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Comments on FR Doc 04 -7984

David A. Kidwell, Ph.D.

I believe that my educational background and experience in the testing of alternative matrices for drugs of abuse makes me an expert in this field. [1] I have a number of comments to make on the proposed F ederal Guidelines for testing of alternative matrices. [2] In general, I have no problems with the use of hair and sweat testing under limited conditions and I have proposed reasonable scenarios for their use. [3] However, for their use in Federally mandated t esting, I do not believe that these technologies have been fully evaluated nor that SAMSHA has fully considered all the problems that their use would entail. The drug testing community looks to SAMSHA to propose fair guidelines for the detection of drug u se. For the reasons setout below, I do no believe that FR Doc 04 -7984 meets SAMSHA's high scientific standards.

A brief history of my involvement with hair testing and sweat testing

In the mid 1980s, the Bureau of Naval Personnel (BUPERS) was approache d by Werner Baumgartner about a novel way to screen individuals for drug use through the use of hair analysis. At that time, the Navy had one of the largest (if not the largest) urine drug testing operations in the world and was always open to new ways to conduct its testing. NRL was tasked by BUPERS to oversee and fund a preliminary study, using personnel in drug rehabilitation at a Navy facility, to evaluate hair testing for cocaine and THC detection. This initial study showed some promise. Because the Navy required two independent confirmations of the presence of drugs before a positive sample could be reported and only Radioimmunoassay (RIA) testing of hair was employed at that time, I was tasked by BUPERS to develop a confirmation test using mass spe ctrometry. I presented the results of my research at the American Society for Mass Spectrometry Conference in 1988 and the first international hair testing meeting held at the National Institutes of Standards and Technology (NIST). During the NIST meetin g, I proposed that the then current concept of hair trapping drugs in inaccessible regions only from the blood was probably incorrect. Instead, I proposed what is now accepted by the scientific community, of multiple sources for drugs appearing in hair. In 1988, I developed the following four concepts:

> Hair traps drugs from internal and external sources - sweat and sebum being one source of the external contamination. Drugs can appear in sweat from two sources: Use and exposure.
>
> The external sources o f drugs confound the data interpretation between user of drugs and mere exposure. [4]
>
> Different hair types have differencing susceptibility to internal uptake and external contamination and therefore a "hair type bias" is likely.
>
> Detection of low use is diffi cult and unproven.

In the intervening 15 years, I have conducted a number of research programs on these four issues. I have published 9 papers in the peer -reviewed literature, several book chapters, and have authored or co -authored over 30 presentations at scientific meetings and technical working groups on hair testing. The Navy has been conducting urine testing for over 20 years and currently tests about 1.5 million urine samples/year for seven drugs of abuse. The Navy has not replaced their urinalysi s program with hair testing.

Since 1990 I have been working on the alternative matrices of sweat and saliva. During this work, coauthors and I evaluated the Pharmcheck ™ Sweat patch and found it to be susceptible to false positives from environmental contamination, which we termed Contamination From WithIn and Contamination From WithOut. We have published four papers in this area and made a number of presentations. The se results will be detailed below.

General Concerns

As discussed below, both hair and sweat testing [5] measure exposure to a substance rather than only ingestion of that substance. One of my concerns in employing this technology in the Federal mandated pr ograms is that exposure cannot be eliminated as an explanation for a positive result. Exposure can come from many sources both knowing and unknowing. For example, living with a drug user or having intimate relations with a drug user may be a common route for exposure. Except for very limited law enforcement and intelligence positions, who an employee associates with after hours is none of the employer's business. In fact for the Government to prohibit freedom of association may go against the 1 st Amendm ent and numerous other laws. How does hair and sweat testing restrict these rights? For example, if an employee's spouse, son, daughter, mother, father, relative, or living conditions [6,7] puts him/her in contact with drugs, they may very well become posit ive with these tests. In fact several studies SHOW that this is the case. Additional sources of drugs may be intimate contact with a drug user. Who wants to admit to frequenting prostitutes? An employee, who is identified as a drug user under common ci rcumstances such as this, must then prove their innocence and reveal highly-personal information to their employer. Afterwards it is up to the employer to fairly evaluate this information – something that most are unequipped to do. We have medical review officers in the loop for prescription medications and false positives resulting from them to protect the privacy for the employee. This appears lacking for hair and sweat testing. Current medical review officers would NOT have the proper training to eva luate the living habits of an individual even if that individual could point to a specific proximal cause of his/hers false positive result. Thus, I foresee substantial invasion of privacy issues with these two technologies that have never been explored w ith urine testing. Substantial resources went in to exploring the envelope where passive exposure to drugs produces false positives in urine testing. Except for studies sponsored by the Navy and ONDCP, no studies have been undertaken by SAMSHA on this crucial question. Yet SAMSHA appears to be allowing individuals in Federally regulated testing to become the guinea pigs and use their own private resources to undertake these studies by trying to demonstrate their innocence in court when they become positi ve though external exposure.

Some of the problems with hair testing, that will be discussed at length below and that have not been included in SAMSHA guidelines, include:

- Hair testing measures exposure to a drug rather than use. Most Federally mandated programs are based on safety. Positives resulting from exposure to drugs cannot meet that premise because exposure has little or no consequences to health at levels that would cause false positives in hair testing. In fact, if we look at trace enough leve ls, everyone has exposure to drugs on a daily basis.
- Hair testing shows bias. Hair is very heterogeneous and therefore not all hair behaves the same when exposed to drugs. In general, hair from African Americans picks -up and retains drugs more readily th an other types of hair making these individuals more likely to be falsely accused of drug use from just exposure. Because drug use tends to be more highly concentrated (more use per area) in less affluent areas, individuals living in those areas are more likely to be exposed. Additionally, because people of color tend to inhabit less affluent areas, this puts then at increased risk of falsely being accused of

drug use, likely loosing their job, and then being blacklisted from gainful employment. Expandin g the reach of these technologies will put more individual at risk.

- Additionally, some religions forbid cutting of hair. Will an exception be allowed for this practice if hair testing is the only technology allowed in certain industries? What if head hair is not available? Is SAMSHA authorizing the cutting of other body hair?

Some of the problems with sweat testing, that will be discussed at length below and that have not been induded in SAMSHA guidelines, include:

- The patch (the ONLY FDA cleared devic e and thus actually what is being approved by SAMSHA) can become contaminated from environmental exposure. Thus, like hair testing, sweat testing measures exposure to drugs rather than use of drugs. Most Federally mandated programs are based on safety. Positives resulting from exposure to drugs cannot meet that premise.
- Like hair testing, binding of drugs to skin may have a melanin component. Thus, people of color may be more likely to retain drugs on their skin and be considered drug users. As mention ed above for hair, people of color are also more likely to be exposed to drugs. These two factors – selective retention and selective exposure – put people of color at a higher risk.

A small problem with saliva testing, that can be addressed here, is tha t that SAMSHA should make clear that the cut -off levels for drugs in saliva are being set essentially at technical cut -off levels. These levels do NOT reflect impairment in anyway and are being set lower than necessary to prove impairment to reinforce the deterrence value of saliva testing. I have proposed alternative methods (which SAMSHA should consider – perhaps in a conference format) to set levels to more reflect impairment (Table 1), which is a likely goal in using saliva. These levels are substa ntially different than proposed in the SAMSHA guidelines.

Table 1 - Summary of calculated saliva levels that likely indicate some form of impairment. Reference 8 should be consulted for calculation method and literature references.

Drug	[Saliva (ng/mL)]
Cocaine	185-600
Heroin	7 (Morphine)
MDMA	1000
Marijuana	20-30
	150-300

Specific Sectional Issues

Some of the sectional issue comments are to call SAMSHA's attention to inconsistencies i n the proposed guidelines.

Section 3.4

On the SAMSHA website for several years, you have published proposed cut -off levels and other criteria to report a cocaine positive for hair. These previous levels were carefully crafted at a four hair testing work ing group meetings (HTWG), in which two I participated. The levels and criteria were a compromise to reduce reporting (but NOT eliminate) innocently exposed individuals as cocaine users and unfairly ruining their reputations. Previously, the cut -off for cocaine was 1000 pg/mg (I am using your units. However see endnote 9) with a 10% BE rule. The previous levels and criteria have been cut arbitrarily in half in section 3.4. Some

commercial companies may suggest that they have sophisticated enough decont amination procedures to distinguish environmental contamination from active use (I disagree – see below) and that too many occasional users would be missed by hair testing if the cut -off level were raised. However, we set urine levels to reduce (but not e liminate) passive exposure and thereby miss active use. If we give -up detecting all use by urine to reduce falsely accusing innocent individuals, then why do we insist on catching everyone with hair testing? The levels suggested by YOUR scientific commit tee should stand.

