The Oral Fluid Matrix and The Mandatory Guidelines

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Presentation scope

- Brief history of DHHS guideline development
- Brief discussion on alternative matrices
- Current state of the art in Oral Fluid testing
- Comparability of Oral Fluid to urine in detecting drug use
- Begin today’s discussion on how Oral Fluid might fit into the Federal Guideline paradigm

History of Guidelines I

- September 1986 - Executive Order 12564, HHS Sec. tasks NIDA to develop Guidelines
- February 1987 – Initial version issued
- July 1987 – Congress passes PL-100-71
- April 1988 – Final notice of new Guidelines for federal employees
  - Standards for collection
  - Standards for screening and confirmation testing
  - Certification program for laboratories
- DOT/NRC adoption expanded impact

History of the Guidelines II

- Over the next 15 years fine tuning [1988-2004] program moves from NIDA to SAMHSA
- In 2004 SAMHSA Proposed changes to include alternative matrices: oral fluid, hair, sweat
- 2008 Final notice that urine would remain only approved matrix for federal programs. Comments indicated the technology for hair, OF, and sweat not sufficiently mature to include at this time
- 2011 - the science and technology for detecting drugs in oral fluid has reached a point where further consideration appears merited

Goals for Today

- Begin a process of discussion to identify the issues regarding the possible inclusion of OF in the Federal testing programs:
  - Technical issues
  - Regulatory issues
  - Lab certification issues
  - MRO issues
  - Legal defensibility of the technology etc.

Choosing a matrix: Variables to Consider

- Reason for test?
- How often to test?
- Window of detection required?
- Which drugs to test for?
- Requirement for immediate results?
- Availability of device/assay?
- Venue

Drug Detection Windows

Specimen	**Timeframe**
Blood	Minutes to days
Oral fluid	Minutes to days
Urine	Hours to weeks
Sweat	Hours to months
Hair	Days to years

Pros/Cons of Oral Fluid Testing

- Pros
  - Less invasive than urine
  - Evidence of very recent exposure
  - Presence of active drug
  - Lab assay and POCT devices available
- Cons
  - Shorter window of detection [Lab better than POCT]
  - Collection method is critical
  - Contamination issues
  - Assay availability
  - POCT only good for some drugs

Oral Fluid History in Drug Testing

- Studies reporting the detection of drugs in OF since the 1970s
- RTI has a bibliography that runs 29 pages
- Widely used in:
  - TDM
  - Pharmacokinetic studies
  - Detection of illegal drug use
- Labs specializing in workplace/business testing for risk management use OF to test for:
  - Cotinine [smoking]
  - HIV
  - Illegal drug use

Lab-based OF Testing

- Screening:
  - ELISA – Heterogeneous assays for most drugs available
  - EIA -Homogeneous fully automated oral fluid drugs of abuse assays available
- Confirmation:
  - GC/MS
  - LC/MS/MS

Oral Fluid POCTs

- Number of devices available
- Most visually interpreted
- Some have readers available
- Specificity, sensitivity, and accuracy depends on drug and device
- Overall performance is poor compared with lab based testing

ROSITA II – Joint US and EU Field Evaluation of Oral Fluid devices

- 2246 DUI suspect subjects in 4 US States and 6 European Countries
- Blood & 2 OF specimens collected
- % Positive samples (lab tested oral fluid)

Drug	**Percentage, %**
Amphetamines	20
Benzodiazepines	32
Cannabis	36
Cocaine	19
Opiates	8

Evaluated devices

- American Biomedica Oralstat
- Branan Medical Oratect [I, II]
- Cozart Bioscience RapiScan (US only)
- Dräger/Orasure DrugTest/Uplink
- Lifepoint Impact

Evaluated devices

- Securetec Drugwipe
- Sun Biomedical Oraline
- Ultimed Salivascreen
- Varian OraLab

Device failures

Device	Failed	Total	%
Cozart RapiScan	0	40	0
Securetec Drugwipe	50	1364	4
American Biomedica Oralstat	3	52	6
Dräger DrugTest	52	592	9
Vairan Oralab	61	234	26
Lifepoint Impact	14	44	32
Branan Oratect II	20	53	38
Sun Oraline	15	38	39
Ultimed Salivascreen	33	70	47
Branan Oratect	87	118	74
Total	3356	2605	

Rosita II Conclusions

- Lab Analysis of Oral Fluid excellent
- POCT oral fluid drug tests less accurate
  - 6/10 devices tested > 25 % failed to run
  - Cannabis: < 50% of positives detected
  - Amphetamines, cocaine: 80% detected
  - Benzodiazepines 67%
  - Opiates 60%
- Report downloadable from http://www.rosita.org

Comparing Oral Fluid with Urine

- Results of 2M urine tests compared with 650K oral fluid tests
- All test results from single MRO source
- All unregulated tests
- Included all test results in comparison
- All blind QC samples were excluded from the analysis of data

OF Methods

- Records for ~650K OF specimens were obtained from a single MRO data source
- The OF specimens were collected during the 5-year period, 2003-2007
- The majority of the OF specimens were analyzed by two large laboratory systems

OF Data Summary

Specimens	**Number**
Specimens tested	648,372
Lab confirmed positives	27,750

Result	**Percentage, %**
Laboratory positive rate	4.3
MRO verified positive rate	95.6
MRO reversal rate	4.4
Non-negative [Invalid/rejected]	1.3

MRO Verified OF Positives by Drug

Drug	**Percentage, %**
Marijuana	60.4
Cocaine	24.1
Methamphetamine	6.4
Amphetamine	4.3
Opiates	3.9
PCP	0.5

Urine Data Methods

- Records for 2 million unregulated urine tests were obtained from same MRO source
- Specimens collected in 2006 and 2007
- Specimens analyzed in NLCP certified labs

% Verified Positives by Drug Oral Fluid vs. Urine

Drug	**Urine, %**	**Oral fluid, %**
Amphetamine	3.4	4.3
Methamphetamine	2.5	6.4
Cocaine	17.7	24.1
Marijuana	72.0	60.4
Opiates	4.5	3.9
PCP	0.4	0.5

Non-Regulated Tests

Matrix	Urine	Oral Fluid
% Lab Confirmed Positives	4.15	4.30
% MRO Verified Positives	76.4	95.6
% MRO Reversals	23.6	4.4

Urine v. OF Summary

- Lab positive rates appear comparable between urine and oral fluid
- Overall the MRO verified positive rate for oral fluid specimens [95.57%] is higher than typically observed with urine test results [76.4%] – not sure why
- Majority of MRO reversals appear to be due to prescription use of opiates and amphetamines in both urine and oral fluid

Summary

- Guidelines have survived nearly 25 years
- Technology has changed significantly
- Opportunity to improve the program and increase efficiency and cost effectiveness
- Today is the beginning of a process to inform and discuss the current state of the art in oral fluid drug test methods to explore the suitability for the Federal programs