Discordant Findings and Error Types Observed in Urine Drug Screens: An External Quality Assessment Program Perspective

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BACKGROUND

- Drugs are screened in urine for suspected overdose or compliance with treatment programs.
- Single-use tests based on immunoassay methods are often employed due to their ease of use, quick availability of results, and multi-panel design for common drugs.
- The Institute for Quality Management in Healthcare (IQMH) provides ISO 17043:2010 accredited Proficiency Testing (PT) programs for urine drug screens.
- The limitations of these drug screens were reflected in discordant PT results, which were reviewed for their error types and root causes.

METHODS

- Eighteen surveys distributed between May 2010 and October 2018 were included.
- PT samples consisted of drug-free, single-donor urine supplemented with specific drugs.
- A total of 54 challenges (six per year) were included in the study period.
- Participants’ results were assessed against the reference laboratory, and confirmed by participant consensus. Discordant findings were investigated by the participating laboratory using a standardized report.
- Drugs or drug classes currently assessed in the IQMH DRUG DA proficiency testing survey include:
  - Amphetamine/Methamphetamine Group
  - Benzodiazepines
  - Buprenorphine
  - Cocaine Metabolites
  - Cannabinoid Metabolites
  - Barbiturates
  - Methadone Metabolite
  - Ecstasy (MDMA/MDA)
  - Tricyclic Antidepressants
  - Methamphetamine
  - Methadone
  - Opiates
  - Tricyclic Antidepressants

RESULTS

- Currently, 177 participant laboratories are enrolled within Canada.
- The number of positive drugs per challenge ranged from 1–4, and a total of 111 intended positive drug results were distributed during the study period.
- The error types for 637 discordant findings, as determined by the participants, are shown by category in Figure 1.

- The mean number of discordant findings per positive drug result was 5.9 discordant findings per positive drug result.
- After normalizing for the number of positive challenges, the most frequently misreported drug results were:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Discordant Findings</th>
<th>Positive Drug Results</th>
<th>Discordant Findings per Positive Drug Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methamphetamine</td>
<td>136</td>
<td>11</td>
<td>12.4</td>
</tr>
<tr>
<td>Methadone</td>
<td>69</td>
<td>8</td>
<td>7.6</td>
</tr>
<tr>
<td>Amphetamine(s)</td>
<td>46</td>
<td>10</td>
<td>6.7</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>53</td>
<td>9</td>
<td>5.9</td>
</tr>
</tbody>
</table>

• For the clerical and interpretation categories, the most frequent errors were noted for methamphetamine (19.8%), methadone metabolite (14.2%), and amphetamine(s) (12.2%).

• For the assays that had the most frequent discordances, the following observations were made on the root or contributing causes. Note that amphetamine(s) includes both the individual drug and class of related compounds, which may be distinct tests depending on the kit. Methadone or its metabolite were always distinct tests.

AMPHETAMINE / METHAMPHETAMINE / GROUP

Methodological

- Most kits report a cut-off of 1000 ug/L. However, some differ in the detection limit. While a drug level in the indeterminate range was avoided, sometimes it occurred and led to discordant findings.
- False positive results for amphetamine and/or methamphetamine (not the group) due to cross-reactivity with MDMA or MDA.
- It was important to include in the survey response any comments appended to a patient report to clarify the cross-reacting compounds or preliminary positive results that may require confirmation. The omission of the report comments may result in a discordant finding.

Clerical or Interpretation

- The user should have knowledge of which drugs are detected under the amphetamines group rather than the specific compound (i.e. d-amphetamine or d-methamphetamine).
- Laboratories using an assay for the class of amphetamines should include a comment clarifying that amphetamines give a positive screening result in the presence of methamphetamine, methadone, MDMA, MDA and/or MDEA as indicated by the manufacturer.

METHADONE / METHADONE METABOLITE

Methodological

- Although the methadone package insert indicated that at concentrations 50% above the threshold of 300 ug/L (i.e. at 450 ug/L), 100% accuracy for positive results should be achieved, this was not apparent for one-quarter of the users for certain kits.
- Re-evaluation of results compared to different lot numbers of reagent or a different method gave the expected (positive) result, suggesting lot-to-lot variation in the detection limit and therefore sensitivity.

Clerical or Interpretation

- Results for methadone were also reported under methadone metabolite, which was a separate test in the survey. Laboratories reported a data entry error because they did not test for the metabolite but only for the parent drug.
- The error for a laboratory using LC-MS/MS was a transcription error due to lack of experience in reporting Proficiency Testing results and omission of secondary review.

BARBITURATES

Methodological

- Laboratories with kits that are calibrated based on one specific barbiturate (e.g. secobarbital or butabarbital) may have incorrectly reported a negative result due to differences in cross reactivity to other barbiturates in the PT samples.

CONCLUSIONS

- The errors identified within PT surveys occurred throughout the testing process that potentially impact the reporting and interpretation of patient results.
- Although immunoassay drug screen results are considered preliminary or presumptive, their limitations are not necessarily apparent and known to end users.

Practices implemented by participants:

- By 2013, the majority of laboratories indicated one or more of the following comments on their patient reports:
  - A screening or preliminary test
  - There are possible interferences
  - The manufacturer’s cut-off concentration for a drug or class
  - Caution is indicated if the result does not fit the clinical picture

Reference


• Recommendation on page 364 states: “When immunoasays are used, the laboratory should list the major cross-reacting substances for each drug class when a positive result is reported. It may also be appropriate to indicate in a final report (e.g. in the ‘notes’ section) that a negative urine drug result does not indicate absence of all drugs of abuse.”