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From: "Dahlberg,Deborah" <ddahlberg@medtox.com>
To: "'wvogl@samhsa.gov'" <wvogl@samhsa.gov>
Date: 7/12/04 4:55PM
Subject: RE: Comments to the Proposed Revisions to Mandatory Guidelines for Federal Workplace Drug Testing

To: The Department of Health and Human Services

Please find the attached files submitted electronically on behalf of MEDTOX Laboratories on the above referenced topic. Hard copies will follow by facsimile. Should you have difficulties opening either file please notify me and I will resend the attachments.

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MEDTOX®
LABORATORIES, INC.

July 9, 2004

The Department Health and Human Services
5600 Fishers Lane, Rockwall II, Suite 815
Rockville, MD 20857
Attn: Docket No. 04-7984
By email: wvogl@samhsa.gov
By Facsimile: 301 443-3031

To Whom It May Concern:

The following comments are in reference to the Proposed Revisions to Mandatory Guidelines for Federal Workplace Drug Testing Programs (FR Volume 69, No.71). These comments are submitted on behalf of MEDTOX Laboratories, Inc., electronically and by facsimile.

MEDTOX supports the Department's efforts to present the guidelines in a simplified and straightforward manner and to incorporate newer technologies into the program. We would like to take this opportunity to address some specific areas and issues, presented in accordance with the working document.

Subpart B – Specimens
2.1 Types of Specimens: The Department proposes to add additional specimen types to the program including head hair, oral fluid and sweat. We submit the following general comments regarding the alternative specimens:

Oral Fluid: Published scientific data indicates that concentrations and detection windows of drugs in oral fluid more closely mirror blood than urine. Thus, the more limited detection times may result in decreased detection rates. While it seems as if the ability to observe the collection makes it more difficult to adulterate a specimen, products such as mouth rinses and oral cleansing tablets are already available (http://www.passyourdrugtest.com/kits/saliva-test.htm) and will certainly have the same potential impact as urine adulterants.

MEDTOX agrees that the lack of diffusion/secretion of THC from the blood into oral fluid is a valid concern and that distinguishing environmental contamination from ingestion requires use of a urine specimen. However, the working document fails to address the fact that the presence of THC in oral fluid only from ingestion-related buccal contamination and not from secretion greatly reduces the detection window for this highly used drug. Data generated from paired oral fluid/urine specimen collections performed in a corrections population demonstrated that the correlation for THC was only 47%; i.e. of the confirmed carboxy-THC urine positives, only 47% of the donor-matched oral fluid specimens screened positive for THC. This data indicates that all of the co-collected urine specimens should be tested for THC metabolite rather than only those with positive oral

fluid screens to ensure that detection rates are **consistent** within the program. We strongly believe that the goals of the Federal Workplace Drug Testing Guidelines have been and should continue to be deterrence of drug use and promotion of safe work environments, to ensure the safety of the general public and to ensure the accuracy of test results for protection of employees. Reducing detection rates of abused drugs is contrary to these goals; introduction of alternative specimens and testing modalities must incorporate all procedures necessary to maintain the integrity of the program.

Hair: MEDTOX agrees with the concerns expressed regarding environmental contamination and variability in uptake of drug into different hair types/colors. The document points out that identification of the metabolites of cocaine, marijuana and methamphetamine can differentiate use from contamination, however, this does not address environmental exposure to PCP and amphetamine since no metabolites are identified. In addition, while the department indicates that limited population studies show no significant association between hair color/race and drug content, there is published scientific data that demonstrates differential uptake which could impact use of this matrix in employment testing. The lag in time between drug use and detectability (7 – 10 days) raises the concern that recent use may be overlooked. The department may want to consider co-collection of a different specimen type to monitor recent use when hair is the primary sample and extended detection times are desired.

