POCT and Drugs of Abuse

Mag. Maksimiljan Gorenjak, EurClinChem
Department for Laboratory Diagnostics
UKC Maribor, Slovenia

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POCT and Drugs of Abuse (DOA)

- For many settings, the availability of POCT devices, designed to detect abused drugs in urine, is an attractive alternative to collection, transport, and subsequent laboratory analysis.

NACB Guidelines POCT 2007 (Chapter 7)
Classification of POCT devices

• According to technology
  - agglutination reaction
  - chromogenic antibodies
  - chromogenic drug-conjugates
  - ……

• According to result evaluation
  - visual reading
  - semi-automated or automated endpoint reading
Sample

- Urine
- Saliva (oral fluid)
- Breath
- Sweat
- Other matrices
Technical solutions

- Strips and dip cards
- Cassette devices
- Test cups
- Automated readers
Strips and dip cards

- Similar to classic urine analytics
- Easy use
- Possible contamination
- Problems with absorbents
Cassette devices

- Pipette applied device
- Manual use of a disposable transfer pipette to apply the urine sample to the absorbent pad
- Single or multidrug devices
- Mistakes regarding the same optical appearance
Test cup

- Immunoassay POCT device is built into a collection container
- No manual intervention
- Special seal for Chain of custody
- High costs
Automatic readers

- Closed or open systems
- No subjectivity
Lateral flow immunoassay (LFI)

• The technical basis of the LFI was derived from the latex agglutination assay
• RIA Yalow and Berson (end of 50s)
• Major patents on this technology (early 80s)
• The main application driving the early development was the human pregnancy test
Architecture of LFI

Fig. 1.1 Typical configuration of a lateral flow immunoassay test strip

Assay components

• The membrane
• The sample pad
• The backing materials
• The conjugate pad
• The wick
• Labels for detection
Immunoassay

- Competitive solid-phase (inhibition) IA
- Direct-sandwich IA
Nitrocellulose strip

The wick

The control line - immobilized Ab to the control Ag

The test line - immobilized Ab to the drug of interest

Antigens for control line

The conjugate

The absorbent pad
The control line is present = test OK

The colored line is present = the test result is NEGATIVE

3-5 min.

No drug in urine
The control line is present = test OK

No visual line on test line = the test result is POSITIVE

3-5 min.

Positive sample - the drug is present in urine
## Analytes and Their Cutoffs

**Effective Date:** October 1, 2010

**Reference:** Federal Register, November 25, 2008 (73 FR 71858), Section 3.4

<table>
<thead>
<tr>
<th>Initial test analyte</th>
<th>Initial test cutoff concentration</th>
<th>Confirmatory test analyte</th>
<th>Confirmatory test cutoff concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana metabolites</td>
<td>50 ng/mL</td>
<td>THCA(^1)</td>
<td>15 ng/mL</td>
</tr>
<tr>
<td>Cocaine metabolites</td>
<td>150 ng/mL</td>
<td>Benzoylecgonine</td>
<td>100 ng/mL</td>
</tr>
<tr>
<td>Opiate metabolites</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Codeine/Morphine(^2)</td>
<td>2000 ng/mL</td>
<td>Codeine</td>
<td>2000 ng/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Morphine</td>
<td>2000 ng/mL</td>
</tr>
<tr>
<td>6-Acetylmorphine</td>
<td>10 ng/mL</td>
<td>6-Acetylmorphine</td>
<td>10 ng/mL</td>
</tr>
<tr>
<td>Phencyclidine</td>
<td>25 ng/mL</td>
<td>Phencyclidine</td>
<td>25 ng/mL</td>
</tr>
<tr>
<td>Amphetamines(^3) AMP/MAMP(^4)</td>
<td>500 ng/mL</td>
<td>Amphetamine</td>
<td>250 ng/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methamphetamine(^5)</td>
<td>250 ng/mL</td>
</tr>
<tr>
<td>MDMA(^6)</td>
<td>500 ng/mL</td>
<td>MDMA</td>
<td>250 ng/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MDA(^7)</td>
<td>250 ng/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MDEA(^8)</td>
<td>250 ng/mL</td>
</tr>
</tbody>
</table>

\(^1\) Delta-9-tetrahydrocannabinol-9-carboxylic acid (THCA).
\(^2\) Morphine is the target analyte for codeine/morphine testing.
\(^3\) Either a single initial test kit or multiple initial test kits may be used provided the single test kit detects each target analyte independently at the specified cutoff.
\(^4\) Methamphetamine is the target analyte for amphetamine/methamphetamine testing.
\(^5\) To be reported as positive for methamphetamine, a specimen must also contain amphetamine at a concentration equal to or greater than 100 ng/mL.
\(^6\) Methylenedioxymethamphetamine (MDMA).
\(^7\) Methylenedioxyamphetamine (MDA).
\(^8\) Methylenedioxyethylamphetamine (MDEA).
Interferences and cross-reactivity

