July 9, 2004 5:00 p.m.

Docket # 04-7984

Walter F. Vogl, Drug Testing Section, Division of Workplace Programs, CSAP

Comments on Proposed Revisions to Mandatory Guidelines for Federal Workplace Drug Testing Programs, 69 FR 19673 (April 13, 2004)

Dr. Vogl:

We submit these comments on the Department of Health & Human Services (HHS) proposed rules for federal workplace testing programs on behalf of the nearly 200 employees of OraSure Technologies, the company with the greatest experience in the collection and testing oral fluid specimens through its Intercept collection system.

Our oral fluid immunoassay systems specifically-directed to oral fluid testing have been used in commercial laboratories for nearly 10 years to analyze more than 15 million specimens. Oral fluid testing for HIV has been well established as the test of choice for public health setting. The ability to eliminate blood and urine collection has improved safety, patient care and user acceptance in these areas of great importance to the global healthcare mission of HHS.

For perspective, oral fluid testing for drugs of abuse has been effectively used in insurance risk assessment since the early 1990s. Public health and insurance testing represent more than 15 million specimens collected using the OraSure Technologies oral specimen collection device that together have helped make critical health-related decisions in the U.S. and abroad. It is worth noting the testing algorithm for those 15 million specimens is similar to the advantages HHS seeks by allowing oral fluid drug testing in the federal workplace program. The advantage of an FDA-cleared oral fluid collection device is the elimination of time, cost and resource demands for appropriately collected urine specimens. Today there are 17 laboratories in the Unites States, Canada and the U.K. processing oral fluid specimens for drugs of abuse testing using the OraSure Technologies FDA-cleared products.

Specific to workplace drug testing, the adoption of oral fluid testing has grown significantly in the past four years, driven by the FDA-cleared Intercept products. In January 2001, one laboratory in the United States processed just 1,000 oral fluid specimens. Today, more than 45,000 oral fluid workplace specimens are processed monthly for workplace drug testing in <u>all</u> testing scenarios encompassed by the federal guidelines. Workplace oral fluid testing is growing at a rate of 65% per year. Workplace oral fluid testing laboratories – including two of the largest SAMHSA-certified urine labs – have established procedures that achieve the same "standard of care" for oral fluid analysis as has been exhibited in their SAMHSA-certified urine testing programs. Proficiency testing for workplace laboratories has expanded and seeks to match those in place for urine testing. Laboratory data affirms that oral fluid testing programs have comparable detection rates – and therefore similarly effective deterrence value – as traditional urine testing programs.

Since oral fluid drug testing was introduced to private sector workplace testing, more than 930,000 specimens have been successfully collected and analyzed using the FDA-cleared

Intercept collection device and immunoassay screening kits – the specifications of which were used to develop the cutoffs HHS now proposes for its federal workplace program.

OraSure Technologies, Inc., significantly contributed to the Drug Testing Advisory Board process, beginning with the first meeting in April 1997 and continuing through creation of the final draft Guidelines. Working collaboratively with our laboratory partners and leading toxicologists, OraSure Technologies led the DTAB Industry Working Group on oral fluid testing as the recognized industry leader. This work helped to ensure that HHS and its regulated agencies benefit from oral fluid testing in a reliable manner.

Our FDA-cleared collection device has been the subject of numerous scientific studies in the peer reviewed published literature. An appendix of study citations is attached. Furthermore, OraSure has generated an extensive portfolio of published data and scientific analysis in the area of oral fluid drug testing, some at the direct request of HHS scientists seeking to evaluate this rapidly expanding technology. This data has helped establish the process for expanding the definition of a split specimen to recognize the utility and appropriateness of bi-lateral device collection, has defined the cutoffs for oral fluid screening and confirmation tests, and has provided HHS with sufficient science to conclude, "Many studies support the use of oral fluid as a specimen for forensic drug testing." (69 FR 19676)

Additionally, OraSure has worked closely with the USDOT to pioneer training and testing guidelines for saliva alcohol testing (49 CFR Part 40). Intercept oral fluid screening has been chosen as the "gold standard" by which all other oral fluid devices would be evaluated in the European Commission's ROSITA (roadside testing and analysis) project. This project has gone on for more than two years and in seven different countries, with the aim of finding law enforcement solutions to deal with the growing concern of "drugged driving." Oral fluid is the chosen testing medium for this important endeavor (www.ROSITA.org).

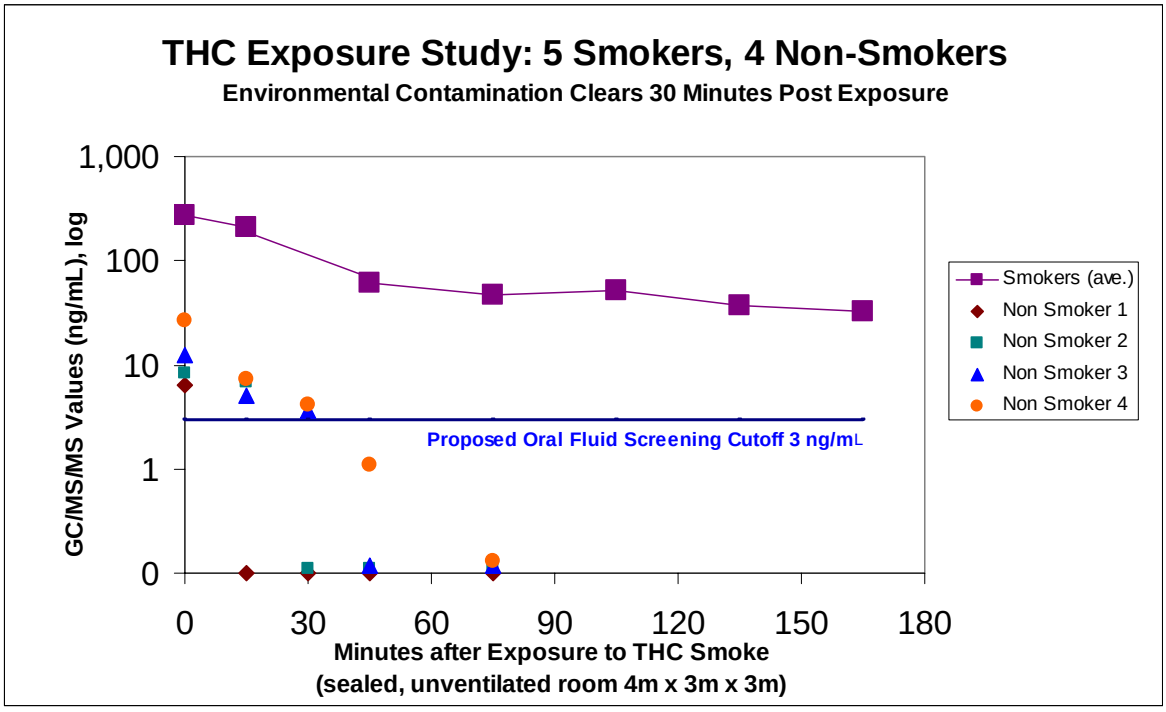
We commend HHS and its staff for their exemplary efforts in drafting proposed revisions to the Mandatory Guidelines for Federal Workplace Drug Testing Programs, availing itself of advances in drug testing technologies to allow more effective drug testing programs.

We also appreciate the opportunity to provide information to HHS in response to its request for information regarding its proposed drug testing procedures published in the Federal Register April 13, 2004 "Proposed Revisions to Mandatory Guidelines for Federal Workplace Drug Testing Programs," (69 FR 19673) and to assist HHS in fulfilling its statutory responsibility to "establish comprehensive standards for all aspects of laboratory drug testing and laboratory procedures to be applied in carrying out Executive order Numbered 12564, …including standards which require the use of the best available technology for ensuring the full reliability and accuracy of the drug tests …" Pub. L. 100–71, Title V, § 503 (a)(1)(A)(ii)(I).

In the document that follows, we address those sections of the Proposed Rules on which we wish to comment, and follow-up with recommendations for the language in the Mandatory Guidelines. As you review those comments, you will see that we stake out five important positions:

1. Commercially available, FDA-cleared collection devices have been used to produce scientific data demonstrating the equivalence of oral fluid and urine analysis for drugs of abuse testing in FDA clearances and numerous clinical studies (see Appendix references). These devices, with some modifications, can reduce specimen collection variability, thereby increasing performance, allowing HHS to maintain the continuity and benefits of oral fluid testing as it is implemented today, which is clearly critically important to the drug testing community and the public. Specifically, we believe that collection of oral fluid using an absorbent pad with a defined capacity with subsequent placement into a fixed volume of preservative is both an acceptable and preferred collection method.

2. New scientific data demonstrates that the potential for positive oral fluid THC test results from any realistic environmental exposure situation is not an issue. Even in extreme conditions, any minimal risk is completely eliminated 30 minutes after exposure (see chart and Appendix, "Passive Cannabis Smoke and Oral Fluid Testing"). We believe the proposed additional specimen (urine) collection, for the purpose of addressing the possibility of positive oral fluid THC test results from environmental contamination to cannabis smoke, is unnecessary and burdensome.



Appendix: "Passive Cannabis Smoke Exposure and Oral Fluid Drug Testing,"

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3. OraSure Technologies established oral fluid cutoffs as part of submission and FDA-clearance of the assays, which were validated through a large population study of more than 77,000 oral fluid and 5.2 million urine drug test results in a general workforce population (see Appendix, JAT 2002). From this landmark study, HHS was provided with data that established comparable positive prevalence rates for the NIDA-5 drug panel. That large population evaluation has been expanded to include more than 600,000 oral fluid specimens, and the data again is presented for HHS to review (see Appendix, "2002-2003 Prevalence Data"). This data confirms the appropriateness of the drug cutoffs listed here.