There appears to be an inconsistency in BE rule. The proposed rule is 5% rather than the previous rule of 10%. If a sample were at the cut -off for cocaine of 500 pg/mg, then BE must be only 25 pg/mg to report that sample as positive. The proposed guidelines suggest that it be 50 pg/mg.

Neither cocaethylene, nor nor -cocaine, nor BE are unique metabolites of cocaine but are present in the environment. Thus, their presence alone does not indicate use. Rather than an absolute amount, th e proposed guidelines should require a relative amount to cocaine to reduce environmental exposure indicating drug use. [10] Of course, this does not eliminate passive exposure from the sweat of a drug user rather than from drug in the environment. Sweat appears to be transferred during intimate contact or the sharing of clothing and may not be rare.

Of all the proposed drugs, only THC carboxylic acid (THCCOOH) appears to be a unique metabolite of an illicit substance. All the others have the same problem as cocaine. However, THCCOOH could reasonably be assumed to arise from non -biological processes, if THC were incorporated into the hair from marijuana smoke. [11] Because of these non -biological processes, laboratories should be required to report both the THC and THCCOOH levels in the hair. This ratio may be diagnostic of contamination. If after years of experience, this ratio is not useful, then SAMSHA could revisit the guidelines and eliminate the reporting requirement for both THC and THCCOOH.

Criteri a for reporting of sweat positives

The confirmation requirements for sweat testing are much worse than for hair testing. Hair testing at least tries to reduce passive exposure with decontamination and metabolite criteria. The proposed sweat testing total ly lacks these criteria. In fact, for cocaine it appears that either cocaine only or BE only would be considered positive. At least require a percentage of BE to cocaine be present and that a BE only patch should raise suspicion.

Section 8.4

The requi rement for an individual to be searched for adulterants to a sweat patch is ludicrous. The patch is placed on by the collector. Nothing in an individual's pocket can adulterate the patch during the application. If this section stays, what are examples f or adulterants – a knife, glue, money, soap? Also, why just the pockets and not purses, briefcases, cars, and houses as adulteration can occur at anytime during the wearing of the patch?

Like testing done at SAMSHA, in our laboratory testing with only a few individuals we have observed allergic reactions. Therefore the comment that:

> On rare occasions, the sweat patch can produce an allergic reaction similar to that for other adhesive bandage products. When this occurs, the donor shall return to the colle ction site and the collector must remove the sweat patch and then request permission from the Federal agency to collect another type of specimen. The sweat patch procedure is cancelled by the collector and notifies the medical review officer and the Federa l agency.

needs strengthening to that a n individual experiencing allergic reactions is NOT a good candidate to wear the patch and MUST be tested by alternative technology. Rather than requesting permission to use alternative technology. In fact the indiv idual undergoing testing should be given the option to wear another patch after explaining the alternatives. However that choice should BE UP TO THE SUBJECT AND NOT THE FEDERAL AGENCY. Otherwise, a Federal agency could be accused of torture by insisting that an individual wear a device that was not suitable for that individual.

Requiring a split specimen for the patch WILL cause many problems. What if the results do not agree because one patch was contaminated on application or removal and the other wa s not? What if the contamination were at different levels – say one patch at 100 ng and the other at 5. Does the 5 ng/patch confirm the 100 or just reflect less contamination? Additionally, contamination CAN occur during analysis. Two patches are bette r than one but it truly depends on cleanliness to amounts of drugs 1000s of times below the visible level.

The patch requires far more careful laboratory analysis than does a urine sample. This is because more steps are involved, less material is being e xtracted (making trace contamination more problematical), a solid matrix must be extracted whereas urine is analyzed directly, the drug levels are lower, and the parent drug (which is in the environment) is being sought. Thus, SAMSHA should require far mo re blanks by the testing laboratory for QC purposes than for urine testing and this requirement SHOULD be part of the proposed regulations.

Although it does not appear to be directly addressed, the sweat patch sometimes fails to adhere. Many studies have confirmed this fact, including our own. Additionally, this failure appears to be more frequent on certain individuals and those who exercise (and thus sweat) heavily. Some agencies consider the failure to adhere a violation just as severe as a positive result. The proposed regulations should clearly address this circumstance and if an individual has repeated failures, then they should be placed under alternative testing. At the very MINIMUM, photographs of all "compromised" patches must be taken and th is requirement must be part of the proposed regulations.

Section 11.15

Only GC/MS is currently allowed as the confirmatory procedure for a presumptive urine drug positive. The proposed guidelines add GC/MS/MS, LC/MS, and LC/MS/MS as three new analytical methods for confirmation testing.

I am concerned that the addition of tandem mass spectrometry and LC as confirmatory detection methods will degrade the reliability of drug testing because these techniques (AS CURRENTLY PRACTICED IN THE COMMERCIAL ENVI RONMENT) have lower information content than GC/MS by a substantial fraction. [12,13] Minimal standards for confirmatory testing should require the same number of ions (generally accepted as three) for all technology. LC/MS, GC/MS/MS, and LC/MS/MS frequently produce only a single ion (or a single daughter ion from the parent). While these procedures can be more sensitive, the results are less specific (as often PRACTICED) and therefore less reliable than if three ions were used. [14,15] GC/MS has been a reliable confirmatory test method under the existing guidelines for millions of samples. That is a lot of experience to discard without a through review. I believe that the addition of alternative confirmation procedures, WITHOUT stringent guidelines imposed (as discussed in references 12 and 13), is unnecessary, unwise, and will needless produce false positives when employed on a large scale. Thus, SAMSHA must break new ground and propose minimal standar ds for confirmation testing rather than leave it to the laboratory to run

the samples with the cheapest and fastest methods possible without regard to quality as long as they have the magic words MS in their title.

Selected Scientific Considerations for H air Testing

Proponents of hair testing appear to be fixated on the concept of soaking hair in solutions of drugs is not likely to occur in the real world without any evidence to support their hypothesis. Nevertheless, they appear to sidestep the problem that hair exposed to external substances incorporates those substances into the hair structure and they cannot be removed. This has long been known for heavy metals and has made heavy metal analysis a measure of exposure rather than ingestion (see: 16,17,18,19, and 20). It is not surprising that I found the same result almost 16 years ago to also be true for drugs of abuse. [21,22] Since that time, numerous researchers have confirmed this initial observation that negative hair exposed to solutions of drugs become s positive as if the hair was from a drug user. In fact, SAMSHA's contractor, RTI, uses exposure to drug solutions to prepare hair samples to send to the commercial laboratories to test their procedures. [23] Long exposure times are not necessary for efficie nt incorporation. We clearly showed over 10 years ago that only a few minutes exposure would suffice to incorporate some drug and that the incorporation rate was linear with time and amount, a result predicted by a diffusion model for incorporation. [29]

Even some commercial laboratories agree that hair testing measures exposure rather than merely use. In fact, Dr. Kelly while director of toxicology at Associated Pathologists Laboratories in Las Vegas (now Quest) and Dr. Moore, laboratory director at U.S. Drug Testing Laboratory in Chicago, Illinois (the third and forth largest, commercial hair testing organizations at the time) have stated at SAMSHA conferences on alternative matrices that hair testing measures e xposure. For example, Dr. Kelly, at a SAMSHA conference [24] stated:

> We have at times – I should indicate, before we even get into the external contamination issue, kind of where we stand. Based on the data that is available today, I don't think that you can flatly state that somebody is a drug user and was not externally contaminated based upon the finding of a parent drug in hair alone. You can come close to doing that with metabolites but there are still some unanswered questions in that realm. There have been situations where, with employers that have extremely credible donors, we have recommended that if they wish to hire that individual, that they hire them subject to random urine testing over a period of time, such as six months. I am uncomfortable sti ll, guess, with just flatly stating that somebody is a drug user, even though obviously the majority of people who test positive are drug users.

At the same conference, Dr. Moore stated her agreement that hair is difficult to decontaminate and that meta bolites may not make reliable markers of use. She said:

> It has been shown by numerous researchers that drug powders and smoke can be incorporated into the hair. It has been suggested that one can distinguish between active use and passive exposure using the wash kinetics that we have heard about. Unfortunately, as Dr. Kelly said, no one has been able to reproduce this. Therefore, you don't have a scientific consensus on whether or not this type of approach actually works. There have been suggestions that we would use cutoff levels. You have just heard my reasons for thinking that is not a good way to good. The presence of metabolites or parent metabolite ratios is a good suggestion. I think it has some merit. Benzoylecgonine, unfortunately, doesn't prove c ocaine use.

Only one commercial company appears to hold that hair testing measures use and use alone, if the decontamination is done properly. Yet they have repeatedly stated that one can prepare standards in the laboratory by exposing hair to solutions of drugs that pass ALL their internal quality controls and make the hair look like a drug user's hair. So the only unsettled question is does exposure occur in the real world? The short answer appears to be - yes.

