding to a 3-month period is used for testing.³¹ Dilution of the positive hair may bring it below the cut-off to call it positive.

Equal Treatment

Besides the source of drugs, other issues still need to be addressed in hair testing. Different hair samples absorb differing amounts of drugs under identical conditions of time, temperature, pH, buffer, exposure concentration, and drug structure. For example, Figure 5 shows different absorption concentrations for several hair samples exposed, *in vitro*, to trace amounts of cocaine or morphine. Ratios of cocaine and morphine with differences of up to 32 fold can be seen between Caucasian black hair and African American black permed hair. Similar variations have been observed for individuals administered identical doses of cocaine³² or other medicinal drugs.³³ There is no clear explanation for these differences in drug binding but it is likely related to melanin content, porosity of the hair, hair texture, prior hair cosmetic treatments, and other factors. Some have interpreted this different uptake from the environment as bias and more inflammatory as racial bias.³⁴ Undoubtedly, cosmetic influences play a major role with differing groups having differing cosmetic preferences. For example, chemically treating hair to straighten it tends to increase drug uptake. Likewise, application of oils and moisturizers should allow for more efficient transfer of drugs from the environment into the hair. Until the factors are better understood, some individuals with absorptive hair will be more likely identified as drug users, either from actual use or exposure, vs. those with resistant hair. More importantly, some individuals may be misidentified as drug users from uptake of the drug into their hair from the environment.

Figure 5 - Binding of drugs to various hair types. Hair was exposed for 1 hr at 37°C to 5 µg/ml of drug. A microgram of drug is 1/10,000 to 1/100,000 of a normal cocaine dose. This amount is not visible to the human eye.



Low Use Detection

When an individual ingests drugs, most of the dose is excreted in the urine. Only a very small fraction, millionths of a percent, appears in the hair. Additionally, in animal and human experiments, drugs bind to and appear in hair selectively. Drugs that can bind through ionic interactions, such as cocaine, amphetamines, and heroin appear in greater concentrations than do substances that not having charged groups, such as marijuana and steroids. Estimates have been made on the minimal amount of drugs that must be ingested per month to reach a given cut-off level in hair and be called positive. The values are given in Table 1. However, many of these estimates are based on self-reported use, which may be unreliable. Calculations based on controlled dose studies are also shown in Table 1. Note that the estimates based on these studies are higher than those based on self-report. Because of the relatively large amounts of drugs that need to be ingested to reach a hair positive level, for many drugs of abuse, a negative hair analysis result cannot be used to refute a positive urinalysis result. In such a case, the individual could be an occasional user of the drug.

Table 1 – Estimates of minimal amount of drug use to reach commercial cut-off levels. Data are in units/month. The dosage units are an estimate based on the average dosage needed by a user. Users may take multiple dosages in one sitting.

