An Evaluation of Rapid Point-of-Collection Oral Fluid Drug Testing Devices

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Background

In the current environment of increased testing for drugs of abuse in traffic safety initiatives there are inherent advantages to testing oral fluid. A number of studies and review articles have examined saliva/oral fluid as a diagnostic matrix for detecting drugs of abuse (1,2,3,4,5,6,). Mixed saliva or oral fluid, is perhaps the most accessible matrix used for the detection of drugs. Oral fluid consists primarily of secretions from the submaxillary (65%), parotid (23%) and sublingual (4%) glands (1,5). Detection times for drugs in oral fluids are roughly similar to that in blood, approximately 1-24 hours [An extensive discussion on detection times in oral fluid by drug is provided by Huestis and Cone (1)]. Oral fluid normally contains parent drug rather than drug metabolites as are most commonly detected in urine. Collection of oral fluid is generally considered less invasive than either blood or urine, and oral fluid could be an excellent matrix to relate drug use with behavioral impairment (1,2,5,6,7).

In the past, the analysis of oral fluid has normally been conducted in a laboratory. However, a number of rapid immunoassay testing devices and devices using newer technology [e.g. Upconverting phosphor] have recently become available that permit immediate testing of the oral fluid specimen at the point of collection [e.g. a police station or in some cases even at the roadside]. Many of these devices use methods that appear to be similar to the rapid POC testing devices that have been shown to be useful for urine drug testing. Some of the newly developed oral fluid devices are modifications of urine test kits and reports comparing POC oral fluid devices with other matrices have found them user friendly, but generally not as accurate as the POC urine testing devices (8,9). Studies examining the effectiveness of specific oral fluid devices to detect drugs and comparing results with lab-based assays have yielded varying results (10,11,12,13). A few of the newly available POC oral fluids testing devices have potential for use in roadside testing, while others utilize desktop instruments and would need to be used at police stations in a manner similar to evidentiary breathalyzer devices.

Currently, there are no nationally accepted standards or cutoff values for detecting drugs in oral fluids [either workplace or criminal justice] and, for most analytes there are significant differences in cutoff values across currently available POC oral fluid testing devices [i.e. sensitivity to detect drug].

Objectives

The objectives of this study were twofold: 1) To identify currently available rapid POC oral fluid drug testing devices; and 2) To evaluate these devices for their ability to detect drugs at manufacturers' claimed cutoff levels, and at proposed U.S. federal standards.

Methodology

The evaluation was performed jointly by The Walsh Group (TWG), Bethesda MD, and the Center for Human Toxicology (CHT) at the University of Utah, Salt Lake City, UT. We reviewed the literature, researched the Internet and contacted a variety of sources to identify the currently available POC oral fluid devices that were on the market or in development. The identified manufacturers were contacted, the evaluation explained, and their participation was solicited. Based on the manufacturers' responses and device availability, the following products were made available for the evaluation: OralLab®, Ansys Technologies, Inc. [Now Varian], Lake Foster, CA (Ansys); RapiScan, Cozart Bioscience Ltd., Abingdon, Oxfordshire UK (Cozart); Drugwipe, Securetec, Ottobrunn, Germany (Securetec); SalivaScreen®, Ulti-Med, Ahrensberg Germany (Ulti-Med); Uplink® OraSure Technologies Inc/Draeger [USA/ Germany] (OraSure); and Oratect®, Branan Medical Corporation [USA] (Branan). These devices represent six of the eight POC oral fluid testing products commercially available in the world at the time of this study.

Using the manufacturers' product information and The Substance Abuse and Mental Health Services Administration (SAMHSA)'s draft guidelines (14) for the analysis of oral fluids, target drug concentrations for the evaluation protocols were established. These target concentrations and the procedures used to prepare the human oral fluid specimens are described in detail in Walsh et. al.(15). The protocol was designed such that each device was challenged with a low, medium, and high concentration of the target drug as well as with a drug-free (negative) control. As a general rule, the low concentration was one-half of the proposed SAMHSA cutoff, the medium concentration was twice the proposed cutoff, and the high concentration was 10 times the proposed cutoff. The cannabinoid concentrations were the only exception. It was clear from the product information provided that none of the devices could test for THC in the range suggested by SAMHSA [i.e. 4 ng/mL]. Therefore, for THC, the low concentration was 1.25 times the proposed SAMHSA cutoff and the medium and high concentrations were 5 times and 25 times, respectively, the SAMHSA concentration.

