

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

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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:

| Readability (g): | $u_{mass}$ (g): |
|------------------|-----------------|
| 0.00001          | 0.0002179       |
| 0.0001           | 0.0003689       |
| 0.001            | 0.002823        |
| 0.01             | 0.04581         |
| 0.1              | 0.2488          |

$$u_{mass} = \sqrt{u_{bal}^2 + u_{process}^2}$$



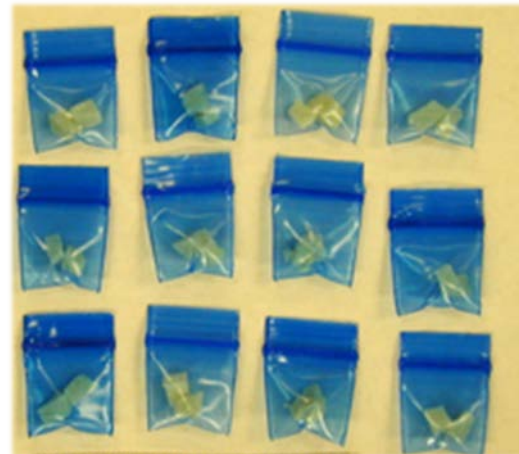
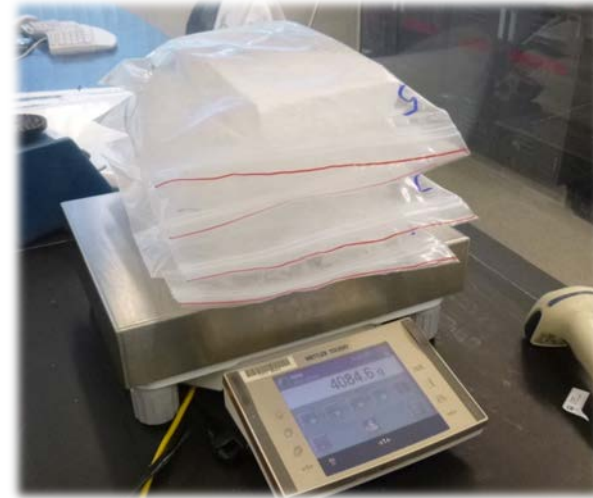
# How are NW Obtained?

- Direct measurements
- Extrapolations
- Combinations
- Dosage Units
- Liquids



# How are NW Obtained?

- Direct measurements:



# How are NW Obtained?

- Extrapolations:



30



650



# 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)

- 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



Chemist: Corbin Case # Ex. #  
Date: 9/1/16 Laboratory # Quant ID#  
Weight ID# W-1186  
For Direct Weighing Cases Only (no extrapolation):

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

| Enter direct weights measured                |   | Enter the No. of weighing events for each balance used |                        |   |   |
|--|---|--|------------------------|---|---|
|  | (g)                                       | Balance readability (g)                                | No. of weighing events | u(mass) (g)   | u(w) (g)  |
| Direct weighing of all full containers: (g)  | 18.24<br>16.16<br>15.84<br>13.06<br>12.82 |  |                        | 0.0002179<br>0.0003619<br>0.0003619<br>0.0003619<br>0.0003619 | 0.0000000<br>0.0000000<br>0.0000000<br>0.0000000<br>0.0000000 |
| Direct weighing of all empty containers: (g) | 6.02<br>5.90<br>5.98<br>5.82<br>5.91      |  | 10                     | 0.04581   | 0.45810   |
|  |   |  |                        | 0.2488  | 0.0000  |
|  |   |  |                        |   | 0.45810   |
|  |   |  |                        |   | 0.45810   |
| Net weight (g):                              | 44.39                                     |  |                        |   | 0.91620   |

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

|             |       |   |        |   |               |
|-------------|-------|---|--------|---|---------------|
| Net weight: | 44.39 | ± | 0.9162 | g | Relative (1%) |
| Report:     | 44.3  | ± | 0.9    | g | 2.0%          |

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

| Enter purity (%)     |     | For dosage units:                          |     |
|----------------------|-----|--|-----|
| Purity               | %   | Enter total number of dosage units counted |     |
| Report:              | N/A | ±  | N/A |
| Amount of pure drug: | N/A | ±  | N/A |
| Report:              | N/A | ±  | N/A |