We would also raise the concern regarding equitable treatment of employees within a given testing program. There is, to our knowledge, no scientific data that demonstrates equivalence of drug levels and cutoffs across these different specimen types. Results of a hair test may demonstrate drug use within a 7 – 90 day window while results of a urine test may demonstrate drug use within the previous 3 – 4 days. How does an employer properly administer a drug testing program when more than one sample type may be collected if, for example, an individual does not have sufficient head hair to provide a sample? Many arbitrations come down to the question of whether all employees are treated fairly and equitably under the company's drug testing program. We would argue that this model introduces new opportunities for legal challenge to the program.

Sweat: MEDTOX believes that based on the unsettled issues of external contamination and potential stigma associated with visibility of patches that this specimen is impractical for use in a workplace population.

2.2 Reasons for Test

We submit the following comments regarding the appropriateness of the use of the alternate specimens under routine testing circumstances:

Urine: MEDTOX believes that urine continues to be an appropriate specimen for all categories of testing. Collection procedures are well established, detection times are relevant and the adulteration issue, although cogent, affects only a limited number of specimens and can be minimized through ongoing training and enforcement at collection sites.

Hair: MEDTOX believes that since drug use may not detectable in hair for 7 – 10 days after use that hair is not an appropriate specimen for pre-employment, random and reasonable suspicion testing since recent use may be overlooked. In addition, we would also raise concerns regarding the ADA definition of 'current use' if a pre-employment drug test detects the presence of drugs used 30 – 60 days prior to the sampling. It has always been our understanding that the Federal Workplace Drug Testing Program is intended to be a 'deterrent' rather than a zero tolerance program.

Oral Fluid: Based on more limited detection times for drugs in oral fluid, MEDTOX believes that it is an appropriate specimen for random, reasonable suspicion/cause and post accident testing only.

Sweat: Appropriate for return to duty and follow-up, if at all.

2.3 Allowing collection of an alternate specimen type when problems occur during collection (e.g. shy bladder) would seem to unduly complicate the collection process and routine specimen handling for laboratories. It is unclear what is envisioned; i.e. would an Agency set up alternative specimen collection protocols up front or would each incidence be addressed individually? Would the collection site have to stock collection kits for different sample types in the event that a problem occurs? We would again express concern that this creates uncertainty as to whether individuals are treated in a consistent manner throughout the program.

2.5 Specimen collection requirements: The requirement to collect the specimen directly into a tube rather than a 'device' disregards the fact that there is currently a quantitative collection device available. We believe that the guidelines should require that the collection of oral fluid is performed in a quantitative manner and that collection devices that provide quantitative measurement should be permitted.

C. Drug and Validity Tests

3.4 – 3.7: Some of the new and revised cutoffs may be difficult to implement based on the requirement to routinely and accurately detect and quantitate these compounds at 40% of the cutoff for retests. Specifically, THC-COOH in hair, THC in oral fluid and THC in sweat. These levels may be pushing the limits of sensitivity even with the higher levels of sensitivity achieved with tandem MS methods.

3.9 Validity testing on oral fluid samples: The use of IgG to determine oral fluid specimen validity is not addressed in any detail nor is any normal range data provided to support the 0.1 – 1.0 acceptable range suggested by the department. The variability of IgG in oral fluid related to the condition of the gums and transudate of the donor may impact the use of this marker for validity testing. In addition, the requirement for 'additional validity testing' is not well defined.

Subpart D – Collectors
4.2(d) indicates that a trained collector must complete a training course by an established organization. 4.3(b)(2) defines what training and experience is required for a collection trainer. These two statements appear to be inconsistent. We recommend that the phrase "established organization" be expanded to include "established organization or individual with documented and appropriate training and experience". In addition, 'established organization' should be defined and should include training organizations, TPA's, laboratories and POCT manufacturers.

Subpart E – Collection Sites
In the preliminary discussion, the department proposes that head hair is the only type of hair that can be collected; MEDTOX believes that this is appropriate.

5.4(a)(6) requires that the specimens are transported to an HHS-certified laboratory in containers that minimize the possibility of damage with specific reference to boxes or padded mailers. MEDTOX recommends that references to shipping requirements refer to packaging requirements of the shipper and IATA.