I have authored and coauthored extensi ve reviews of my work and others and much of this evidence for passive exposure will not be repeated here. [25,26,27,28,29] However, several papers in the scientific literature frequently are used to argue that passive exposure does not occur. For example, in a paper with a limited study of police officers with unknown (but assumed some) exposure, [30] Dr. Mieczkowski's discusses his concept of passive exposure and contrasts it with mine. After this discussion, Dr. Mieczkowski describes the older procedure used by Psychemedics to decontaminate hair, [31] explores environmental contamination and how papers reported to show environmental contamination are wrong, and finally describes his data set. His data set consisted of hair samples (40) collected from officers who cl aim some drug contact as part of their work. [32] A detailed questionnaire was obtained from 39 of these 40 individuals discussing, among other issues, frequency of drug handling and types of drug contact. [33] One of the 40 officers was positive above Psychemed ics cut-off level (at 5.2 ng/10 mg of hair) and another showed the presence of cocaine, but below the cut -off level. The positive officer was tested four months later and found to be negative. [34] Dr. Mieczkowski explained this positive result as "microinge stion", a novel concept. [35] In previous papers, Dr. Baumgartner calculated that it would require ingestion of 234 mg/month of cocaine to reach a positive hair level of 5 ng/10 mg of hair. [36] Therefore, using Dr. Baumgartner's estimates (which controlled stud ies indicate are low) this officer would have needed to ingest (supposedly by "taste testing") 10 mg/day (or 5 -10 samples/day) for each of the 20 workdays in a month. Using estimates from more controlled studies, the officer would have had to "microingest " 150 mg/day (or 75 -150 samples/day). Such an undercover officer should be awarded a metal. If either estimate meets Dr. Mieczkowski's definition of "microingestion", I believe that such "microingestion" is extreme. Passive exposure is the most likely r oute to this positive.

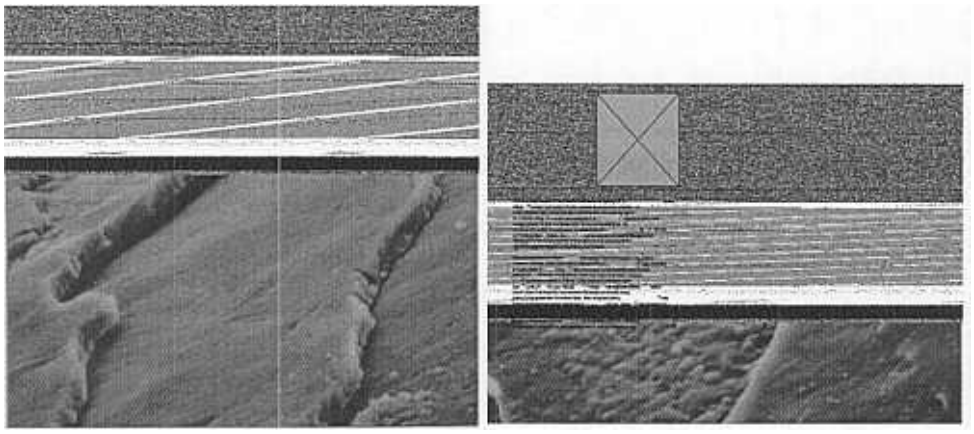
Mere opportunity for exposure is insufficient to cause a false positive. An additional difficultly of examining individuals who are in the vicinity of drugs is that moisture may absent. Moisture (or similar hydroxylic solvents) i s necessary for efficient transfer of the exposure to the hair (as discussed below). In addition, exposed individuals may not have the appropriate hair type or cosmetic practices for efficient incorporation of external substances.

An earlier paper, [37] often cited to demonstrate that external contamination can be removed, does not apply modern decontamination procedures; more importantly, the contamination events are unrealistic. The authors exposed cut hair to crack cocaine vapors and decontaminated the h air by washing. The authors then analyze the "decontaminated" hair by an extraction procedure that likely does not fully account for all the drugs in the hair. Because all the drugs are not extracted for analysis, extraction procedures can produce false negatives and give a false sense that the hair was decontaminated where in actuality the analysis was lacking.

An additional major issue with this paper is how the authors contaminate the human hair. They expose cut, dry hair to crack cocaine vapors. H air is a complex organ. It is composed of a number of sub -structures, but for the purposes of this discussion, I will only consider two: (1) The cortex or the inner part of the hair, thought to be the repository of the absorbed drugs, and (2) The cuticle , or the outer part of the hair, which protects the inner part from external contamination. A micrograph of intact human hair is shown in Figure 1a. The scale -like entities are the cuticle. In aqueous environments, the cuticle opens -up and allows molecu les to

penetrate into the cortex. [38] Furthermore, the liquid, which swells the cuticle, provides a vehicle for the rapid transport of materials. When the liquid is removed, the cuticle closes and helps entrap the drugs. Therefore, contamination applied in the dry state to hair, as was done in this paper, is easily removed, whereas contamination applied in solution is not. By inappropriately contaminating hair, the authors reach the incorrect conclusion that environmental contamination is easily removed.

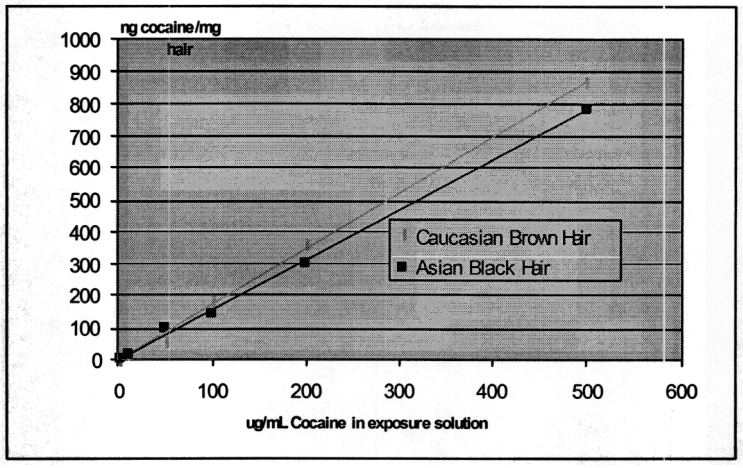
Figure 1 – Structure of human hair cuticle. [39] Micrograph (A) is normal human hair. Micrograph (B) is hair that has a damaged cuticle due to cosmetic treatment.



from the sweat of drug users or as impurities in the source cocaine. Clearly, the money was not metabolizing cocaine and that clearly "metabolites" are being transferred to inanimate objects, such as money.

Although I could discuss our previous data at length, I rather review the data from the leading hair testing laboratory in the country. [46] In this paper, 14 negative hair samples are exposed to 1 ì g/mL of cocaine for 1 hour at room temperature [47] and then decontaminated using three procedures. None of the procedures removes 100% of the drugs. However, the remaining drug concentrations were below their current cut-off criteria and they considered the hair decontaminated. But wait. We showed long ago that the uptake into hair from the external environment was linear with the concentration of drug in the exposure solution (See Figure 2). [25] Additio nally, we showed that 1 ì g/mL, as employed here, would NOT normally reach the 0.5 ng/mg cut-off necessary to call a sample positive. **Because hair may be passively exposed to any quantity of drug in the real-world,** one could have just as well used 10 ì g/mL, a longer time, or higher temperatures. As shown in our previous studies, all these conditions would have increased the cocaine uptake. If the authors had exposed their hair samples to 10 ì g/mL of cocaine (1/10,000 th of a typical dose), two of their sam ples (#16&17 in Table III) would have met ALL their wash criteria and be considered positive, true drug-user specimens. [48] A 20% false positive rate is not reassuring for a claim of an effective decontamination procedure.

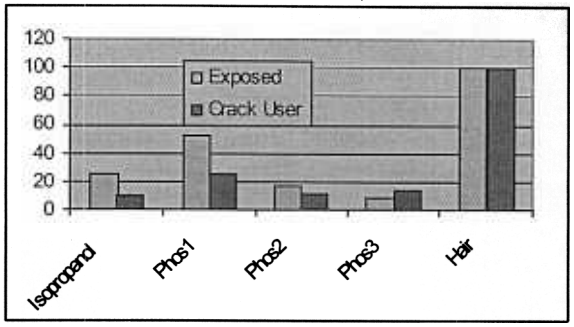
Figure 2 – Effect of concentration on the incorporation of cocaine into hair. Two types of hair were exposed to cocaine for 1 hr and were dried overnight before extraction. Source: Blank and Kidwell, reference 25. Under the conditions that these two hair specimens were exposed, they DID reach 1 ng/mg at the 1 ì g/mL exposure solution. However, many hair samples in other experiments did not, when exposed at this level.



