

APPENDIX A to Comments of National Federation of Federal Employees, Drug Policy Alliance, and DKT Liberty Project regarding Proposed Revisions to Mandatory Guidelines for Federal Workplace Drug Testing Programs, FR DOC # 04-7984, SAMHSA, HHS

THE SCIENTIFIC ISSUE: HOW ACCURATE ARE POSITIVE SWEAT PATCH TEST RESULTS AS AN INDICATOR OF RECENT DRUG USE BY THE TEST SUBJECT?

Commenters do not dispute that drugs will appear in the sweat of an individual who has ingested them. Nor do they dispute that, if a 10 ng/ml cutoff level is used, the sweat patch will give positive results for most individuals who have ingested drugs while wearing it. These accepted scientific conclusions, however, do not end the inquiry about the accuracy and reliability of sweat testing and do not speak to the critical issue with regard to workers: how often will the sweat patch yield a positive test result for test subjects who have *not* recently ingested drugs?

Even PharmChem does not claim that the sweat patch is infallible in this regard. As discussed below, research has established beyond a doubt that the sweat patch is susceptible to environmental contamination. A subject's skin can be contaminated with drugs prior to attachment of the patch; in addition, drugs can pass directly through the membrane that covers the patch, thus contaminating the sample. See Kidwell, Smith, "Susceptibility of PharmChek Drugs of Abuse Patch to Environmental Contamination," 116 Forensic Science International 89 (2001) (hereinafter Naval Research Lab 2001 Study). In either of these scenarios, the outcome would be a positive test result, indistinguishable from a result based on intentional ingestion. *Ibid.*

PharmChem does not dispute that environmental contamination of the sweat patch is *possible*. The question is, *how likely* is contamination? In court cases, PharmChem has taken the position that environmental contamination is "unlikely" or

“unlikely in real life.” But this *qualitative speculation* – unsubstantiated by any data proffered by PharmChem or published in peer-reviewed journals – wholly fails to provide the Agency with useful guidance. Instead, the Agency must look to research for some *quantitative indication* of the technology’s real-life error rate.

Every study in which sweat patch results have been compared to urine test results has indicated substantial numbers of false positives with the sweat patch. Studies indicate that seven to forty percent of drug-abstinent individuals tested through the patch will falsely test positive. In light of this quantitative data, numerous independent scientists have expressed serious reservations about the reliability of sweat patch in peer-reviewed, published articles.

Part of the growing body of research casting doubt on the reliability of sweat testing includes published research indicating that drugs can be stored in the skin for long periods of time and then released into the sweat patch, falsely indicating recent drug use. See Levisky, Bowerman, Jenkins, and Karch, “Drug Deposition in Adipose Tissue and Skin: Evidence for an Alternative Source of Positive Sweat Patches,” 110 *Forensic Science International* 35 (2000) (hereinafter Skin Storage Study). Much remains to be learned about why and how the long-term storage and eventual release of drugs occurs in the body, but the fact is that this process does indeed take place. PharmChem, which markets its sweat patch as a reliable indicator of recent drug use, has not taken account of this fact in the design, marketing or defense of its product – and does not even claim to know how long drugs can be stored in the body before they are excreted in sweat.

As noted earlier, PharmChem has done next to nothing to assess the problem of

false positive results from its sweat patch. But independent researchers have investigated this issue, and a review of published research indicates that:

- studies investigating the problem of false positives for sweat testing find substantial numbers of false positives;
- the possibility that environmental contamination can cause a false positive is well-established;
- the possibility that long-term storage of drugs in skin can cause a false positive is well-established;
- results indicating false positives through the sweat patch occur both in laboratory tests and in real-world situations;
- there is no scientific consensus as to the reliability of the sweat patch; and
- the technology has not reached the level of general acceptance in the forensic toxicology community.

The studies on which these statements are based are discussed below. **As far as commenters know, there are *no studies*, published or unpublished, refuting the results of the research substantiating these points. Every time the sweat patch has been studied in an effort to investigate accuracy of positive test results, a substantial number of false positives has been the result.** Any assertion that real-life false positives due to environmental contamination are “rare” or “unlikely” is based on speculation, not research.

Following are descriptions of the relevant studies.

A. “Real-Life” studies.

PharmChem has routinely criticized studies performed in laboratories by speculating that the results were not likely to be replicated in “real-life” settings.