In most cases, each device was challenged at four drug concentration levels (Negative, Low, Medium, and High) for each drug class (Methamphetamine, Opiates, Cocaine, Amphetamine, and Cannabis [delta-9-THC]). The challenges consisted of 10 replicate tests at each of the spiked concentration levels and five replicate tests for the negative challenge. Therefore, depending on the number of parameters available on each device approximately 100-125 tests were conducted per device. On each day of the evaluation, a control solution was selected and thawed. Ten devices from each manufacturer were unpackaged and labeled. The analyses were performed according to the manufacturers' specifications and the test results were read and recorded by the principal analyst. For devices in which the results were visually interpreted, a second analyst also read and recorded his/her results. Discrepant results between the primary and secondary analyst were noted. (Only two discrepancies were encountered in the entire evaluation and these were interpreted in favor of the device). The procedure was repeated until all of the devices were evaluated with the selected control solutions.

Results and Analyses

The principal goal of the study was to evaluate these devices for the ability to detect target drugs at manufacturers' claimed cutoff levels, and to examine the performance of the devices around the proposed U.S. federal standards.

Figures [A-F] illustrate performance of the devices at each test concentration and as compared to the **SAMHSA** proposed standards. In the Figures below, the **SAMSHA** cutoff

line represents the theoretical concentration at which a screening device should be able to differentiate a negative specimen from a presumptive positive specimen. These **SAMSHA** cutoff concentrations are based on draft guidelines for testing oral fluids that have been proposed for Workplace Testing.

Figure A. Methamphetamine Results
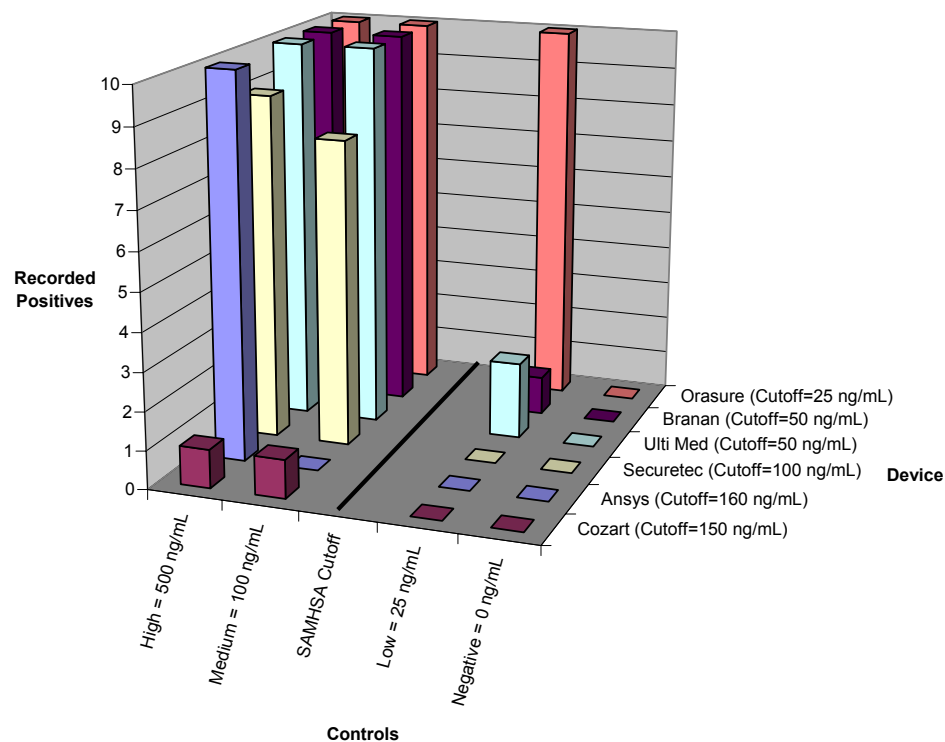
Methamphetamine - Overall, the ability of these devices to detect methamphetamine in oral fluids was reasonably good. While there were differences in sensitivity, Ansys, Branan, OraSure, Securetec and Ulti-Med devices performed well detecting methamphetamine at their stated cutoffs values. The OraSure device was shown to be the most sensitive and performed without error at half the proposed SAMHSA cutoff level.