An accidental, independent test of commercial wash procedures was provided by Dr. Mieczkowski. [30] As a control, he sent had analyzed three hair samples of known origin. Two were exposed hair and one was the hair of a known cocaine user. One of the exposed hai rs and the hair from the cocaine user are displayed in Figure 3. Visual examination of this plot shows that the wash-kinetic curves are very similar. The exposed hair passes all of commercial wash criteria, [49] whereas the hair from the crack user fails the Rew and Rc criteria. [50] In this

example, we have the negative, exposed hair looking like a user and the user hair looking like it is contaminated.

Figure 3 – Comparison of wash kinetics from a user and exposed hair. The hair was exposed to 10 ì g/mL of cocaine. It is not clear if this sample was washed before submission, which would further skew the extraction kinetics. The two specimens are normalized to help visualize the decontamination process.



Besides not always being effective, wash criteria ar e based on an unproven model of drugs binding to hair and the assumption of "inaccessible regions". In our studies, the presence of microscopic, inaccessible regions, were not evident. [51] One does not need the presence of "inaccessible regions" to account for the decontamination curves. We proposed an alternative model of simple diffusion. [52] This model is not new, having been proposed and verified for dyeing of hair and wool many years ago. [53] Without "inaccessible regions", which have never been shown to e xist, wash kinetics can fail for one simple reason – people wash their hair. Wash kinetics relies on contamination being present. If some or most of this contamination is removed though normal hygiene, then the contamination would not be present to "trip " the wash kinetics. Essentially, a clean head - passively exposed to cocaine - may make you a drug user.

One may ask, "Can external contamination occur in real -life?" Basically yes. We conducted a study on the children of cocaine -addicted mothers. [54] Because these were young children (1 -13 years of age), knowing use of cocaine was unlikely. The pattern of cocaine concentration in the hair of the children varied widely by household. However, on aggregate, their levels mirrored the cocaine using mot hers such that no cut -off would separate the two populations. [55] This study was criticized because we had minor differences between our decontamination procedure and commercial decontamination procedures. To partially resolve this issue, we sent some of th e hair samples to a commercial laboratory. Their results were similar to ours. [56] An additional criticism is that the children may be microingesting cocaine. However, one subject, a one -year old child, had 100ng of cocaine/mg of hair in his/her hair. [57] Even taking into consideration differences in body weight, it is not clear that this child could have ingested that much cocaine. [58] Furthermore, when the hair sample was taken, a urine sample was also obtained. No cocaine metabolite was found. Thus, the ma croingestion [59] would have had to stop several days before the hair sample was obtained, which is unlikely. This is not the only study on the children of drug using parents. A major, commercial, hair -testing laboratory employs hair testing of children for several social service organizations. [60] Positive hair findings, of which there are many, are part of the evidence for removing children from a drug -using environment.

Finally, one may ask are there any *in vivo* studies where drug-negative adults have been exposed to cocaine and have hair positive results? Again, the answer is yes. Romano, *et al.*, exposed four individuals to cocaine by placing cocaine on their hands and having them rub their hair.[61] Hair was taken nearly immediately and periodically after the contamination for 70 days. Every sample was positive and the hair was still positive at the end of the study. More importantly, the "metabolite" benzoylecgonine started to form in the hair, *in vitro* and reached a level of approximately 30% of the cocaine level in the hair. Additionally, all four subjects would have been positive in each of the 13 hair samples (total of 52 samples) throughout the 70 day study period, if only the cut-off level were applied. Furthermore, the authors decontaminated the hair in a similar manner to commercial procedures so that these wash criteria could be applied.[62] Applying this wash criteria to the data from 20 of the hair samples where all the data is presented (data stopped being reported at 15 days), showed two interesting effects: (1) Hair collected within one hour of contamination appeared contaminated by the wash criteria. (2) One day later some samples passed all the wash criteria and as time went on, more and more passed the criteria. This reinforces the statement that **people wash their hair** and this washing confounds the wash kinetic analysis. In contrast, freshly-contaminated, dry hair is easily decontaminated or detected as contaminated by wash criteria.

In summary, there are a large number of authors that have exposed hair to drugs and have been unable to completely decontaminate the hair. Examining children, living in an environment where drugs are used or had been used, indicates that passive exposure can occur and generate false hair test results. Examining adults, who have been intentionally contaminated, also shows that contamination is difficult to remove and lingers for months. This body of literature indicates that hair testing, more likely than not, measures exposure to drugs rather than only use.

Metabolites

For most drugs of abuse, the predominant drug found in hair is the parent compound. Because the parent drug is often also in the environment, and wash kinetics are not completely effective, then external contamination is difficult to unequivocally distinguish from use. Frequently, laboratories use the presence of metabolites to unambiguously call a sample positive with the assumption that metabolites can only come from the drug passing though the human body.[63] In the case of cocaine in hair, benzoylecgonine is the major metabolite. Benzoylecgonine (BE) can be produced by decomposition of cocaine in inside the hair. During a Hair testing Working Group meeting, I proposed that a BE rule be adopted. Basically, for a sample to be considered positive, the BE/Cocaine ratio had to be at least 10%. Additionally, I proposed a cut-off level of cocaine in hair of 1 ng/mg of hair. Although this was an arbitrary ratio and cut-off, I believed would help distinguish passive exposure from active use, in the majority of cases.[64] After much discussion, this rule was adopted with one dissention. Later though correspondence, Werner Baumgartner argued that a BE/Cocaine ratio was useless because BE can be present in illicit cocaine in any ratio.[65] SAMSHA has overruled their own Working Group and proposed the 5% BE/cocaine ratio and a lower cut-off (1/2 that recommended) to call a sample positive. This increases the risk of false positives with very little documented improvement in detection ability.[66]

The presence of other, more presumably more unique "metabolites" is considered to override any BE or cut-off rule. However, I question that these "metabolites" are definitive of cocaine passing though a human body. One "metabolite" of interest is norcocaine. Norcocaine is a demethylated form of cocaine, presumed to be formed in the liver. However, cocaine may be demethylated with oxidants *in vitro*. One such oxidant is potassium permanganate.[67] Because

of its use in processing, clandestine cocaine may have up to 2.5-3 % nor-cocaine present.[68,69] Thus, although more unique than cocaine or benzoylecgonine, norcocaine cannot serve as a definitive marker of use.

In summary, no marker of use exists for cocaine that can demonstrate definitive use vs. exposure.

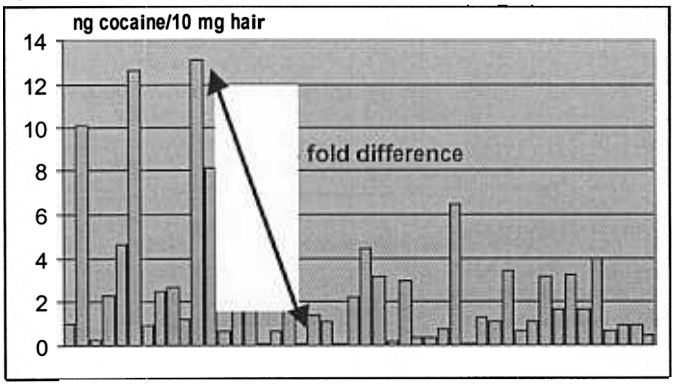
Bias

There is no more contentious issue than bias in hair testing. Originally, we referred to the differential uptake of drugs into different hairs as hair type bias. Other authors have taking these earlier statements, amplified them into racial bias, and then published papers reporting to show that racial bias does not exist.[70,71] Several well-controlled studies, where known amounts of drugs are administered, do show a difference in drug incorporation by race or hair color. In a recent study, Rollins, *et al.*, administered ofloxacin and codeine to healthy volunteers.[72,73,74] He observed a trend where black > brown > blond > red for the incorporation of these drugs. He noted: "These data clearly demonstrate that, in a controlled study, the hair pigmentation pattern has a major effect on the incorporation of codeine and ofloxacin into human hair." Additional studies in several animal models shows that drugs are incorporated far more frequently into pigmented hair than into non-pigmented hair. In limited human studies, drugs are also incorporated into black hair in much greater amounts than in gray hair, on the same head! Finally, a number of in vitro studies show that drugs bind preferentially to melanin AND cocaine shows one of the larger preferences to all the drugs of abuse.

There is no need to discuss the bias issue here as it is not relevant to hair testing. If there were bias in hair testing (as I believe that it has been shown), then consider two people, say an African American female and a Caucasian male. They both use drugs and because of differential uptake in conjunction with cut-off levels[75] the African American female is identified in a hair test as a drug user whereas the Caucasian male is not. Contrast this to the situation where the same two individuals are in the <u>presence</u> of drugs (maybe unknowingly), get the same exposure, and again due to the <u>differential</u> uptake in conjunction with cut-off levels the African American female is identified in a hair test as a drug user whereas the Caucasian male is not. The first scenario, use, is certainly unfair (but a drug user does get identified) and if it happens often enough possibility grounds for not using hair testing. However, the latter scenario, exposure, is a tragedy that should never happen as an innocent individual has her life, liberty, or livelihood at risk.