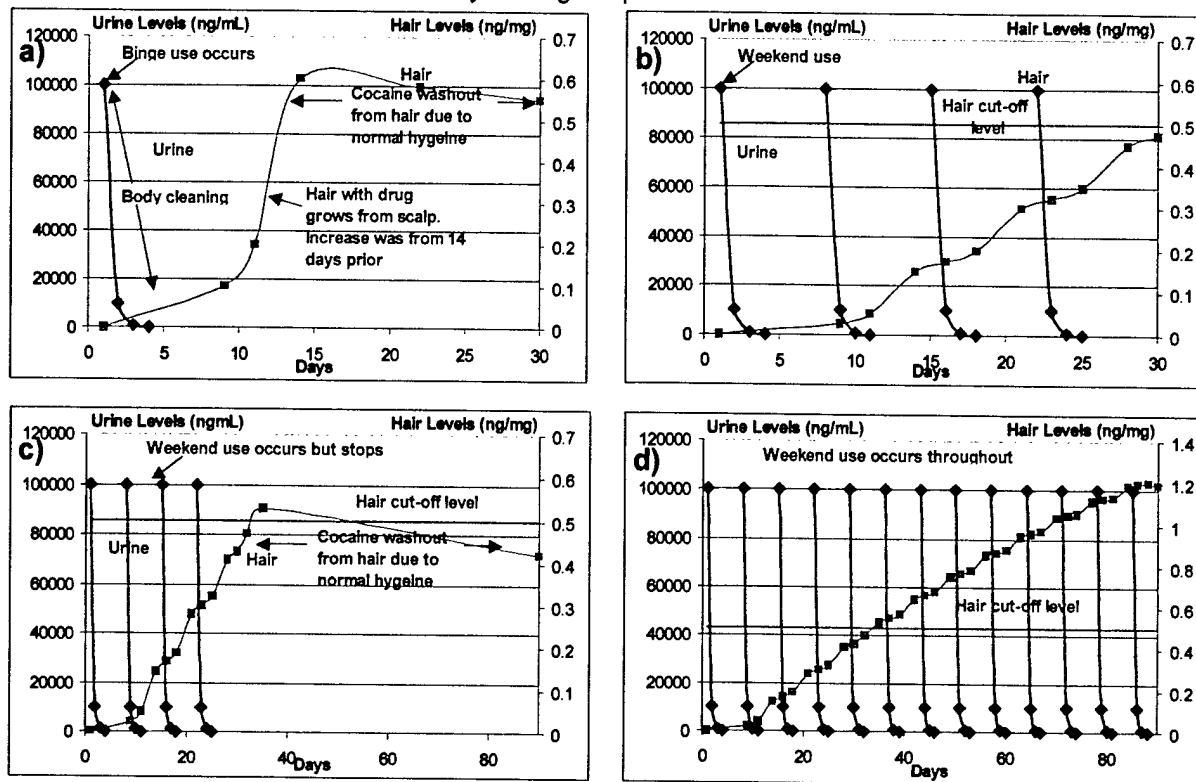
Drug	Self-reported Data ³⁵	Controlled Studies	Dosage Units
Cocaine	260 mg 16 mg (Black hair) ³⁶ 270 mg (Brown hair) ³⁶ 1100 mg (Blonde hair) ³⁶	1100 mg (IV – 14 Caucasians) ³⁷ 250 mg (IV – 3 Non-Caucasians) ^{Error! Bookmark not defined.} 2800 mg (Nasal – 7 Caucasians) ^{Error! Bookmark not defined.} 600 mg (Nasal – 9 Non-Caucasian) ³⁸ 50 mg (Subcutaneous - 8 African-Americans) ³⁹	2-11
Morphine (opiates)	21 bags	800 mg codeine (oral – 8 African-Americans) ^{Error! Bookmark not defined.}	21
Methamphetamine	1320 mg		33-66
PCP	1.8 Sherms		1-2

Which Matrix is Best?

The matrix that has the best chance of detecting drug use depends on the use pattern. Of the five matrices discussed, hair and the sweat patch are integrating matrices – the drug stays in the matrix while the matrix is on the human body, *i.e.* the drug is cleaned from the matrix at a slow rate compared to the lifetime of the matrix on the body. Urine and saliva (and to some extent skin swabs) are pulse matrices – the drug is cleaned from the body at some rate much faster than the availability of the matrix. Because of these differences, which matrix is best highly depends on the use pattern. Consider two use patterns of cocaine (binge and weekend), depicted in Figure 6.

In this example, an individual has used sufficient amount of drug to trip each assay, with hair requiring more than urine. Cocaine would be detectable by urinalysis for 4/30 days (13%) of the time for the binge use pattern (Figure 6a) and 16/30 days (53%) of the time for the weekend use (Figure 6b). In contrast, cocaine would be detectable by hair 16/30 days (53%) of the time after the binge use and no time (0%) during the 30 days after the weekend use as the cocaine has not had sufficient time and amount to reach the cut-off level. Continuing this example to 90 days where the weekend drug use stopped in the first month is shown in Figure 6c. In this case, urine would detect use 16/90 (18%) of the time and hair 17/90 (19%) of the time. Finally, consider the example shown in Figure 6d where the weekend pattern continued for the whole 90 days. In this case, urine would detect use 52/90 (58%) of the time and hair 56/90 (62%) of the time. Of course, if the weekend user or the binge user was in an announced urinalysis program,⁴⁰ there would be no chance of detecting drug use by urinalysis, if they stopped using drugs. In such a situation, depending on the decontamination attempts by the individual (for example daily hair washing or cosmetic treatments) and time window, hair also may have no chance of detecting intermittent drug use.

Figure 6 – Drug use scenarios. For the binge use, the individual had used sufficient cocaine to reach the hair analysis cut-off in a short period of time. For the weekend use, this amount is spread out over 4 weekends. For the continued weekend use, this amount is used every 30 days. In Figure 6a and 6c, the drop-offs in cocaine concentration is only due to hygiene. Growth of negative hair would reduce the window of detection in hair even further by diluting the positive hair.



