Proficiency Testing Programmes by Health Sciences Authority Singapore, with assigned values determined by a reference method

9th EURACHEM PT Workshop
Portorož, Slovenia, 9-12 Oct 2017

Cheow Pui Sze
Senior Scientist
Chemical Metrology Laboratory
Applied Sciences Group
Health Sciences Authority, Singapore

Outline

• Overview of HSA Chemical Metrology Laboratory

• Overview of HSA Chemical Metrology Laboratory’s PT/EQA Programmes

• Benefits of Participating in a PT Programme – deriving the assigned value from a reference method

• Performance of the Participating Laboratories
About the HSA Chemical Metrology Laboratory

HSA is a Designated Institute responsible for developing the chemical metrology programme to enhance the accuracy of chemical measurements in Singapore. Our areas of focus are healthcare, food, pharmaceuticals & health products.

The HSA Chemical Metrology Laboratory

- **Quality system**
  - ISO/IEC 17025 & ISO Guide 34 - The Lab was assessed by Singapore Accreditation Council (SAC) and peer reviewed by a team of experts from the international chemical metrology community.
  - ISO/IEC 17043 - The Lab is accredited by SAC as a PT Provider since August 2013.

- **Chemical metrology activities**
  - Since 2008, the laboratory participates actively in regional & international chemical metrology activities, including over 40 relevant regional & international comparisons.
  - HSA is a full member of the Asia Pacific Metrology Programme (APMP) since 2008.
  - HSA is also a member of the Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM).
The HSA Chemical Metrology Laboratory

- **Laboratory facilities**
  - The laboratory is housed in a cleanroom with a rating of ISO Class 7.
  - A special “metal free” section was created in the laboratory for inorganic analysis.
  - The laboratory has a wide array of instruments to support its measurement activities.

HSA's PT/EQA Programmes

In the HSA PT/EQA programmes, the assigned values are independently determined by Chemical Metrology Laboratory (CML) and are **traceable to the International System of Units (SI)**.

Each assigned value has an associated measurement uncertainty, estimated after rigorous investigation of all possible sources of uncertainties\(^1,2\).

**Objective**

Enables participating labs to assess the **COMPARABILITY** and **ACCURACY** of their test results

---


\(^2\)Eurachem Guide on Quantifying Uncertainty in Analytical Measurement
HSA PT Programmes For Chemical Testing Labs (2011-2017)

Additives in Food
- Benzoic acid in orange juice (2011)
- Benzoic acid, methyl paraben & n-butyl paraben in soy sauce (2013)
- Saccharin & sodium cyclamate in fruit juice (2015)
- Acesulfame potassium & sucralose in cake mix flour (2016) – APLAC PT Co-organised with SAC
- Preservatives in food sauce (2018)

Elements in Food/Beverage
- Arsenic, calcium, cadmium & lead in mushroom powder (2012)
- Lead in alcoholic beverage (2014)
- Toxic and Essential Elements in brown rice flour (2017)

Elements in Water
- Calcium, cadmium, lead & nickel in drinking water (2011)
- Arsenic, chromium, copper and molybdenum in drinking water (2014)
- Aluminium, calcium, cadmium, lead, nickel, arsenic, chromium, copper and molybdenum in drinking water (2016)

Elements in Cosmetics
- As, Pb & Hg in cosmetic cream (2015)
- Toxic elements in lipstick (2018)

Others
- Oil & grease in water (2016)
- Trihalomethanes in water (2017)

Advantages of HSA's PT Programmes

- Survey and gap analysis are conducted regularly to establish the needs for testing laboratories and to ensure relevancy to local needs.

- To ensure comparability of results, in some of the PT programmes like preservatives in soy sauce and artificial sweeteners in fruit juice, high purity reference standards were also offered to the participating laboratories for use as calibration standards.