We strongly believe that the HHS proposed cutoffs for Amphetamines class drugs and for PCP are not supportable with large and well controlled scientific data. Importantly, lowering the Amphetamines class cutoffs will stimulate more false positive screening test results from over-the-counter medications, creating confusion, adding costs, and jeopardizing public confidence and credibility.

Drug Target Cutoffs (ng/mL)	Screening	Confirmation
THC (parent or metabolite)	3 (parent)	1.5 (parent)
Cocaine metabolites	15	6 (Benzoylecgonine)
Opiate metabolites	30	
6-Acetylmorphine		3
Morphine		30
Codeine		30
Phencyclidine	3	1.5
Amphetamine	300	120
Methamphetamine	120[1]	120
MDMA		120

[1]One assay for either Methamphetamine or MDMA that also must cross-react at least 100% with the other target.

Drug Testing Positive Prevalence Rates

	2002-2003 Oral Fluid Intercept *(n=527K)*	January - June 2003 Drug Testing Index - Urine Gen. Workforce *(n=2,800K)*	Federal *(n=600K)*
Total Positives	4.62%	5.00%	2.50%
Marijuana	3.08%	3.02%	1.39%
Cocaine	1.32%	0.74%	0.58%
Opiates	0.19%	0.34%	0.19%
Amphetamines	0.47%	0.46%	0.29%
PCP	0.03%	0.03%	0.04%

Notes: Oral fluid analysis by LabOne, Inc., Lenexa, KS
Drug Testing Index courtesy of Quest Diagnostics, Inc., Teterboro, NJ

4. Oral Fluid is appropriate for return to duty and follow-up testing. Our laboratory partners compare positive prevalence rates for their Intercept and urine testing programs. Intercept results compare favorably to urine testing results in every category, including return-to-duty and follow-up testing. Further, it is generally known that drug users will employ various methods to tamper with their urine specimens, including adulteration products, dilution by drinking high volumes of fluid, or by substituting their own urine with clean specimens. Oral fluid testing, by the basis of a directly observed collection and the inability to dilute the specimen, eliminates most, if not all, tampering concerns. This may explain why oral fluid testing positive rates sometimes are higher than those of urine testing. Consequently, oral fluid should be permitted for every testing scenario. The table below provides details.

Drug Testing Positive Prevalence Rates (2003)

	Oral Fluid	**Urine**	
Reason for Test	**Intercept**	**Non-Federal**	**Federal**
Lab A	*(n=273K)*	*(n=1,271K)*	*(n=660K)*
Pre-employment	4.3%	4.7%	2.3%
Random	3.0%	6.0%	1.3%
Post-accident	10.6%	4.0%	2.7%
Suspicion	22.0%	15.0%	10.5%
Follow-up	***14.8%***	***9.0%***	***3.2%***
Return-to-duty	***3.6%***	***4.1%***	***5.8%***
Lab B	*(n=36K)*	*(n=5,900K)*	*(n=1,200K)*
Pre-employment	4.1%	4.1%	2.9%
Random	3.6%	6.6%	1.9%
Post-accident	4.7%	5.7%	3.1%
Suspicion	15.8%	28.0%	13.0%
Follow-up	***8.3%***	***9.6%***	***3.4%***
Return-to-duty	***4.6%***	***5.6%***	***2.8%***

5. Quality control standards for oral fluid ELISA technology require a different metric than those applied to urine EIA testing. To achieve the greater sensitivity required to detect the majority of drug targets in oral fluid samples – as well as hair and sweat samples – the current available technology (ELISA) that is FDA-cleared for oral fluid testing can resolve a positive control at two times the cutoff and a negative control at one half of the cutoff concentration. Appropriate quality control standards for oral fluid immunoassays are -50%, +100% (½x, 2x) of the cutoff. The HHS proposed screening controls of ±25% are those currently applied to urine screening, which uses a different type of immunoassay technology that allows for this type of differentiation between a control and cutoff. The number of steps in the ELISA process results in the need for these control levels of ½x, 2x.

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Comments to HHS Discussion in Preamble

In the preamble of its proposed revisions to the Guidelines, HHS discussed several points and conclusions with regard to oral fluid testing of which we provide commentary/perspective.

"The department asks whether commenters are aware of any other studies or data that would cast more light on the appropriateness of using any of the alternative specimens or on limitations on how the specimens should be used." (69 FR 19675)

Comments:

HHS is aware of data published in the *Journal of Analytical Toxicology* demonstrating the strong comparability of prevalence rates between results from 77,000 oral fluid specimens and 5.2 million urine specimens collected in 2001 from general workforce populations. Additional data is being provided to HHS (see Appendix, "2002-2003 Prevalence Data") validating this same comparative detection capability over a data set of more than 600,000 oral fluid specimens. Clearly, this is the most comprehensive analysis of oral fluid testing HHS can hope to review.

Further, HHS has been recently notified of a landmark study on environmental contamination by marijuana smoke exposure that has been accepted for publication by the *Journal of Analytical Toxicology*[1]. This study concludes unequivocally that the individual for whom HHS expresses concern for being "in a room where others smoked marijuana" (69 FR 19676) is not at risk of having a positive oral fluid test solely on the bases of environmental contamination. This study shows the scenario for that individual to test positive is to be sealed in a small ($36m^3$), unventilated room with the smokers, be permitted no food or drink, and be tested within 30 minutes of exposure. We envision no scenario under which a federal worker would encounter these conditions, nor would we expect a federal agency to define this type of exposure as "passive."

OraSure and its laboratory partners have been leaders in developing the science of oral fluid testing. One of our current goals is to investigate the possibility of identifying specific markers in oral fluid that are indicative of active drug use. In testing for cannabis use, additional cannabis components may be present and as yet undiscovered. In particular, our current focus is upon the identification of metabolic products that are excreted in oral fluid following active cannabis use. For example, if the carboxy-acid metabolite of THC were identified in oral fluid, it might serve as further evidence of active cannabis use. Of course, any target identification will require validation with respect to separating active use from environmental contamination. OraSure and its laboratory partners are committed to continued research targeted toward improving the reliability and validity of oral fluid testing. We look forward to reporting our results on these exciting topics in peer-reviewed scientific literature in the near future. In the meantime, data generated clearly proves that screening and confirmation of THC in oral fluid provides acceptable differentiation between active cannabis use and environmental contamination.

[1] Accepted with minor revisions, publication date to be determined.

"However, the active component of marijuana (delta-9-tetrahydrocannabinol (THC)) does not diffuse into oral fluid.[26, 31,32] The only way to detect marijuana use is through the presence of the patent drug (THC) in the oral fluid because the parent drug was present in the oral cavity. Unfortunately, further scientific study is needed to be able to differentiate between whether the parent drug was present in the oral cavity due to drug use or environmental contamination i.e., the individual was present in a room where others smoked marijuana, for example." (69 FR 19676)

"In order to protect Federal workers from incorrect test results for marijuana, the Department proposes that a second biological specimen, a urine specimen, will need to be collected under the current guidelines at the same time the oral fluid specimen is obtained." (69 FR 19676)

"The department will revise the Guidelines when the science is available to differentiate between actual use and environmental contamination." (69 FR 19676)

"With regard to testing oral fluid specimens for marijuana, there is scientific evidence that the parent marijuana compound (THC) in oral fluid is not from plasma, but is residual THC present either from smoking a marijuana cigarette or from oral contamination. To ensure that a THC result on an oral fluid specimen is from active exposure, the Department is proposing to always collect a urine specimen with an oral fluid specimen that would be available if the oral fluid specimen was positive for THC. The Department is requesting comments on this proposed policy." (69 FR 19687)

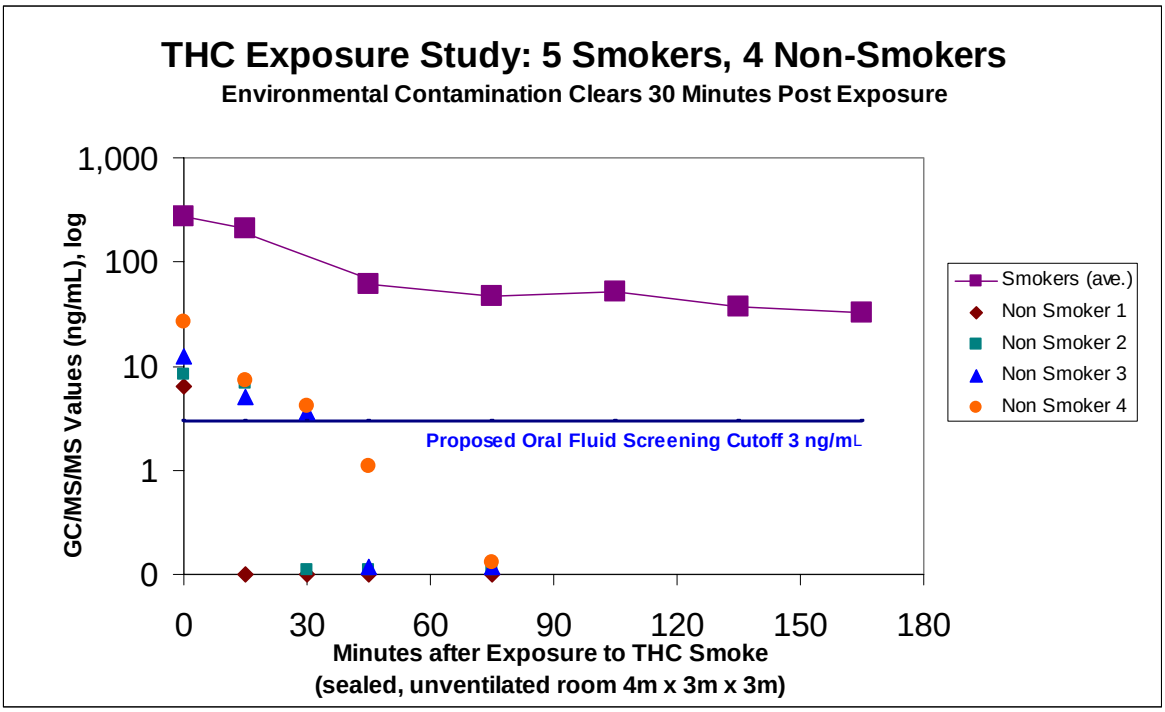
Comments:

As noted, a well-controlled study, accepted for publication by the *Journal of Analytical Toxicology*, concludes that an individual present in a room where others smoked marijuana is not at a practical risk of having a positive oral fluid test. In an extreme condition, with five smokers and four non-smokers together in a small room ($36m^3$) with no ventilation, environmental contamination was measurable for a period of only 30 minutes. There is no evidence that environmental contamination can create a risk of a positive oral fluid result for THC in any reasonable scenario. Further, even in extreme conditions, any minimal risk is completely eliminated 30 minutes after exposure. This study has been repeated under even more extreme conditions – an eight-passenger van – with similar results. These findings will be presented at the 2004 Society for Forensic Toxicology (SOFT) annual meeting.

More than 15,000 Intercept oral fluid tests have been confirmed positive for THC without a single challenge of environmental contamination, according to the leading workplace oral fluid testing laboratory. Further, this technology has been employed for more than

four years in criminal justice and drug treatment settings – a population with significantly more frequent THC use – and there have been no challenges of environmental contamination on positive THC results.

The science is now available to revise the Guidelines, and it is submitted here for your review.



Appendix: "Passive Cannabis Smoke Exposure and Oral Fluid Drug Testing,"

"To avoid saliva stimulation some recommend spitting into a cup, but some donors may be opposed to spitting, especially when observed, and may experience dry mouth." (69 FR 19676)

Comments:

The act of spitting induces salivary stimulation. Spitting to provide an oral fluid specimen is impractical, unpleasant, and undignified for professional workplace testing. This requirement does not allow for convenient collection by any of the numerous reliable collection devices in current use today. Use of an FDA-cleared collection device should be included, if not preferred. In a survey of human resource managers (n=67) at the Society for Human Resource Management (SHRM) annual conference, 100% said they would prefer to have donors use an FDA-cleared collection device vs. having the donor spit into a tube (survey summary enclosed in Appendix). For both the end-user and the testing administrator, the practice of spitting into a tube would be unacceptable for a professional testing program.

"Therefore, despite these known limitations, the Department proposes to incorporate this new technology as an optional selection for Federal agencies because oral fluid testing may be useful in certain missions and tasks that only individual Federal agencies can identify." (69 FR 19676)

"Because of the short detection window, oral fluid is not suited for return to duty, and follow-up testing." (69 FR 19679)

Comments:

Since its introduction to the marketplace in February 2000, private companies have found that oral fluid testing with an FDA-cleared collection device and related assays is useful in the full spectrum of "missions and tasks," and more appropriate for their workforce than urine testing. Oral fluid has been successfully used in all testing scenarios covered in the federal Guidelines.

It is generally known that drug users will employ various methods to tamper with their urine specimens, including adulteration products, dilution by drinking high volumes of fluid, or by substituting their own urine with clean specimens. Oral fluid testing, by the basis of a directly observed collection and the inability to dilute the specimen, eliminates most, if not all, tampering concerns. This may explain why oral fluid testing positive rates sometimes are higher than those of urine testing. Details follow:

Drug Testing Positive Prevalence Rates (2003)

	Oral Fluid	Urine	
Reason for Test	**Intercept**	**Non-Federal**	**Federal**
Lab A	*(n=273K)*	*(n=1,271K)*	*(n=660K)*
Pre-employment	4.3%	4.7%	2.3%
Random	3.0%	6.0%	1.3%
Post-accident	10.6%	4.0%	2.7%
Suspicion	22.0%	15.0%	10.5%
Follow-up	***14.8%***	***9.0%***	***3.2%***
Return-to-duty	***3.6%***	***4.1%***	***5.8%***
Lab B	*(n=36K)*	*(n=5,900K)*	*(n=1,200K)*
Pre-employment	4.1%	4.1%	2.9%
Random	3.6%	6.6%	1.9%
Post-accident	4.7%	5.7%	3.1%
Suspicion	15.8%	28.0%	13.0%
Follow-up	***8.3%***	***9.6%***	***3.4%***
Return-to-duty	***4.6%***	***5.6%***	***2.8%***

For pre-employment testing, companies find oral fluid testing more convenient to the donor, reduces the chances of adulteration, creates significant cost savings, and ultimately accelerates the hiring process. Testing at the hiring location, and eliminating the trip to the urine collection site, is more convenient for the donor, who may otherwise have been required to take additional time off from a current job to provide the urine specimen for the new job. Further, since most donors are given 24-48 hours to report to collection sites, the hiring agency expects urine drug testing results 48-72 hours after instructing the

donor to provide a specimen. With the oral fluid specimen provided right at the hiring location and sent directly to the laboratory, the agency has a result within 24 hours. This time acceleration is significant when trying to meet business and project demands with adequate staffing. In addition, any delay prior to collection provides an opportunity for any drugs to clear the donor's system, or for the donor to take steps to mask their presence. In summary, the described urine procedure may result in the loss of 1-2 days before a urine specimen is provided, creating an opportunity to allow metabolism and excretion of the drug. A timely oral fluid collection eliminates this delay and chance of escaping detection of recent drug use.

For random testing, the timesaving usefulness of oral fluid testing is even more pronounced. When workers are sent off-site to urine collection facilities, the disruption in their productivity is significant. Employers report that this paid time away from work averages more than 60 minutes. With oral fluid testing, the Donor can provide a specimen within a few minutes. Employers using Intercept testing report Donors are back at their appointed tasks within 10-15 minutes – a downtime reduction of more than 75% over traditional testing. In just one of many examples, a large private employer determined that the savings discussed above in reducing "time away from task" and hiring delays would save that employer approximately $240,000 per year on its drug free workplace program. In another example, Intercept oral fluid testing enabled a large retail employer to expand its drug free workplace throughout 18 divisions for the same budget consumed for urine testing in only six divisions. These savings can be used to expand drug testing, consistent with the goals of the Federal Guidelines. These examples represent the common experience of Intercept oral fluid drug testing clients. Given the use of taxpayer dollars to finance these programs, Federal agencies should have the opportunity to run their drug free programs as efficiently as possible, while maintaining the highest quality to protect donor rights.

For post-accident testing and suspicion-based testing, oral fluid is the obvious choice, given its bias toward "real time" use. As you have determined from your research of the literature, oral fluid detects drug use sooner after use than any other testing matrix except blood.

For return-to-duty testing, oral fluid testing offers the best opportunity to distinguish current from historic use. As HHS is aware through the work of its Center for Substance Abuse Treatment (CSAT), drug-treatment programs deal with the variability of urine drug elimination rates by using confirmation levels as an indication that a person is successfully completing a substance abuse recovery program. Oral fluid better reflects the recent activity of the person completing the recovery program reducing the potential for an inaccurate accusation. Data comparing the positive prevalence rates of oral fluid and urine testing in workforce populations (see table above) show each is valid for this testing scenario.

For follow-up testing, oral fluid offers the same advantages, just discussed, for return-to-duty testing. In addition, oral fluid testing offers the advantage of minimizing the risk of tampering. We have several documented examples of workers who avoided detection under urine "follow-up" programs, but had their drug use discovered the first time the company switched to Intercept oral fluid testing. In one example, the Donor was

surprised and reportedly nervous when told he would give an oral fluid specimen instead of a urine specimen. This particular donor called his supervisor two hours after providing his specimen and admitted he had been adulterating his urine tests and had been using marijuana throughout his urine follow-up program.

We recognize that HHS has taken several steps to address the prevalence of adulterants, dilution and substitution in urine drug testing. Sensitive to donor rights, HHS has lowered the creatinine thresholds for dilute and substituted specimens. Further, we understand HHS monitors the thousands of websites offering products to "beat a drug test" and knows that a Donor has regular control by diluting a specimen through drinking copious amounts of fluid. Oral fluid testing makes each of these concerns irrelevant. It has become very clear that: "cheaters" do not have a way to manipulate an oral fluid collection – since it is done under direct observation, using a fluid that cannot be diluted through fluid intake, nor substituted or adulterated after delivery. Therefore, oral fluid is the most appropriate specimen for both protecting donor rights while enforcing compliance with their treatment.

"Non-instrumental POCTs for oral fluid have been characterized by only one group of independent investigators.[59]" (69 FR 19677)

"The investigators felt that "there is every reason to be optimistic about the future for drug testing using oral fluid matrix."[59](69 FR 19678)

"POCT testing of oral fluid is most suited for situations that require quick, negative results such as in emergency/crisis management. It is most suited for reasonable suspicion/cause and post-accident. It may be least suited for random testing. Oral fluid is not suited for return to duty, follow-up testing and pre-employment." (69 FR 19678)

Comments:

HHS has taken the appropriate steps to establish cutoffs, performance standards and certification requirements for oral fluid testing. Therefore any oral fluid technology, whether laboratory-based or POC, should be permitted under the federal program when it can meet all HHS requirements.