- Interferences could arise from chemicals (matrix effect) and other methods of adulteration/manipulation
- Cross-reactivity to drugs and metabolites
- NACB guideline 85: users of POCT devices need to be aware of any known interferences from drugs or metabolites that could affect result interpretation
POCT device evaluation and method validation

- Comparisons between POCT measurement and result obtained using instrument based immunoassay
- Sensitivity, specificity, efficiency, ease of operation
- Only discordant samples-results were evaluated
- Only trained laboratory personnel included
Use of POCT for detection of DOA

- Clinical settings (ED, visiting nurses, transport vehicles …)
- Non-clinical settings (WDT, prisons, army, police (DRUID), security, at home …)
Alternative matrices

- **Urine is the best established matrix for POCT**
- **If alternative matrices are to be used, the antibodies and cutoffs must be optimized to detect the parent drug or metabolite most abundant in that matrix.**

NACB Guidelines
New technologies

• None of the POCT devices currently available are sufficiently specific to be considered a confirmatory test, with exception of breath-alcohol analyzers.
• Other measuring principles (NIR etc.)
• Oral fluid devices
• Breath analyzers
Oral fluid devices

- Ease to use in real world applications
- Fast
- Significant interest in the field of detecting driving under the influence of drugs
- 2 big studies (ROSITA-ROSITA 2 and DRUID)
- The results from ROSITA 2 study showed that none of the available POCT devices were suitable for DRUID detection.
Amphetamines Detected in Exhaled Breath from Drug Addicts: A New Possible Method for Drugs-of-Abuse Testing

Olof Beck¹,*, Kathinka Leine¹, Göran Palmskog¹, and Johan Franck²

¹Department of Medicine, Section of Clinical Pharmacology and ²Department of Clinical Neuroscience, Division of Psychiatry, Karolinska Institutet, Stockholm, Sweden

**Figure 1.** Outline of the sampling device used to collect exhaled breath samples on a modified silica surface (SPEC DAS cartridge). The subject was able to breath normally during the sampling time. Any expired saliva was trapped in the mask.
Detection of drugs of abuse in exhaled breath using a device for rapid collection: comparison with plasma, urine and self-reporting in 47 drug users

Olof Beck\textsuperscript{1,3}, Niclas Stephanson\textsuperscript{1}, Sören Sandqvist\textsuperscript{1} and Johan Franck\textsuperscript{2}

\textsuperscript{1} Department of Medicine, Section of Clinical Pharmacology, Karolinska Institutet, Stockholm, Sweden
\textsuperscript{2} Department of Clinical Neuroscience, Division of Psychiatry, Karolinska Institutet, Stockholm, Sweden

E-mail: olof.beck@karolinska.se

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Drugs of Abuse (DOA)

• A drug that is taken for nonmedicinal reasons (usually for mind-altering effects);

• Drug abuse can lead to physical and mental damage and (with some substances) dependence and addiction.
Drugs of Abuse

- *Alcohol*
- Amphetamines
- Barbiturates
- Benzodiazepines
- Cannabis
- Cocaine
- Ketamine
- LSD
- Methadone
- Opiates
- Propoxyphene
Designer drugs – new kids in town

- Cannabinoids
- Cathinones
- GHB
- Piperazines
- Bath Salts, K2-Spice…
- “Natural products”
Commonly abused drugs

http://www.drugabuse.gov/publications/media-guide/commonly-abused-drugs
USA - Nearly 23000 ED visits in 2011
New drugs in Europe, 2012


Headline activities in 2012

- 73 new psychoactive substances were officially notified for the first time through the EU Early warning system (EWS) in 2012, up from 49 in 2011, 41 in 2010 and 24 in 2009.

Figure 1: Number of new psychoactive substances notified for the first time to the EWS since May 2005 (22)
Quality assurance

• Quality control varies between manufacturers and suppliers;
• For some (most) POCT devices there is no formal QC, making their analytical precision at best uncertain;
• Lack of formal accrediting organization;
• The accuracy of the devices claimed by the manufacturer will have no external verification or validation against external standards;
Conclusions

• POCT drug testing has grown exponentially in last years
• POCT should be used within a clearly defined framework
• The objective of testing should be clear and benefits and risks recognized
• Important role of laboratory professionals
• Quality issues, maintenance, recordkeeping, and cost/benefit also required consideration

NACB Guidelines POCT 2007 (Chapter 7)
Thank you for your attention!