The issue of bias in exposure has never been studied in so called large N studies but has in laboratory situations. Rather than discuss my own and others extensive data, where the decontamination procedures have been claimed to be misunderstood, let's examine some commercial exposure data. Figure 3 plots data from two of their studies where they exposed different hair samples to 1 ì g/mL of cocaine (1/100,000th of a dose) for 1 hour.[76] However, different hair "types", incorporate widely varying amounts of cocaine. This result does not appear to depend only on hair color (the hair color was reported for some of the hair samples). Joseph, *et al.*, observed a similar pattern and saw a statistically significant difference between hair types with African American hair binding substantially more cocaine (*ca.* 2x) than Caucasian hair.[77] More importantly, is that the RATE of uptake in African American hair is FASTER. This has direct bearing bias.[78]

Figure 3 – Incorporation of cocaine into different hair types. Data from [46,79]



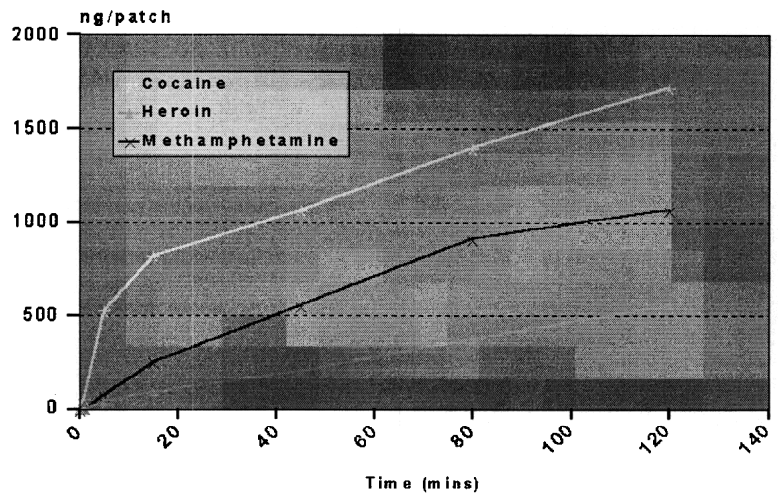
If not hair color, then what could account for this approximately 144 -fold difference in incorporation rates in these 45 di fferent hair "types"? [80] We have postulated several factors: genetics, hair color, and cosmetic treatment (among others) to account for different incorporation rates. Because hair color plays only a small role, we have termed this bias "cultural bias" wit h the implication that cosmetic treatment may be the dominant factor. [81] To cause a hair positive, first there must be the opportunity for contamination to occur. Then the drugs must penetrate the cuticle and enter the cortex, which contains the melanin gr anules. Although melanin, and therefore hair color, plays a role in the final amount of binding (if equilibrium is reached), the first step is getting past the cuticle. As mentioned in above, water (or sweat) is important in swelling the cuticle, which f acilitates penetration of the drugs into the hair. Additionally, prior cosmetic treatment is also important because it damages the cuticle (see Figure 1b) and reduces the requirement for water. [82] Furthermore, some of the cosmetic treatments placed on cosm etically straightened hair to add shine and prevent breaking can enhance transfer and binding of drugs. Most often these treatments contain oil and glycerol. Glycerol serves are a replacement for water and is known to aid in drug transfer from keratin to an inert object. [83] Furthermore, the oil absorbs cocaine. Thus, anyone applying such materials to their hair have a ready system for hair contamination: the oil absorbs and concentrates cocaine from the environment, the glycerol swells the hair and provi des a vehicle for drug transfer, the conditioning treatment is not replaced frequently providing lengthy exposure times (such as 48 -72 hours), the damaged hair is less resistant to drug transfer, and binding of the drugs occurs inside the cortex, perhaps a ided by the melanin present. [84] We have proposed two methods to rank hair on its damage and possibly correct for drug uptake in some hair types. [75] Interestingly, commercial laboratories have had a methylene blue staining technique to measure cosmetic damage for at least 10 years but do not appear to use it routinely. [85]

In summary, different hair "types" have different rates of contamination from the environment. Cosmetically treated hair, because of damage and re sidual chemicals, absorbs drugs more readily then untreated hair. To the extent that African Americans more readily treat their hair, for genetic and cultural reasons, they as a group would be more susceptible to environmental contamination and the result ing false positives from that contamination.

Selected Scientific Considerations for Sweat Testing

There are two types of contamination possible with the sweat patch: (1) Contamination From WithIn (CFWI). In this case, drugs were present on the skin pri or to application of the sweat patch. The cleaning procedure is insufficient to remove all the drugs before the patch is applied. Sweating releases the bound drugs, which migrate into the patch and are detected as if the individual had used drugs rather than was in contact with drugs. Like hair testing, skin is also susceptible to contamination from the external environment. Once drugs come in contact with the skin, they appear to bind tightly [86] and are difficult to completely remove with any cleansing procedure. [87,88] Complete decontamination is much more difficult if enough time elapses after exposure and before removal of the drugs is attempted. [87] Like hair, the skin can be contaminated with any amount of dru gs. Therefore, complete removal is necessary to avoid CFWI. We have tried numerous cleaning procedures and none removed 100% of the applied drugs. (2) Contamination From WithOut (CFWO). In this case the patch is porous to externally applied materials. It is very difficult to design materials that allow water vapor to freely escape and yet not allow other molecules to enter. We showed that the polyurethane membrane of the patch is permeable to drugs applied to the outside at a rapid rate (Figure 4). It would not be unreasonable for a individual to touch the patch because is can be an irritant and during heavy sweating the individual undergoing testing may be concerned that the patch may come loose (which it sometimes does). Under these conditions, if t he individual had drugs on the surface of their hands, some would be transferred to the surface of the patch, penetrate the membrane, and contaminate the interior.

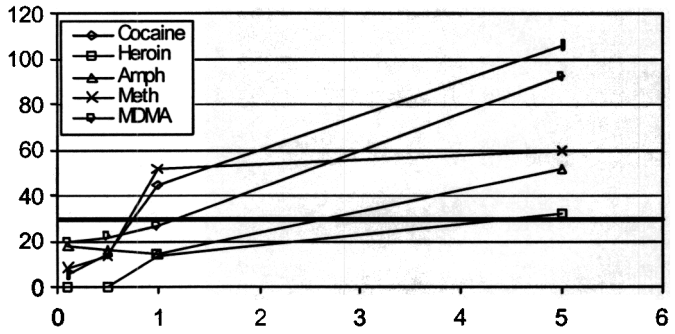
Figure 4 - Penetration of drugs into the patch from the external environment. Data from re ference 83.



SAMSHA is proposing that soap and water will be sufficient to decontaminate the skin and avoid CFWO. We have tried numerous cleaning procedures and none removed 100% of the applied drugs. SAMSHA appears to be relying on a non -peer-reviewed paper showing that after application of 1 ìg of drugs to a limited area, soap and water reduced the amounts to below the cut-off level for the patch. This study has a number of problems. For one, the authors o nly investigated a single, very low concentration (1/100,000 of a dose) of drugs (because of the

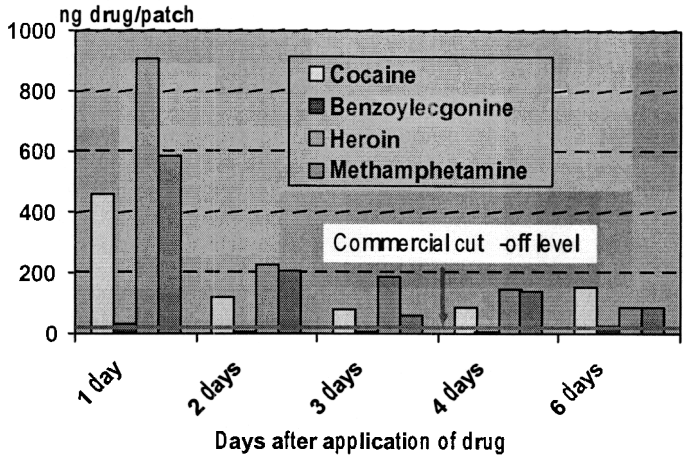
application method of spraying it is not even clear that the amounts are correct). Based on our work (Figure 5), 1 ìg of drugs would put most of the drugs bel ow the commercial cut -off after a similar decontamination procedure but WITH substantial elapsed time. Additionally, it is not clear that the authors waited long enough for the drugs to sufficiently bind to the skin. Finally, if the drugs were bound to t he skin, sufficient sweating, though exercise, must occur to release the bound drugs.