Figure B. Amphetamine Results
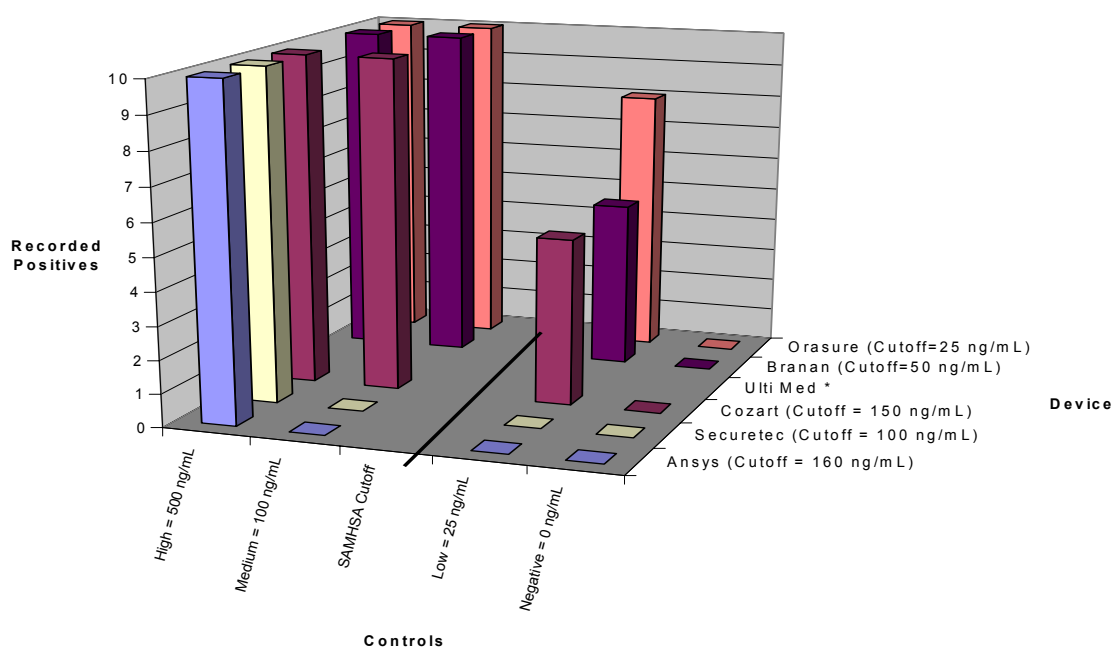
All of the devices detected amphetamine at the high concentration. OraSure, Branan, and the Cozart devices performed well above and below the proposed SAMHSA cutoff value and met or exceeded their claimed cutoffs.