- Forum discussion sessions are organised at the end of the PT programmes to provide feedback and recommendations to improve the performance of the participating laboratories.
Underpinning Measurement Capabilities – Participating in International Comparisons

Purity Assessment of Organic Compounds & Peptides

01 CCQM-K55.b: Characterisation of organic substances for chemical purity - aldrin

02 CCQM-K55.c: Characterisation of organic substances for chemical purity - L-valine

03 CCQM-K55.d: Characterisation of organic substances for chemical purity - folic acid

Additives, Contaminants & Elements in Food/Water

01 CCQM-K124: Trace elements in drinking water

02 APMP.QM-S8: Benzoic acid, methyl paraben and n-butyl paraben in soy sauce

03 CCQM-K108: Total arsenic and arsenic species in brown rice flour

04 CCQM-K95.1 Polycyclic aromatic hydrocarbon in tea
Underpinning Measurement Capabilities – Participating in International Comparisons

Clinical Chemistry

01 CCQM-K107: Elements in human serum
02 CCQM-K6.2: Total cholesterol in human serum
03 CCQM-K12.2: Creatinine in human serum
04 CCQM-K109: Urea and uric acid in human serum

HSA EQA Programme for Clinical Labs

An accuracy-based EQA Programme (organised since 2011), where assigned values are independently determined by CML.

In human sera
1. Creatinine
2. Glucose
3. Total cholesterol
4. Triglycerides
5. Urea
6. Uric acid
7. Calcium
8. Sodium
9. Potassium
10. Magnesium
11. Iron
12. Chloride
13. Low-density lipoprotein cholesterol (LDL)
14. High-density lipoprotein cholesterol (HDL)

In human blood
Glycated haemoglobin (HbA1c)

In urine
1. Creatinine
2. Albumin
How are Assigned Values Determined by HSA CML?

In HSA CML, high accuracy gravimetric and/or isotope dilution mass spectrometric (IDMS) methods are used, whenever possible.

Evaluation of Participating Laboratories’ Results

\[
z = \frac{x_i - x_{pt}}{\sigma_{pt}}
\]

- \(x_i\) is the participating laboratory’s result
- \(x_{pt}\) is the assigned value determined by CML
- \(\sigma_{pt}\) is the standard deviation for proficiency assessment

- \(|z| \leq 2.0\) “satisfactory” result
- \(2.0 < |z| < 3.0\) “questionable” result
- \(|z| \geq 3.0\) “unsatisfactory” result

\[
\zeta = \frac{x_i - x_{pt}}{\sqrt{u_i^2(x_i) + u^2(x_{pt})}}
\]

- \(x_i\) is the participating laboratory’s result
- \(x_{pt}\) is the assigned value determined by CML
- \(u_i(x_i)\) is the standard uncertainty reported by the participating laboratory
- \(u(x_{pt})\) is the standard uncertainty of the assigned value \(x_{pt}\)

- \(|\zeta| \leq 2.0\) “satisfactory” result
- \(2.0 < |\zeta| < 3.0\) “questionable” result
- \(|\zeta| \geq 3.0\) “unsatisfactory” result
Benefits of Participating in a PT Programme – deriving the assigned value from a reference method

STY-0026A Preservatives in Soy Sauce (2013)

**Benzoic acid**

Results were wrongly evaluated if arithmetic mean was used

<table>
<thead>
<tr>
<th>Laboratory Code</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>-3.2</td>
</tr>
<tr>
<td>18</td>
<td>-2.1</td>
</tr>
<tr>
<td>25</td>
<td>-1.0</td>
</tr>
<tr>
<td>26</td>
<td>0.0</td>
</tr>
<tr>
<td>28</td>
<td>1.0</td>
</tr>
<tr>
<td>33</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Assigned value = 871 mg/kg
Arithmetic mean = 905 mg/kg

**Methyl paraben**

Result was wrongly evaluated if arithmetic mean was used

<table>
<thead>
<tr>
<th>Laboratory Code</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>-4.5</td>
</tr>
<tr>
<td>18</td>
<td>-3.4</td>
</tr>
<tr>
<td>25</td>
<td>-2.3</td>
</tr>
<tr>
<td>26</td>
<td>-1.2</td>
</tr>
<tr>
<td>28</td>
<td>0.0</td>
</tr>
<tr>
<td>33</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Assigned value = 238 mg/kg
Arithmetic mean = 266 mg/kg
Benefits of Participating in a PT Programme – deriving the assigned value from a reference method

STY-0026A Preservatives in Soy Sauce (2013)

n-Butyl paraben

Results were wrongly evaluated if arithmetic mean was used

Assigned value = 93.7 mg/kg
Arithmetic mean = 102.1 mg/kg

z-Scores for n-butyl paraben evaluated by assigned values from CML (colour-filled columns) and robust means from participating laboratories’ results (horizontal stripe columns).