Figure 5 – Amount of drug found in patches after increasing skin contamination. Varying amounts of drug were applied to ca. 9 cm ^{2} of human skin the day prior to patch a pplication. Personal hygiene and two cleanings with isopropanol swabs occurred prior to patch application. Amounts listed are the averages of two trials. Note that the retention of drugs on the skin varies with the drug. Unknown amounts of drug are los t in personal hygiene, cleaning, and strong binding of the drug to the skin. Therefore only a fraction of the applied drugs are recovered in the patches. Data from : 88.



After application of 10 ìg to the skin, we showed that drugs can remain on the skin for up to 6 days and appear in the patch (Figure 6). Furthermore, "metabolites" (mainly BE) appeared in the patch even though only cocaine was applied to the skin. Cocaine is known to be hydroly tically unstable and it is not surprising that some degrades to BE. Thus, the presence of BE is insufficient to prove use even if BE were somehow excluded from being contamination from the environment.

Figure 6 - Applying Patches after Varying Times Fro m Drug Application. All patches worn for three days.



Conclusions

Both hair and sweat testing measure use and exposure to drugs rather than use alone. In a number of areas the proposed guidelines fail to adequate address this fact. Additionally, because these matrices are more challenging, the proposed guidelines should make the criteria for their use and testing more stringent than for urine testing rather than less stringent. Hair and sweat testing may disproportionately and falsely accuse people of color of drug use because of their living arrangements and the rate at which drugs bind to melanin. This problem must be more thoroughly explored before these procedures are allowed for Federal drug testing. Those intent on freedom of movement and ass ociation without having to justify or release personal information to their employer should be wary of accepting this technology for workplace testing. After all, drug testing is justifiable because illicit drug use may affect job performance and public safety. Illicit drug use is a safety issue. Contamination is not.

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[1] My educational background includes a Bachelor of Science Degree in Chemistry, *Magna cum Laude*, from the Uni versity of North Carolina in Greensboro (1977), a Doctor of Science degree in Organic Chemistry from the Massachusetts Institute of Technology (1982), and a National Research Council Post Doctoral Associateship at the Naval Research Laboratory (1982 -1984). I have been a member of the American Chemical Society since 1977, the American Association for the Advancement of Science since 1983, and the Society of Hair Testing. I have been certified as an expert witness in Federal District Court, State Courts, Mi litary Courts Martial, and several Military Administrative Board Hearings.

[2] Although I am employed by the Department of the Navy and I have been working on alternative matrices for the detection of drugs of abuse for approximately 20 years, the opinions e xpressed are my own and they do not necessarily represent the DoD or U.S. Government policy. These comments are being given as a private citizen at my own effort.

[3] D.A. Kidwell, "Selecting the Best Drug -Testing Procedures", NRL Memorandum Report 6170 -03-465, November 28, 2003.

[4] The concept of external contamination being a problem in hair analysis for drugs may have been novel at the time but it was well known for heavy metals such as zinc and lead. For example, deliberately contaminated hair could no t be decontaminated. See: P. Manson, "Hair analysis – a critical review", *Can. Med. Assoc.* , 133 (1985) 186 -187.

[5] For the purposes of this discussion, when I am referring to sweat testing, I am referring to the use of the Pharmchek ™ Sweat Patch.

[6] For example, in some public housing in the inner city or staying at less expensive hotels.

[7] The US prison system uses Ion Mobility Mass Spectrometry (IMS) to search visitors at many prison locations. IMS will reveal trace levels of drugs on the skin and clothing and presumably indicate that that individual had been in recent contact with drugs and therefore may be smuggling contraband into the prison. According to the U.S. Department of Corrections, they warn visitors to correction facil ities that employ trace detection that staying in less expensive hotels the night before may increase their risk of environmental contamination. Additionally, living in a drug using environment and not freshly washing their clothes before the prison visit also puts them at risk. Although some prison systems just turn away positive individuals for that day (a huge inconvenience for less affluent individuals that may have traveled a long distance for the visit), other system deny access for substantial peri ods of time. If SAMSHA wished to study exposure in the general population, then airport security screening systems may make a good test bed. IMS technology is already being used for explosives; with minimal changes, the same technology could be used for drugs. Our studies of airports do show trace levels of drugs on certain surfaces, showing that sources of contamination exist in unlikely places.

[8] D.A. Kidwell and L.A. Riggs, "Testing for Driving Under the Influence of Drugs: Setting Impairment Levels", Proceedings of ONDCP 2003 International Technology Symposium, San Diego, CA, July 9, 2003.

[9] The international units for hair testing are in ng/mg. Why SAMSHA wishes to change to pg/mg is unclear. In numerous discussions with commercial companies, thei r chief scientists have stated to the effect that pg/mg "makes the units look bigger". This is NOT just semantics. In court trials, where I have been the expert witness for the defense and where reasonable scenarios for passive exposure have been put forth, it is much harder to convince the jury that a 1000 pg/mg positive resulting from passive exposure is possible because the number appears too big. On the other hand, a 1 ng/mg positive make eminent sense. Thus, I encourage using the international unit s so that lay people can grasp at the truly low levels we are reporting for hair testing. Otherwise, if we want really big and impressive numbers, then why not femtograms/mg or atto -grams/mg?

[10] There are issues with the fact that hair does not incorporate all drugs equally from the environment so that the ratios should be larger than the amount of "metabolite" in street cocaine AND reflect the differential incorporation rate. Additionally, this does not eliminate the "metabolites" coming from the sweat of a drug user. An example of the latter is cocaine on money where BE and cocaethylene are found. The sources of these "metabolites" are unclear and they may reflect handling of the money by a drug user or from traces of street drugs. Handling of an inert object by a drug user reconfirms than intimate contact transfers trace amounts of drugs. Alternatively, contaminating the money from the environment confirms that the environment contains "metabolites". In either case, the presence of unique "metabolite s" is not definitive of use because there are no unique metabolites yet discovered for the majority of illicit drugs.

[11] For example, the Fenton reaction (discovered in the late 1800's) has long been used to generate metabolites of drugs *in vitro*. Although there are many variations on the theme of the Fenton reaction, basically they all generate OH radicals. Additionally, the Fenton reaction's chemistry uses chemicals identical to the chemistry used in hair dying. Therefore, one could reasonably propose t hat hair could be passively exposed to marijuana smoke, incorporating THC, and then undergo some form of cosmetic treatment (of which there are too many to scientifically study) converting only a trace (far less than 1%) of the THC to "metabolites". Beca use the THC concentration can be any arbitrary amount in the hair, we MUST consider all trace chemistry - something that has never been thoroughly studied. Knowing the THC level in the hair will help, once we determine that the Fenton reaction, or its man y cousins, only produces say 1% THCCOOH.

[12] D.A. Kidwell, "Minimal Standards for Instrumental Analysis Derived from Information Theory", 3rd European Conference on Hair Analysis, Crete, October 6 -8, 2003.

