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July 12, 2004

Via Federal Express Facsimile and E-mail

Substance Abuse and Mental Health Services Administration
Drug Testing Division
Division of Workplace Programs
CSAP
5600 Fishers Lane, Rockwall II, Suite 815
Rockville, MD 20857

Attn: Walter F. Vogl, Ph.D.

Re: Quest Diagnostics Comments on the Notice of Proposed Revisions to the Mandatory Guidelines for Federal Workplace Drug Testing Programs Docket Number 04-7984

Dear Dr. Vogl:

Attached are the comments of Quest Diagnostics Incorporated ("Quest Diagnostics") on the **Notice of Proposed Revisions to the Mandatory Guidelines for Federal Workplace Drug Testing Programs (69 FR 19673, April 13, 2004, FR Doc#04-7984)**. Quest Diagnostics is the nation's leading provider of diagnostic testing, information and services, providing insights that enable healthcare professionals to make decisions that improve health. The company offers the broadest access to diagnostic testing services through its national network of laboratories and patient service centers, and provides interpretive consultation through its extensive medical and scientific staff. Quest Diagnostics is the leading provider of esoteric testing, including gene-based medical testing, and provides advanced information technology solutions to improve patient care. Quest Diagnostics performs Federal workplace drug testing through our network of six SAMHSA-certified laboratories.

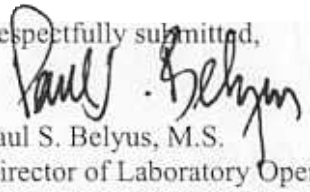
We would like to commend the Department on its efforts in preparing the NPRM for publication. Quest Diagnostics' customers utilize many of the technologies envisioned by these guidelines. The incorporation of alternative specimens and testing methods into the Mandatory Guidelines publication will facilitate the standardization of these new technologies much like the original Guidelines facilitated standardization of the urine drug testing industry. Furthermore, many employers perform both Federally-mandated testing and other types of drug testing in

accordance with company-policy. The publication of this NPRM is the first step in enabling the harmonization of drug testing policies within companies that perform both types of testing.

Our comments on the proposed mandatory guidelines are organized by Section number as they are enumerated in the NPRM.

For further clarification on any issue or comment cited above, please do not hesitate to contact me directly at 610-454-4173.

Respectfully submitted,



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

Quest Diagnostics generally agrees with the definitions set forth in this section. We have several comments pertaining to the definition:

- ***Certifying Technician (CT)*:** In some circumstances a CT should be permitted to certify an invalid result (e.g. immunoassay interference, inconsistent creatinine and specific gravity results, abnormal pH, abnormal oxidant activity, etc, on 2 aliquots). Furthermore, **Sections 14.3 – 14.7** imply that a CT may certify invalid results since an IITF may report invalid results to the MRO.
- ***Instrumented Initial Test Facility (IITF)*:** The definition should be clarified to specify whether an IITF must be a fixed location or whether "mobile" facilities would be permitted.

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

The data below summarizes positivity by reason for test from over 10 million tests performed by Quest Diagnostics between January 2003 and May 2004. This data suggests employers believe that hair, oral-fluid, and urine specimens are suitable and effective specimens for all reasons listed. Nevertheless, we would agree with the Department that hair is not the preferred specimen for post accident and reasonable suspicion/cause tests. (**Note:** FMSS=Federally-Mandated Safety Sensitive; GW=General Workforce)

Testing Reason	Urine		Hair (*N*=~113K)	Oral-Fluid (*N*=~77K)
	FMSS (*N*=~1,700K)	GW (*N*=~8,300K)		
Follow-up	3.5%	9.8%	29.1%	12.7%
Periodic	0.6%	2.1%	9.3%	5.3%
Post-Accident	3.1%	5.7%	5.2%	3.7%
Pre-Employment	2.9%	4.2%	6.5%	3.9%
Random	1.8%	6.8%	16.6%	4.2%
Reasonable Suspicion/Cause	14.0%	28.4%	38.8%	19.6%
Returned to Duty	2.9%	5.5%	4.6%	3.9%

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

- We disagree with the requirement to collect a urine specimen whenever an oral fluid specimen is collected based on the following:
    1. It is our understanding that some of the data reviewed by the Department in making its proposed recommendation and more recent data generated by the manufacturer of the FDA-cleared oral-fluid testing system, suggest that even

under extreme conditions of passive-exposure, the detection of THC above cut-off is very transitory (30 minutes or less), making the test results highly dependent upon timing of the collection.

2. An oral-fluid collection is most often administered by the employer. In this situation, the donor is in a more controlled environment (e.g. job application process, at the jobsite, etc.) and would not have the opportunity to be exposed to marijuana smoke in a closed environment. Furthermore, the collection process for oral fluid requires that the donor be observed for 10 minutes prior to the collection to ensure that he or she has had nothing by mouth prior to the collection. Consequently, the time course of the collection process would ordinarily exceed the 30 minute window of detection.
3. Operationally, it would be very difficult to coordinate the collection of both the urine and the oral fluid specimens at the collection site. There would be an additional burden on the laboratory to coordinate the selective testing of the oral fluid and/or urine.
4. Overall, there would be additional operational burden on the collection site, employer, laboratory, and MRO in addition to an added cost to the program (i.e., Federal Agency).
5. While we believe that the combination of the time course following exposure and the administrative cutoff in most cases would preclude positive results due to passive inhalation, recent preliminary data suggest there may be an additional marker for active THC use. Recent studies of specimens from several oral fluid testing labs suggest that marijuana metabolite (THCA) may be detectable in oral-fluid specimens reported positive for THC. At this point, this data is very preliminary and additional studies are required prior to making any recommendations with respect to THCA testing in oral fluid.

- While we agree that it might be desirable to collect an alternative specimen if a problem develops during the collection of another type of specimen, logistical and operational impediments to documenting and obtaining the necessary written permission may outweigh the benefits.

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

- ***(a) Hair*:**
  1. We recommend that the requirements for collecting a hair specimen should specify that the hair specimen be cut from the root end closest to the scalp and that the hair sample be placed in two separate foil packages - "A" (Primary) and "B" (Split).
  2. In order to ensure a sufficient quantity of specimen for both the "A" and "B" tests, we also would recommend that the hair specimen be subdivided ~70/30, respectively. This is consistent with the current requirements and/or recommendations for urine and oral fluid. If splitting the hair 70/30 is not feasible and an equal division of hair is required,

then we would propose collecting a larger amount (e.g. 150 mg) to ensure an adequate amount of specimen for the initial test, confirmatory test(s), and any necessary reanalysis.

3. Any recommendation/requirement in the *Final Rule* for subdividing the hair collection into "A" & "B" specimens, should be worded so as ***not*** to imply that the specimen should be weighed at the collection site to ensure compliance with the specified minimum quantities. We believe that requiring the weighing or semi-quantitative subdivision of the sample at the collection site is not practical and could lead to specimen contamination or mismatches.

- ***(b) Oral Fluid:***
  1. The *Proposed Guidelines* would require that the oral fluid be collected as a neat specimen, rather than using a device for specimen collection. Currently, the only FDA-cleared oral fluid testing system uses a device (e.g. "applicator pad", "collector") for specimen collection. We strongly urge the Department to permit the use of a collection device for the collection of the oral-fluid specimen. This type of collection is currently used by many employers and is more efficient and hygienic. This device could be an applicator pad that is subsequently placed in a buffer solution (the current FDA-cleared system) or an absorbent pad (or foam) that is subsequently "expressed" (several POCT systems use this approach) into a collection vial.
  2. We believe that it is important that the collection system reproducibly (within 10-20%) collect a specified volume of oral fluid. The volume collected may be dependent on the collection/testing system used. Consequently, a requirement for 2 mL of the "original" oral fluid may be significantly more than is required and may exceed the capacity of the collection device. Rather than requiring a fixed 2 mL collection of oral fluid, we recommend that the minimum collected volume of oral fluid (including any dilution with buffer) be sufficient for the initial test (screen), confirmatory test(s), and some reserve for reanalysis. This minimum volume would be determined by requirements of the FDA-cleared collection/test system (~100-125 µL of "original" oral fluid, including dead volume) and the validated confirmatory procedures (which typically require <100 µL of "original" oral fluid).
  3. The requirement for collection and subsequent subdivision of "neat" oral-fluid for the "A" and "B" specimens would require the use of a pipette or some other device by the collector. Use of a pipette may be operationally difficult at collection sites. Moreover, some donors may view the introduction of a transfer pipette into the original specimen as a mechanism for contaminating their specimen. Therefore, we recommend the allowance for the collection of "A" and "B" specimens using two devices.
  4. The definition of a *Split Specimen* in **Section 1.5** would permit a "concurrent" (e.g., bi-lateral), subdivided, or "nearly simultaneous" collection.