Performance of the Participating Laboratories

Distribution of z-scores (2011-2016)

Number of laboratories achieved satisfactory z-scores from Year 2011 to 2016.
Performance of the Participating Laboratories

Distribution of $\zeta$-scores (2011-2016)

- In the past PT Programmes, about 90% of the participating laboratories reported their measurement uncertainties.

![Bar chart showing distribution of $\zeta$-scores from 2011 to 2016]

CRMs for Continuous Monitoring of Quality of Testing

- Test and characterise material in accordance with ISO/IEC 17043 and ISO 13528
- Characterise material and perform stability monitoring in accordance with ISO 17034 and ISO Guide 35
Our Certified Reference Materials

We Provide
- Pure substance CRMs as Calibrants
- Matrix CRMs for Quality Controls and Methods Validation

High Purity Substances
- HRM-1002A: Benzoic Acid
- HRM-1003A: Methyl Paraben
- HRM-1004A: n-Butyl Paraben
- HRM-1018A: Sorbic Acid
- HRM-1005A: L-Valine
- HRM-1006A: L-Leucine
- HRM-1013A: L-Lysine
- HRM-1014A: L-Phenylalanine
- HRM-1016A: L-Proline
- HRM-1007A: L-Isoleucine
- HRM-1008A: L-Leucine
- HRM-1009A: L-Leucine
- HRM-1010A: L-Leucine
- HRM-1011A: L-Leucine
- HRM-1012A: L-Leucine
- HRM-1013A: L-Leucine
- HRM-1014A: L-Leucine
- HRM-1015A: L-Leucine
- HRM-1016A: L-Leucine

Clinical Chemistry
- HRM-2002A: Ca, K & Na in Human Serum
- HRM-2005A: Ca, K, Na, Mg, Fe & Cl in Human Serum
- HRM-2011A: Na, Cl, Cu, Se & P in Human Serum
- HRM-3002A: Creatinine, Glucose, Total Cholesterol, Total Glycerides, Urea & Uric Acid in Human Serum
- HRM-3002B: Creatinine, glucose, total cholesterol, HDL-cholesterol, total glycerides, urea & uric acid in Human Serum
- HRM-3003A: Glycated haemoglobin A1c (HbA1c) in Human Blood
- HRM-3003B: Glycated haemoglobin A1c (HbA1c) in Human Blood

Food & Others
- HRM-1005A: Benzoic Acid, Methyl Paraben & n-Butyl Paraben in Soy Sauce
- HRM-2003A: As, Cd, Ca & Pb in Mushroom Powder
- HRM-2006A: Pb, As & Hg in Cosmetic Cream
- HRM-2008A: Cd, Pb, Total As and As species in apple juice
- HRM-2009A: Cd, Pb, Total As and As species in apple juice
- HRM-3002A: Creatinine, Glucose, Total Cholesterol, Total Glycerides, Urea & Uric Acid in Human Serum
- HRM-3002B: Creatinine, glucose, total cholesterol, HDL-cholesterol, total glycerides, urea & uric acid in Human Serum

Values of HSA's PT Programmes

- Provides an objective evaluation of the performance of a participating laboratory
- Serves as a platform for participating laboratory to gauge the comparability of its results with other laboratories
- Complements commercial programmes, enabling participating laboratories to assess the accuracy and comparability of their test results by viewing the deviation from the "true value"
- Allows participating laboratories to monitor the consistency of their test results
For More Information

For enquiries concerning PT programme: HSA_CMLPT@hsa.gov.sg

Thank you

E-mail: Cheow_Pui_Sze@hsa.gov.sg