However, three different studies have compared patch results to urine test results in a

real-life setting, and each has found substantial numbers of false positives.

These three real-life studies bolster the conclusions of the laboratory studies, demonstrating that the possibility of environmental contamination in a real-life setting is more than theoretical. It bears repeating that *there are no studies that reach a different conclusion on this point*. The fact that PharmChem has never chosen to study this issue in a real-life setting is itself revealing.

1. The Naval Research Laboratory 2003 Study – Real-Life Comparison of Patch and Urine Test Results

Several forensic toxicologists affiliated with the United States Naval Research Laboratory recently performed a detailed study of the sweat patch. The U.S. Naval Research Laboratory is an independent, government-operated research facility, unaffiliated with PharmChem or other corporate drug testing interests. Results of this study were published in April 2003, in a peer-reviewed article in *Forensic Science International*. See Kidwell, Kidwell, Shinohara, Harper, Roarty, Bernardt, McCaulley, Smith, “Comparison of Daily Urine, Sweat, and Skin Swabs Among Cocaine Users,” 133(1-2) *Forensic Science International* 63 (2003) [hereinafter Naval Research Lab 2003 Study].

In this study, test subjects were given daily urine tests, and wore two sweat patches at all times during the four-week study. *Id.* at p. 3. These subjects were recruited from a cocaine dependence treatment program. Some subjects lived with current drug users, and some did not; some used cocaine during the course of the study, and some did not. *Id.* at p. 2-5. Subjects were thus a cross-section of “real-life” scenarios, such as those experienced by the pool of individuals on federal supervised release.

The relevant aspect of the study for the Agency was the sweat patch test results for individuals who did not use drugs while wearing a sweat patch. Drug abstinence for such individuals was established by daily urine testing, confirmed through GC/MS analysis of urine samples.

When drug-abstinent subjects were tested, the sweat patch gave false positive results seven percent of the time. There were three subjects in the study each of whom posted daily urine test results of *less than 25 ng/ml* – far below the cutoffs that would indicate actual drug use. Over the course of the study, these three subjects were patch-tested 27 different times. Two of these twenty-seven sweat patches – seven percent – came up positive for cocaine, even though the subjects had not ingested cocaine. The studies’ authors observed, “Consistently blank urine specimens accompanied by above cut-off positive sweat patches are consistent with environmental contamination and inconsistent with cocaine ingestion.” *Id.* at 7.

The study also swabbed the skin of test subjects prior to the application of sweat patches on the skin. These pre-application swabbing tests found that the skin of individuals who live in environments where there is or had been drug use is frequently contaminated with those drugs, irrespective of whether the subject has ingested those drugs. *Id.* at 9-12. This finding supports the likelihood of environmental contamination leading to false positive patch test results for individuals living in contaminated environments.

The primary importance of this study is that it demonstrates a significant possibility of false positive sweat patch test results when the patch is used in a real-life situation. PharmChem had speculated that earlier research results indicating the

possibility of false positives through environmental contamination would not be replicated in a real-life setting. In this real-life study, however, the authors did indeed find substantial numbers of false-positives.

2. The Preston Comparison study: Real-Life Comparison of Patch and Urine Test Results.

A 1999 study tested dozens of drug users by both sweat and urine testing in order to evaluate the accuracy of the sweat patch testing system in monitoring cocaine use. See Preston, Huestis, Wong, Umbricht, Goldberger, and Cone, “Monitoring Cocaine Use in Substance-Abuse-Treatment Patients by Sweat and Urine Testing,” 23 *J. Analytical Toxicology* 313 (1999) (hereinafter “Preston Comparison Study”). This “real-life” study found that sweat testing produced a very large number of false positive test results.

The study was carefully designed to ensure that urine tests would detect any drug use that a subject engaged in while wearing the sweat patch. Sweat patches were placed on subjects on Tuesdays, and then urine tests were performed every second or third day thereafter for the duration of the time the subjects wore the patches. As the test subjects were recent drug users, their home environments may well have been contaminated with drugs.