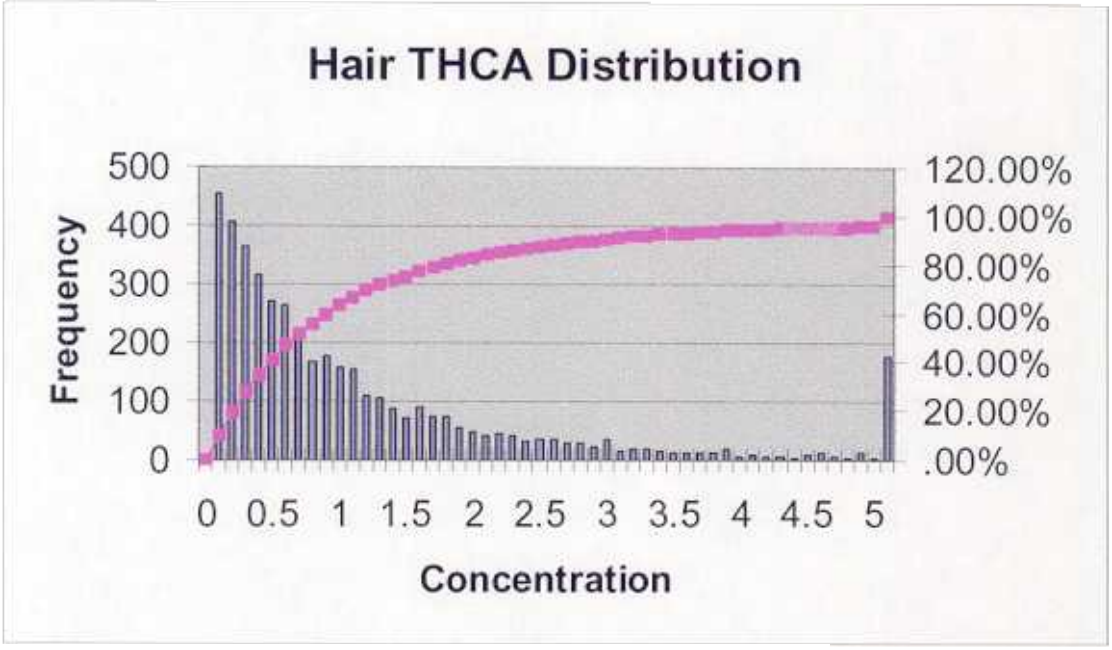
Section 3.4 What are the cutoff concentrations for hair samples?

- ***Initial Test***
  - *Cocaine Metabolites* – Cutoff for cocaine should be lowered to 300 pg/mg (See data below)
  - *Amphetamines* –
    1. Cutoff for amphetamines should be lowered to 300 pg/mg (See data below)
    2. A separate immunoassay for MDMA should not be required if the FDA-cleared immunoassay for amphetamines (methamphetamine as target analyte) has cross-reactivity >=80% with MDMA. Currently, the initial test immunoassays targeting methamphetamine have sufficient cross-reactivity to detect MDMA use.

Confirmatory Test

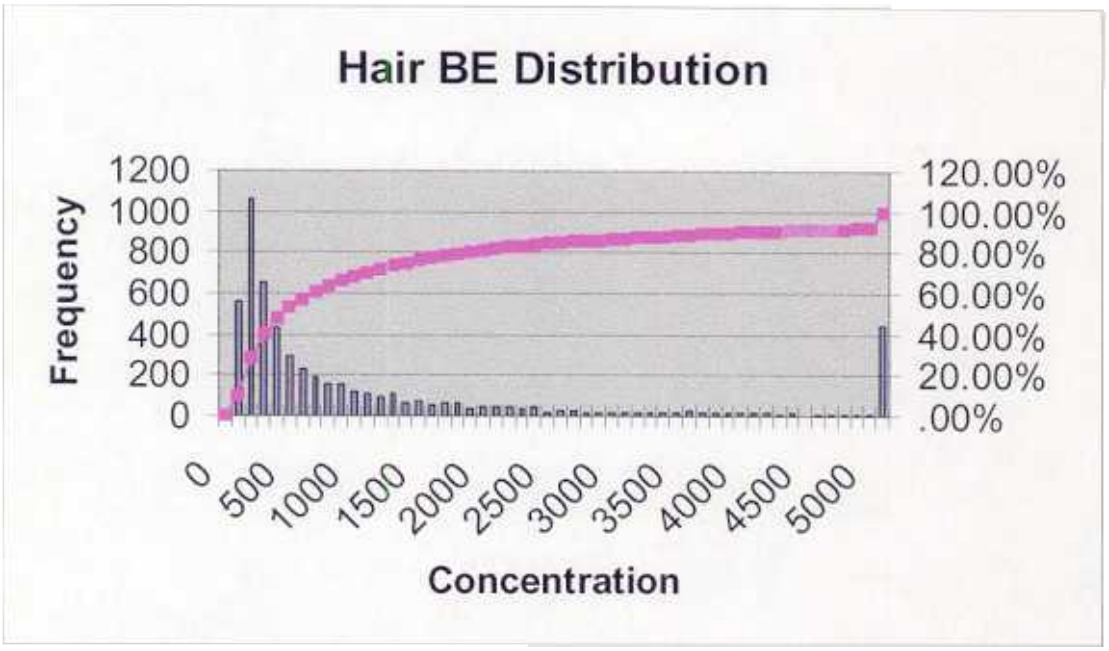
- *Marijuana Metabolite*:
  1. The confirmatory cutoff should be 0.1 pg/mg in order to meet commonly applied identification criteria (2-ion MS/MS identification) and ensure the ability to "retest" at 40% of cutoff.
  2. Pilot PT results, to date, would also support raising the cutoff to 0.1 pg/mg. As technology improves, it would be appropriate to revisit the cutoff and lower it if appropriate in manner that is being contemplated for Benzoylecgonine confirmation in urine. Our data reflects that ten percent (10%)of the THCA positive results are equal to 0.1 pg/mg and nine percent (9%) of the THCA positive results fall between 0.1 and 0.2 pg/mg.

Distribution of Marijuana Metabolite (THCA) positives (*N*= 4441). Data from positive specimens reported between September 2003 and May 2004

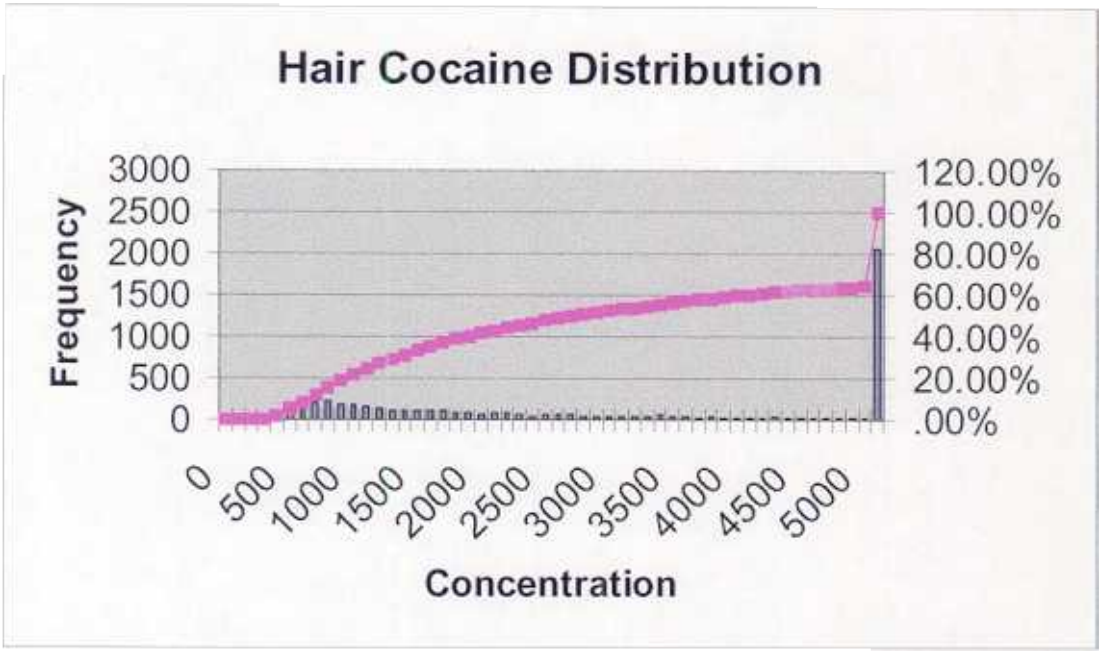


- *Cocaine & Metabolite*:
  1. Cutoff for cocaine should be lowered to 300 pg/mg. Our data reflects that five percent (5%)of the cocaine positive results and thirteen percent (13%) of the BE positive results fall between 300 and 500 pg/mg. (See data below)
  2. We suggest dropping norcocaine as a ***required*** confirmation analyte.
  3. Benzoylecgonine should be permitted as a separate analyte in the "cocaine class" at a cutoff of 300 pg/mg.
  4. We suggest revising the wording of footnote 2 as follows:
     "[2] Cocaine concentration is greater than or equal to confirmatory cutoff and Benzoylecgonine (BZE)/Cocaine ratio is greater than or equal to 0.05; or Cocaethylene (CE) greater than or equal to 50 pg/mg."
     With this proposed change, a cocaethylene at or above cutoff could stand alone in the absence of cocaine at or above cutoff.

