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To: "'wvogl@samhsa.gov'" <wvogl@samhsa.gov>
Date: 7/12/04 4:52PM
Subject: Response for Proposed Regulation of Oral Fluid Drug Testing

Dr. Vogl, attached please find my response to the proposed HHS regulations, docket number 04-7984.

Thank you for your consideration.

Lance Presley
LabOne

<<HHS Oral Fluid Response.doc>>

CC: "Mike Asselta" <Mike.Asselta@LABONE.com>, "Joe Benage" <Joe.Benage@LABONE.com>

July 12, 2004

Walter F. Vogl, Ph.D.
Division of Workplace Programs
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Via e-mail, wvogl@samhsa.gov

Federal Register Docket Number 04-7984

Dear Dr. Vogl,

I would like to thank you and your office for all of the work that you have put into the "Proposed Revisions to Mandatory Guidelines for Federal Workplace Drug Testing Programs". I have reviewed the section of the proposed regulations relating to alternative matrix testing and am commenting with the following response. Most of my comments deal directly with the proposed regulations concerning oral fluid testing.

Introduction

Lab*One* has tested biological specimens for the risk assessment industry since our inception in 1972. We began routine testing of oral fluid specimens in 1995. We currently test over 5000 oral fluid specimens per day for cotinine, cocaine and HIV for our risk assessment business. We also test over 1000 specimens per day for drugs of abuse in our forensic toxicology laboratory. Our customers range in size from many of the largest life insurance companies in the world to small third party administrators.

Overall, our experience with the testing of oral fluid has been very favorable. Companies that use oral fluid like the simplicity of an observed collection that all but eliminates the possibility of adulteration. Companies also like the noninvasiveness of an oral fluid collection. The collection is easily done by a supervisor or human resources staff member and does not have the same privacy requirements as a urine collection. From a laboratory perspective, oral fluid is an easy specimen to handle and test. It does not present any new handling or procedural challenges as compared to routine serum or urine testing.

We began testing drugs of abuse in oral fluid in 2000. We were able to combine the years of experience from our insurance lab with the day to day practical skills in forensic regulatory guidelines of our certified urine testing lab. Our oral fluid program today has many if not all of the same standards for testing as our urine testing program.

We would like to thank you for considering oral fluid as an alternative matrix for drugs of abuse testing for Federal workplace programs. We feel that oral fluid testing is a valuable deterrent and useful matrix for detecting drugs of abuse. In the last two years, our experience includes testing of over 500,000 oral fluid samples for drugs of abuse. We have published articles and made presentations of our experiences with oral fluid testing and we have represented our results in unemployment hearings. We believe we have significant experience, perhaps more than any other laboratory, with the forensic

testing of oral fluid samples for drugs of abuse.

Response

Reasons for Testing

The chart in section 2.2 lists the different specimen types and the reasons for testing when each type may be used. Oral fluid is not allowed for follow-up or return to duty. Earlier in the Subpart B introduction on FR page 19679 it is stated that "because of the short window of detection oral fluid is not suited for return to duty and follow-up testing".

The federal drug testing program was designed as a deterrent program. As such, drug testing is a tool of regulated employers to help insure a drug free workplace. I feel that restricting the use of oral fluid from follow-up and return to duty limits its use as a deterrent. Stating that oral fluid is not appropriate to use in these two situations because of a short detection window goes counter to the philosophy of a deterrent program and the data below.

We have published data from our oral fluid testing program comparing the percentage of positive samples to those found in a non-regulated urine population (1). Even though the data was not categorized by reason for test the overall positive rate was similar for the two matrices. Another peer-reviewed article shows that oral fluid is an effective matrix for determining heroin abuse (2).

We have also compared our oral fluid data from 2003 to our federally regulated urine data. In 2003 we tested over 270,000 oral fluid specimens. The specimens that were tested as "Follow-up" tests had a positive rate of 14.8%. The specimens that were tested as "Return to Duty" had a positive rate of 3.6%. By comparison we tested over 660,000 federally regulated urine samples. Only 3.2% of the "Follow-up" tests were positive and 5.8% of the "Return to Duty" were positive. Please see the table below.