"In order to provide an equivalent program of on-going quality assurance for POCT devices, the Department proposes a certification process under which POCT device manufacturers would provide tests for evaluation to be placed on the list of SAMHSA-certified devices published by the Secretary. This would be followed by periodic additional testing as new lots of manufactured tests become available as well as PT sample requirements, training of POCT testers, and on-going quality assurance requirements." (69 FR 19678)

"Section 12.2 establishes criteria for the Secretary to certify a POCT for the use in the Federal drug testing program. The device must be FDA-cleared for the purposes of detecting drugs of abuse and it must be determined by the Secretary that it effectively determines the presence or absence of drugs and the validity of a specimen, either as an integral function of the POCT device or as a set of compatible devices or procedures. Section 12.5 provides manufactures a list of what they must provide the Secretary in order to have their device or devices included on the list of SAMHSA-certified devices." (69 FR 19684)

Comments:

A SAMHSA-certified list of approved products, similar to the NHTSA Conforming Products List, is a responsible way to provide consistent standards for all device manufacturers. We support this proposal.

"For oral fluid, the Department is proposing that 2 mL be collected in a collection tube rather than allowing oral fluid to be collected directly into a collection device that does not provide an accurate measurement of the volume of oral fluid collected. This approach allows establishing specific cutoffs for oral fluid testing." (69 FR 19680)

"For oral fluid, the Department proposes that the donor provide an oral fluid specimen directly into an appropriate container. This approach will ensure that a minimum amount of oral fluid is collected and can then be split for on-site testing or sent to a laboratory for both initial and confirmatory testing." (69 FR 19682)

Comments:

Based on our experience with more than 1.9 million oral fluid specimen collections for drugs of abuse analysis performed with an FDA-cleared collection device with an absorbent pad and preservative solution, we believe that oral fluid specimen collection can be most effectively performed using such an FDA-cleared device. Specimen collections can be performed reliably and conveniently with this method, minimizing donor reluctance or distaste for expectoration, while ensuring adequate and repeatable specimen volumes.

It should be noted that significant variances in specimen characteristics are currently accepted for urine specimens under long-existing regulations, as well as for hair and sweat specimens under the proposed guidelines. Urine specimens from individuals are known to vary significantly in concentration due to intentional and unintentional physiological dilution, and yet these variances are effectively disregarded absent the specimen being so dilute as to not be possible under normal human physiology. Typical urine creatinine levels are on the order of 150 mg/dL (J. Cook et al., The Characterization

of Human urine for Specimen Validity Determination in Workplace Drug Testing: A Review. J. Anal. Toxicol., 24, 579 (2000)), and yet no significant program responses accrue until urine specimens have creatinine values more than 50 times lower. These variances are entirely capable of being manipulated by the donor through intentional physiological dilution, as has been well recognized.

Furthermore, there is little control over specimen collection in sweat patch testing where significant differences in the amount of sweat collected may occur between and within individuals. With sweat patch testing here is no measure whatsoever of the amount of specimen collected. Nonetheless, as configured, it proves useful drug detection and deterrence.

In this context, we strongly believe oral fluid, FDA cleared collection devices are within the accepted scientific variances of defensible forensic testing. Reliable data for scientific studies, FDA clearances on nine drugs of abuse assays, and positive prevalence results have been generated using a collection device and ELISA testing systems. This data encompasses all systematic variability from the collection device through laboratory analysis, and yet the results show comparability to urine positive prevalence rates.

We believe, as the experts, that collection devices represent the best collection method in the market. In general, reducing sample volume variability is a reasonable longer-term goal in terms of continuous improvement of the current devices. We are committed to this goal in our process of continuous improvement. However, in the immediate future, the combination of a reliable, repeatable collection device and a fixed volume of preservative is a better option than forcing professional federal workers to spit into a tube.

Spitting into a tube to obtain a “neat” specimen does not necessarily represent the “best available technology,” nor do we believe this collection method would be practical. Donors appreciate the dignity of an oral fluid collection, which we do not believe exists should Donors be required to spit into a container. The additional cost and time required for collecting and dividing “neat” specimens could be significant. The collection environment would require control and possibly sanitizing, and the allowance of 15 minutes to provide a specimen is five times longer than the collection process with the FDA-cleared oral specimen collection device. The requirement to handle saliva would compel Federal agencies to rely on external collection resources, which have associated costs both in fees and the paid time a Federal worker spends away from the job. We have extensive experience in obtaining “neat” oral fluids used in the development process. Neat oral fluid is not easily pipetted, even in a laboratory environment. Collection of “neat” saliva samples will not be accepted by donors and administrators.

Human Resources professions, surveyed at the annual meeting of the Society for Human Resource Management (SHRM), unanimously preferred use of a collection device to spitting in a tube. The 67 professionals surveyed all chose the collection device. These HR professionals found the spitting recommendation, “unpleasant,” “disgusting,” “unreasonable,” and “stupid.”

"As previously stated in the preamble, the Department is proposing to adopt the cutoff concentrations that were recommended by the industry working groups. The Department believes that each laboratory testing a specific type of specimen for a particular drug must be able to accurately determine the concentration as well as concentrations equal or greater than the cutoff. The Department is specifically requesting comments on the appropriateness of these cutoff concentrations and the ability of laboratories to meet this requirement." (69 FR 19680)

"The Department is specifically interested in obtaining information on the ability of the various immunoassay test kits to detect MDMA, within the amphetamine class of drugs. The Department believes that the only sensitive and specific manner to perform the initial test for methamphetamine, amphetamine, and MDMA is to use two separate initial tests, one for methamphetamine and amphetamine and a second initial test for MDMA. Recommendations on using a single amphetamine test kit or the need to use separate test kits are requested." (69 FR 19680)

Comments:

We agree with HHS that laboratories must be able to accurately and consistently identify drug concentrations in oral fluid specimens and appropriately compare them to the administrative cutoffs. To establish the cutoffs presented by the oral fluid working group, OraSure Technologies and LabOne collaborated on a large population study of more than 77,000 oral fluid drug test results in a general workforce population. From this landmark study, HHS was provided with data on the appropriateness of cutoffs for the NIDA-5 drug panel. That large population evaluation has been expanded to consider more than 600,000 oral fluid specimens, and the data again is presented for HHS to review.

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Amphetamines	0.47%	0.46%	0.29%
PCP	0.03%	0.03%	0.04%

Notes: Oral fluid analysis by LabOne, Inc., Lenexa, KS
Drug Testing Index courtesy of Quest Diagnostics, Inc., Teterboro, NJ

The data shared in the table above confirms the appropriateness of the following drug cutoffs:

Drug Target Cutoffs (ng/mL)	Screening	Confirmation
THC (parent or metabolite)	3 (parent)	1.5 (parent)
Cocaine metabolites	15	6 (Benzoylecgonine)
Opiate metabolites	30	
6-Acetylmorphine		3
Morphine		30
Codeine		30
Phencyclidine	3	1.5
Amphetamine	300	120
Methamphetamine	120[1]	120
MDMA		120

[1]One assay for either Methamphetamine or MDMA that also must cross-react at least 100% with the other target.

The recommendation by HHS for a single immunoassay kit to simultaneously detect amphetamine and methamphetamine is confusing given the data generated for HHS over the past several years. The only FDA-cleared immunoassay test kits to detect amphetamine and methamphetamine are in fact separate immunoassays. These kits have been used in more than 930,000 workplace drug tests since February 2000, secured FDA-clearance based on accuracy and reliability comparable to traditional urine assays, and demonstrated comparable detection capabilities to generally-accepted, FDA-cleared urine tests. The FDA-cleared immunoassay for methamphetamine also detects MDMA (Methylenedioxymethamphetamine), with a cross-reactivity of greater than 100%. It is possible this statement of the Department belief around "the only sensitive and specific manner" to detect amphetamine, methamphetamine and MDMA is based on its knowledge of urine testing assays. Copies of the package inserts for the FDA-cleared immunoassays for amphetamine and methamphetamine are included.

We strongly believe that the HHS proposed cutoffs for Amphetamines class drugs and for PCP are not supportable with large and well controlled scientific data. Importantly, based on our experience, lowering the Amphetamines class cutoffs will stimulate more false positive screening test results from over-the-counter medications, creating confusion, adding costs, and jeopardizing public confidence and credibility.

"If the FDA has cleared a collection device, it has been determined that the device does not affect the specimen collected. If the FDA has not cleared a collection device, the Federal agency must only use a collection device that does not affect the specimen collected." (69 FR 19682)

"It is reasonable to believe that new and different specimen collection devices will be used to collect Federal employee drug

test specimens. The department requests specific comments on this requirement." (69 FR 19682)

Comments:

Based on our experience with more than 1.9 million oral fluid specimen collections performed with an FDA-cleared collection device for drugs of abuse analysis, we believe that oral fluid specimen collection can be most effectively performed using such an FDA-cleared device. Specimen collections can be performed reliably and conveniently with this method, minimizing donor reluctance or distaste for expectoration, while ensuring adequate specimen volumes.

Reducing sample volume variability is a reasonable position. The combination of a reliable, repeatable collection device and a fixed volume of preservative is a better option than forcing professional federal workers to spit into a tube.