The study found that, when urine testing showed that an individual had abstained from cocaine use in a given week, sweat patch tests nonetheless gave positive test results almost **forty percent** of the time.¹

¹ Interpreting the study’s results in this regard requires use of some scientific terminology. The study reports for the aggregated test results “specificity ranging from 60.5 to 62.9%.” (Preston Comparison Study at 320). “Specificity” indicates what proportion of those who are actually negative will test

Perhaps because of this alarmingly high rate of false positives, the study's authors inquired further into the 75 false positive test results. The authors looked more closely at both the positive sweat patches and the negative urine tests. Even if one adjusts the study's test results conservatively, to (1) take into account GC/MS analysis of the positive sweat patches, and (2) eliminate some of the possibly drug-free individuals by lowering the cutoff level for a urine test to be considered negative, this study nevertheless yields a false positive rate for the sweat patch of **twenty-six percent**.²

3. The Levisky Comparison study – Real-Life Comparison of Patch to Urine Test Results.

Six scientists, including four who authored the Skin Storage Study described below, published a recent peer-reviewed study that is strongly critical of the sweat patch. (See J.A. Levisky, Bowerman, Jenkins, Johnson, J.S. Levisky, Karch, "Comparison of Urine to Sweat Patch Test Results in Court Ordered Testing," 122 Forensic Science International 65 (2001) (hereinafter "Levisky Comparison study"). This "real-life" study compared sweat patch test results to a comprehensive sequence of urine tests: urine tests were performed on the days before and after each patch was applied, and every weekday while the patch was worn. (Levisky Comparison study at 66). The subject for this test was an individual undergoing court-ordered drug testing.

negative; the remainder will test falsely positive. The study reports specificity of 60.5 to 62.9%, meaning that almost 40% of individuals whose urine tests were negative tested falsely positive through the sweat patch.

² For the subjects who apparently tested false positive, ninety-three percent of the sweat patches were confirmed as positive through GC/MS. For these same subjects, sixty percent of the urine test results were negative even when the cutoff was dropped to the limit of detection. Adjusting the results in these proportions still gives a specificity of 74% – meaning that 26% of drug-

Of thirteen sweat patches placed on this individual during the study, five were positive. Because every urine test associated with each of the sweat patches was negative, the authors determined that **all five sweat patches were false positives**. The authors note that these findings confirm those of an earlier study finding a high number of false positives with the sweat patch. (Levisky Comparison study at 65, referring to Preston Comparison study, described above.)

The study mentions two possible sources for these false positive test results: long-term drug storage in skin, and environmental contamination. The authors note:

Individuals who must wear sweat patches have husbands, live-in lovers, and friends who may continue to use drugs. It is not surprising that the sweat patch wearer may unknowingly be exposed to these drug sources.

(Levisky Comparison study at 68).

The article closes with a strong call for the courts to reject use of the sweat patch until further research is performed:

Whether one or all of these mechanisms contribute to the problem [of false positives] is not known, and will never be known until the appropriate studies are undertaken. **Until such studies are undertaken the appropriateness of the sweat patch methodology, at least for use by the courts, remains in doubt.**

(Levisky Comparison study at 68). Even standing alone, this study would also be sufficient to demonstrate that there is no “scientific consensus” on the reliability of sweat testing.

B. Laboratory Studies.

In addition to the real-life studies described above, the vulnerability of the sweat patch to environmental contamination has been repeatedly studied in the laboratory. As

abstinent individuals will test falsely positive with the sweat patch.

with the real-life studies, every laboratory study has confirmed the possibility of environmental contamination – even those studies performed by PharmChem.

It bears emphasis that these studies contradict claims made for years by PharmChem regarding the reliability of its device. In the past, PharmChem officials have testified in court that the membrane that covers the patch is absolutely impermeable to drugs; and that a single isopropyl alcohol rub is sufficient to remove any contaminants from the test subject's skin. Both of these crucial contentions were proven false by laboratory research, described below.

1. The Naval Research Laboratory 2001 study.

The United States Naval Research Laboratory performed extensive research on the sweat patch in 1999, investigating various environmental contamination scenarios. Results of this research were published in a peer-reviewed article. See the Naval Research Lab 2001 Study, also released as a United States Naval Research Laboratory publication, NRL/MR/6170-99-8414 (November 3, 1999).