Testing Scenarios

Any testing system initially should test frequently (at least once a week) to emphasize the seriousness of drug use. For frequent testing either urine, saliva, or skin swabs could be employed with the frequency of testing determined by the window of detection for that matrix coupled with the drug of choice. After several weeks to months of frequent testing, the individual could graduate to a matrix with a longer window of detection such as the sweat patch or hair testing. This would still require contact with the client on a weekly or semiweekly basis and reinforce the seriousness of drug use. After several months of this type of testing the individual could graduate to hair testing every 3–4 months. Important in this system is the realization that some matrices, such as hair, sweat patches, and skin swabs can give false positives due to environmental exposure. Therefore, NO adverse action should be based solely on one of these tests. Instead, individuals who test positive, but deny use, would be placed in the previous testing regime. Only a positive from urine or saliva test would be the basis of disciplinary action. This staged testing is shown schematically in Figure 7 for a 2-year supervised-release monitoring program. The number of tests needed for this program are listed in Table 2 and compared with that needed for conventional urine/saliva testing. Although the number of tests is much less in a combined program, the costs for testing are similar because companies may charge more for the

alternative matrices.⁴¹ Nevertheless, labor costs should be lower in a combined testing program without compromising detection.

Figure 7 – Example of a comprehensive testing program. An individual who failed in any of the alternative matrices would be placed back at the start. The initial urine tests could be substituted by saliva or skin swabs. However, only a positive (urine or saliva) would result in disciplinary action.

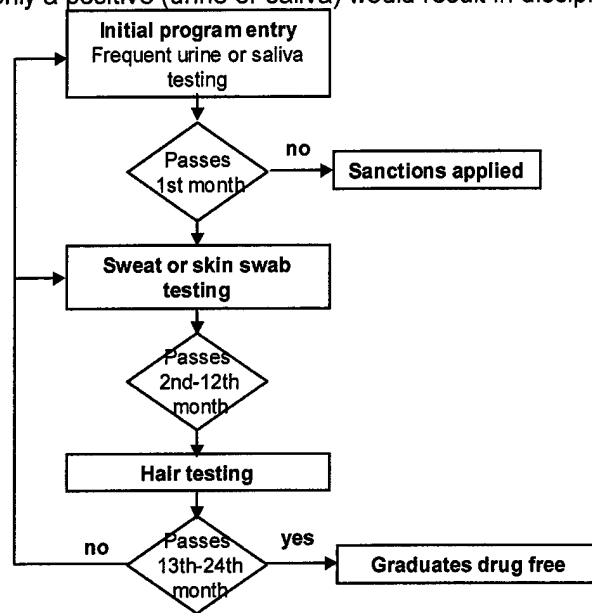


Table 2 – Number of tests employed in the system outlined in Figure 7

	Urine or saliva only (2 tests/week initially and then 1 test/week)	+ Sweat and Hair (Sweat every 2 weeks and hair every 2 months)
1 st month	8 tests	8 tests
Month 2-12	11 * 4 = 44 tests	11*2 = 22 tests
Month 13-24	12 * 4 = 48 tests	6*1 = 6 tests
Total tests	100 tests = 100 visits	36 tests = 36 visits

The longer window of detection or more convenient tests (skin swabs, hair, or sweat) would only be used to classify individuals into those whose contacts with drugs or drug users, hair type, and cosmetic practices make them suitable for testing by that matrix. If an individual was detected to be positive OR exposed⁴² to drugs by this alternative test and has other reasons for the positive result, such as environmental exposure, then that individual would be placed in a frequent, random urinalysis program. Only if that individual were positive by urinalysis would adverse action be taken.⁴³ Periodically, the individuals in the random urinalysis program would be offered the chance to “graduate” to a hair testing program if they believed that such a program were more beneficial.⁴⁴ The type of testing should be the choice of the individual as only he/she can access their exposure to drugs based on their changing living conditions.⁴⁵ The inconvenience of undergoing frequent urine tests would be a deterrent to the bouncing back-and-forth from alternative testing to urinalysis to alternative testing to urinalysis. Individuals bouncing between testing regimes could be offered less frequent urine tests (after “graduating” from the initial urine-testing program, rather than testing by alternative matrices). The cost of such a policy should be

less than the urinalysis only program, and yet provide a better deterrent to drug use by providing flexibility and incentives for "graduating" to a different testing regime.

For detection of drug use in the employment sector, the testing methods selected would depend on the goals of the program. If the goal were to deter drug use because of discipline, medical, or inventory control issues, then a program as outlined above for the criminal justice system would be desirable. If the goal is to ensure performance or public safety and drug use off the job was not a concern, then saliva testing should be used.