Spitting into a tube to obtain a "neat" specimen does not necessarily represent the "best available technology," nor do we believe this collection method would be practical. Donors appreciate the dignity of an oral fluid collection, which we do not believe exists should Donors be required to spit into a container. The additional cost and time required for collecting "neat" specimens could be significant. The collection environment would require control and possibly sanitizing, and the allowance of 15 minutes to provide a specimen is five times longer than the collection process with the FDA-cleared Intercept oral specimen collection device. This additional time and control would be economically burdensome for the Federal agency.

"Again with regard to oral fluids, the preamble mentions a possibility of an individual having 'dry mouth.' The Department would appreciate any comments on whether the Department should adopt a specific procedure for 'dry mouth' as it has for 'shy bladder' under urine." (69 FR 19687)

Comments:

Based on the collective experience of hundreds of workplace end-users and more than 930,000 specimens processed for workplace drug testing, a condition which HHS calls "dry mouth" has not presented itself. We have no documented complaints from customers or end users of a Donor unable to provide an oral fluid specimen on an FDA-cleared collection device due to "dry mouth."

The use of an FDA-cleared oral fluid collection device according to the manufacturer's recommendations has been well established. The incidence of volume collection below the volume needed for processing a specimen in the laboratory is very low.

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OraSure Technologies hereby submits recommended language for certain sections of the new proposed guidelines, as indicated below.

Section 1.5 What do the terms used in these Guidelines mean?

Split Specimen. For oral fluid, one specimen collected that is subdivided or two specimens collected almost simultaneously.

Recommendation:
We agree with the proposed language for this section.

Justification:
Simultaneous (bi-lateral) collection of oral fluid specimens has been shown reliable in scientific studies presented to the Society of Forensic Toxicologists (see Appendix, SOFT 2001) and published in the Journal of Analytical Toxicology (see Appendix, JAT Vol. 25, 2001).

Section 2.2 Under what circumstances can the different types of specimens be collected?

Oral Fluid… Pre-employment, random, reasonable suspicion/cause, post-accident

Recommendation:

Section 2.2 - Under what circumstances can the different types of specimens be collected?

"Oral Fluid …Pre-employment, random, reasonable suspicion/cause, post-accident, return to duty, follow-up"

Justification:
A review of large population data demonstrates that oral fluid has sensitivities comparable to urine for detection of drug use in a workplace population. A large-scale, peer-reviewed study published in the *Journal of Analytical Toxicology* comparing workplace testing results of 77,000 oral fluid specimens with 1 million federally mandated urine specimens and more than 5.2 million general workforce urine specimens concluded that, "it is clear that the value of oral fluid for drug detection is at least equivalent and in some cases may be superior to urine drug testing." (Cone et al. Oral Fluid Testing for Drugs of Abuse: Positive Prevalence Rates by Intercept Immunoassay Screening and GC-MS-MS Confirmation and Suggested Cutoff Concentrations. *J. Anal. Toxicol*. 26: 541-46 (2002).)

These findings have been validated through a review of more than 600,000 oral fluid tests performed for all workplace testing scenarios, the results of which continue to compare with the detection capabilities of urine testing in both the federally mandated and non-

mandated workforces. This new data is provided for your review. Furthermore, there are no significant differences between the purposes and detection windows between return-for-duty and pre-employment tests and follow-up and random tests. Thus we can see no reason to preclude the use of oral fluid as a specimen for these situations.

It is generally known that drug users will employ various methods to tamper with their urine specimens, including adulteration products, dilution by drinking high volumes of fluid, or by substituting their own urine with clean specimens. Oral fluid testing, by the basis of a directly observed collection and the inability to dilute the specimen, eliminates most, if not all, tampering concerns. This is one reason why oral fluid testing positive rates sometimes are higher than those of urine testing.

Drug Testing Positive Prevalence Rates (2003)

	Oral Fluid	Urine	
Reason for Test	**Intercept**	**Non-Federal**	**Federal**
Lab A			
Follow-up	***14.8%***	***9.0%***	***3.2%***
Return-to-duty	***3.6%***	***4.1%***	***5.8%***
Lab B			
Follow-up	***8.3%***	***9.6%***	***3.4%***
Return-to-duty	***4.6%***	***5.6%***	***2.8%***

For return-to-duty testing, oral fluid testing offers the best opportunity to distinguish current from historic use. As HHS is aware through the work of its Center for Substance Abuse Treatment (CSAT), that drug-treatment programs deal with the variability of urine drug elimination rates that they will sometimes compare confirmation levels as an indication that a person is successfully completing a substance abuse recovery program. Oral fluid better reflects the recent activity of the person completing the recovery program. Oral fluid reduces the potential for an inaccurate accusation. Data comparing positive prevalence rates of oral fluid and urine testing in workforce populations show each is valid for this testing scenario.

For follow-up testing, oral fluid offers the same advantages just discussed for return-to-duty testing. In addition, oral fluid testing offers the advantage of minimizing the risk of tampering. We have several documented examples of workers who avoided detection under urine "follow-up" programs, but had their drug use discovered the first time the company switched to Intercept oral fluid testing. In one example, the Donor was surprised and reportedly nervous when told he would give an oral fluid specimen instead of a urine specimen. This particular donor called his supervisor two hours after providing his specimen and admitted he had been adulterating his urine tests and had been using marijuana throughout his urine follow-up program.

Oral fluid testing is also uniquely able to detect illicit drug use. A worker trying to cheat on an SAP program is very likely to attempt to tamper with urine specimens by diluting or adulterating them, or by substituting clean urine. Oral fluid testing provides a directly observed collection that virtually eliminates the opportunity to tamper with specimens.

In summary, we believe oral fluid testing is appropriate for all testing scenarios. It is clearly suited for Return-to-Duty and Follow-Up testing, because it detects recent drug use. A worker successfully completing a substance abuse recovery program and staying clean from drugs will appropriately test clean soonest with oral fluid testing. Therefore, oral fluid is them most appropriate specimen for both protecting donor rights while enforcing compliance with their treatment.

Section 2.3 - Can more than one type of specimen be collected at the same time from the same donor?

(a) When an oral fluid specimen is collected, a urine specimen must also be collected;

Recommendation:

We recommend that this section be removed from the Mandatory Guidelines.

Justification:

We recognize that at the time of the drafting of these Proposed Revisions scientific data on the effect of environmental contamination by cannabis smoke on oral fluid tests had not been published in the peer reviewed literature. We now wish to present to HHS the results of authoritative scientific studies, which allow for the differentiation of actual use and environmental exposure. These studies were designed to specifically address this issue. The results of these studies have been accepted by the *Journal of Analytical Toxicology* for peer review and publication, with permission to submit them here for your consideration.

In this controlled study, 4 subjects were passively exposed to marijuana smoke generated by 5 marijuana smokers each smoking a single marijuana cigarette (1.75% THC) over 20 minutes in an unventilated sealed room of 36 m^3. Oral fluid specimens were collected from all 9 subjects, both the 5 active smokers and as well as the 4 passively exposed subjects, over the next 4 hours. Specimen collection began at the end of the 20-minute exposure period (T=0). Only 8 of 12 specimens collected from the passively exposed subjects between 0–30 minutes after exposure were confirmed positive for THC (avg. 9.5ng/mL, 3.6–26.4). Of these 8 positive oral fluid specimens, only 2 were above 10ng/mL (12.3 and 26.4ng/mL), and both were collected immediately at the end of the smoking exposure period. At 30 minutes after the exposure period only 1 subject tested positive in the immunoassay (at 3.6ng/mL).

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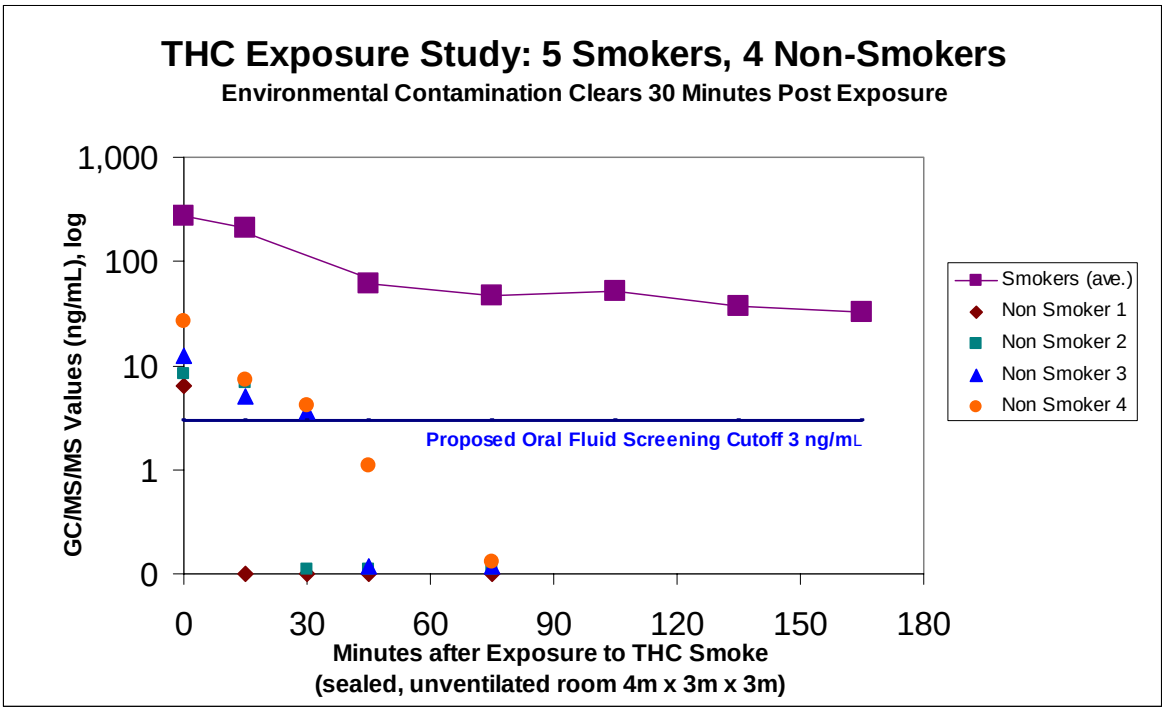

Appendix: "Passive Cannabis Smoke Exposure and Oral Fluid Drug Testing,"

This research demonstrates that although THC may be detected in the oral fluid of subjects passively exposed to cannabis smoke, it is only under relatively extreme exposure conditions (several joints in a small room) and at relatively low levels for only short periods of time (30 minutes) after environmental contamination.