[13] D.A. Kidwell and L.A. Riggs, "Comparing Two Analyt ical Methods: Minimal Standards in Forensic Toxicology Derived from Information Theory", *Forensic Science International* , in press.
[14] F.P. Smith and D.A. Kidwell, "Minimal standards in forensic toxicology derived from information theory", American Academy of Forensic Sciences, Reno, NV, February 21 -25, 2000.
[15] D.A. Kidwell and F.P. Smith, "Minimal standards for the performance and interpretation of toxicology test in legal proceedings", *J. Forensic Sciences,* 45(1) 237-9 (2000).
[16] J. Lenihan, *Measuring and M onitoring the Environment* , J. Lenihan and W.W. Fletcher, eds., Academic Press, New York, 1978, pp. 66 -86.
[17] M. Wilhelm, F.K. Ohnesore, I. Lombeck, and D. Hafner, "Uptake of Aluminum, Cadmium, Copper, Lead, and Zinc by human scalp hair and elution of the ad sorbed metals", *J. Anal. Tox.,* 13 17, 1989.
[18] V. Valkovi, *Human Hair Trace Element Levels, Volume II,* CRC Press, Inc., Boca Raton, FL, 1988.
[19] H.C. Hopps, "The biologic basis for using hair and nail for analysis of trace elements", The Science of the Total Environment, 7 71, (1977).
[20] A. Chatt and S.A. Katz, *Hair Analysis: Applications in the Biomedical and Environmental Sciences,* New York: VCH Publishers, Inc., 1988, pp. 14 -16 and pp. 77 -81.
[21] D.A. Kidwell, "Analysis of Drugs of Abuse in Hair by Tandem M ass Spectrometry", American Society for Mass Spectrometry Conference, San Francisco, CA, 6 -10 June 1988.
[22] D.A. Kidwell, "Analysis of Phencyclidine and Cocaine in Human Hair by Tandem Mass Spectrometry", *Journal of Forensic Science* , 38 272-284(1993).
[23] I was told by John Mitchell at RTI that he exposes hair to 10 ì g/mL of drugs for several days for preparing round -robin standards. When I mentioned that this length of time is not necessary, he stated that he wanted to prepare uniform standards rather than t est the decontamination procedures of the commercial laboratories. I agree with this premise. However, this lengthy exposure demonstrates that external substances can be incorporated into hair and at least this exposure provides an upper limit where expo sure mimics use for ALL current procedures.
[24] Transcript from Substance Abuse And Mental Health Services Administration, Drug Testing Advisory Board, Scientific Meeting On: Drug Testing Of Alternative Specimens and Technologies (PART II), September 10, 19 97.
[25] D.L. Blank and D.A. Kidwell, "External Contamination of Hair by Drugs of Abuse; An Issue in Forensic Interpretation", *Forensic Science International* 63 145-156(1993).
[26] D.A. Kidwell and D.L. Blank, "Comments on Sample Preparation Techniques", *Forensi c Science International* 63 137-143(1993).
[27] 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).
[28] D.A. Kidwell and D.L. Blank, "Mechanisms of Incorpora tion of Drugs into Hair and the Interpretation of Hair Analysis Data", In: E.J. Cone, M.J. Welch, and M.B. Grigson Babecki, eds., *Hair Testing for Drugs of Abuse: International Workshop on Standards and Technology,* National Institutes of Health Publ. #95 -3727, Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 1995, pp. 19 -90.
[29] 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, Boc a Raton, FL, 1996, pp. 17 -68.
[30] T. Mieczkowski, "Distinguishing passive contamination from active cocaine consumption: assessing the occupational exposure of narcotics officers to cocaine" *Forensic Science International* , 84 (1987) 87 -111.
[31] The time frame in which Psychemedics switched from their older procedure to their newer procedure is not clear. Their older procedure provided valuable criteria lacking in the newer procedure.
[32] How these officers were selected was not reported. However, the selection appears to be a hodgepodge of the subjects available, rather than a random sample. Only 5/40 handled cocaine daily or near daily. This sample included 4 evidence technicians and it is likely that they were in the 5/40, who handled cocaine daily, given t he amount of cocaine trafficking in Florida. But handling cocaine does not equate to exposure because it is likely that evidence technicians take measures to control contamination of themselves and the evidence; otherwise, trace evidence would be useless.
[33] The survey questions are not correlated with the analytical results making it impossible to discern a pattern.

[34] I discussed this officer at length with Dr. Mieczkowski. Dr. Mieczkowski claimed that the officer had dramatically changed his appearance between the two hair samples. Part of the change was bleaching his hair and growing it much longer. Because of the 4 month interlude, the second hair sample didn't even cover the same time-frame as the first. Additionally, it is not clear that the officer's duties still required contact with cocaine. This and the cosmetic treatment (which degrades cocaine and can generate false negatives) would easily account for the negative with the second sample.

[35] One approximately 60 year old evidence technician had trace amounts of drugs in his hair (below the normal cut-off level, but ABOVE the LOD and presumably the safety net level). It is unlikely that the evidence technician was even "micoingesting" cocaine as part of his work. Thus, finding any cocaine in his hair is surprising.

[36] This number is based on self-reports and is likely too low. Based on the well-controlled dose studies of Henderson, Harkey, and Jones, at level of approximately 3000 mg of cocaine could be calculated to be necessary to reach the 5 ng/10 mg cut-off in Caucasian individuals and about 8 times less in non-Caucasian individuals.

[37] G. Koren, *et. al*, "Hair analysis of cocaine: differentiation between systemic exposure and external contamination", *J. Clin. Pharmacol.*, 32 (1992) 671-675.

[38] Hair also swells in high humidity environments and in the presence of sweat. Since 1775, hygrometers have been constructed using the swelling properties of hair to measure humidity.

[39] From an article in *Science News*.

[40] M.I. Schaffer, W-L. Wang, and J. Irving, "An evaluation of two wash procedures for the differentiation of external contamination versus ingestion in the analysis of human hair samples for cocaine", *J. Analytical Toxicology*, **26** (2002) 485-488.

[41] We have used times as short as 5 minutes and have observed incorporation of cocaine.

[42] For non-novice users, one needs to inject about 30 mg of pure cocaine to produce an effect. Intranasal or oral ingestion is about three times less effective and consequently requires more drug.

[43] These studies obtained money from the Naval Research Laboratory Federal Credit Union. According to the bank, this money comes from the Baltimore Federal Reserve Bank. Baltimore has a high incidence of cocaine use, which may account for the large positive rate.

[44] The source of drugs on money is not clear. Based on finding benzoylecgonine, methyl ecgonine, and cocaethylene on some bills, I believe that some of the contamination could come from the sweat of drug users. Alternatively, our concept of "metabolites" must be greatly expanded. Cocaine likely binds to the fibers or ink of the currency. The money MUST be extracted to efficiently determine the amount present. It is unlikely present as particles unless closely associated with drug use.

[45] Rubbing money between the palms of <u>dry</u> hands does not transfer much of the drug present. However, handling the money with damp palms can transfer 100-300 ng of cocaine from the bill. Of course, one would then need to transfer this drug to the hair. I previously believed that this transfer is highly unlikely until a recent court case were the client described a scenario for transfer (to a sweat patch, not hair) that was reasonable. For details see: DA Kidwell and WP Gardner, "Testing for illicit drugs via sweat and saliva analysis: application to the detection of body packers", 1999 ONDCP International Technology Symposium, March 8-10, 1999, Washington, DC, pp. 21-1 to 21-15.

[46] M.I. Schaffer, W-L. Wang, and J. Irving, "An evaluation of two wash procedures for the differentiation of external contamination versus ingestion in the analysis of human hair samples for cocaine", *J. Analytical Toxicology*, **26** (2002) 485-488.

[47] There are several significant differences between the reported exposure procedures and our published work. We exposed our hair samples to drugs in phosphate buffer at 37 °C. They used distilled water and the room temperature (assumed to be 20-25°C). Higher temperatures and the presence of buffer tend to incorporate more drugs into the hair by diffusion. Generally, reaction rates double with each 10 °C rise in temperature. Also, the hair was not thoroughly dried. Dried hair is harder to hydrate and remove the drugs during the decontamination process. Although these differences may be minor, they would tend to bias the experiments towards generating negative results.

[48] The metabolite criteria, as discussed later, would not be met. This is expected because the authors used chemically pure cocaine and environmental degradation had not been allowed to occur. Thus, to say that this criterion is required in these cases is unreasonable.

[49] These are the older criteria called Rc, Rsz, and Rew.

[50] The laboratory has changed their criteria from the older criteria that used Rew and Rz and that had been employed on hundreds of thou sands of hair samples to another criteria employed on these hair samples. No adequate justification for this change has been provided.

[51] We employed fluorescent dyes and showed that they were incorporated throughout the hair. Others have preformed simila r experiments and produced similar results. Although we have not precluded molecular -size, inaccessible regions, they seem unlikely.

[52] S.F. DeLauder and D.A. Kidwell, "The Incorporation of Dyes into Hair as a Model for Drug Binding", *Forensic Science In ternational*, 107 (2000) 39 -61.

[53] Dyeing of wool and hair fibers have long been studied and modeled because of their obvious commercial importance. One needs cost -effective dyeing yet cannot afford to have uneven color being present. Dyes and drug molecul es have similar diffusion properties. In fact, due to the lack of a strong binding (a chemical gradient), drug molecules should diffuse into hair fibers faster than dyes.

[54] Actually, this was two separate studies. The first study produced such surprising ly high results that the protocol was repeated. The second study also produced the same results.

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

[58] Actually, the commercial laboratory agreed with our analysis in most samples except one, which was much higher. After much work, we discovered that our analysis method UNDER estimated the cocaine in some hair types. Therefore, some of the children woul d have been even more positive than was reported. We have since corrected our procedure.

[57] According to the commercial analysis and confirmed by our revised and current procedure.

[58] One may ask, if not ingestion, what could cause a one -year old have so m uch drug present? A simple possibility is that these children were bottle -fed. During bottle -feeding, a mother supports the head of the baby with the palm of her hand. Or a cocaine -using mother, contamination on her hands is likely from use as well as h andling cocaine. Thus, the baby's hair would be rubbed repeatedly with cocaine from the sweat of the mother, allowing cocaine and metabolite transfer to occur.

[59] With this large amount of cocaine present "microingestion" should not even be a consideration .

[60] For example see: Lewis, D., C. Moore, P. Morrissey and J. Leikin, "Determination of drug exposure using hair: application to child protective cases", *Forensic Science International*, 84 (1997) 123 -128.