Conclusions

Frequent testing acts as a deterrent to drug use. Because of ease of collection, hair, sweat, and skin swab testing should be considered where environmental contamination permits. Hair, sweat, and skin swab testing measure use AND exposure to drugs. Exposure may provide valuable intelligence. However, if use is the only goal – exposure must be eliminated. The order of detectability of drugs in the alternative matrices is not clear at this time, but it likely is: Cocaine (most detectable), Methamphetamine and Heroin (less detectable), Marijuana (much harder to detect). For marijuana users, urinalysis is the preferred matrix. Money and personnel costs can be saved through use of a combined testing program that recognizes the strengths and weaknesses of all the matrices being employed. A summary of the advantages and disadvantages of the various matrices is given in Table 3.

Table 3- Summary of the advantages and disadvantages of each matrix.

Matrix	Advantages	Disadvantages
Urine	<ul style="list-style-type: none"> • Well known system • Lowest cost/specimen • Self cleaning - not very susceptible to environmental contamination 	<ul style="list-style-type: none"> • Must be collected under observation to prevent adulteration • Females harder to observe • Moderate window of detection • On-demand sampling not always possible
Saliva	<ul style="list-style-type: none"> • Easily collected under observation • Best correlation with under the influence • Self cleaning – not susceptible to environmental contamination 	<ul style="list-style-type: none"> • Low drug levels require sensitive instrumentation • Short window of detection
Sweat Patch	<ul style="list-style-type: none"> • Easily collected under observation 	<ul style="list-style-type: none"> • Susceptible to environmental contamination • Moderate window of detection • Patches don't always adhere well • Scientific information limited
Skin Swabs	<ul style="list-style-type: none"> • Easily collected under observation • Inexpensive testing available 	<ul style="list-style-type: none"> • Susceptible to environmental contamination • Moderate window of detection • Little scientific information available
Hair testing	<ul style="list-style-type: none"> • Easily collected under observation • Long window of detection 	<ul style="list-style-type: none"> • Susceptible to environmental contamination • Some individuals lack head hair • Cosmetic concerns • Moderate drug use required • Not all hair behaves the same

References and Notes

¹ K.L. Preston, M.A. Huestis, C.J. Wong, A. Umbricht, B.A. Goldberger, and E.J. Cone, "Monitoring cocaine use in substance-abuse-treatment patients by sweat and urine testing", *Journal of Analytical Toxicology* **23** (1999) 313-322.

² J. Ambre, T.T. Ruo, J. Nelson, and S. Belknap, "Urinary excretion of cocaine, benzoylecgonine, and ecgonine methyl ester in humans", *Journal of Analytical Toxicology* **12**(6) (1988) 301-306.

³ G.F. Jackson, J.J. Saady, and A. Poklis, "Urinary excretion of benzoylecgonine following ingestion of Health Inca Tea", *Forensic Science International* **49**(1) (1991) 57-64.

⁴ R.C. Baselt and R. Chang, "Urinary excretion of cocaine and benzoylecgonine following oral ingestion in a single subject", *Journal of Analytical Toxicology* **11**(2) (1987) 81-82.

⁵ Most programs use the cut-off levels set by the Substance Abuse and Mental Health Administration Guidelines for workplace drug testing. In this case, the levels were set high enough to avoid passive exposure except under extreme conditions. Since most testing laboratories follow these guidelines, the larger number of samples lowers the cost relative to specialized testing at lower cut-off levels. However, because most instrumentation is highly automated, even a low volume testing facility should be able to adjust the cut-off levels to lower values without substantial cost penalties.

⁶ Most drugs have a 2-4 day window of detection. However, marijuana, because it is more fat soluble, is generally assumed to have a window of detection of 5-7 days for a single use. Therefore, urine testing is generally more effective for this drug.

⁷ We do not test sweat collected as a liquid. Rather, the residue from dried sweat, sebum, and dead skin cells is used, and we do not try to differentiate between the various species. All these materials have differing ability to bind substances of interest. For moderate to long-term testing after the fact, skin cell proteins are the likely repository for the substances of interest because the other surface materials will be removed by normal hygiene. Also skin tends to be moist, which facilitates binding.