There is no evidence that environmental contamination can create a risk of a positive oral fluid result for THC in any reasonable scenario. Further, even in extreme conditions, any minimal risk is completely eliminated 30 minutes after exposure.

More than 10,000 Intercept oral fluid tests have been confirmed positive for THC in the leading workplace oral fluid laboratory without a single challenge of environmental contamination. Further, this technology has been employed for more than four years in criminal justice and drug treatment settings – a population with significantly higher THC positive prevalence rate – and no challenges of environmental contamination on positive THC results.

Thus we do not believe that passive inhalation is a reasonable defense or that significant exposure can occur through passive inhalation to cause an oral fluid specimen to be reported positive. In fact this is precisely the language HHS published in its Mandatory Guidelines for Federal Workplace Drug Testing Programs in 1994: "The Department does not believe that passive inhalation is a reasonable defense or that significant exposure can occur through passive inhalation to cause a urine specimen to be reported positive." (59 FR 29908)

The remote possibility of testing positive in oral fluid from environmental exposure to cannabis smoke is analogous to the situation for urine drug testing where it is

acknowledged that it is scientifically possible to test positive by environmental exposure to cannabis smoke (as demonstrated in the published peer-reviewed scientific literature) but importantly only under the most extreme exposure conditions. This remote possibility of positive urine test results from environmental exposure has not precluded the use of urine drug testing to assess cannabis use in federal workplace drug testing programs. The minimal risk of positive oral fluid test results from extreme exposure should not preclude or encumber oral fluid collection and analysis.

Thus the mere possibility of contamination of oral fluid from environmental exposure is so remote that there is no firm scientific basis on which to justify mandating a concomitant urine specimen.

Section 2.5 What is the minimum quantity of specimen to be collected for each type of specimen?

(b) Oral Fluid: 2 mL collected as a "neat specimen" (divided as follows: at least 1.5 mL for the primary specimen and at least 0.5 mL for the split specimen)

Recommendation:

Section 2.5 - What is the minimum quantity of specimen to be collected for each type of specimen?

(b) Oral Fluid: a bilateral collection with a volume of combined oral fluid and preservative collected by each collection device that is sufficient for screening, confirmation and retesting as needed for the testing system used. The volume of remaining fluid after confirmation should be at least 25% of the initial volume.

Justification:

We can understand the desire to collect a "neat" specimen in such a way that minimizes inter- and intra-subject variability in specimen collection and would supposedly supply a consistent specimen independent of collection device. However, expectoration into a tube does not necessarily represent the "best available technology." The UN has already published a document addressing the use of alternative specimens including oral fluid for drug testing and stated that saliva collection devices including Intercept "are recommended over passive collection of saliva." [United Nations Drug Control Programme. Guidelines for Testing Drugs Under International Control in Hair, Sweat, and Saliva. For Use by National Laboratories. United Nations, 2001.]

It is burdensome and unreasonable to require transfer of saliva between containers when the definition of "Split Specimen" provides for two collected specimens, and when the FDA has cleared devices appropriate for the purpose of collecting oral fluid specimens.

Section 3.5 What are the cutoff concentrations for oral fluid specimens?

Initial Test Cutoff Concentration (ng/mL)
THC Parent drug and metabolite.... 4
Cocaine metabolites..... 20
Opiate metabolites[1]..... 40
Phencyclidine..... 10
Amphetamines[2]..... 50
MDMA 50
[1] *Labs are permitted to initial test all specimens for 6-AM using a 4ng/mL cutoff*
[2] *Methamphetamine is the target analyte*

Confirmatory Test Cutoff Concentration (ng/mL)
THC Parent drug..... 2
Cocaine[1]..... 8
Opiates
Morphine..... 40
Codeine..... 40
6-Acetylmorphine 4
Phencyclidine..... 10
Amphetamines
Amphetamine..... 50
Methamphetamine[2]..... 50
MDMA..... 50
MDA..... 50
MDEA..... 50
[1] *Cocaine or Benzoylecgonine*
[2] *Specimen must also contain Amphetamine at a concentration greater than or equal to the limit of detection*

Recommendation:

Drug Target Cutoffs (ng/mL)	Screening	Confirmation
THC (parent or metabolite)	3 (parent)	1.5 (parent)
Cocaine metabolites	15	6 (Benzoylecgonine)
Opiate metabolites	30	
6-Acetylmorphine		3
Morphine		30
Codeine		30
Phencyclidine	3	1.5
Amphetamine	300	120
Methamphetamine	120[1]	120
MDMA		120

[1]One assay for either Methamphetamine or MDMA that also must cross-react at least 100% with the other target.

Justification:

The cutoffs established by the oral fluid working group were based almost exclusively on the FDA filings by OraSure Technologies for the Intercept assays and collection device. To validate these cutoffs, OraSure Technologies and LabOne collaborated on a large population study of more than 77,000 oral fluid drug test results in a general workforce population. From this landmark study, HHS was provided with data on the appropriateness of cutoffs for the NIDA-5 drug panel. That large population evaluation has been expanded to consider more than 600,000 oral fluid specimens, and the data again is presented for HHS to review. The US FDA has asserted its authority over workplace drug testing. Therefore, HHS should give most credence to assays with FDA clearances, and rely on the cutoffs established by those assays, especially when validated by such comprehensive real world data.

Drug Testing Positive Prevalence Rates

	2002-2003 Oral Fluid Intercept *(n=527K)*	January - June 2003 Drug Testing Index - Urine Gen. Workforce *(n=2,800K)*	Federal *(n=600K)*
Total Positives	4.62%	5.00%	2.50%
Marijuana	3.08%	3.02%	1.39%
Cocaine	1.32%	0.74%	0.58%
Opiates	0.19%	0.34%	0.19%
Amphetamines	0.47%	0.46%	0.29%
PCP	0.03%	0.03%	0.04%

Notes: Oral fluid analysis by LabOne, Inc., Lenexa, KS
Drug Testing Index courtesy of Quest Diagnostics, Inc., Teterboro, NJ

We strongly believe that the HHS proposed cutoffs for Amphetamines class drugs and for PCP are not supportable with large and well controlled scientific data. Importantly, based on our experience, lowering the Amphetamines class cutoffs will stimulate more false positive screening test results from over-the-counter medications, creating confusion, adding costs, and jeopardizing public confidence and credibility.

Section 3.9 What validity tests must be performed on an oral fluid specimen?

(a) For each primary (Tube A) oral fluid specimen, an HHS-certified laboratory or IITF must:
(1) Determine the immunoglobulins (IgG) concentrations on every specimen; and

Recommendation:

(1) Determine that the IgG concentration is at or above a level of 1.5 mcg/mL.

Justification:

We recognize the Department's interest in insuring that an oral fluid specimen is a valid human specimen, although considering the direct observation of specimen collection we

think substitution would be highly unlikely. Nonetheless, we acknowledge the utility of a determination of IgG. Based on laboratory experience with workplace and insurance testing (more than 15 million specimens), we believe that a suitable minimum level of IgG expected for a human oral fluid specimen would be 1.5 mcg/mL by immunoassay. The presence of IgG above a specified cut-off representative of minimum levels expected for valid specimens should suffice for this purpose.

Section 3.16 What criteria are used to report an oral fluid specimen as substituted?

A primary (Tube A) oral fluid specimen is reported substituted when the IgG concentration is less than 0.10 mcg/mL.

Recommendation:
A primary (Tube A) oral fluid specimen is reported substituted when the IgG concentration is less than 0.30 mcg/mL.

Justification:
Any specimen with no IgG detected in the screen could be reported as substituted. The concentration of 0.30 mcg/mL is the limit of detection for commercial IgG assays.

Section 4.3 How is a collector's training documented?

(a) A trainer must monitor and evaluate the knowledge and performance of the individual being trained, in person or by means that provides real-time observation and interaction between the trainer and trainee, and attest in writing that the mock collections are error-free.

Recommendation:
Section 4.3 How is a collector's training documented?

(a) A trainer or approved training tool must evaluate the knowledge and performance of the individual being trained, in person or by means of documenting that the collector's procedural knowledge and mock collections are error-free.

Justification:
We suggest that training can be effectively accomplished through video or CD-based training materials. In 1996, the US DOT reviewed and approved a video-based training tool for certification of Screening Test Technicians complying with 49 CFR Part 40. For the past four years, employers have successfully trained oral fluid Collectors using an interactive CD-based training tool. This tool requires a level of proficiency is the testing program before the student is deemed ready to collect oral fluid specimens. A sample of this training product is enclosed for your review.