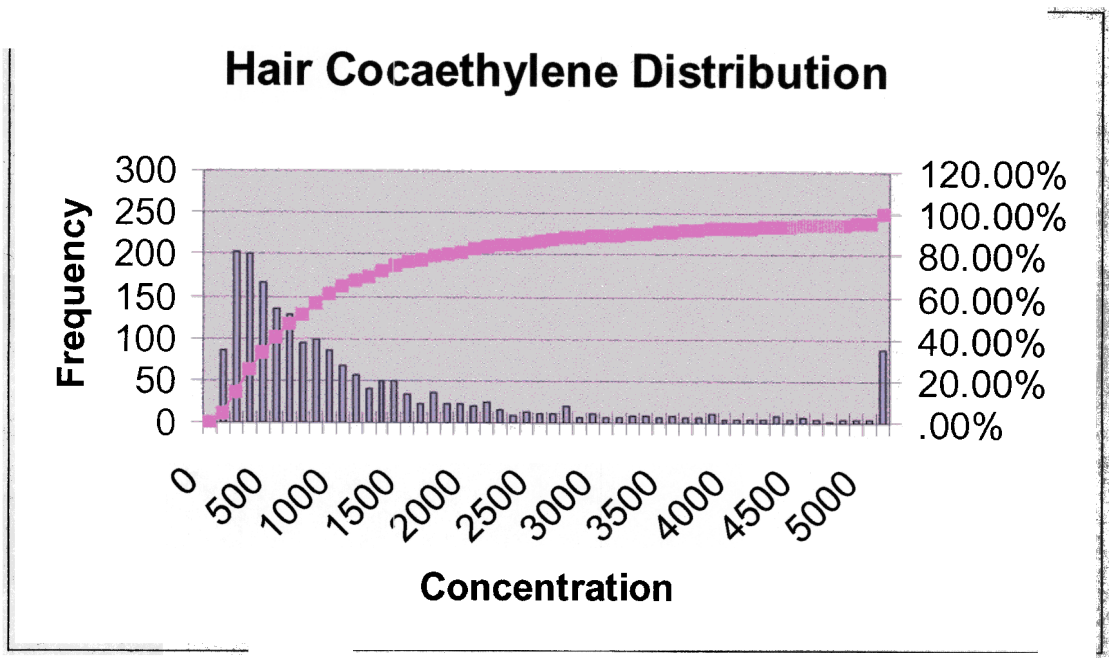
Distribution of Benzoylecgonine (BE) positives (*N*= 5634). Data from positive specimens reported between September 2003 and May 2004



Distribution of Cocaine positives (*N*= 5802). Data from positive specimens reported between September 2003 and May 2004



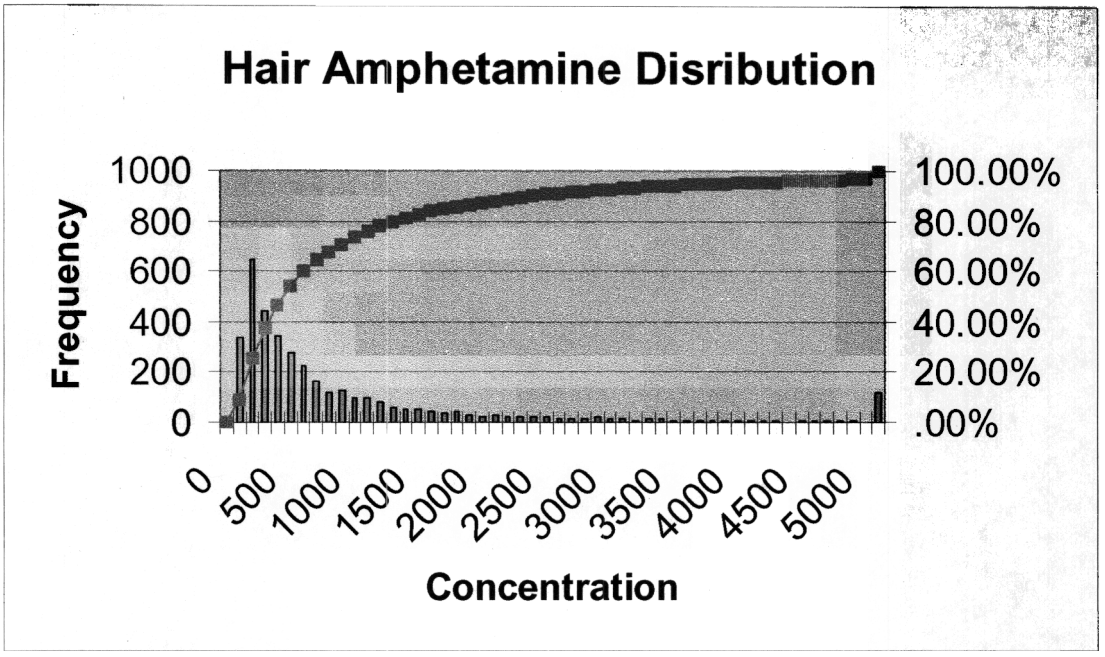
Distribution of Cocaethylene (CE) positives (*N*= 1958). Data from positive specimens reported between September 2003 and May 2004



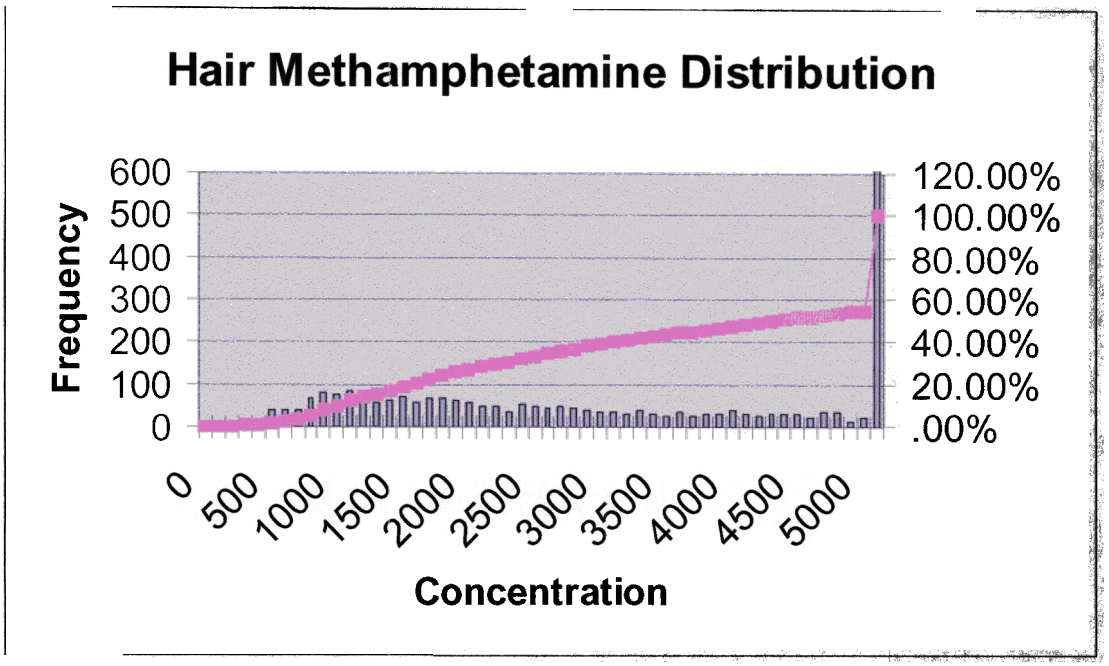
- *Opiates*:
  1. We suggest deleting footnote 3 and suggest that 6-AM be permitted as a separate analyte in the "opiate class" irrespective of the morphine concentration. Some specimens may be 6-AM positive and morphine negative. Furthermore, this change is consistent with the current proposed rules for 6-AM in oral-fluid and the sweat patch.
- *Amphetamines*:
  1. Cutoff for amphetamines should be lowered to 300 pg/mg. Sixteen percent (16%) of the amphetamine positive results, nine percent (9%) of the MDMA positive results, and thirteen (13%) of the MDA positive results fall between 300 and 500 pg/mg. (See data below)
  2. With a properly validated confirmation procedure, laboratories can document that there is no conversion of ephedrine to methamphetamine in the laboratories' confirmation procedure. Consequently, to eliminate false negative results for methamphetamine, we recommend that the requirement for the concomitant identification of amphetamine at a concentration >=50 pg/mg be eliminated. If the Department believes that a requirement for the detection of amphetamine should remain, we recommend changing the requirement to ">=LOD". Changing to >=LOD is consistent with the NPRM language for oral fluid and sweat patch.