This study demonstrated unequivocally that environmental contamination can cause false positives in the sweat patch. The study refuted two central claims that PharmChem had repeatedly made in defense of its sweat patch over a period of years: (1) that an isopropyl rub performed immediately prior to application of the sweat patch removes drug residue present on the subject's skin; and (2) that the membrane that covers the absorbent patch is not permeable to drugs. The study demonstrated that false positive sweat patch test results may occur because both of these claims are false.

a. “Contamination from within”: The ineffectiveness of the isopropyl alcohol rub in cleaning skin prior to application of the sweat patch.

PharmChem has always recommended that the relevant portion of the subject’s skin be swabbed with an isopropyl alcohol rub prior to application of the sweat patch. However, even before the Naval Research Laboratory 2001 study was performed, literature had demonstrated that an isopropyl alcohol rub does not remove drug residue on an individual’s skin, and the drug residue can remain on an individual’s skin for several days.³

The resulting danger of false positives is plain: if an individual has drug residue on her skin that is not removed with an isopropyl alcohol rub and the sweat patch is applied to that area of skin, the drug residue would be detected in the sweat patch, appearing as if the individual had excreted that amount from that small portion of the individual’s skin. As an earlier published study explained:

[A] simple cleaning of the skin with isopropanol may be insufficient to remove residual, previously deposited drug. The residual drug may then be transferred by sweat into the collection device and mimic use.

See Kidwell, Holland, and Athanaselis, “Testing for Drugs of Abuse in Saliva and Sweat,” 713 *J. Chromatography B* 111, 124 (1998).

The Naval Research Laboratory 2001 Study bears out this concern. Non-drug-using study subjects had sub-microscopic, trace amounts of cocaine, heroin, or methamphetamine applied to their skin, then engaged in normal hygiene, including showers. (The amount of drug placed on subjects’ skin was comparable to the amount

³ See Kidwell, Blanco, & Smith, *Cocaine Detection in a University Population*, 84 *Forensic Science International* 75 (1997) (Exhibit J); see also Kidwell, Holland, and Athanaselis, *Testing for Drugs of Abuse in Saliva and*

that another study has found on the skin of individuals unintentionally exposed to drugs through environmental contamination. See Naval Research Laboratory 2001 Study at 99). The subjects' skin was then *twice* swabbed with an isopropyl alcohol rub – even though PharmChem's protocols for sweat testing at the time called for only a single swab.

Sweat patches applied after this procedure repeatedly found drugs at levels many times in excess of PharmChem's recommended cutoff level for a positive test. (Naval Research Laboratory 2001 Study at 99-101.) Moreover, sweat patches tested positive for all drugs even when the patches were applied *six full days* after the skin was contaminated by the drug, and even after the subject showered at least once per day. (Naval Research Laboratory 2001 Study at 99-101). The study concluded:

False positive interpretations may arise from prior presence of drugs on the exterior of the skin which are not removed by the cleaning process.

(See Naval Research Laboratory 2001 Study at 98). As discussed below, *all* subsequent studies of this issue — even those belatedly performed by PharmChem — have replicated the core results of the Naval Research Laboratory study on this point.

b. “Contamination from without”: The permeability of the membrane covering the sweat patch.

PharmChem has additionally long claimed that the membrane covering the sweat patch is impermeable to drugs when affixed to the skin. The findings of the Naval Research Laboratory 2001 Study belie this fundamental claim.

After application to an individual, the sweat patch is covered by a membrane made of a material called TegadermTM, which is used for a variety of medical purposes.

Sweat, 713 J. Chromatography B 111 (1998) (Exhibit I).

Water vapor can travel freely through the membrane. PharmChem repeatedly claimed in court that drugs could not pass through the membrane and contaminate the patch.

The Naval Research Laboratory 2001 Study demonstrated that, contrary to PharmChem's assertions, drugs can indeed pass directly through the membrane and contaminate the sweat patch. This scenario can cause false positive test results in environments contaminated with drugs.

The Naval Research Lab researchers tested the permeability of the membrane under a variety of conditions. They found that several common factors increased the permeability of the membrane to the point where drugs in the environment could pass through it and contaminate the patch. Factors increasing the likelihood of this type of environmental contamination include:

- (1) the tested individual actively sweating;
- (2) the exterior of the patch becoming wet; and
- (3) the exterior of the patch being exposed to a material with a pH level greater than seven, such as many common soaps and shampoos.⁴

(Naval Research Laboratory 2001 Study at 94). Everyday routines of course involve all of these factors.

