Assessing the Uncertainty of Net Weight Measurements throughout the Drug Enforcement Administration (DEA) Laboratory System

Sandra E. Rodriguez-Cruz, Ph.D., ABC-F
DEA Southwest Laboratory
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Disclaimer

- The views expressed during this presentation are those of myself alone and do not represent the view of the Drug Enforcement Administration, the United States Department of Justice or the United States Federal Government.
Outline

• Background
• A system-wide approach to uncertainty
• Assessing uncertainty factors
• How are NW obtained?
• DEA uncertainty calculator
  • Excel-based uncertainty calculator
  • Weighing methods
  • Incorporation into LIMS
• Training
• Most valuable lessons (MVL) learned
Background

• What is net weight (NW)?
  • Only the drug material (no wrapping, containers)
  • Powder, crystalline, liquid, plant, etc.
• Importance of NW:
  • Sentencing levels
  • State statutes
• Importance of NW uncertainty:
  • Transparency
  • Quality of result
  • Exculpatory information
Background

• ISO 17025 (2005):
  • 5.4.6.2 Testing laboratories shall have and shall apply procedures for estimating uncertainty of measurement.

• 2007:
  • Purity uncertainty included in reports

• 2009:
  • NW uncertainty included in reports
  • Revision of purity uncertainty budget
  • Amount pure substance uncertainty added

• 2014:
  • First re-assessment of uncertainty factors
A System Approach

- 8 laboratories
- > 270 analysts
- > 300 balances
- Different balance types

To Assess Variability Across:

- Laboratories
- Environments
- Operators
- Balances
Uncertainty Assessment

• Balance calibrations (annual):
  • By external provider
  • 0.1 g thru 0.00001 g readability
  • Linearity, sensitivity, repeatability, etc.
  • Short-term variability

• Performance verification procedures:
  • Monthly checks (accuracy, repeatability, etc.)
  • Different laboratories
  • Different operators
  • Different reference weights
  • Long-term variability (1-yr data)
System-wide $u_{mass}$ values

- Combination of all uncertainty factors
- Per balance type:

<table>
<thead>
<tr>
<th>Readability (g):</th>
<th>$u_{mass}$ (g):</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00001</td>
<td>0.0002179</td>
</tr>
<tr>
<td>0.0001</td>
<td>0.0003689</td>
</tr>
<tr>
<td>0.001</td>
<td>0.002823</td>
</tr>
<tr>
<td>0.01</td>
<td>0.04581</td>
</tr>
<tr>
<td>0.1</td>
<td>0.2488</td>
</tr>
</tbody>
</table>

$$u_{mass} = \sqrt{u_{bal}^2 + u_{process}^2}$$
How are NW Obtained?

- Direct measurements
- Extrapolations
- Combinations
- Dosage Units
- Liquids
How are NW Obtained?

- Direct measurements:
How are NW Obtained?

• Extrapolations:
How are NW Obtained?

- **Combinations:**
  - Direct + extrapolation
  - Sub-groups

- **Dosage Units:**
  - NW Weight $\rightarrow$ Counts
  - Average dosage weight

- **Liquids:**
  - NW Weight $\rightarrow$ Volume
  - Density
NW Policy & Procedures

• Standardization

• Minimum weight thresholds:

  To ensure (95% level of confidence) that the relative uncertainty associated with the balance used is no greater than 1% of the weight measurement recorded.

• Ensure appropriate balance use
NW Policy & Procedures

• Less than 10 units:
  • Direct weighing

• 10 or more units:
  • Direct weighing OR extrapolation
  • Extrapolation:
    • Weigh 9 individual units (RSD < 10%)

• Extrapolation:
  • Contents
  • Containers
### DEA Uncertainty Calculator (2009-2016)

**A. Direct Net Weight and Uncertainty:**

<table>
<thead>
<tr>
<th>Balance Readability (g)</th>
<th>No. of Weighing Events</th>
<th>u(mass): (g)</th>
<th>u(w): (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.000001</td>
<td>10</td>
<td>0.0002179</td>
<td>0.0000000</td>
</tr>
<tr>
<td>0.001</td>
<td>10</td>
<td>0.0006818</td>
<td>0.0000000</td>
</tr>
<tr>
<td>0.1</td>
<td>10</td>
<td>0.045110</td>
<td>0.0000000</td>
</tr>
<tr>
<td>0.1</td>
<td>18</td>
<td>0.2481</td>
<td>0.0000000</td>
</tr>
</tbody>
</table>