3. We recommend the deletion of MDEA as a ***required*** confirmation analyte. In our general workforce urine testing, we have never detected any positives for this analyte.

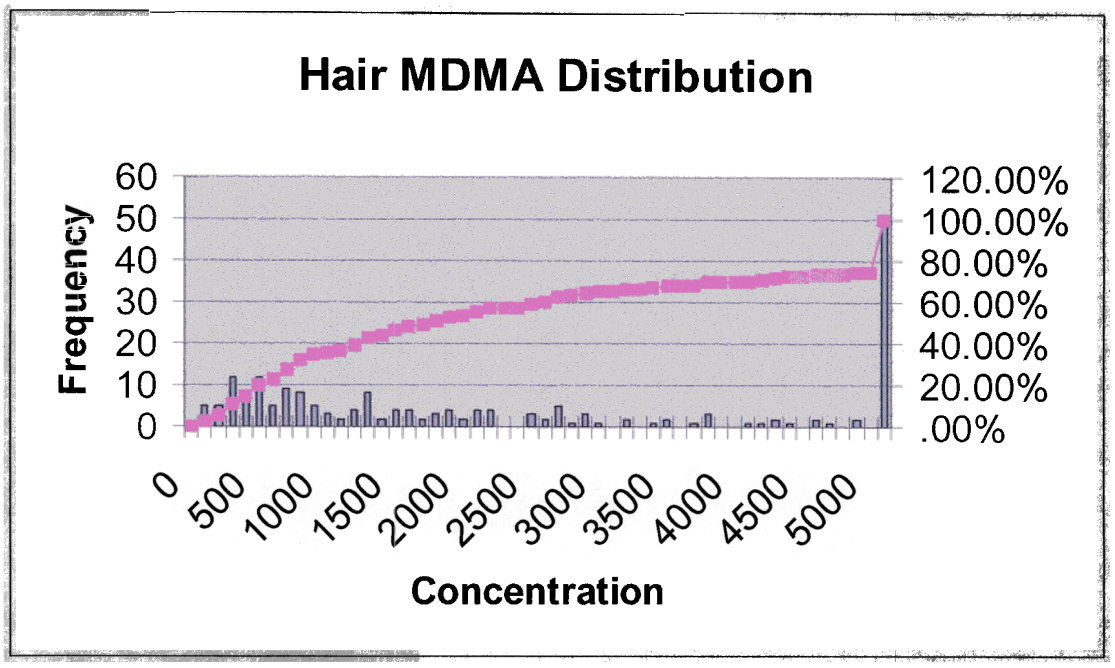
Distribution of Amphetamine positives (*N*= 3780). Data from positive specimens reported between September 2003 and May 2004.



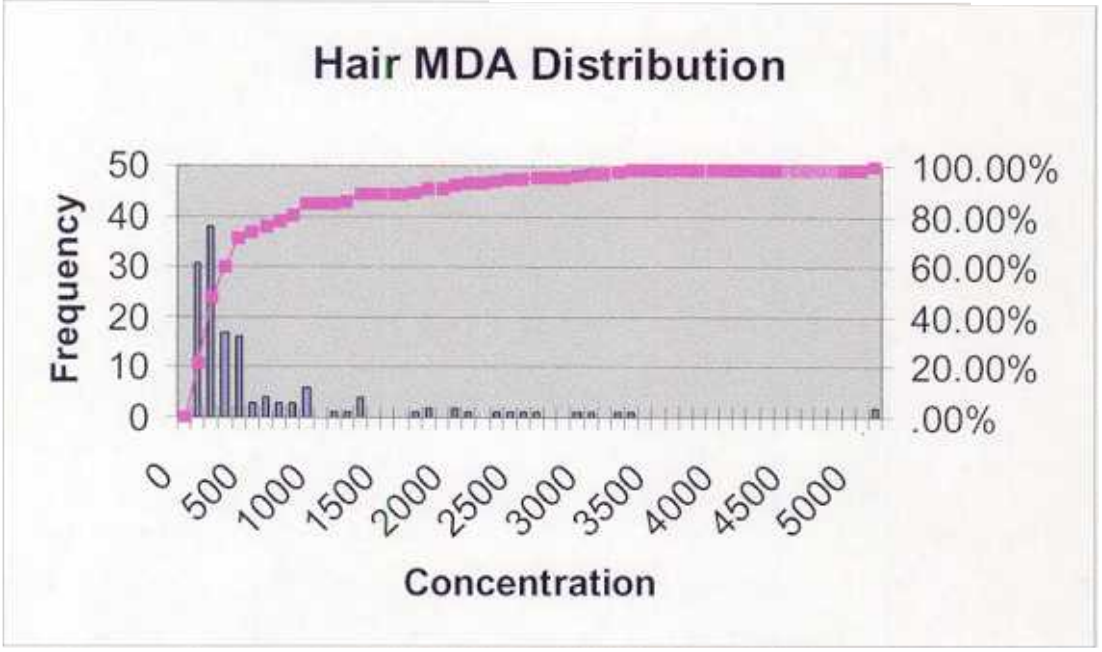
Distribution of Methamphetamine positives (*N*= 3811). Data from positive specimens reported between September 2003 and May 2004.



Distribution of MDMA positives (*N*= 196). Data from positive specimens reported between September 2003 and May 2004.



Distribution of MDA positives (*N*= 196). Data from positive specimens reported between September 2003 and May 2004.



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

The cutoffs for oral fluid specimens in the NPRM were based largely on the cutoffs used by the only FDA-cleared oral-fluid test system. The early drafts of the Proposed Guidelines assumed a 4-fold dilution of "original" oral-fluid with a buffer. However, both the manufacturer and our laboratory has documented that the FDA-cleared oral fluid test system produces an approximately 3-fold dilution of "original" oral-fluid. Consequently, at a minimum, we recommend that the cutoffs in the *Final Rule* should be based on this 3-fold dilution in the FDA-cleared system. Using the standard cutoffs in the FDA-cleared testing system, our positive prevalence in oral fluid is similar to that observed in urine.

Overall positivity rates and positivity rates by drug category for urine and oral fluid drug testing by Quest Diagnostics between January 2003 and May 2004. (***Notes***: 1) FMSS=Federally-Mandated Safety Sensitive; GW=General Workforce; and 2) a single initial test is used for "amphetamines" in urine and two different immunoassays are used for amphetamine and methamphetamine in oral-fluid.)

Drug Category	Urine		Oral-Fluid (*N*=~77K)
	FMSS (*N*=~1700K)	GW (*N*=~8300K)	
Overall	2.4%	5.0%	4.1%
Amphetamines	0.30%	0.50%	0.14%
Methamphetamines			0.49%
Cocaine	0.57%	0.74%	1.20%
Marijuana	1.34%	2.98%	1.96%
Opiates	0.19%	0.33%	0.66%
Phencyclidine	0.04%	0.02%	0.03%

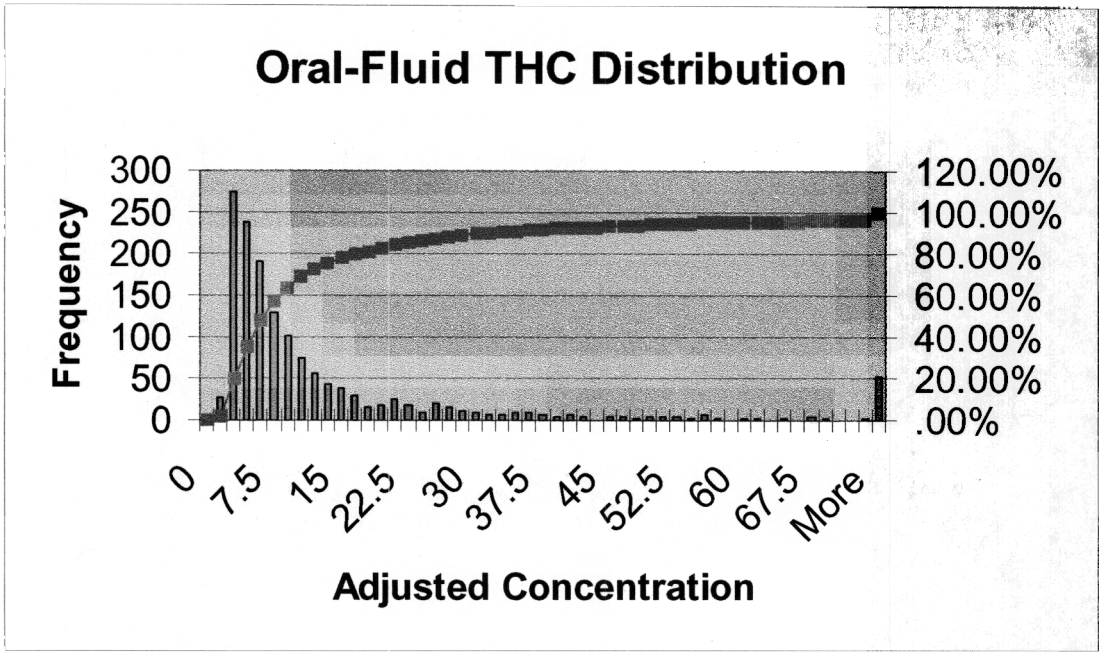
Our specific comments and suggested cutoffs (***in "original" oral fluid***) for each class/analyte are set forth below (included in this section are charts of the distribution of drug concentrations found in positive specimens):