⁸ Drinking large amounts of water will dilute the drug levels in the urine and may bring them below the cut-off level. Therefore, many programs measure creatinine or specific gravity and the urine sample must be above a certain level (SAMSHA recommends a specific gravity ≥ 1.003 and creatinine >20 mg/dL) or be it will be considered adulterated and untestable. However, a better approach would be to test these samples at the limit of detection of the analytical procedure. These levels are often so low as to make adulteration by physiological dilution actually counter productive. This would also treat individuals who have certain physiques (small-framed females) or jobs that tend to produce low creatinine levels naturally (dehydrating conditions such as physical labor or flight attendants) in a fairer manner.

⁹ In this scenario, reusable instrumentation would be required to keep the costs reasonable. For example, ion mobility mass spectrometry (such as the Ion Track or Ion Scan systems) could be used to test drugs in saliva or the inexpensive ion selective electrode systems being developed at NRL.

¹⁰ For individuals that chew on items (fingernails, pencils, etc.) or smoke, these could be contaminated and contaminate their saliva. However, waiting 10-20 minutes before obtaining the saliva, will allow these contamination sources to be eliminated.

¹¹ A.J. Jenkins, J.M. Oyler, and E.J. Cone, "Comparison of heroin and cocaine concentrations in saliva with concentrations in blood and plasma", *J. Analytical Toxicology* **19** (1995) 359-373.

¹² We use Salivettes manufactured by Sarstedt, which come in their own storage container. These are relatively inexpensive (\$0.40) collection devices that can collect approximately 1 mL of saliva in a few minutes. This amount is more than adequate for most testing scenarios.

¹³ A small proportion of the population suffers from dry mouth, which is a reduced saliva flow. Some drugs exacerbate this condition. Chewing on the saliva collection device tends to stimulate saliva flow in individuals with reduced saliva production.

¹⁴ M. Burns, R.C. Baselt, "Monitoring drug use with a sweat patch: an experiment with cocaine." *J. Anal. Toxicol.* **19**(1) (1994) 41-48.

¹⁵ Seven days is the recommend time of the manufacturer.

¹⁶ P. Kintz, "Drug testing in addicts: a comparison between urine, sweat, and hair", *Therapeutic Drug Monitoring*, **18** (1996) 450-455.

¹⁷ M. Burns and R.C. Baselt, "Monitoring drug use with a sweat patch: an experiment with cocaine", *J. Anal. Toxicol.*, **19**(1) (1994) 41-48.

¹⁸ M.J. Long and D.A. Kidwell, "Improving the PharmChek™ Sweat Patch: reducing false positive from environmental contamination and increasing drug detection", NRL Memorandum Report 6170-01-8597, December 19, 2001.

¹⁹ D.A. Kidwell and F.P. Smith, "Susceptibility of PharmChek™ Drugs of Abuse Patch to Environmental Contamination", NRL Memorandum Report 6170-99-8414, November 3, 1999.

²⁰ D.A. Kidwell, J.D. Kidwell, F. Shinohara, C. Harper, K. Roarty, K. Bernadt, R.A. McCaulley, and F.P. Smith, "Comparison of daily urine, sweat, and skin wipes among cocaine users", *Forensic Science International*, **133**(1-2), 63-78, 2003.

²¹ F.P. Smith, D.A. Kidwell, "Susceptibility of PharmChek™ Drugs of Abuse Patch to environmental contamination", *Forensic Science International* **116**(2-3) (2001) 89-116.

²² G. Skopp, L. Potech, H.P. Eser, and M.R. Moller, "Preliminary practical findings on drug monitoring by a transcutaneous collection device", *J Forensic Sci.* **41**(6) (1996) 933-937.

²³ D.J. Crouch, C.L. Metcalf, M.H. Slawson, and J. Baudys, "An assessment of the potential for vapor phase contamination of the PharmChek™ Sweat Patch", *Bulletin of the International Association of*

Forensic Toxicologists. **32**(3) (2002) 7-10.

²⁴ F.P. Smith and D.A. Kidwell, "Cocaine in hair, saliva, skin swabs, and urine of cocaine users' children", *Forensic Science International* **83** (1996)179-189.

²⁵ The drugs probably remain much longer but are so difficult to remove that rapid testing is not possible.

²⁶ W.A. Baumgartner, V.A. Hill, and W.H. Bland, "Hair analysis for drugs of abuse", *J. For. Sci.*, **34**, 1433 (1989).

²⁷ D.L. Blank and D.A. Kidwell, "Environmental Exposure - The Stumbling Block of Hair Testing", in *Drug Testing in Hair*, Pascal Kintz, Ed., CRC Press, Boca Raton, FL, 1996, pp. 17-68.

²⁸ D.L. Blank and D.A. Kidwell, "Decontamination Procedures for Drugs of Abuse in Hair. Are They Sufficient?", *Forensic Science International*, **70** 13-38 (1995).