Reason for Test	Federally Regulated Urine Percent Positive	Oral Fluid Specimens Percent Positive
Follow-up	3.2	14.8
Post Accident	2.7	10.6
Pre-employment	2.3	4.3
Random	1.3	3.08
Reasonable Cause/Suspicion	10.5	21.9
Return to Duty	5.8	3.6
Other	1.9	4.3

Simultaneous Urine Collection

Section 2.3 requires that a urine specimen be collected as part of every oral fluid collection. Section 8.3 lists the requirement as part of the collection procedure for oral fluids. Section 11.27 requires that "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". The explanation in the introduction section on page 19676 of the federal register states that "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". Page 19679 states that a urine specimen is necessary to protect federal workers from incorrect test results for marijuana.

I strongly disagree with this requirement. believe that oral fluid is in itself an effective matrix for drugs of abuse testing.

In 2003 Lab*One* reported over 7800 specimens as positive for THC. I had questions from clients concerning passive inhalation but there were never any challenges of the positive results. This statistic alone is a strong indicator of the lack of passive inhalation in marijuana positive specimens. Niedbala, et al., published the test results of two subjects that were passively exposed to marijuana smoke (3). The subjects' oral fluid tested positive only by EIA screen at one hour after exposure. No sample confirmed positive for the presence of THC.

Recently, OraSure has performed more detailed, extensive studies on the possibility of testing positive for THC as a result of passive exposure. In one study, subjects were in a room only 36 M^2. Five people actively smoked marijuana while four people were passively exposed. In the second study four people smoked marijuana and four people were passively exposed while sitting in a van. In both studies, the subjects that were passively exposed showed a presence of THC up to 30 minutes after being exposed. After 30 minutes only the people smoking marijuana tested positive for THC. The levels of THC found were also much higher than in those who were passively exposed.

The two paragraphs above justify the use of parent THC as an indicator of marijuana use in oral fluid. However, Lab*One* and Northwest Toxicology are preparing to publish data that shows the presence of THC-COOH (THCA) in oral fluid specimens. We have developed a procedure for the extraction and confirmation of THCA in oral fluid. The procedure uses chemical ionization on a tandem GC/MS and has shown to be sensitive and rugged. Many samples have been analyzed by the procedure to date and show that THCA is found in oral fluid.

I believe that the requirement for the collection of a urine specimen with an oral fluid can be eliminated. The use of THC alone for confirmation analysis has shown to be an effective analyte. The possibility of using THCA as the confirmation analyte as it used in the urine program offers another justification for not requiring the additional collection of a urine specimen as part of an oral fluid test.

Collection and Collection Device

Section 2.4 requires a split specimen be collected for every matrix. Section 2.5 requires the split specimen for oral fluid be collected as a neat specimen and divided into 1.5 and 0.5 mL portions.

I disagree with the requirement that one neat specimen be collected and separated by the collector into a 1.5 mL portion and a 0.5 mL portion.

Neidbala, et al., have shown that placing oral fluid collection devices simultaneously in either side of the mouth gave equivalent results when testing for drugs of abuse in oral fluid (3). Two devices placed simultaneously into the oral cavity will give the same end result as a single, neat specimen divided into two parts. Using two devices will also ease the handling requirements of the collector. Both collection devices would be packaged and sealed individually and forwarded to the lab where the split specimen testing procedures are followed. One advantage of oral fluid testing is the ability of employers to collect the sample at the workplace, avoiding extra time and expense associated with a urine collection.

Section 7.1 requires a single use plastic device. Section 7.2 requires that the collection device not affects the specimen and/or is FDA cleared for the purpose of testing a specimen. Section 8.3 describes the oral fluid collection process in detail. The section states that a clean specimen tube be given to the donor, the donor begins to expectorate into the tube until 2mL of oral fluid has been collected or until 15 minutes has past. The collector must then separate the sample into "A" and "B" containers for shipping. The justification for requiring a single use container that the donor expectorates into is described in the oral fluid introduction section, p. 19676. The collection procedures are justified by stating that the proposed "oral fluid collection procedures are not functionally different than other specimen collection difficulties currently encountered with urine". The justification above also mentions the potential for changes in pH to alter the concentration of drugs in an oral fluid specimen. The section also says that insertion of a collection device into the mouth might stimulate saliva flow, increase the pH and alter the concentration of drug in a donor's specimen.

I again disagree with the requirements and procedures described for an oral fluid collection.