- ***Initial Test***
  - *Marijuana (parent drug)* – suggested cutoff: 3 ng/mL
  - *Cocaine Metabolites* – suggested cutoff: 15 ng/mL
  - *Amphetamines* –
    1. Cutoff for amphetamines (methamphetamine as target analyte) should be 120 ng/mL. The NPRM's proposed cutoff of 50 ng/mL would produce a significant and unacceptable number of false positive screens.
    2. If the FDA-cleared immunoassay for amphetamines (methamphetamine as target analyte) has cross-reactivity >=80% with MDMA, a separate immunoassay for MDMA should not be required. Currently, the initial test immunoassays targeting methamphetamine have sufficient cross-reactivity to detect MDMA use.
    3. The Department should consider adding Amphetamine as a separate analyte for oral fluid testing. The ELISA methamphetamine immunoassays are specific for methamphetamine (and MDMA) and have poor cross-reactivity with amphetamine. In our experience, 10% of "amphetamine" positives, confirmed by Quest Diagnostics in oral fluid, are for amphetamine alone without any methamphetamine detected at or above the cutoff. The screening cutoff of the FDA-cleared assay used for this testing is 300 ng/mL.
  - *Opiates* – suggested cutoff: 30 ng/mL
  - *Phencyclidine*:
    1. The cutoff should be 3 ng/mL.

2. A lower cutoff is recommended for adequate detection of PCP users. At this cutoff, the positive prevalence rate in oral fluid is similar to urine.

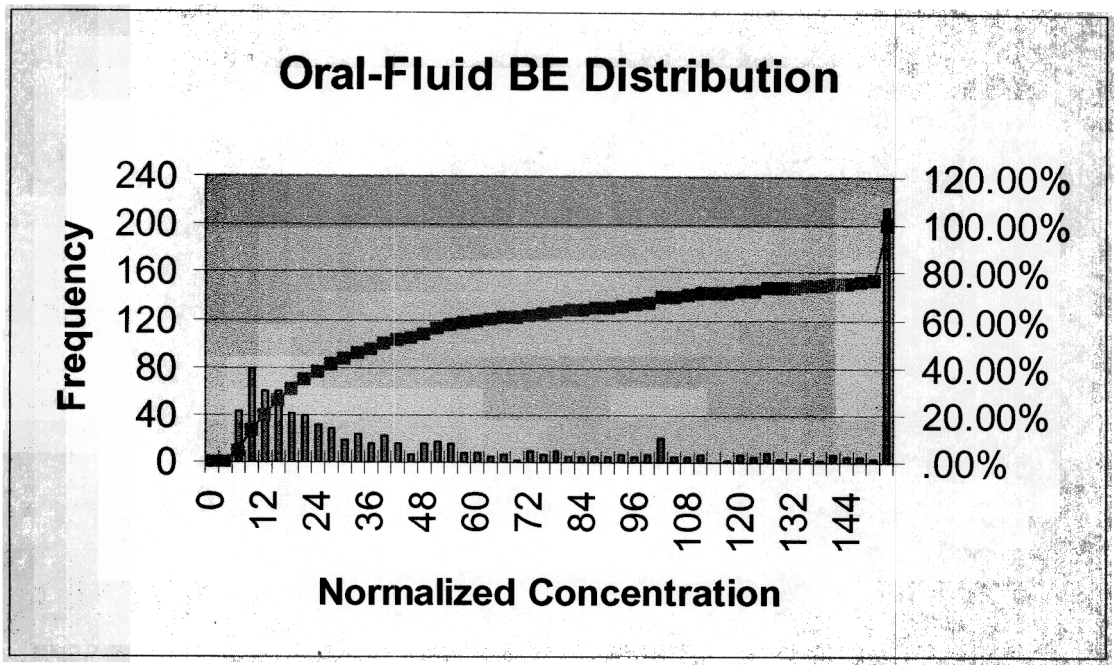
- ***Confirmatory Test***
  - *Marijuana (Parent Drug)* – suggested cutoff: 1.5 ng/mL. Eighteen percent (18%) of the THC positives fall between 1.5 and 3 ng/mL. (See data below)

Distribution of Marijuana (THC) positives (*N*= 1509). Data from positive specimens reported between January 2003 and May 2004 – ***Note:*** Concentration adjusted to compensate for dilution (~3-fold) of original fluid – i.e., "on-device" concentration multiplied by three (3).



- *Cocaine*:
  1. Cutoff should be 6 ng/mL. More than 8% of the benzoylecgonine positive results fall between 6 and 9 ng/mL. (See data below)
  2. We agree with footnote 1 (cocaine or benzoylecgonine)

Distribution of Benzoylecgonine (BE) positives (*N*= 932). Data from positive specimens reported between January 2003 and May 2004 – ***Note:*** Concentration adjusted to compensate for dilution (~3-fold) of original fluid – i.e., "on-device" concentration multiplied by three (3).



- *Amphetamines*:
  1. Cutoff for all amphetamines (amphetamine and methamphetamine groups) should be 120 ng/mL.
  2. We suggest deleting footnote 2. With a properly validated confirmation procedure, a laboratory can document that there is no conversion of ephedrine to methamphetamine in the laboratory's confirmation procedure. Consequently, to eliminate false negative results for methamphetamine, the requirement for the concomitant identification of amphetamine at a concentration >=LOD should be eliminated.
  3. We recommend the deletion of MDEA as a ***required*** confirmation analyte. In our general workforce urine testing, we have never detected any positives for this analyte.

- *Opiates*:
  1. Cutoff for all opiates should be 30 ng/mL.
  2. Strongly suggest raising cutoff for 6-AM to 30 ng/mL as the other opiates to facilitate routine confirmation of 6-AM in every specimen. In our testing, 50% of the morphine positive specimens are also positive for 6-AM and there have been isolated instances of specimens with 6-AM only above cutoff with no morphine at or above cutoff.
- *Phencyclidine* – suggested cutoff: 1.5 ng/mL

Section 3.7 What are the cutoff concentrations for urine specimens?

Initial Test

The lower initial test cutoff levels for *Cocaine Metabolite* and *Amphetamine* required by the NPRM are achievable. However, due to the higher confirmation rate for these substances that will occur, an unintended consequence of this change will be to increase the overall cost of testing to the Federal agency/employer.

- *Cocaine Metabolites* – In 1998, two of our laboratories performed a study of specimens that were immunoreactive for cocaine but below cutoff on the initial test. The data from this study suggests that the confirmed positivity rate for cocaine would increase significantly if the proposed cutoff changes for this analyte were implemented.
- *Amphetamines* –
  1. With the implementation of a 500 ng/mL cutoff for *Amphetamines*, laboratories will also experience more false positives as a result of donor's use of over the counter drugs (OTC).
  2. For MDMA, we believe that a cutoff level at 250 ng/mL is more appropriate for the initial test than a cutoff of 500 ng/mL, from a workplace-related viewpoint. (See Data Below)
  3. Currently, a separate test for MDMA is required for urine samples to avoid an unacceptably high number of false positive screens. However, if there was an FDA-cleared immunoassay for amphetamines (methamphetamine as target analyte) with MDMA cross-reactivity >=150%, a separate immunoassay for MDMA should not be required.