Subpart F – Federal Drug Testing Custody and Control Forms
6.1(b) MEDTOX recommends that the program use a single form designed to accommodate all specimen types if possible to minimize problems selecting the appropriate form at the collection site. In addition, based on our experience, we do not believe that it is practical to prohibit alteration of the form. At the point of collection, it

is sometimes necessary to modify a form to properly identify the employer/account number.

Subpart G – Collection Device

7.1(c) The definition of an oral fluid collection device as a single-use plastic tube does not incorporate FDA-cleared oral fluid collection devices that include a collection pad in addition to the plastic tube for storing/transporting oral fluid. Neither does it acknowledge the potential for development of new collection technologies. We believe this definition is too narrow and should be expanded to include FDA-cleared devices or collection technologies.

H. Specimen Collection Procedure

8.3(a)(6) This protocol appears to prohibit the use of oral fluid collection devices that utilize a pad coupled with a plastic tube for specimen storage/transport. The requirement for expectorating directly into a tube appears to be inconsistent with 7.2 which discusses the use of FDA-cleared devices. MEDTOX believes that the guidelines should allow the use of FDA-cleared volumetric devices that incorporate a 'collection pad' or other collection technology into the collection procedure. These devices simplify the collection of oral fluid and minimize collector contact with the specimen. Incorporation of this section as written may discourage innovation of new collection methodologies and devices. There is no incumbent reason to mandate neat sample collection if other paradigms can demonstrate consistent and useful methods of collecting oral fluid samples.

8.3(a)(16) MEDTOX endorses the concurrent collection of a urine specimen to ensure the integrity of the program.

8.6(b) Based on the number of collection sites utilized for Federal Workplace Drug Testing Programs and the variation in collection volumes, annual inspections of each site by the agency is both expensive and impractical. For example, our internal statistics indicate that in a recent 3 month period, more than 7,000 different collection sites were utilized by our client base. Based on an implied imputed cost of $2,000 per one day inspection per site, inspection costs for this sampling would exceed $14,000,000.00.

I. Certification of Laboratories and IITFs

9.5(a)(2) PT samples should contain concentrations of drugs consistent with performance specifications of each specimen type or modality. For example, visually-read POCT devices do not demonstrate the same precision as instrumented immunoassay tests; nor do manually pipetted ELISA test systems. PT samples at 20% above the cutoff may yield inconsistent results between paradigms. We believe that each modality should be challenged aggressively, but within the expected precision of the test.

9.22(d) Rather than conduct full inspections for each specimen type, MEDTOX recommends that the department develop a 'General' checklist that would apply to all specimen types and separate specific individual checklists for each specimen type. Inspections should occur concurrently with inspection teams comprised of individuals with the appropriate experience for each specimen type.

K. Laboratory

11.5 The requirement of a certifying technician, and certification and reporting of negative results is inconsistent for laboratories, IITFs and POCT (12.22). Requirements for certification of negative results must be applied uniformly across all modalities.

11.10 MEDTOX endorses the requirement that samples received after POCT are processed as if no other testing had been performed. Based on our experience, when specimens received from POCT sites are re-screened in the laboratory, a percentage are negative. Approximately 10% initially screen positive on-site versus

7% in the laboratory. While some appear to be 'borderline', others are consistent with a true negative. We believe that this can be attributed to collector/tester training and turn-over, variability in visual acuity when reading devices, particularly when results are equivocal and differences in cross-reactivity of related compounds between the devices and laboratory-based reagents. Retesting all specimens at the certified laboratory reduces the variability and subjectivity in the process.

11.12(c) MEDTOX supports the requirement for FDA-clearance of all initial drug test kits.

11.17 This appears to limit analytical methodology to single point calibration paradigms. We believe that this section should not specify whether assay calibration uses a single point or linear regression. Multi-point calibration protocols and use of historical calibration curves are well established procedures currently utilized by many laboratories. Based on current PT performance records for the urine program, laboratory-to-laboratory precision is quite good, regardless of calibration modality. There would appear to be no particular advantage or improvement in requiring single point calibration over multi-point historical curves and incorporating this into the guidelines places an undue burden of additional method validation on those laboratories currently utilizing alternate calibration protocols.