Figure C. Opiate Results
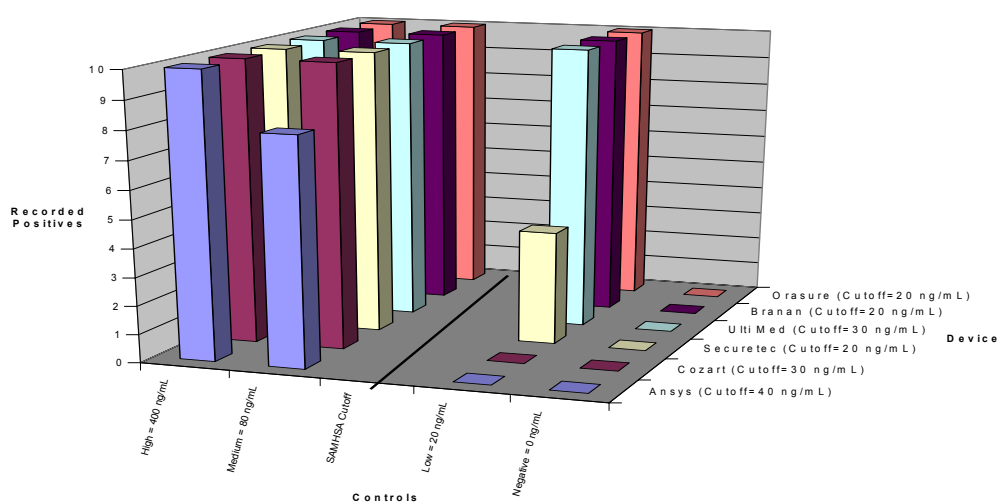
All of the devices detected opiates at the medium and high concentrations and all performed in accordance with claimed cutoff values. The OraSure, Branan, Ultimed, and Securetec devices performed well even at the low concentration below the proposed SAMHSA cutoff.

Figure D. Cocaine Results

The Branan, Ansys, and Securetec devices performed in accordance with claimed cutoff values. Clearly, the Ansys device was most sensitive to the Cocaine challenge and performed well both above and below the proposed SAMHSA cutoff value.
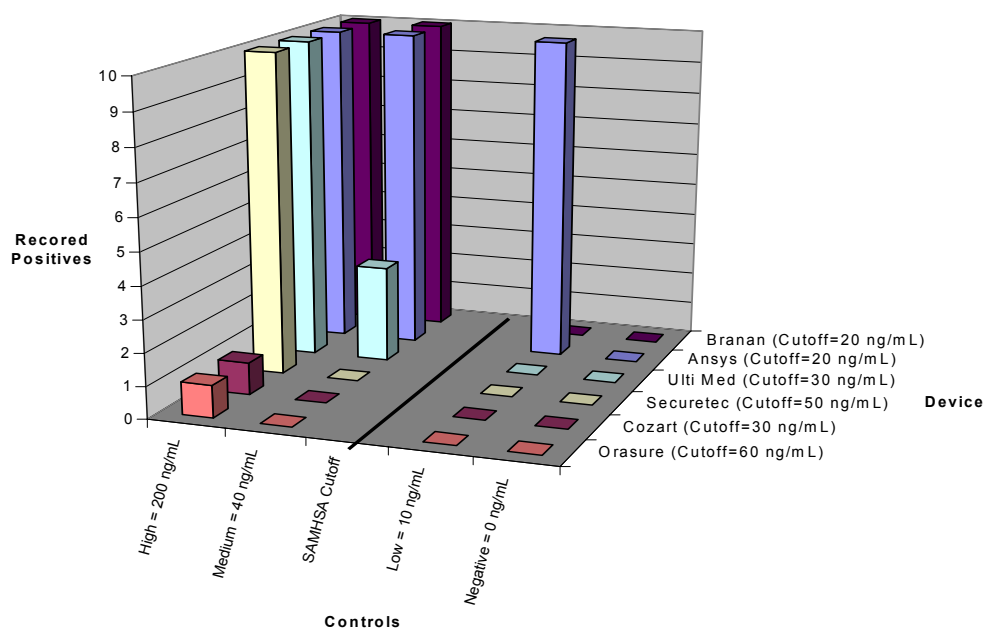
Figure E: Marijuana [Delta 9 Tetrahydrocannabinol (THC)] Results
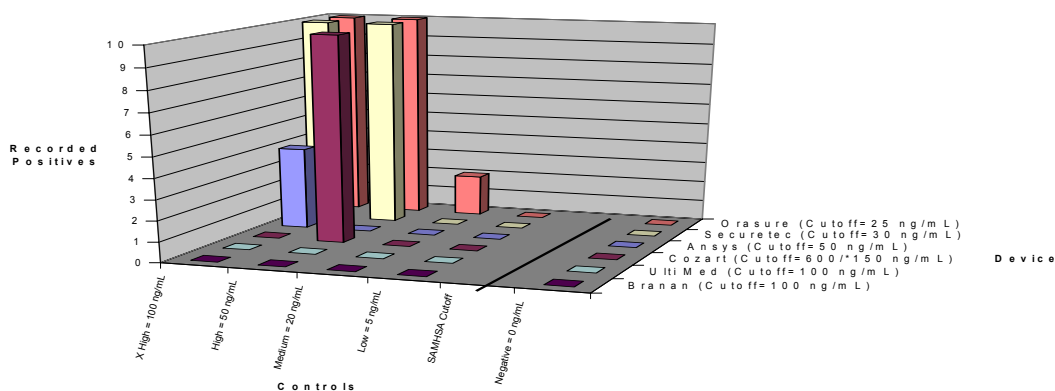
Overall, the ability of these devices to detect delta 9 THC in oral fluids was quite variable. There were substantial differences in the manufacturers' cutoff values: Ansys @ 100 ng/mL, Branan @ 100 ng/mL, Cozart @ 600 /*150 ng/mL [*In the initial evaluations the Cozart cutoff for THC was 600 ng/ml in neat oral fluid. During the final phases of this evaluation, Cozart provided new THC kits with improved sensitivity at 150 ng/mL which had been in development during the course of the study], OraSure @ 25 ng/mL, Securetec @ 30 ng/mL, and Ulti-Med @ 100 ng/mL. Figure E illustrates that in this evaluation only the OraSure device was able to detect the low positive challenges at 20 ng/ml. The OraSure, and Securetec devices were able to detect the medium [50 ng/mL] and high [100 ng/mL] challenges without error. Cozart's new THC kits, with improved sensitivity, [150 ng/ml cutoff] detected all 50 ng/ml challenges. The Ansys device was only able to discriminate the high positive challenge from the negatives but that device had a 60% false negative rate at its stated cutoff. Neither the Branan nor Ulti-Med devices were able to