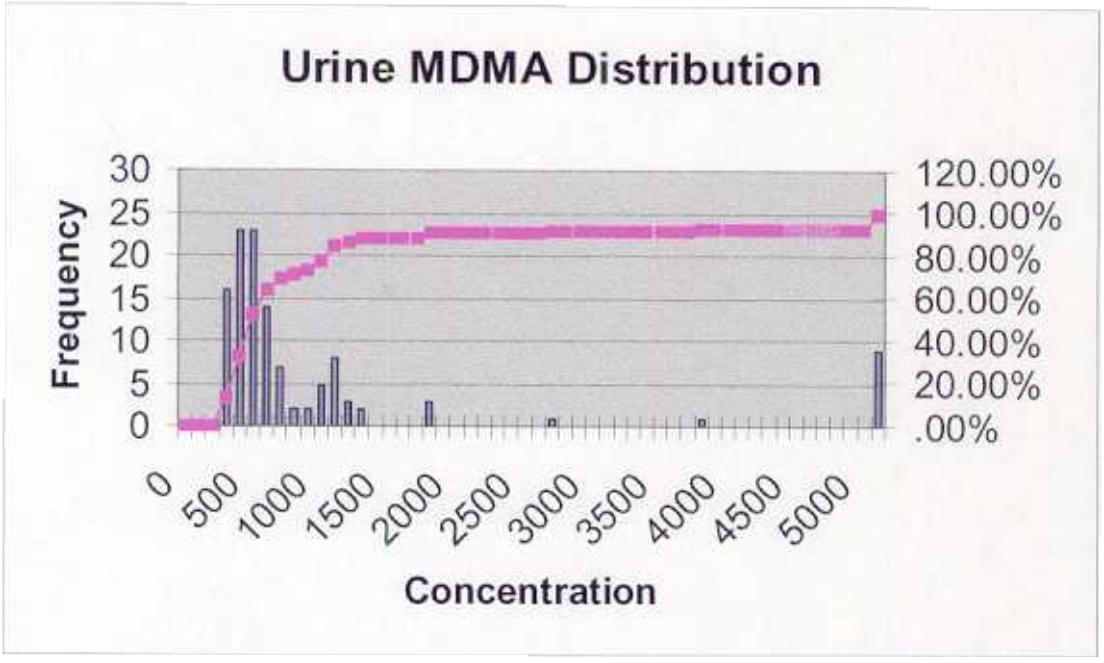
Confirmatory Test

- *Amphetamines*:
  1. We agree that the cutoff for all amphetamines and MDMA should be 250 ng/mL.
  2. We suggest the deletion of footnote 4. With a properly validated confirmation procedure, laboratories can document that there is no conversion of ephedrine to methamphetamine in their confirmation procedure. Consequently, to eliminate false negative results for methamphetamine, the requirement for the concomitant identification of amphetamine at a concentration >=100 ng/mL should be

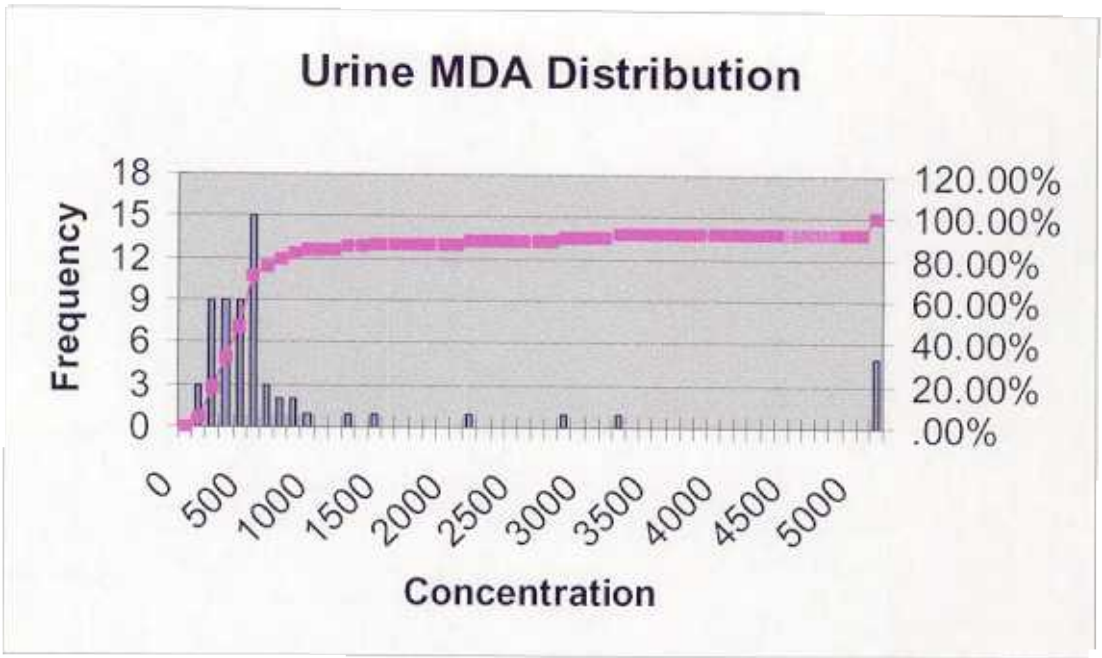
eliminated. If the Department believes that a requirement for the detection of amphetamine should remain, we would suggest changing the requirement to ">=LOD". This later suggestion is consistent with the NPRM language for oral-fluid and sweat patch.

3. We recommend the deletion of MDEA as a ***required*** confirmation analyte. In our general workforce testing, we have never detected any positives for this analyte.

Distribution of MDMA positives (*N*= 103). Data from positive specimens reported between September 2002 and June 2004



Distribution of MDA positives (*N*= 52). Data from positive specimens reported between September 2002 and June 2004.



Section 3.8 What validity tests must be performed on a hair sample?

The NPRM does not describe in detail the tests proposed by the Department, making it difficult to provide specific, constructive comments. However, as a general comment, the proposed tests appear to be manual, costly, and unduly burdensome on the laboratory. A validity test should be able to differentiate head hair that is commingled with other synthetic hair – i.e., hair extensions, wigs, weaves and other synthetic hairs. However, it is not clear if a validity test could easily differentiate these different types of "hairs" from "natural" hair.

We support a requirement to perform some simple procedure for validity testing. However, this procedure(s) should be easily incorporated into the laboratory workflow; and, preferably, would be automated like the current SVT tests (creatinine, pH, oxidants) for urine specimens and the IgG test for oral fluid.

It is unclear what specimen validity tests would be considered appropriate to satisfy the conditions articulated in section 3.8(a)(5)(i) through (iii). It appears as though laboratories are being given authority to perform specimen validity tests without established criteria for determining and further reporting the findings in a standardized manner. This section also does not specify what tests would be required, as opposed to which tests would be optional at the discretion of the laboratory, to respond to the observed indicators.

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

It is unclear what specimen validity tests would be considered appropriate to satisfy the conditions articulated in section 3.9(2)(a)(i) through (iii). It appears as though laboratories are being given authority to perform specimen validity tests without established criteria for determining and further reporting the findings in a standardized manner. This section also does not specify what tests would be required, as opposed to which tests would be optional at the discretion of the laboratory, to respond to the observed indicators.

Section 3.10 What validity tests must be performed on a sweat patch specimen?

It is unclear what specimen validity tests would be considered appropriate to satisfy the conditions articulated in section 3.10(2)(a)(i) through (iii). It appears as though laboratories are being given authority to perform specimen validity tests without established criteria for determining and further reporting the findings in a standardized manner. This section also does not specify what tests would be required, as opposed to which tests would be optional at the discretion of the laboratory, to respond to the observed indicators.

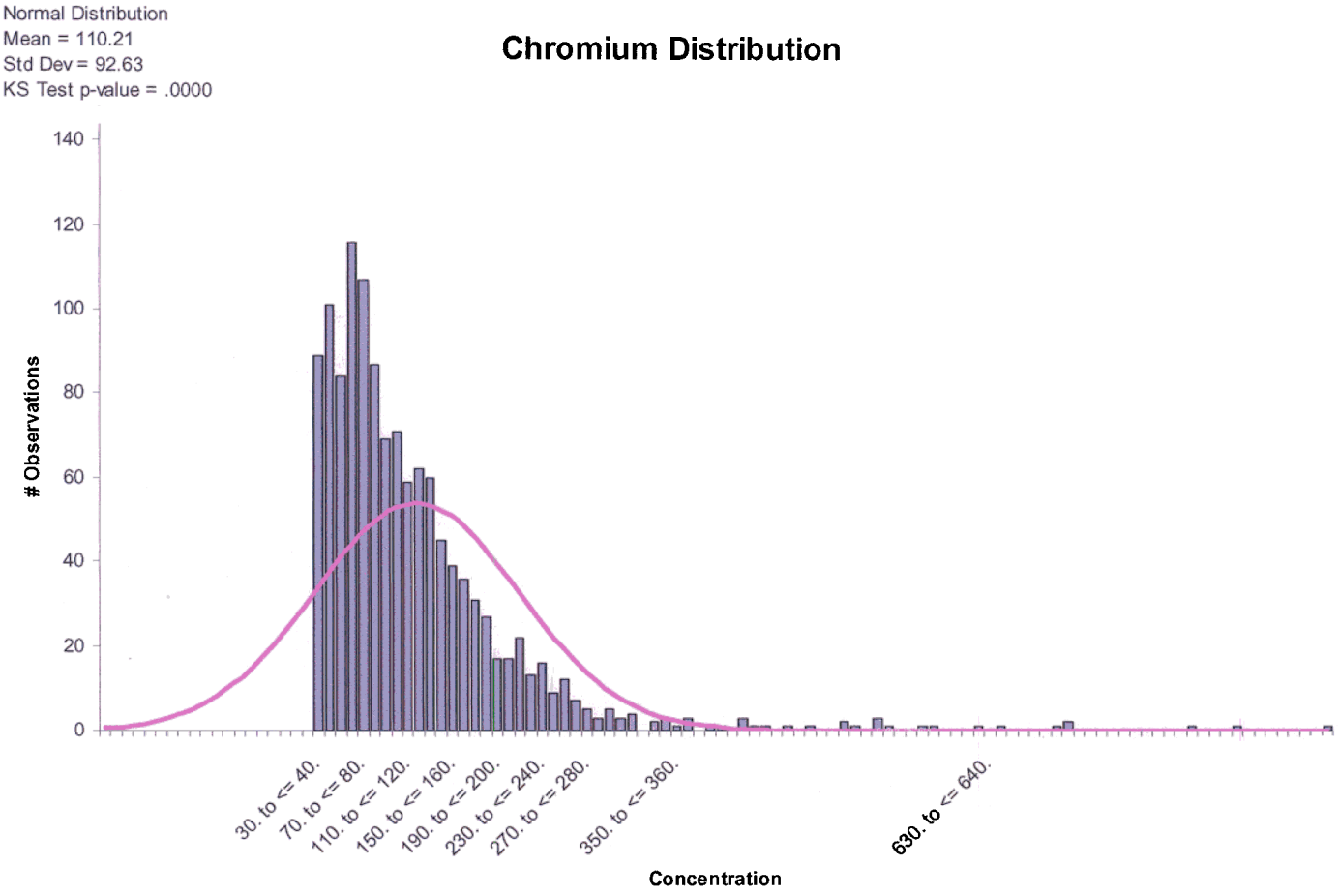
Section 3.11 What validity tests must be performed on a urine specimen?