11.27(c) This section implies that if an oral fluid specimen screens positive for THC, that a confirmation test is performed on oral fluid. It appears that the urine specimen is tested only if the oral fluid specimen confirms as positive. Because detection times for THC in oral fluid are limited by the lack of drug diffusion/secretion into oral fluid, MEDTOX believes that the co-collected urine specimen should be screened for carboxy-THC concurrent with an oral fluid screen. If either the urine or oral fluid screen as non-negative, the urine specimen should be processed for confirmation testing. This model will overcome both the issue of environmental contamination and the limited availability of THC in the oral fluid.

11.26 – 11.29 Reporting quantitative results for drug positives: While laboratories are capable of providing this information, it has been our experience that when quantitative results are provided there may be a tendency to 'over-interpret' the meaning or value, particularly in urine.

L. Point of Collection Test (POCT)

12.5(e) Since device manufacturers vary greatly in both lot size and the number of lots in current distribution, a firm number of 100 may not be the most appropriate way to evaluate the device. MEDTOX recommends that the number of devices submitted should be based on the number of lots in distribution and be statistically significant for the protocol selected for device performance evaluation.

12.6(a)(5) POCT devices are screening tests and should not be considered a definitive result for either drug or validity tests. POCT devices should have a high negative predictive value. To ensure specimens that require further testing by the laboratory are correctly identified the positive predictive value may be lower. For adulteration testing, some colorimetric tests used in the laboratory for screening demonstrate cross-reactivity with other compounds – for example, tests for nitrites may cross-react with high concentrations of other oxidants. It may not be appropriate to evaluate results of validity tests in the same context as drug tests for inclusion on a conforming products list. Criteria for evaluating POCT for drug tests and SVT should be viewed more as a first initial test, identifying true negatives and ensuring other samples are sent to the laboratory for a second initial test and subsequent confirmation if merited.

12.7(a) MEDTOX recommends that the notification requirement be defined in accordance with changes that would require notification to the FDA (i.e. change in intended use requiring a special 510(k) or traditional 510(k).

12.7(b) Our comment to 12.5(e) is also applicable to the submission of 50 devices annually.

12.8 This section appears to be overly burdensome for the Agency that wishes to utilize POCT in a workplace drug testing program. MEDTOX recommends that 12.8 be revised to allow all or some of the program management to be provided by third parties, including manufacturers.

12.9(b) We reiterate our comments from I - 9.5 regarding the importance of challenging testing procedures in a manner consistent with modality. MEDTOX recommends revising this section to define PT challenges at concentrations that ensure true negatives are identified and that non-negatives are sent to a certified laboratory for further testing.

12.9(f) and (g) MEDTOX believes that PT samples should challenge POCT's in a manner consistent with the intended use; i.e. to distinguish normal samples from abnormal samples. It is likely that discerning small variations in creatinine concentration and specific gravity will be difficult for visually read colorimetric tests.

12.12 POCT failures: For POCT testing, definition and identification of a 'failure' may not be straightforward. It is important to define 'failures' in terms of device vs lot vs tester failure when determining the course of action taken when results are discrepant. The performance specifications required for the FDA 510(k) clearance of a POCT device are inconsistent with the requirements described in section 12. Reasons for which the Secretary would notify the FDA should be further clarified.

12.18 MEDTOX strongly endorses the paradigm for conducting POCTs as described in this section. We believe that the process whereby a sample is collected, chain of custody executed and testing performed after the donor has left the site most closely mimics the current well established procedures and maintains the integrity of the testing process. The POCT is a screening test and results should only be made available after all testing is completed; this would include initial determination of negative/non-negative and laboratory follow-up testing if required.

12.18(e) As indicated in our introductory comments and in section 11.27(c), MEDTOX believes that the discrepancy between THC positive rate in co-collected urine and oral fluid specimens merits testing of all urine specimens for THC-COOH regardless of the results of the oral fluid test. We believe that this is important for protection of employees, workplace safety and preserving the integrity of the program.