²⁹ G. Romano, N. Barbera, and I. Lombardo, "Hair testing for drugs of abuse: evaluation of external cocaine contamination and risk of false positives", *Forensic Science International*, **123** (2001) 119-129.

³⁰ G. Romano, N. Barbera, G. Spadaro, and V. Valenti, "Determination of drugs of abuse in hair: evaluation of external heroin contamination and risk of false positives", *Forensic Science International*, **131** (2003) 98-102.

³¹ Hair growth varies widely among individuals and even on different locations on the body. Generally, the posterior vertex (top-back) of the head has the most consistent growth. The growth rate in this area is often quoted as 0.8-1.3 cm/month. Some commercial laboratories use a 3.9 cm section of hair, which is claimed to represent a 3-month window of detection. However, this window does vary.

³² G.L. Henderson, M.R. Harkey, C.H. Zhou, R.T. Jones RT, and P. Jacob, "Incorporation of isotopically labeled cocaine into human hair: Race as a factor", *J. Anal. Tox.*, **22** 156-165 (1998).

³³ D.G. Wilkins, A. Mizuno, C.R. Borges, M.H. Slawson, and D.E. Rollins, "Ofloxacin as a reference marker in hair of various colors", *J. Analytical Toxicology*, **27** (2003) 149-155.

³⁴ T. Mieczkowski and R. Newel, "An analysis of the racial bias controversy in the use of hair analysis" in *Drug Testing Technology – Assessment of Field Applications*, Ed. By T. Mieczkowski, CRC press, New York (1999), pp. 313-348.

³⁵ W.A. Baumgartner and V.A. Hill, "Hair analysis for organic analytes: methodology, reliability issues, and field studies" in *Drug Testing in Hair*, ed. by P. Kintz, CRC Press, 1996, pp. 223-265.

³⁶ Calculated from: F. Ursitti, J. Klein, E. Sellers, and G. Koren, "Use of hair analysis for confirmation of self-reported cocaine use in users with negative urine tests", *Journal Of Toxicology-Clinical Toxicology* **39** (2001) 361-366.

³⁷ Calculated from: G.L. Henderson, M.R. Harkey, and R. Jones, "Hair analysis for drugs of abuse. Final Report on Grant Number NIJ 90-NIJ-CX-0012 to National Institutes of Justice", Sept. 1993.

³⁸ Calculated from: G.L. Henderson, M.R. Harkey, C. Zhou, R.T. Jones, and P. Jacob, III "Incorporation of isotopically labeled cocaine into human hair: race as a factor", *J. Analytical Toxicology*, **22** (2000) 156-165.

³⁹ Calculated from: J.D. Roper-Miller, B.A. Goldberger, E.J. Cone, and R.E. Joseph, Jr., "The disposition of cocaine and opiate analytes in hair and fingernails of humans following cocaine and codeine administration", *J. Analytical Toxicology*, **24** (2000) 496-508. These authors used weekly head shavings instead of whole hair. It was assumed that the average time the drug was visible was 2 weeks, the average cocaine concentration was 1.75x the peak value reported, a constant growth rate of the hair, and a linear dose-response curve. Additionally, the doses were split into 3 administrations over a week period, which may enhance incorporation.

⁴⁰ For example: preemployment programs that require urinalysis several weeks after the job offer or employment programs that test at defined times like birthdays.

⁴¹ Because of competition, methodology, and automation, urine tests are substantially cheaper than current alternative testing on a per test basis. However, this could change as more competition enters this marketplace.

⁴² In this case, the testing laboratories would use LOWER cut-off levels than for routine testing because the additional safety provided by higher cut-off levels from environmental exposure would not be necessary.

⁴³ In some programs, individuals must have several positive tests before adverse action is taken. It is not clear that an individual testing positive by the initial urinalysis should be offered drug treatment or an

additional chance. However, to be placed in the urinalysis program a second time, that individual would need to argue that the alternative test was incorrect and drug treatment was unnecessary. Therefore, any urine positive (after graduation from the initial program) should have substantial sanctions applied.

⁴⁴ The type of testing should be the choice of the individuals as only they can access their exposure to drugs based on their changing assignments. Additionally, exposure to cocaine, which can cause a false urine positive under certain circumstances, can be easily documented with urinalysis but not with hair analysis.

⁴⁵ An example is moving into an apartment where drugs had been used. Sufficient drugs can remain in the environment to produce a positive by sweat or hair testing with some individuals.