The study showed that when the exterior of a sweat patch becomes wet, with either sweat or tap water, methamphetamine can permeate the membrane and enter the patch in amounts large enough to cause positive test results. (Naval Research Laboratory 2001 Study at 98).

⁴ See Sellers, Smith, Gruszecki, Clouette, *Effect of Shampoo on Cocaine Uptake in Hair*, Proceedings of the TIAFT/SOFT 1994 Joint Congress Abstracts

2. The Crouch Environmental Contamination study.

Another published study similarly investigates one of the environmental contamination scenarios found in the Naval Research Laboratory study. (See Crouch, Metcalf, Slawson, *An Assessment of the Effectiveness of the PharmChek Sweat Patch Skin Cleansing Procedure*, 32 Bulletin of the International Association of Forensic Toxicologists 5 (2000) [hereinafter Crouch Contamination Study]). This study replicated the Naval Research Lab's "contamination from within" scenario by placing drugs on a non-drug-user's skin, cleaning the skin twice with isopropyl alcohol, and testing a sweat patch placed on that area.

The study repeatedly found that the isopropyl alcohol rub was *ineffective* in removing the drug from the subjects' skin, and the sweat patches absorbed a substantial amount of the drug – often enough to cause a false positive test result. When 1000 ng of methamphetamine was placed on the skin, **all five subjects showed methamphetamine in the sweat patch, at an average concentration of 10.8 ng/ml – an amount above the cutoff level for a positive test**; two of five subjects tested above the cutoff level. When 1000 ng of cocaine was placed on the skin, four out of five subjects – or 80% – showed cocaine in their sweat patch test (the study does not indicate how many were above the cutoff level for a cocaine positive test).

These results replicate the basic finding of the Naval Research Laboratory study: that drug deposited on skin is not removed by isopropyl alcohol, and that false positive results can therefore occur.

(1994) at 118.

3. The Skin Storage study.

In 2000, another peer-reviewed article was published, questioning the reliability of the sweat patch on entirely different grounds. See Skin Storage Study. None of the four authors of this study was involved with the Naval Research Laboratory study described above.

Levisky et. al. undertook their study because, despite the claims of “[p]roponents” of the sweat patch, “a number of questions about the process remain unanswered.” (Skin Storage Study at 36.) The authors cited widely accepted and as yet unrebutted scientific reports that drugs are stored in skin and adipose tissue, and noted that:

The observation [of drug deposition] is of considerable forensic significance, since if drugs do accumulate in fat and other tissues, then **results of sweat patch testing may falsely suggest that new episodes of drug use have occurred.**

(Skin Storage Study at 36). The study went on to find that drugs are indeed deposited and stored for long periods of time in adipose tissue and skin. The authors performed autopsies on eight different deceased drug users, and every analysis of skin or adipose tissue came up positive for substantial amounts of drugs. (Skin Storage Study at 39-41).

These findings cast doubt on the validity of positive sweat patch test results in two different ways. First, a positive sweat test result could be from drugs deposited in the skin or adipose tissue an “extremely long” time before the sweat patch had been applied, rather than from current drug use. (Skin Storage Study at 45). Second, as the authors of the Skin Storage Study explain:

According to patch manufacturers, a sweat patch test is considered

positive when more than 10 ng /ml solvent . . . is detected and confirmed . . . The process [that PharmChem used for determining the cut-off] presumes that the only route for drug entry into the patch is sweat, and that drugs enter the sweat from the blood. But the results presented here, and the results of previously published studies, strongly suggest that other processes may be involved . . . These findings suggest that **other mechanisms leading to positive patch tests are possible** . . .

(Skin Storage Study at 44).

These four independent and established authors openly question the validity of the cut-off level PharmChem has set for positive sweat patch tests – and cast crippling doubt on PharmChem’s core biological assumptions on which the company based its entire sweat testing regimen. This study, standing alone, contradicts any claim that sweat testing has reached a level of general acceptance in the scientific community.

4. PharmChem’s Internal Studies.

Perhaps in hopes of rebutting the results of the studies discussed above, PharmChem at one point performed internal studies on the issue of environmental contamination. PharmChem has never published the results of these studies, and (unsuccessfully) fought efforts to make the studies public.