It is unclear what specimen validity tests would be considered appropriate to satisfy the conditions articulated in section 3.11(5)(a)(i) through (iii). It appears as though laboratories are being given authority to perform specimen validity tests without established criteria for determining and further reporting the findings in a standardized manner. This section also does not specify what tests would be required, as opposed to which tests would be optional at the discretion of the laboratory, to respond to the observed indicators.

Section 3.15 What criteria are used to report a urine specimen as adulterated?

We believe that the cutoff of 50 µg/mL of chromium (VI) on the initial screen and confirmatory is too high. Quest Diagnostics has been performing quantitative chromium (VI) assays since 2001 and has used 20 µg/mL as the screening cutoff. If the cutoff is increased to 50 µg/mL, many specimens that are in fact adulterated will be reported as negative. Data below is from a preliminary analysis of chromium (VI) positive specimens by our certified laboratories from 2002 to 2004. The Histogram indicates that of 1251 specimens that were positive, 263 or 21% would have been reported as negative instead of as adulterated at a cutoff of 50 µg/mL. A subset of this data including only Federally-regulated specimens also provided the same approximate percentage of specimens that would have been reported as negative with the 50 µg/mL cutoff. We believe that this is a significant issue and adoption of the higher cutoff would certainly be a departure from our commitment to identify and report drug testing subversions. Increasing the cutoff to 50 µg/mL will encourage further adulteration of specimens using a lesser amount of the adulterant to achieve the same purpose. We are in the process of performing a study to document

the concentration of chromium(VI) that will create a false negative for marijuana and other analytes. Upon completion, we will make this data available to you upon your request.



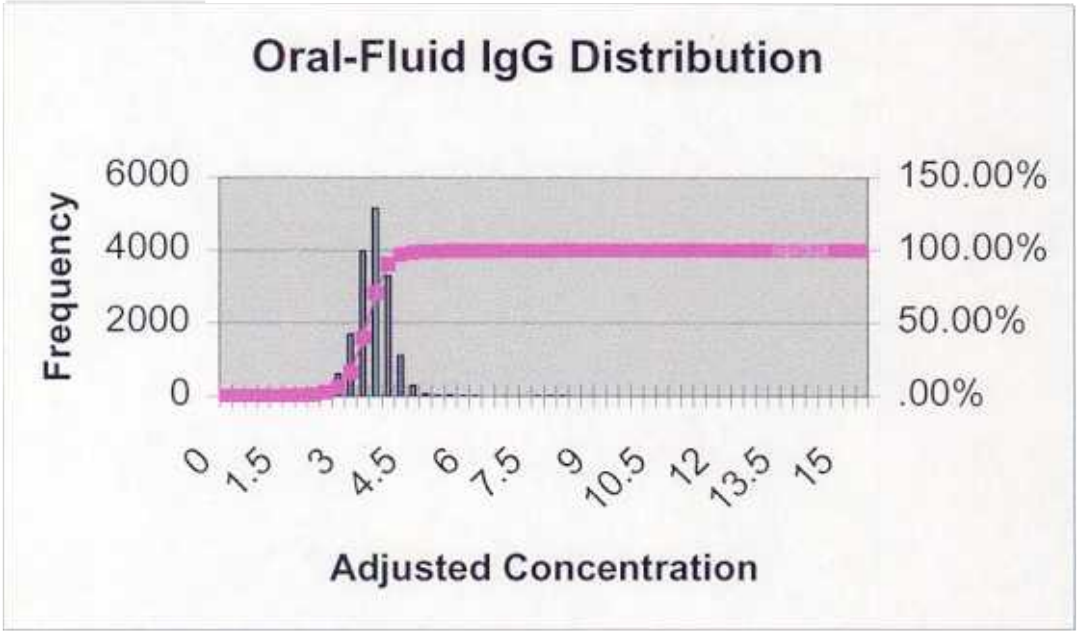
Section 3.19 What criteria are used to report a hair sample as an invalid result?

We recommend that subsection 3.19(d), which deals with the physical appearance of the two specimens, be eliminated or clarified. Individuals with "salt and pepper" hair or those that use "highlighting" may have "clearly different" "A" and "B" specimens. Moreover, in a typical hair collection – specimen wrapped in foil, which is then inserted in an opaque envelope – neither the primary ("Lab A") or the retest ("Lab B") laboratory would have the opportunity to visually compare the "A" and "B" specimens.

Section 3.20 What criteria are used to report an oral fluid specimen as an invalid result?

IgG is used by many oral fluid testing laboratories as an indicator of specimen validity. After correcting for the 3-fold dilution using the FDA-cleared oral-fluid testing system, the suggested cutoff for specimen validity is 1.5 µg/mL (See distribution of IgG results below). We believe it would be appropriate for the Guidelines to define an "abnormal" range above the cutoff for substitution and below the normal range where an oral fluid specimen would be considered invalid. Our data reflects that 0.05% of the oral-fluid IgG results are less than 1.5 µg/mL.

Distribution of Oral-Fluid IgG (*N*= 16776). Data from a 45-day period, May & June 2004 – ***Note:*** Concentration adjusted to compensate for dilution (~3-fold) of original fluid – i.e., "on-device" concentration multiplied by three (3).



Section 4.1 Who may collect a specimen?

- *Subsection 4.1(b)*: The proposed prohibition of a supervisor being the collector should not apply, generally, for pre-employment tests since there is no employer-employee relationship at that point. Furthermore, we do not see a conflict of interest in a supervisor collection of a hair, oral fluid, or urine specimen that will be tested in a laboratory, especially for pre-employment testing.
- *Subsection 4.1(c)*: A POCT site should not be considered a "testing facility" for the purposes of this section.

Section 5.8 What are the privacy requirements when collecting a urine specimen?

The requirements in this section are generally consistent with the current DOT rules. However, the requirement that *visual privacy* must be given to the Donor unless the test is a *follow-up* or *return-to-duty* test is inconsistent with the DOT (**§ 40.67** (b)"*..employer, you may direct a collection under direct observation..*") and would increase the cost to the Federal agency program.

Subpart F –Federal Drug Testing Custody and Control Forms

We believe that a single Custody and Control Form (CCF) would provide more flexibility if alternate matrices are permitted to be collected. We also recognize that it may not be possible to accommodate all of the specimen specific information and the variety of specimen seals that may be required on a single 8.5"x11" form. We would encourage the Department to host meetings or a "consensus conference" with all stakeholders to develop the new form(s). This process previously worked well in the development of the current Federal CCF.

Section 7.1 What is a collection device?

As we commented earlier in Section 2.5(b), this section should not preclude the use of an applicator pad or absorbent pad to collect the oral fluid from the oral cavity.

Section 8.1 What must the collector do before starting a specimen collection procedure?

Please clarify what type and extent of collector identification the collector must make available to the donor. Is an employee ID sufficient? Is a picture ID required? Collectors may be concerned if asked to display their driver's license that may include private information such as their home address or social security number.

Section 8.2 What procedure is used to collect a head hair sample?

Please refer to our earlier comments in Section 2.5(a). In addition, we would like to comment on the requirement that only head hair may be collected. Head hair is generally more abundant than hair from other sources. Furthermore, mandating a single source for the hair specimen, facilitates equal treatment of different donors. If other sources are permitted under the *Final Rule*, we strongly believe that pubic hair should be excluded as a hair source

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

Please refer to our earlier comments in Section 2.3 and Section 2.5(b). In addition, we would like to add the following comments:

- The use of an applicator pad as a collection device for oral fluid is already a well-accepted and FDA-cleared procedure for oral fluid drug testing.
- "Spitting" to collect "neat" oral fluid, is an unhygienic procedure that may have a greater potential for the transmission of infectious disease, especially if the donor expectorates or brings up sputum.