detect positive challenges even at 100 ng/mL [the stated cutoff value for Branan and Ultimed].

Figure E clearly illustrates that OraSure demonstrated better sensitivity than the other devices but was not able to discriminate THC around the proposed SAMHSA cutoff level of 4 ng/ml. None of the devices could reliably detect marijuana at less than 50 ng/ml.

Discussion

Overall, the performance of the rapid point-of-collection [POC] oral fluid drug-testing devices evaluated was variable. Some devices performed well in the analysis of some drugs, but poorly for others. No single device consistently outperformed the others. In general, most of the devices detected amphetamine, methamphetamine and opiates well, but performed marginally in detecting marijuana and cocaine. One of the major difficulties in conducting this evaluation was that there are no standard cutoff values for oral fluid testing and there was a lack of consistency in cutoff levels across devices for almost every drug.

The detection of marijuana use in oral fluid appears to be especially difficult. None of these devices come close to the proposed SAMHSA cutoff value for workplace testing. Since cannabis is the most widely abused drug and most frequently associated with impaired and injured drivers, the ability to detect recent marijuana use is critical. Only the OraSure, Cozart and Securetec devices were able to reliably detect THC at 50 ng/ml. Based on available literature, detecting delta-9-THC at 50 ng/mL or greater would provide a relatively short window of detection [approximately 1-2 hours] which may not be sufficient to be effective.

Conclusion

This assessment has demonstrated that the six POC oral fluid devices evaluated performed well in detecting amphetamine, methamphetamines, and opiates. For cocaine detection, some devices are effective while others are not. The ability to detect cannabis varied significantly across devices. Even the most sensitive devices could not detect delta-9-THC at levels five times the proposed SAMHSA cutoff levels. The state of the art in oral fluid testing is evolving rapidly. There have been significant improvements over the last five years, and new methods and devices are currently in development. The search for a marijuana assay that can provide a reasonable window of detection appears to be the major hurdle for all of the device manufacturers. However, with the current focus of technology development in oral fluid testing, we believe there is every reason to be optimistic about the future for drug testing using the oral fluid matrix.

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