[61] See: G. Romano, N. Barbera, and I. Lombardo, "H air testing for drugs of abuse: evaluation of external cocaine contamination and risk of false positives", *Forensic Science International*, 123 (2001) 119 -129. Although not explicitly stated, I assume that the volunteers in this study were actually the au thors. In that way, the authors could be sure that drug use did not occur during the study. Additionally, the hair care of the subjects could be closely monitored. Although no subject reported unusual cosmetic treatment, one participant rinsed her hair with vinegar after shampoo application. In this case, her hair was the only hair that did not show the production of benzoylecgonine. Interestingly, *in vivo*, cocaine is more stable in acid than in base. By making her hair acidic after applying basic sham poos, she may have been reducing the degradation of the cocaine in the hair. I would never have considered washing hair with vinegar "normal", which reinforces that cultural differences (in this case participants from Italy) influence hair care and makes studying "normal" hygiene difficult.

[62] The authors claimed to follow Psychemedics procedure. However, a close examination of the reported data shows that they actually exceeded Psychemedics older washing procedure (washed too much). Fortunately, the wash data can be recombined to reproduce the Psychemedics wash. Furthermore, their analysis did not dissolve the hair and therefore it should UNDER REPORT the hair drug concentrations. Thus, even more samples may have passed the kinetic wash criteria if the analysis exactly followed Psychemedics procedure. For my statistical analysis, I used the published data to reconstruct Psychemedics procedures from the over -washed hair.

[63] Assuming that this is true, we cannot exclude metabolites from arising in the hair of a non-drug user from contact with the sweat of a drug user (which would contain the metabolites). Such transfer has been experimentally demonstrated. Henderson, Harkey, and Jones allowed individuals to hold negative hair in their hands after being ad ministered cocaine. The negative hair became positive. The amount of drugs transferred to the negative hair in the Henderson experiment may be lower than in real life because the subjects were administered drugs under laboratory controlled conditions and did not have the opportunity to contaminate their hands. Therefore, they would have lower drug levels on their hands than a typical drug user and less drug to transfer.

[64] SAMSHA uses a similar concept with morphine for urinalysis. The original cut-off level for morphine was raised from 300 ng/mL to 4000 ng/ml to avoid falsely accusing an individual of opiate use from eating poppy seeds. However, this was a compromise level as even this level can be achieved by eating poppy seed cake and certain Greek pastries. Thus, SAMSHA reduced the harassment of the majority of bagel eaters but not all individuals by adjusting the cut-off level.

[65] I partially agree with his analysis. However, he fails to consider that the binding ratio is different for the two compounds and that this ratio was never intended to eliminate all possibility of external contamination.

[66] Part of the rational for less stringent criteria is that too many presumed-legitimate users of cocaine would be called negative. We set cut-offs for urine testing higher than instrumentally possible to reduce (but not eliminate) passive exposure. Lower cut-offs for urinalysis would certainly catch more users an falsely accuse more innocent individuals. One only needs to remember the fiasco with morphine levels in urine due to poppy seed ingestion to realize that too low of levels WILL false accuse individual not actively using drugs.

[67] This oxidant is often used in Columbia to purify cocaine, but not all clandestine processors use potassium permanganate because of its limited availability and the reduction in drug yield by up to 10%. However, it does yield a whiter and purer product that is more in demand.

[68] JM Moore and JF Casale, "Cocaine profiling methodology – recent advances", *Forensic Science Review*, 10 (1998) 13-46.

[69] K. Janzen, "Concerning norcocaine, ethyl benzoylecgonine, and the identification of cocaine use in human hair", *J. Analytical Toxicology*, 16 (1992) 402.

[70] T. Mieczkowski and R. Newel, "An evaluation of patterns of racial bias in hair assays for cocaine: black and white arrestees compared", *Forensic Science International*, 63 (1993) 85-98.

[71] T. Meckowski 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.

[72] D.E. Rollins, D.G. Wilkins, A. Mizuno, M.H. Slawson, and C.R. Borges, "The role of pigmentation in the disposition of drugs of abuse in human hair", Clinical Pharmacology & Therapeutics.

[73] 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.

[74] Rollins DE, Wilkins DG, Krueger GG, Augsburger MP, Mizuno A, O'Neal C, Borges CR, Slawson MH, "The effect of hair color on the incorporation of codeine into human hair", *J. Anal. Tox.*, 27 (8) (2003) 545-551.

[75] D.A. Kidwell, E.H. Lee, and S. F. DeLauder, "Evidence for Bias in Hair Testing and Procedures to Correct Bias", *Forensic Science International*, 107, 93-104(2000).

[76] As discussed above, this exposure level will not produce a hair sample with sufficient drug present to meet the proposed SAMSHA cut-of levels if one employs wash criteria. However, three (see Figure 3) WILL meet the proposed SAMSHA cut-off levels if the levels are taken at face value!

[77] RE Joseph, W-J Tsao, T-P Su, and EJ Cone, "*In vivo* characterization of cocaine binding sites in human hair", *J. Pharmacology and Experimental Therapeutics*, 282 (1997) 1248-1241.

[78] Joseph, et al., measured both the rate and the equilibrium level. For most exposures, the equilibrium level would never be reached as it takes days. African-American females took-up drugs far faster than Caucasian females with the same hair color. This is likely due to cosmetic damage and what we termed "cultural bias".

[79] This data was attached to a letter received January 22, 2001 from Werner Baumgartner and supplied to the members of the Hair Testing Working Group.

[80] Rate is an important parameter. To prepare hair samples that mimic hair from real users, the Research Triangle Institute (RTI) exposes hair for one week to drugs and then washes the hair extensively, (to remove external contamination). I would agree that a one-week exposure is excessive and probably unnecessary. However, it appears that this very long exposure breaks down the kinetic barrier to drug diffusion and provides hair with a uniform drug content – just what is needed for standards. RTI apparently has not varied this procedure to determine the minimum criteria for exposure.

[81] It is an interesting legal question if what we term "cultural bias" is actually prohibited discrimination because it has some preference aspect to it rather than pure genetics. However, religion also has a large preference aspect and in that case discrimination is prohibited. For an example of preference,

Mieczkowski gives an example of sunbathers and skin cancer. Assume that excess sun exposure resulted in excess skin cancer and that groups may have a cultural preference for sun bathing. He asks, "Would we be inclined to call a test that identifies these cancers 'biased'?" Of course not. Now change the facts slightly. Suppose there was an established religion where the members worshiped the sun and one of the tenets of this religion was to spend significant amounts of time sunbathing. Because of this practice, the lighter-skinned members of this religious group have excess skin cancer rates. It would be an interesting legal test case if the Government tried to deny health benefits to lighter-skinned members of this religious group only based on their membership. What is missing in the discussion of bias in hair testing is that genetics gives one a basis to work with but culture defines the norm. If the norm of beauty in the African American culture were straight, black hair, then that almost requires frequent chemical straightening and the damage that this entails to the hair cuticle. Genetics does not provide this norm directly (althou gh some African Americans may have straight hair naturally). Frequently washing causes breakage on treated hair. Thus, African Americans tend to wash their hair less frequently and apply oil to keep it pliable. For a survey on African American hair trea tments see: http://www.blackhaircare.com/books.htm (accessed 6/1/2003). For a non-scientific discussion of African American hair see: http://www.razzamatazz.net (accessed 6/1/2003).

[82] Interestingl y, J. Sagal, "Acid and base binding behavior of white and pigmented hair", Textile Research Journal, (1965) 672-673 observed that treated African American hair (with straightening agents) had more acid bind capability than untreated hair but Caucasian hai r had no similar differences.

[83] D.A. Kidwell and F.P. Smith, "Susceptibility of PharmChek ™ Drugs of Abuse Patch to Environmental Contamination", *Forensic Science International*, 116 89-106 (2001). In this case, drugs were transferred from skin, which cont ains similar proteins to hair, to a pad placed on the surface. This transfer was approximately 2 fold better with glycerol in the pad than sweat alone. Part of the reason is that glycerol remains (does not dry-out) whereas the presence of sweat is transi ent.

[84] Most authors, including us, remove this cosmetic treatment before laboratory contamination experiments are done. This is partly to better control the procedure. Different laboratory pretreatments of the hair can account for different ordering of h air types in their uptake of drugs. Additionally, there is no hair available to provide standards, making comparisons between laboratories difficult.

[85] The exact procedure that they use has never been specified, and it appears to be somewhat subjective.

[86] Drugs have long been shown to bind to hair and it has been postulated that they bind to the protein matrix though first ionic and then van der Waals interactions. The keratin in hair and skin have much in common. Thus, it is not surprising that drugs al so bind to skin and we could use our extensive experience with hair contamination to predict that skin decontamination will be difficult..

[87] D.A. Kidwell, M.A. Blanco, and F.P. Smith, "Cocaine Detection in a University Population by Hair Analysis and Skin Swab Testing", *Forensic Science International*, 84 75-86(1997).

[88] M. 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.