12.19(a)(1) POCT devices are self-contained, single test units with internal controls that verify device performance on each test. Because POCT sites vary greatly in daily test volumes, the requirement for daily external quality control is excessive and costly. Using our previous example of potentially > 7,000 collection sites for our client base, 2 controls a day x 21 days/month x 12 months generates a retail cost of an additional $9,000,000.00 for quality control devices. MEDTOX recommends that external QC be performed monthly at a minimum, and with each new shipment and new lot. This paradigm is sufficient to ensure device performance within manufacturer stability guidelines and integrity during shipping and storage. We recommend the NCCLS Protocol EP18-A, Quality Management for Unit-Use Testing, Approved Guidance.

12.19(b) QC requirements for SVT devices are excessive; we recommend adoption of the above paradigm for QC of all POCT testing.

12.19(c) There is significant variability in numbers of tests performed at test sites which will impact the overall number of samples submitted. While 10% may be too high for high volume sites, some lower volume sites may

not perform 10 tests in a quarter. MEDTOX recommends that the department revise this section to define a quarterly minimum and maximum number of samples that must be submitted to ensure appropriate QA monitoring without undue expense and burden to test sites.

12.20 This section should be revised to ensure that some troubleshooting is performed at the test site before a QC sample is sent to the laboratory. Isolated QC failures may be limited to a single device in a shipment or to tester issues. The site should be instructed to test a second device to eliminate isolated device failure and to troubleshoot potential QC sample issues with the vendor as would be done in a certified laboratory.

12.21(b) We reiterate our comment on section 12.19(c) regarding numbers of specimens required for effective QA monitoring of POCT sites.

12.22(a) Certified laboratories have relatively sophisticated systems for reporting specimen results. This is not true for collection facilities. Vast differences in electronic reporting capabilities at POCT sites make reporting results to MRO's a challenge. MEDTOX recommends that the department allow POCT sites to report to MRO's utilizing the electronic reporting services of a third party provider to ensure that results are transmitted in an efficient, accurate and confidential manner and in a format that MRO's may receive and interpret appropriately.

Additional Comments:
MEDTOX would like to encourage the Department to provide flexibility when it comes to changes that might accommodate improvements in technology both from an analytical perspective and probably more important, in the area of communication. We strongly support the movement to a 'paperless' laboratory system, utilizing electronic signatures, electronic reporting and generation of electronic forms. While criteria must be developed to ensure that appropriate security procedures protect the integrity of the information, MEDTOX endorses the inclusion of electronic technology in storage and transmission of records, chain of custody documentation, remote generation of forms as well as use of electronic signatures in lieu of traditional formats. We believe that these issues should be included in the discussion of appropriate revisions to the mandatory guidelines.

We would also like to reiterate our conviction that the integrity of the program is of the utmost importance and inclusion of any alternative specimen types and testing modalities must meet the same standards of defensibility. Having reflected in totality on the serious concerns and limitations raised in the proposed guidance regarding alternative specimens and testing modalities, scientific validity and impractical and costly administrative requirements, we believe HHS has not defined or developed fully a sound procedural guidance to ensure and maintain the integrity of the program. We recommend withdrawal of this document as a proposed rule at this time.

