

NLCP Implementation of the Revised Mandatory Guidelines 2010

Initial Testing for New Analytes and New Cutoffs

John M. Mitchell, PhD

Co-Director, National Laboratory Certification
Program

Center for Forensic Sciences

RTI International

Revised Program Requirements

- New initial test analytes:
 - Methylendioxyamphetamine (MDMA)
 - Cutoff: 500 ng/mL
 - 6-Acetylmorphine (6-AM)
 - Cutoff: 10 ng/mL

Revised Program Requirements

- Revised initial test cutoffs:
 - Methamphetamine (MAMP) and amphetamine (AMP)
 - Current: 1000 ng/mL
 - Revised: 500 ng/mL
 - Cocaine metabolites
 - Current: 300 ng/mL
 - Revised: 150 ng/mL

Implementation Concerns

- Timeline for implementation
- Awareness of required changes by Laboratories and supporting industries
- Availability of materials for implementation of the changes
- Acceptability of materials
- Readiness of Laboratories

Implementation Timeline 2009-2010

- May-November 2009 – NLCP HHS-certified Laboratories validate new immunoassay (IA) kits prior to November 2009
- November 2009 – Laboratories receive practice samples from the NLCP to verify validation
- January-May 2010 – Laboratories receive qualifying PT samples

Laboratory Awareness

- January 12, 2009: Questionnaire to all Laboratories
 - Have you contacted your immunoassay kit supplier(s) as to when kits for the new analytes and revised cutoffs will be available for validation and testing?
 - Who is your immunoassay supplier contact?

Awareness of Supporting Industries

- February 16, 2009: Questionnaire to 31 immunoassay supplier contacts
 - When will your new immunoassay kits for the new analytes and revised cutoffs be available to the Laboratories for validation and testing?

Availability of Immunoassays (IA)

- Manufacturers of IA tests currently used by Laboratories
 - Roche
 - Siemens
 - Thermo Fisher

Roche Response

- AMP/MAMP/MDMA (500 ng/mL cutoff)
 - *Single Kit, with FDA for review, anticipated 3rd Quarter 2009*
- 6-AM (10 ng/mL cutoff)
 - *No plans to offer*
- COC (150 ng/mL cutoff)
 - Now Available

Siemens Response

- MDMA (500 ng/mL cutoff)
 - Now Available
- AMP/MAMP (500 ng/mL cutoff)
 - Now Available
- 6-AM (10 ng/mL cutoff)
 - *Developed but not yet Submitted to FDA*
- COC (150 ng/mL cutoff)
 - Now Available

Thermo Fisher Response

- MDMA (500 ng/mL cutoff)
 - Now Available
- AMP/MAMP (500 ng/mL cutoff)
 - Now Available
- 6-AM (10 ng/mL cutoff)
 - Now Available
- COC (150 ng/mL cutoff)
 - Now Available

Specificity Data for Amphetamines and MDMA (Ecstasy) IA Kits

What Performance is Desired in an Immunoassay?

- An IA positive result should reflect the presence of drug analytes that are metabolically related to the target analyte used to calibrate the assay
- An IA should be formulated to maximize response to the target analyte used for calibration and metabolically related analytes

Example of Desirable Performance

- Opiates
 - Morphine is used to calibrate the assay
 - Morphine may be produced through the metabolism of heroin, 6-AM and codeine
 - Response to minor metabolites and structurally related compounds such as hydrocodone, hydromorphone, oxycodone, etc. do not exceed that obtained with morphine

Siemens Amphetamines Assay Specificity

| Compound | Concentration (ng/mL) | % Cross Reactivity |
|----------|--------------------------|-----------------------|
| d-MAMP | 500* | 100 |
| MDMA | 9,150* | 5.5 |
| MDA | 1,700* | 29.4 |
| MDEA | 6,800* | 7.3 |

- *Concentration required for response equivalent to 500 ng/mL MAMP

Thermo Fisher (CEDIA) Amphetamines Assay Specificity

| Compound | Concentration (ng/mL) | % Cross Reactivity |
|----------|-----------------------|--------------------|
| d-MAMP | 1,000* | 100 |
| d-AMP | 1,000* | 100 |
| MDMA | 1,500* | 69 |
| MDA | 50,000* | 1.9 |
| MDEA | Not Given | Not Given |

- ***Concentration required for response equivalent to 1000 ng/mL MAMP**

Thermo Fisher (DRI) Amphetamines Assay Specificity

| Compound | Concentration (ng/mL) | % Cross Reactivity |
|----------|-----------------------|--------------------|
| d-MAMP | 1,000* | 100 |
| d-AMP | 1,000* | 100 |
| MDMA | 1,300* | 77 |
| MDA | 2,500* | 40 |
| MDEA | Not Given | Not Given |

- *Concentration required for response equivalent to 1000 ng/mL MAMP

Siemens MDMA Assay Specificity

| Compound | Concentration (ng/mL) | % Cross Reactivity |
|----------|-----------------------|--------------------|
| MDMA | 500* | 100 |
| MDA | 578* | 86.5 |
| MDEA | 528* | 94.6 |
| d-AMP | 430,000* | 0.1 |
| d- MAMP | 130,000* | 0.4 |

- *Concentration required for response equivalent to 500 ng/mL MDMA

Thermo Fisher (DRI) MDMA Assay Specificity

| Compound | Concentration (ng/mL) | % Cross Reactivity |
|----------|-----------------------|--------------------|
| MDMA | 500* | 100 |
| MDA | 900* | 56 |
| MDEA | 600* | 83 |
| d-AMP | 600,000** | 0.1 |
| d-MAMP | 600,000** | 0.1 |

- *Concentration required for response equivalent to 500 ng/mL MAMP
- **Concentration that produces a negative result

Summary I

- NLCP HHS-Certified Laboratories are aware and planning for the implementation of the pending revisions to the Mandatory Guidelines
- Immunoassay manufacturers are aware and preparing to support the needs of Laboratories
- Only one manufacturer has an FDA-cleared immunoassay for 6-acetylmorphine (6-AM)

Summary II

- All manufacturers have FDA-cleared immunoassays for Cocaine
- Two manufacturers have FDA cleared immunoassays for MAMP/AMP and MDMA
- One manufacturer has submitted for FDA clearance a single immunoassay that detects MAMP/AMP and MDMA