Section 8.6 What are the responsibilities of a Federal agency that uses a collection site?

We support inspections but recommend a standard checklist and reasonable written prior notice be provided prior to the inspection. The use of qualified/trained auditors/inspectors is essential to the inspection process.

Section 9.2 Who has the authority to certify laboratories and IITF's that want to test specimens for Federal agencies?

Subsection 9.2(a): The language regarding review of private-sector test results should be clarified to clearly indicate that this requirement would apply only to testing of private-sector employees pursuant to a Federal Agency contract.

Section 9.6 What are the PT requirements for an applicant laboratory to conduct hair testing?

Subsection 9.6(a)(3): For the analytes requiring highly sensitive techniques, e.g., THCA, the requirements of the NPRM are too strict based on the technology that is currently available and PT performance. A more appropriate criterion may be 3 standard deviations.

- *Subsection 9.6(a)(6)*: Currently, there are no quantitative tests for specimen validity in hair. Consequently, it would be difficult to assign quantitative criteria at this time.

Section 9.7 What are the PT requirements for an applicant laboratory to conduct oral fluid testing?

- *Subsection 9.7(a)(3)*: For the analytes requiring highly sensitive techniques, e.g., THC & PCP, the requirements may be too strict based on the technology that is currently available and PT performance. A more appropriate criterion may be 3 standard deviations.

Section 9.10 What are the PT requirements for an HHS-certified laboratory to conduct hair testing?

- *Subsection 9.10(a)(3)*: For the analytes requiring highly sensitive techniques, e.g., THCA, the requirements may be too strict based on the technology that is currently available and PT performance. A more appropriate criterion may be 3 standard deviations.
- *Subsection 9.10(a)(6)*: Currently, there are no quantitative tests for specimen validity in hair. Consequently, it would be difficult to assign quantitative criteria at this time.

Section 9.11 What are the PT requirements for an HHS-certified laboratory to conduct oral fluid testing?

Subsection 9.11(a)(3): For the analytes requiring highly sensitive techniques, e.g., THC & PCP, the requirements may be too strict based on the technology that is currently available and PT performance - 3 standard deviations may be a more appropriate criteria.

Section 11.3 What scientific qualifications in analytical toxicology must the RP have?

- *Subsection 11.3(a)*: This section appears to require that the RP be certified as a laboratory director by the State in Forensic or Clinical Toxicology. Many states do not have this requirement and/or certification. Therefore, this requirement should be eliminated.

Section 11.12 What are the requirements for an initial drug test?

Subsection 11.12(c): While we strongly support the requirement that the initial test immunoassays be FDA-cleared, they need not be cleared for "*commercial distribution*". There are FDA-cleared drug testing systems that are not marketed for "*commercial distribution*" – i.e., they are intended for "in-house" use only.

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

- *Subsection 11.14(a)(1) & (2)*: Currently, hair, oral fluid, & sweat patch drug testing systems utilize ELISA technology. This type of technology is required due to the limited specimen volume and/or concentration of drugs in these specimens. While it is highly accurate and reliable, the concentration-response curve for the ELISA technology is more likely to exhibit crossover at the +/-25% threshold levels and the CV% tend to be higher than in the EIA-based urine drug screening systems. Consequently, the requirements in this section should either be matrix or technology-specific. The FDA-cleared hair and oral fluid assays used by our laboratory are listed with controls at –50% and +100% (i.e. ½ x & 2x) of the cutoff. We recommend that QC requirements for the "alternative" specimens be consistent with the FDA-cleared protocol.

Section 11.17 What are the quality control requirements when conducting a confirmatory drug test?

Currently laboratories have the option of utilizing either single-point or multi-point calibration. We interpret the requirements in this section as requiring a single-point calibration. We recommend multi-point calibration for the following reasons:

- Multi-point calibration enables extension of the linear range and facilitates reporting of quantitative results without sample pre-dilution or reanalysis with dilution. Since these

Proposed Rules would require the automatic reporting of all quantitative results to the MRO, multi-point calibration permits the laboratory to provide an accurate quantification without additional cost or delay.

- If single point calibration is a requirement, then the PT requirements should only have challenges that are around (near) the cutoff. Since linearity is compromised by single point calibration, the accuracy at points other than those around the cutoff is suspect. The PT program should be modified to provide challenges around the cutoff, which is the value of the single point calibrator.

Section 11.23 What are the requirements for conducting each validity test on an oral fluid specimen?

Currently, IgG is the only validity test available for oral fluid specimens and is performed as part of the initial test panel. Due to the limited sample volume, confirmation of IgG concentration by another analytical method may not be feasible or cost effective. We believe that a second IgG test using the same analytical principle as the first IgG test is an acceptable confirmatory test. This technique is similar to current guidance for confirmation testing of creatinine and pH in urine.

Section 11.26 What are the requirements for an HHS-certified laboratory to report a hair test result?

We support the requirements set forth in this section including the mandatory quantitative reporting of non-negative test results in subsection **(h)** and **(i)**.

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

We generally support the requirements set forth in this section, including the quantitative reporting requirements in subsections **(i)** and **(j)**. We strongly disagree with the requirements for urine THCA testing in subsection **(c)**. (In addition, please refer to our comments in **Section 2.3**).

Section 11.29 What are the requirements for an HHS-certified laboratory to report a urine test result?

We support the requirements set forth in this section, including the mandatory quantitative reporting of non-negative test results in subsection **(j)** and **(k)**.

Section 11.32 What statistical summary report must an HHS-certified laboratory provide?

We strongly agree with the requirements in this section. These changes bring the Federal and DOT programs into congruence. It should be noted that the components in the Statistical

Summary Report are urine based. Different analytes will be required for other specimen matrices and should be enumerated in the *Final Rule.*

Section 11.35 What information must an HHS-certified laboratory provide to its private sector clients?

This proposed requirement is not within the scope of the guidelines as it applies to private sector testing. Furthermore, SAHMSA has no regulatory authority or compelling reason to hold a laboratory to this requirement for the laboratory's purely private-sector testing. Therefore, we recommend that this section be deleted in its entirety.

Subpart L - Point of Collection Test (POCT)

We are generally supportive of the POCT requirements and supports FDA-clearance for POCT devices and the concept of a *SAMHSA-certified* list.

Section 12.18 What are the requirements for conducting a POCT?

We agree that the donor should not have access to the device. However, we recommend the following:

- POCT should be collected and documented on a different CCF than that used for laboratory/IITF testing.
- It is problematic for the collector to open the specimen, test the specimen and reseal the specimen if determined to be non-negative for shipping to a *HHS-certified laboratory* for further testing. In order to simplify the specimen chain of custody (COC) and to minimize the possibility of COC omissions and errors, we recommend that the POCT test be performed on residual specimen in the urine collection cup and that the un-opened "A" and "B" specimen be forwarded to the *HHS-certified* laboratory.
- We recommend that you clarify, in this section, that all non-negatives sent to the *HHS-certified laboratory* for further testing must be re-screened and confirmed if presumptively positive at the laboratory.

Section 12.26 What type of relationship is prohibited between a manufacturer of a POCT device or a POCT site operation and an MRO?

The list of prohibited types of relationships is similar to prohibited relationships in a laboratory/IITF-MRO relationship and we support -the consistency in the regulations.

Subpart M - Instrumented Initial Test Facility (IITF)

We are generally supportive of the concept and requirements for an IITF.

Section 13.6 What qualifications must the responsible technician (RT) have?

Since an IITF is essentially a "screening laboratory" that has all of the same processes and procedures as the initial testing portion of an *HHS-certified laboratory* and an IITF may report *invalid* results, we strongly recommend that the RT meet the same requirements as those for an alternate RP. Passage of the RT requirements proposed in this NPRM would lower standards of the current program, in our opinion.

Subpart N - Medical Review Officer (MRO)

We generally support the requirement for certification of MRO's.

Section 16.3 What discrepancies are not sufficient to require a laboratory or IITF to reject a hair, oral fluid, sweat, or urine specimen for testing or an MRO to cancel a test?

Subsection 16.3(c): This section should be clarified to specify whether the "no more than once a month" test for an omission or discrepancy to be considered insignificant applies to an individual collector, the collection site, or the entire collection organization.

Section 17.2 What definitions are used for this subpart?

We recommend renumbering 17.1**(b)** as 17.1**(c)** and including in a new subsection 17.1**(b)** the specific grounds for suspension or revocation of a laboratory's certification.

Section 17.5 When must a request for informal review be submitted?

All time periods should start upon the date of receipt of the notice, not the date of the Notice. This may be accomplished by requiring that all Notices be served by CERTIFIED MAIL, RETURN RECEIPT REQUESTED.