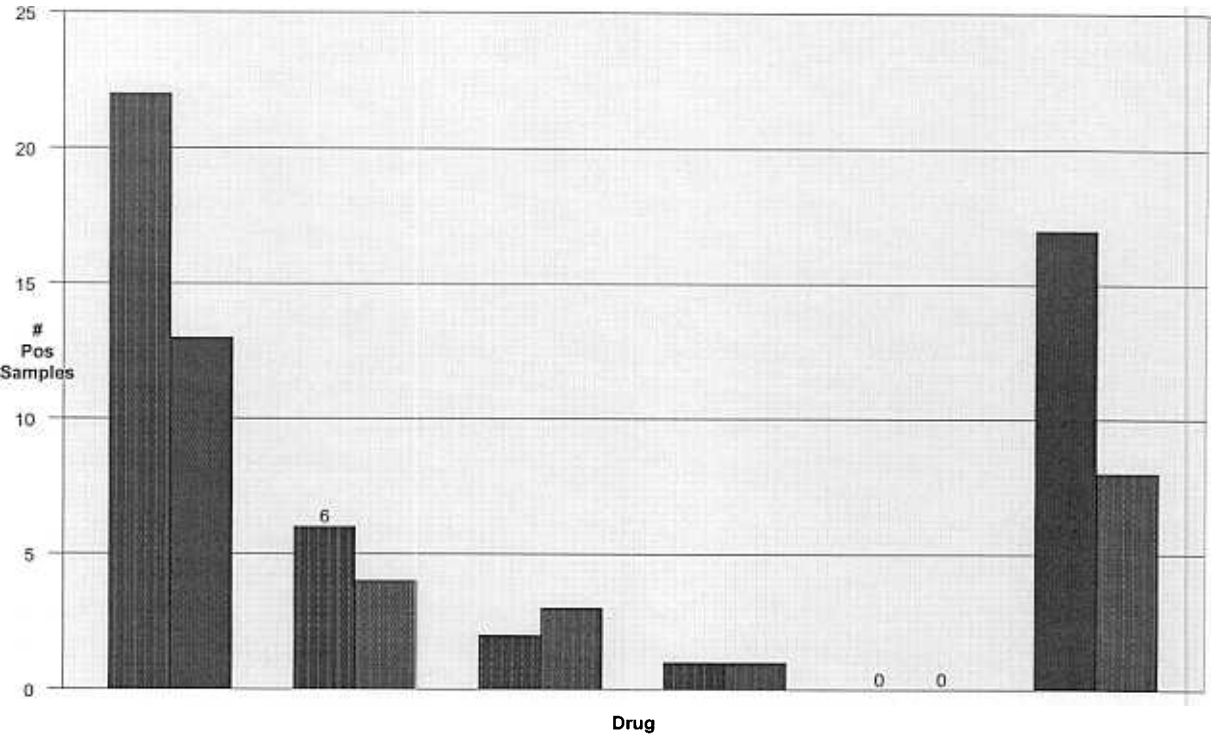
This concludes our comments. We appreciate the opportunity to participate in the revision process. If any additional information or clarification is required, please contact us via email at jcollins@medtox.com or by telephone at (651) 636-7466.

Sincerely,

MEDTOX Laboratories, Inc.

Positive Frequency, Urine/Oral Fluid
07/2004

MEDTOX Laboratories, Inc.,



Paired Oral Fluid/Urine Study Results:

Paired oral fluid and urine samples were collected over several months in cooperation with a local corrections group. When received at the laboratory, urine samples were screened using standard SAMHSA cutoffs; non-negative samples were confirmed by GCMS. Oral fluid samples were screened by ELISA using cutoffs set forth in Rev. 4 of the proposed revisions to the mandatory guidelines. Non-negatives were confirmed by LCMSMS when volume permitted (4/13 were QNS to confirm).

68 Paired Samples Received/Tested

Results Summary:

URINE:		ORAL FLUID:	
	46 Negatives (67.6%)		55 Negatives (80.9%)
	22 Positive Samples (32.4%)		13 Positive Samples (19.1%)
DRUGS DETEC		DRUGS DETECTED	
AMP/MAMP-	6 (27.3%)	AMP/MAMP-	4 (30.8%)
COC-	2 (9.1%)	COC-	3 (23.1)
OPI -	1 (4.5%)	OPI-	1 (7.7%)
THC -	17 (77.3%)	THC-	8 (61.5%)
PCP -	0 (0%)	PCP-	0 (0%)

PAIRED RESULTS: 9/68 Discrepant Results

8 samples positive for THC in urine were negative for THC in OF

2 samples positive for AMPs in urine were negative in OF

1 sample positive for cocaine in oral fluid was negative for BE in urine