**Net Weight (g):** 44.39

**Net Weight Results (k=2):**

- Net weight: 44.39 ± 0.0162 g
- Relative U(%): 0.37

**B. Purity and Amount of Pure Drug Uncertainty (k=2):**

<table>
<thead>
<tr>
<th>Purity (%)</th>
<th>Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

### Extrapolated Net Weight and Uncertainty:

**Extrapolated Net Weight:** 45.6000 g

**Net Weight Results (k=2.306):**

- Avg. NW/Unit (g): 440.689 ± 0.6519 g
- Net weight: 4555.9556 ± 111.26231 g
- Relative U(%): 0.44

### Contents Extrapolation (page 1 of 1)

Uncertainty Calculator (July 2014)
DEA Uncertainty Calculator (2009)

- Validated
- Case identifiers
- All weight measurements
- Minimum weight thresholds
- Uncertainty factors
- Calculate & combine uncertainties
- Expand & round final uncertainty
- Acceptance criteria (%RSD, relative U)
- Truncate final NW
Weighing Methods (2011)

• Standardized balance methods
• No data typing by analysts
• Macros:
  • Balance raw data → Uncertainty Calculator
DEA Uncertainty Calculator (2016)

- Incorporated into LIMS
DEA Uncertainty Calculator Worksheet

Extrapolated Net Weight (Uniform Contents)

Chemist: LIMS #: Laboratory: Mid-Atlantic
Date: 10/21/2015 5:43:04PM  Ordno: 1188  Lab Exhibit #: SR Direct 5

Number of Units in Exhibit: 59

Individual Weight Measurements

<table>
<thead>
<tr>
<th>TaskID</th>
<th>Weight (Full) (g)</th>
<th>Weight (Empty) (g)</th>
<th>Weight (Net) (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T54526</td>
<td>454.0</td>
<td>14.6</td>
<td>439.4</td>
</tr>
<tr>
<td>T54526</td>
<td>455.5</td>
<td>13.7</td>
<td>441.8</td>
</tr>
<tr>
<td>T54526</td>
<td>453.4</td>
<td>13.7</td>
<td>439.7</td>
</tr>
<tr>
<td>T54526</td>
<td>451.5</td>
<td>14.5</td>
<td>437.0</td>
</tr>
<tr>
<td>T54526</td>
<td>457.3</td>
<td>14.8</td>
<td>443.0</td>
</tr>
<tr>
<td>T54528</td>
<td>458.1</td>
<td>14.8</td>
<td>443.3</td>
</tr>
<tr>
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<td>438.9</td>
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<tr>
<td>T54528</td>
<td>454.1</td>
<td>14.9</td>
<td>439.2</td>
</tr>
<tr>
<td>T54528</td>
<td>458.7</td>
<td>14.8</td>
<td>443.9</td>
</tr>
</tbody>
</table>

Uncertainty Factors

Balance (g)  u(mass) (g)
0.1  0.2488

Weight Statistics

<table>
<thead>
<tr>
<th>Avg. NW/Unit (g)</th>
<th>STDEV (g)</th>
<th>% RSD</th>
<th>u(avg) (g)</th>
<th>u(unit) (g)</th>
<th>Extrapolated u(unit) (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>440.63389</td>
<td>2.381</td>
<td>0.54</td>
<td>0.79380</td>
<td>0.8319</td>
<td>48.2491</td>
</tr>
</tbody>
</table>

Net Weight Results (t = 2.306)

| Avg. NW/Unit (g) | 440.63389 +/- 0.8319 |
| Net Weight:      | 25.5600 +/- 1113 g   |
| Reported Values: | 25.5 +/- 0.1 kg      |
Training: DEA Analysts

- Prior to implementation
- Refreshers
- Integration into LIMS
- BFC Classes (Quantico, VA)
- Court testimony

Training: Others

- Case agents
- Attorneys
- Triers of facts
Most Valuable Lessons (MVL) Learned

- Good weighing practices
- Minimum weight thresholds
- External calibration providers
- Performance verification procedures
- Standardization across laboratories
- Awareness of variability of drug samples between laboratories
- Awareness of uncertainty effects
- Adaptability
- Training
Summary

• NW procedures
• Assessment of NW uncertainty factors
• Policy implementation
  • Standardization of weighing procedures
  • Automation of data analysis
    • Excel-based uncertainty calculator
    • Balance weighing methods
    • Incorporation into LIMS
• Training
• Lessons learned
Thank you!

Questions?

sandra.e.rodriguez-cruz@usdoj.gov