Uncertainty Calculator (July 2014) Direct Weighing (page 1 of 1)

# DEA Uncertainty Calculator (2016)

- Incorporated into LIMS

Uncertainty Calculator

### Exhibit Weight and Uncertainty

LabX Weight Events (Methods)

Ad Hoc Event Remove Event Worksheet

| Task ID | Method      | File Name               | File Date          |
|---------|-------------|-------------------------|--------------------|
| TS4528  | Contents... | W-1188-TS4528-Conten... | 10/21/2015 2:32:07 |

Weights

Add Weight Remove Weight

| Weight(Full) | Weight(Empty) | Net Weight |
|--------------|---------------|------------|
| 454.0        | 14.6          | 439.4      |
| 455.5        | 13.7          | 441.8      |
| 453.4        | 13.7          | 439.7      |
| 451.5        | 14.5          | 437        |
| 457.8        | 14.8          | 443        |
| 458.1        | 14.8          | 443.3      |
| 453.7        | 14.8          | 438.9      |
| 454.1        | 14.9          | 439.2      |
| 458.7        | 14.8          | 443.9      |

Enter the Number of Units

No. Units: 58

#### Weight Statistics

| % RSD | STDEV   | u(avg)  | u(unit) | Extrapolated u(unit) |
|-------|---------|---------|---------|----------------------|
| 0.54  | 2.38141 | 0.79380 | 0.83188 | 48.24906             |

#### Uncertainty Factors

| Balance Readability | # of Events | u(mass) (g) | u(w)(g) |
|---------------------|-------------|-------------|---------|
| 0.1                 | 18          | 0.24880000  | 4.4784  |

#### Net Weight Results (t=2.306)

|                   |             |     |           |             |      |
|-------------------|-------------|-----|-----------|-------------|------|
| Avg. NW/Unit (g): | 440.68889   | +/- | 0.83188   | Relative U% |      |
| Net weight:       | 25559.95556 | +/- | 111.26233 |             | 0.00 |
| Report:           | 25.5        | +/- | 0.1       |             | kg   |

# DEA Uncertainty Calculator (2016)

## DEA Uncertainty Calculator Worksheet

### *Extrapolated Net Weight(Uniform Contents)*

|          |                      |                |              |
|----------|----------------------|----------------|--------------|
| Chemist: |                      | LIMS #:        |              |
| Date:    | 10/21/2015 5:43:04PM | Laboratory:    | Mid-Atlantic |
| Ordno:   | 1188                 | Lab Exhibit #: | SR Direct5   |

Number of Units in Exhibit: 58

### *Individual Weight Measurements*

| TaskID | Weight (Full) (g) | Weight (Empty) (g) | Weight (Net) (g) |
|--------|-------------------|--------------------|------------------|
| T54528 | 454.0             | 14.6               | 439.4            |
| T54528 | 455.5             | 13.7               | 441.8            |
| T54528 | 453.4             | 13.7               | 439.7            |
| T54528 | 451.5             | 14.5               | 437.0            |
| T54528 | 457.8             | 14.8               | 443.0            |
| T54528 | 458.1             | 14.8               | 443.3            |
| T54528 | 453.7             | 14.8               | 438.9            |
| T54528 | 454.1             | 14.9               | 439.2            |
| T54528 | 458.7             | 14.8               | 443.9            |

### *Uncertainty Factors*

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

### *Weight Statistics*

| Avg. NW/Unit (g) | STDEV (g) | % RSD | u(avg) (g) | u(unit) (g) | Extrapolated u(unit) (g) |
|------------------|-----------|-------|------------|-------------|--------------------------|
| 440.68889        | 2.381     | 0.54  | 0.79380    | 0.8319      | 48.2491                  |

### *Net Weight Results (t = 2.306)*

|                   |           |     |         |
|-------------------|-----------|-----|---------|
| Avg. NW/Unit (g): | 440.68889 | +/- | 0.83188 |
| Net Weight:       | 25,560.0  | +/- | 111.3 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?

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