We have successfully used a FDA approved oral fluid collection device at Lab*One* since beginning our testing program. The device is a paper pad on the end of a plastic stick. It is very easy for the collector to handle and administer. The donor keeps the pad in their mouth for 2 – 5 minutes and then places the pad in a tube for shipment to the lab. The collector is not required to handle the device or manipulate the donor's saliva sample. I feel that requiring the collector to accurately measure 1.5 and 0.5 mL portions of a saliva sample is functionally different than a urine collection. The collector cannot be assured of the quality or consistency of an expectorated oral fluid sample. Frothy saliva as well as semi-solid matter may be expectorated into a collection container making the volume of collection inconsistent or inadequate. Additionally, it is known that oral fluid could potentially contain infectious pathogens including Tuberculosis, Hepatitis

B or the SARS virus. The potential for these becoming airborne during an expectoration would be an issue. The handling of the specimen by the collector could also cause an additional exposure event.

The use of a FDA approved collection device with an absorbent pad assures the consistency of the oral fluid sample. The sample from one donor is "standardized" and equivalent to samples collected from other donors. Using a standard collection device assures the consistency of all donor samples whereas allowing expectoration into a container allows for any number of variables to alter the sample and thus test results.

Spitting itself can stimulate a saliva flow of 0.5 ml/min. The production of bubbles during expectoration can also cause pH changes in saliva samples (4). Oral fluid pH can range from 6.2 to 7.4. Usually only with stimulation and increased secretion does the pH increase to 7.4. However the pH of stimulated saliva has a narrow pH around 7.4, again making for a very consistent sample between donors (5). Weakly acidic or weakly basic drugs are largely unaffected by pH changes. For example, benzoylecgonine (BE) exists as a zwitterion with pKa values at 2.25 and 11.2. Schramm, et al., showed that the concentration of BE is unaffected by saliva pH (6). Our data that was published in 2002 compared the positive rates of oral fluid specimens to positive rates in urine specimens. The urine rates were obtained from the annual data that are presented by Quest Diagnostics. The positive rates of the non-regulated urine tests were very comparable to the positive rates found in oral fluid. Oral fluid was even found to have a higher percentage of positive cocaine specimens.

Since oral fluid is a directly observed collection, I do not feel that it is necessary to require the donor to remove a coat or empty their pockets.

Cutoff Concentrations

Section 3.5 lists the proposed screening and cutoff concentrations. The oral fluid cutoffs listed are very near the levels we use currently. I suggest that the opiate screening cutoff be lowered to 30 ng/mL and that the phencyclidine screening cutoff be lowered to 3 ng/mL. These suggested levels have proven to give positive prevalence rates similar to urine testing (1).

I also recommend the lowering of the confirmation cutoff levels of cocaine (as benzoylecgonine) to 6 ng/mL, Opiates to 30 ng/mL and phencyclidine to 2 ng/mL. Other confirmation levels are very near our current levels so that positive rates would remain similar to those in urine.

The amphetamine level for screening and confirmation of 50 ng/mL is much lower than the 120 ng/mL that we currently use. This will increase the number of amphetamine samples that screen positive and require confirmation. The cross reactivity of the OTC medications will also increase making many of the additional confirmations unnecessary.

Quality Control Requirements

Sections 11.14 and 11.17 list the quality control requirements for screening and confirmation.

At present, oral fluid screening methods employ ELISA-based systems that are not automated. These systems are highly sensitive, FDA-cleared assays that produce reliable results, but are subject to greater variability in response because of temperature fluctuations and delays in reagent addition. Consequently, less precision around the cutoff is found with ELISA as compared to more automated systems employed in urine testing programs. 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 increased from +/- 25% to -50% and +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.

Point Of Collection Test (POCT) devices

It is generally acknowledged that, in the present urine-testing program, collections are the most common source of errors. To propose a new form of testing that would put the entire program into the hands of collectors is to knowingly introduce the probability of additional extensive errors in the drug-testing program. Use of HHS-approved POCT devices – whatever the quality controls proposed for the devices themselves – necessarily relies on the existence of well-trained and qualified POCT testers.

To conclude, I believe that the proposed regulations should be separated and considered individually by matrix or method. Separating the rule making will allow the individuals or groups that are finalizing the rules and regulations to "divide and conquer".

Thank you for your consideration.

Sincerely,

Lance Presley, Ph.D., DABFT
Sr. VP Toxicology, Lab*One*

References

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