Section 4.5 Frequency of Training

(a) Recertification
(b) Corrective training

Recommendation:

(a) A Collector shall be re-certified every 5 years.
(b) A Collector shall be re-certified when a collection error causes a test to be cancelled by the laboratory.

Justification:

This section was absent in the published Proposed Guidelines while present in Draft #4. We consider recertification a valuable requirement to ensure the accuracy and reliability of the collection process. Given that collectors responsible for oral fluid testing for alcohol testing under current DOT rules are recertified every 5 years, we would prose this period for the Mandatory Guidelines as well.

Section 5.6 What are the privacy requirements when collecting an oral fluid specimen?

The donor provides the sample directly into an appropriate container under the direct observation of the collector. Only the collector may be present while the donor provides the oral fluid specimen.

Recommendation:

The donor provides the sample using an FDA-cleared collection device under the direct observation of the collector. Only the collector may be present while the donor provides the oral fluid specimen.

Justification:

The Department also addressed this requirement in its discussion of Subpart E–Collection Sites where it wrote, "For oral fluid, the Department proposes that the donor provide an oral fluid specimen directly into an appropriate container. This approach will ensure that a minimum amount of oral fluid is collected and can then be split for on-site testing or sent to a laboratory for both initial and confirmatory testing." (69 FR 19682)

We again recommend that the collection of oral fluid specimens allow for collection using an FDA-cleared absorbent device. The wording "appropriate container" may be construed to preclude use of such a device. It has been demonstrated that the FDA-cleared Intercept device collects the minimum amount of oral fluid specimen necessary to split the specimen and conduct initial and confirmation tests.

Section 7.1 What is a collection device?

(c) For oral fluid, it is the single-use plastic specimen container.

Recommendation:
(c) For oral fluid, it is a collection device cleared by the FDA.

Justification:
In its discussion of Subpart G–Collection Device, HHS has indicated, "Since the Department is proposing drug testing using alternative specimens and technologies, it is reasonable to believe that new and different specimen collection devices will be used to collect Federal employee drug test specimens. The Department requests specific comments on this requirement." (69 FR 19682)

Based on our experience with more than 1.9 million oral fluid specimen collections performed with an FDA-cleared absorbent collection device (Intercept) we believe that oral fluid specimen collection can be most effectively performed using such an FDA-cleared device. Specimen collections can be performed reliably and conveniently with this method minimizing donor reluctance or distaste for expectoration while ensuring adequate specimen volumes.

The only commercially available, FDA-cleared means for collecting oral fluid specimens for drugs of abuse analysis are collection devices.

Section 7.2 Which collection devices may be used?

(b) These Guidelines do not determine if a collection device must be cleared by the FDA.

Recommendation:
(b) A collection device must be cleared by the FDA.

Justification:
We believe that only collection devices which have been cleared by the FDA are suitable for use in federal workplace drug testing programs "for ensuring the full reliability and accuracy of the drug tests …" Pub. L. 100–71, Title V, § 503 (a)(1)(A)(ii)(I).

The FDA has asserted its authority for workplace testing, and HHS itself has exhibited the wisdom to require FDA clearance of POCT devices.

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Section 8.3 What procedure is used to collect an oral fluid specimen?

(a) The collector must use the following procedure to collect an oral fluid specimen:
(5) The collector will give the donor a clean specimen tube.
(6) Under direct observation, the collector will instruct the donor to expectorate (to spit) 2 mL of oral fluid into the specimen tube. This can be accomplished over a 15 minute time period or until the appropriate volume of specimen is collected.
(7) Both the donor and the collector must keep the specimen tube in view at all times prior to its being sealed and labeled.

Recommendation:

Section 8.3(a) The collector must use the following procedure to collect an oral fluid specimen:
(5) The collector will give the donor an FDA-cleared collection device.
(6) Under direct observation, the collector will instruct the donor to follow the manufacturers instructions for the FDA-cleared collection device.
(7) Both the donor and the collector must keep the collection device in view at all times prior to its being sealed and labeled.

Justification:

We can understand the desire to collect a "neat" specimen in such a way that minimizes inter- and intra-subject variability in specimen collection and would supposedly supply a consistent specimen independent of collection device. However, expectoration into a tube does not necessarily represent the "best available technology." The UN has already published a document addressing the use of alternative specimens including oral fluid for drug testing and stated that saliva collection devices including Intercept "are recommended over passive collection of saliva." United Nations Drug Control Programme. Guidelines for Testing Drugs Under International Control in Hair, Sweat, and Saliva. For Use by National Laboratories. United Nations, 2001.

The additional cost and time required for collecting "neat" specimens could be significant. The collection environment would require control and possibly sanitizing, and the allowance of 15 minutes to provide a specimen is five times longer than the collection process with the FDA-cleared oral specimen collection device.

Based on our experience with more than 1.9 million oral fluid specimen collections performed with an FDA-cleared absorbent collection device (Intercept) we believe that oral fluid specimen collection can be most effectively performed using such an FDA-cleared device. Specimen collections can be performed reliably and conveniently with this method minimizing donor reluctance or distaste for expectoration while ensuring adequate specimen volumes.

We have recognized a degree of variability in our FDA-cleared collection device, yet the device has proven effective in collecting oral fluid specimens for detecting drugs of abuse substantially equivalent to urine predicate systems. Data for the scientific studies listed

in the attached appendix, the FDA clearances on nine drugs of abuse assays, and the positive prevalence data published in JAT have all been generated using this collection device, with its known degree of variability.

Donors appreciate the dignity of an oral fluid collection, which we do not believe exists should Donors be required to spit into a container. Human Resources professions, surveyed at the annual meeting of the Society for Human Resource Management (SHRM), unanimously preferred use of a collection device to spitting in a tube. The 67 professionals surveyed all chose the collection device. These HR professionals found the spitting recommendation, "unpleasant," "disgusting," "unreasonable," and "stupid." It was unacceptable for professional workplace drug testing.

Specimen collection of oral fluid by an absorbent pad has been shown to be relatively consistent, and the donor is not able to control any variances by attempting to dilute or adulterate the sample. As previously noted, significant variances in specimen characteristics are currently accepted for urine specimens under long-existing regulations. Urine specimens vary significantly in concentration both from intentional and unintentional dilution, and yet these variances are effectively disregarded.

There is little control over specimen collection in sweat patch testing where significant differences in the amount of sweat collected may occur between and within individuals. Sweat patch testing offers no measure whatsoever of specimen collected. Nonetheless, as configured it proves a useful drug detection and deterrence technology.

Hair specimens may also be subject to significant variations in specimen characteristics. Hair may grow at different rates between individuals and for a given individual (references 2, 5, 8, 9, 10, 14 of the HHS document 69 FR 19688). Differences in drug incorporation for hair specimens of varying melanin content have also been repeatedly demonstrated. At least these variances in specimen collection are not under the control of the donor.

Specimen collection of oral fluid by an absorbent pad may be shown to be relatively consistent. In addition, the donor has no willful influence over any variances that might exist (e.g., dilution by hydrating oneself). We have demonstrated fairly consistent specimen collection volumes and believe the overall variance in specimen collection can be reduced to less than 30%. We are committed to this goal in our process of continuous improvement. At least, the variances in oral fluid specimen collection are less than those possible with urine collection, and, at least, those variances for oral fluid are not under the direct control of the donor as HHS concludes they are with current urine testing.

Much of the above discussion and arguments have been published as an Authors' Reply to a Letter to the Editor, Comment on Oral Fluid Testing for Drugs of Abuse: Positive Prevalence Rates by Intercept Immunoassay Screening and GC-MS-MS Confirmation and Suggested Cutoff Concentrations, *J. Anal. Toxicol.*, 27, 169 (2003).

None of this is to say that specimen collection should not be as uniform and unbiased as possible, but there is no basis to unnecessarily burden oral fluid testing with specimen collection procedures when other specimens also have similar collection variances.

Again it must be remembered that the underlying goal of the federal workplace testing program is deterrence rather than detection, while maintaining fairness to the donor.

Section 8.3 What procedure is used to collect an oral fluid specimen?

(8) The collector, in the presence of the donor, mixes the specimen and transfers the oral fluid into two specimen tubes that are labeled Tube A and Tube B. A minimum of 2 mL of oral fluid is required, i.e., 1.5 mL for Tube A and 0.5 mL for Tube B.

Recommendation:

(8) To provide a split specimen, as per the definition in Section 1.5, the donor will use two collection devices and collect specimens almost simultaneously. Each collection device will be sealed in a separate specimen container, labeled Tube A and Tube B. The donor would select which container to label A and which to label B. A minimum of 1 mL of total fluid, including oral fluid and preservative solution, is required for each specimen container.

Justification:

Where we have argued that spitting into a tube is impractical, unpleasant, and undignified, the suggestion that the Collector would mix and pipette an oral fluid specimen to split it worsens an already unacceptable process. Only use of an FDA-cleared collection device or devices to collect the needed A and B volumes is appropriate.

(9) The Tube A specimen, containing a minimum of 1.5 mL of oral fluid, is to be used for the drug test. If there is no additional oral fluid available for the second specimen tube (Tube B), the first specimen tube (Tube A) shall nevertheless be processed for testing.

Recommendation:

(9) The Tube A specimen, containing a minimum of 1.0 mL of oral fluid and preservative, if needed, is to be used for the drug test. If there is no additional oral fluid available for the second specimen tube (Tube B), the first specimen tube (Tube A) shall nevertheless be processed for testing.

Justification:

A volume of 1.0mL of fluid is sufficient for reliable laboratory screening, confirmation and challenge confirmations (as might be required).