Dr. Fred Smith has obtained and review the results of these internal studies. He found that studies gave the following results:

- When 100, 500, and 1000 nanograms of cocaine and cocaine metabolite were applied to skin, and then the skin was repeatedly swabbed with isopropyl alcohol, sweat patches placed on the skin came up positive for cocaine 76% of the time, and for cocaine metabolite 52% of the time. This is further evidence that the isopropyl alcohol swab is ineffective at removing drugs and metabolites that have contaminated the skin.
- When cocaine solution was applied to t-shirt material, and the t-shirt material is worn next to the skin for eight hours, and then the skin was swabbed with isopropyl alcohol, subsequent sweat patches tested positive 60% of the time. This demonstrates that skin contamination can occur from contact with contaminated clothing.

- When a sweat patch was externally contaminated with cocaine in a water solution, 33% of sweat patches tested positive. This is further evidence that sweat patches the membrane that is supposed to protect the sweat patch is permeable to drugs.

These results duplicate the findings of the Naval Research Lab 2001 study on key points. It is understandable that PharmChem has tried to conceal these damning research results.

C. Summary of Scientific Evidence.

The real-life studies indicate widely varying false positive rates for the sweat patch, ranging from seven percent (Naval Research Lab 2003 study) to forty percent (Preston Comparison Study). Thus, according to the current state of the research, when the sweat patch is used on drug-abstinent individuals, **false positive test results will occur somewhere between seven percent and forty percent of the time.**

Commenters believe further research into the issue of false positives is warranted; experts retained by PharmChem will likely agree. However, speculation by experts that further research will reveal lower false positive rates is just that: speculation. Speculation by experts, no matter how well-credentialed, cannot displace the results of actual scientific research. For every expert that foresees that further research will bolster the reliability of the sweat patch, there are other experts whose best guess is that further research will confirm the research thus far, or reveal further problems – from the skin storage issue raised in the research discussed above, from varying rates of perspiration or other bodily factors in individuals, or perhaps from some factor yet to be anticipated.

PharmChem's experts may critique the existing studies, suggesting that they could have been improved with different protocols, or that their results would not be replicated if different, better protocols were followed. However, any study can be criticized with the benefit of hindsight and with varying scientific opinions. Until these hypothetical, different tests are performed, the current research is the best that science has to offer on this question.

Bibliography

- Crouch, Metcalf, Slawson, "An Assessment of the Effectiveness of the PharmChek Sweat Patch Skin Cleansing Procedure," 32 *Bulletin of the International Association of Forensic Toxicologists* 5 (2000). [Crouch Contamination Study.]
- Levisky, Bowerman, Jenkins, Johnson, Levisky, Karch, "Comparison of Urine to Sweat Patch Test Results in Court Ordered Testing," 122 *Forensic Science International* 65 (2001). [Levisky Comparison Study.]
- Levisky, Bowerman, Jenkins, and Karch, "Drug Deposition in Adipose Tissue and Skin: Evidence for an Alternative Source of Positive Sweat Patches," 110 *Forensic Science International* 35 (2000). [Skin Storage Study.]
- Kidwell, Blanco, & Smith, Cocaine Detection in a University Population, 84 *Forensic Science International* 75 (1997). [Kidwell 1997 article.]
- Kidwell, Holland, and Athanaselis, "Testing for Drugs of Abuse in Saliva and Sweat," 713 *J. Chromatography B* 111, 124 (1998). [Kidwell 1998 Article.]
- Kidwell, Kidwell, Shinohara, Harper, Roarty, Bernardt, McCaulley, Smith, "Comparison of Daily Urine, Sweat, and Skin Swabs Among Cocaine Users," 133(1-2) *Forensic Science International* 63 (2003). [Naval Research Lab 2003 Study.]
- Kidwell, Smith, "Susceptibility of PharmChek Drugs of Abuse Patch to Environmental Contamination," 116 *Forensic Science International* 89 (2001). [Naval Research Lab 2001 Study.]
- Preston, Huestis, Wong, Umbricht, Goldberger, and Cone, "Monitoring Cocaine Use in Substance-Abuse-Treatment Patients by Sweat and Urine Testing," 23 *J. Analytical Toxicology* 313 (1999). [Preston Comparison Study.]