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8.3(a)(10) A minimum of 0.5 mL of oral fluid shall be transferred into the second specimen tube (Tube B).

Recommendation:
8.3(a)(10) A minimum of 1.0 mL of oral fluid and any preservative solution shall be collected by the second device and labeled as Tube B.

Justification:
There should be no difference in the volume requirement for FDA-cleared collection devices when such devices are used to collect two specimens almost simultaneously.

8.3(a)(16) After completing the oral fluid specimen collection procedure, the collector must also collect a urine specimen following the procedures described in section 8.5.

We recommend that this section be removed from the Mandatory Guidelines.

Justification:
Since we have provided the scientific data HHS requested to negate the necessity for collection of a urine specimen when collecting an oral fluid specimen (comments to section 2.3), the reference to a concomitantly collected urine specimen should be deleted from the Mandatory Guidelines.

(17) The collector must send the oral fluid and urine split specimens at the same time to an HHS-certified laboratory or IITF or transfer the specimens to the POCT tester (if a POCT is being conducted).

Recommendation:
(17) The collector must send the oral fluid specimens at the same time to an HHS-certified laboratory or IITF or transfer the specimens to the POCT tester (if a POCT is being conducted).

Justification:
Since we have provided the scientific data HHS requested to negate the necessity for collection of a urine specimen when collecting an oral fluid specimen (comments to section 2.3), the reference to a concomitantly collected urine specimen should be deleted from the Mandatory Guidelines.

Section 11.14 What are the batch quality control requirements when conducting an initial drug test?

(a) Each batch of specimens must contain the following QC samples:
(2) At least one positive control with the drug or metabolite

targeted at 25 percent above the cutoff;
(3) At least one control with the drug or metabolite targeted at 75 percent of the cutoff; and

Recommendation:
(2) At least one positive control with the drug or metabolite targeted at 100 percent above the cutoff;
(3) At least one control with the drug or metabolite targeted at 50 percent of the cutoff.

Justification:
We believe that current oral fluid drug testing technology would be most appropriately controlled using a positive control at 100 percent above the cutoff. We believe that current oral fluid drug testing technology would be most appropriately controlled using a below cutoff control at 50 percent of the cut-off.

Quality control standards for oral fluid require a different metric than those applied to urine testing. Appropriate quality control standards for oral fluid immunoassays are -50%, +100% (½x, 2x) of the cutoff. The HHS proposed screening controls of ±25% are those currently applied to urine screening, which uses a different type of immunoassay technology that allows for this type of differentiation between a control and cutoff. However, to achieve the greater sensitivity required to detect the majority of drug targets in oral fluid samples – as well as hair and sweat samples – the current available technology (ELISA) that is FDA-cleared for oral fluid testing can resolve a positive control at two times the cutoff and a negative control at one half of the cutoff concentration. The number of steps in the ELISA process results in the need for these control levels of ½x, 2x.

Setting quality control standards for enzyme immunoassay is highly dependent upon current practices and availability of automated equipment. At present, oral fluid screening methods employ ELISA-based systems. These systems are highly sensitive, FDA-cleared assays that produce reliable results, but are subject to greater variability in response because of environmental influences and assay timing. Despite these current limitations, ELISA-based systems are essential in alternate matrix testing, and in particular for oral fluid testing because of their inherent increased sensitivity over urine-based assays. The requirement that ELISA-based systems attain equivalent precision to highly automated systems is unrealistic. Current performance-based standards for ELISA must be adjusted for these inherent differences in technologies as compared to automated enzyme immunoassay assays designed for detection of substantially higher drug concentrations found in urine. A realistic performance standard for ELISA-based systems should be based on similar principles as in urine testing, i.e., demonstration of linearity around the cutoff concentration, but the limits should be -50% to +100% of the cutoff concentration. ELISA systems can reliably perform within these limits; and presumptive positives can move to confirmation without loss in confidence in the final test outcome.

Section 11.27 What are the requirements for an HHS-certified laboratory to report an oral fluid test result?

(c) A primary (Tube A) oral fluid specimen is reported positive for a specific drug when the initial drug test is positive and the confirmatory drug test is positive. For only those oral fluid tests that result in a confirmed positive for marijuana, the laboratory must not report the result for the oral fluid specimen to the MRO but, instead must test the primary (Bottle A) urine specimen for marijuana and report that result in accordance with section 11.29.

Recommendation:

11.27(c) A primary (Tube A) oral fluid specimen is reported positive for a specific drug when the initial drug test is positive and the confirmatory drug test is positive.

Justification:

Since we have provided the scientific data HHS requested to negate the necessity for collection of a urine specimen when collecting an oral fluid specimen (comments to section 2.3), the reference to testing a urine specimen should be deleted from the Mandatory Guidelines.

Section 12.18 What are the requirements for conducting a POCT?

(b) After the donor leaves the collection site and after the split specimens are labeled and sealed by the collector, a POCT tester (which may be the collector) is permitted to break the label/seal on the primary specimen and remove an aliquot to conduct the POCT.

Recommendation:

(b) After the donor leaves the collection site and after the split specimens are labeled and sealed by the collector, a POCT tester (which may be the collector) is permitted to break the label/seal on the primary specimen and conduct the POCT.

Justification:

We believe that technologies will become available whereby the POCT tester may test the primary specimen without manually removing an aliquot for such testing.

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(e) If the aliquot tests presumptive drug positive, adulterated, substituted, or invalid on the POCTs, the primary specimen must be resealed using a new tamper-evident label/seal and sent with the split specimen to an HHS-certified laboratory for testing. The POCT tester must initial and date the new label/seal that was used to reseal the primary specimen. The POCT tester must report the POCT result on the OMB-approved custody and control form. The aliquot used to conduct the POCTs is discarded. When a POCT is conducted on an oral fluid specimen aliquot and it is presumptive positive for marijuana, the POCT tester must send the urine split specimen bottles to an HHS-certified laboratory for testing rather than the oral fluid specimen tubes. For all other presumptive positive drug test results on an oral fluid POCT, the POCT tester may only send the oral fluid split specimen tubes to the HHS-certified laboratory for testing.

Recommendation:

(e) If the aliquot tests presumptive drug positive, adulterated, substituted, or invalid on the POCTs, the primary specimen must be resealed using a new tamper-evident label/seal and sent with the split specimen to an HHS-certified laboratory for testing. The POCT tester must initial and date the new label/seal that was used to reseal the primary specimen. The POCT tester must report the POCT result on the OMB-approved custody and control form. The aliquot used to conduct the POCTs is discarded.

Justification:

Since we have provided the scientific data HHS requested to negate the necessity for collection of a urine specimen when collecting an oral fluid specimen (comments to section 2.3), the reference to testing a urine specimen should be deleted from the Mandatory Guidelines.

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Section 12.19 What are the quality control requirements when conducting POCTs?

(a) For drug POCTs:
(1) Each day testing is performed using devices with visually read endpoints (i.e., a color appearing or disappearing that indicates a positive result using that device), each individual performing drug tests using these devices must test at least one negative control (i.e., a sample certified to contain no drug or drug metabolite) and one positive control (i.e., a sample with the concentration of the drugs or metabolites in the range of 25 percent above the cutoff concentration) before donor specimens are tested. These quality control samples must be tested and the results interpreted with the positive control testing positive and the negative control testing negative before donor specimens are tested and reported each day.

Recommendation:
Quality control material must be run on each new lot.

Justification:
The US FDA has ruled that certain devices are appropriately controlled when Quality testing is performed once for each lot number used in patient testing. If devices for the HHS guidelines must be FDA-cleared and on the SAMHSA list of approved devices, it is reasonable to expect that these devices will be of the same quality standard as those for which a QC testing once per lot number is appropriate.

(2) Each day testing is performed using devices with semi-automated or automated testing devices with machine read endpoints (i.e., spectrophotometer), at least one negative control (i.e., a sample certified to contain no drug or drug metabolite) and one positive control (i.e., a sample with the concentration of the drugs or metabolites in the range of 25 percent above the cutoff concentration) must be tested on each device used. These quality control samples must be tested and the results interpreted with the positive control testing positive and the negative control testing negative before donor specimens are tested and reported each day.

Recommendation:
(2) On each new lot of POCT devices with semi-automated or automated machine read endpoints (i.e., spectrophotometer), at least one negative control (i.e., a sample certified to contain no drug or drug metabolite) and one positive control (i.e., a sample with the concentration of the drugs or metabolites in the range of 100 percent above the cutoff concentration) must be tested on each device used.

Justification:
We believe that instrumented drug testing technologies exist which have demonstrated stability such that daily controls may not be required. We recommend that for FDA-cleared devices with less frequent quality control schedules that the quality control requirement be at a minimum to follow the test system manufacturer's FDA-cleared quality control practices.

Also, as noted above in section 11.14, We believe that current oral fluid drug testing technology would be most appropriately controlled using a positive control at 100 percent above the cutoff.

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We again thank the Department for this opportunity to provide information to assist it in drafting and finalizing drug-testing guidelines and for their careful consideration of these points. We are eager to offer whatever further information and comments to the Section that will allow it to fulfill its statutory obligations to "establish comprehensive standards for all aspects of laboratory drug testing and laboratory procedures to be applied in carrying out Executive order Numbered 12564, …including standards which require the use of the best available technology for ensuring the full reliability and accuracy of the drug tests …"

Sincerely,

/s/ Keith W. Kardos
Vice President, R&D

/s/ P. Michael Formica
Executive Vice President, Operations

[Signatures provided on hard copy sent via FedEx.]