TRACEABILITY IN EXTERNAL QUALITY ASSESSMENT

HOW WE ENSURE TRACEABILITY IN EQA AND STRESS ITS IMPORTANCE TO USERS

PROGBA (BUENOS AIRES EXTERNAL QUALITY ASSESSMENT SCHEME)
CEMIC UNIVERSITY HOSPITAL
BUENOS AIRES - ARGENTINA

SILVIA QUIROGA (PROGBA)
BUENOS AIRES EXTERNAL QUALITY ASSESSMENT SCHEME

- EQAS services since 1979
- EQA scheme accreditation ISO/IEC 17043:2010, since 2011
- Sample preparation certification, ISO 9001:2008 since 2008
- Home made freeze-dried samples from human origin
- 840 participants from Argentina, Colombia, Ecuador, Perú, Chile, Belgium, Uruguay, Spain, El Salvador, Guatemala, Bolivia
- ProgBA was supported at its beginning by the Special Programme in Human Reproduction from World Health Organisation (WHO – HRP) and the International Atomic Energy Agency (IAEA) through Arcal VIII Project.
- Now supported by CEMIC and participants´fee.
BUENOS AIRES
EXTERNAL QUALITY ASSESSMENT SCHEME

EQAS services
- Courses, seminars and workshops in Latin American countries (Argentina, Mexico, Brazil, Peru, Paraguay and Uruguay)
- Training of fellows from peer hospitals
HOME MADE SAMPLES OF HUMAN ORIGIN
• **Immunoassays**: Growth, Thyroid, Reproductive, Steroid Hormones. Tumor Markers
  Antithyroid Antibodies – Bone markers - Proteins
• **Clinical chemistry**
  Chemistry - Enzymes - Electrolytes
• **Serology**
  Blood Transmitted Diseases –TORCH
• **Newborn screening**
  Hypothyroidism and Metabolic Diseases
• **Glycated haemoglobin**
  HbA1c
• **Coagulation**
  In collaboration with ECAT foundation’s EQAS
HOW WE ENSURE TRACEABILITY

• THE TSH EXAMPLE

• THE PTH EXAMPLE
WHO 2nd IRP (80/558)
In Human serum

ProgBA round XXXI. Sept. 2017

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>MEAN</th>
<th>CV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABBOTT</td>
<td>113</td>
<td>5.65</td>
<td>5.18</td>
</tr>
<tr>
<td>ACCESS</td>
<td>31</td>
<td>5.52</td>
<td>9.77</td>
</tr>
<tr>
<td>CENTAUR</td>
<td>59</td>
<td>5.93</td>
<td>7.37</td>
</tr>
<tr>
<td>IMMULITE</td>
<td>136</td>
<td>5.50</td>
<td>10.25</td>
</tr>
<tr>
<td>ROCHE</td>
<td>325</td>
<td>5.40</td>
<td>5.75</td>
</tr>
</tbody>
</table>

TSH – pool 4
9. COLLABORATIVE STUDY

The candidate pituitary TSH preparation 81/565, along with other pituitary TSH preparations, was evaluated in an international collaborative study in which nine laboratories in six countries took part. Assays contributed were all immunoassays except for a single in vitro assay based on cAMP release from bovine thyroid membranes. The study was designed to:
- compare by immunoassay the ampouled preparations of TSH with local standards presently in use,
- confirm the calibration of the candidate preparation of TSH for use as a potential International Standard,
- confirm the activity of the candidate preparation relative to the original study preparations,
- assess the stability of the candidate preparation using thermally accelerated degradation samples,
- compare rDNA TSH and pituitary TSH in a variety of immunoassay systems.

9.1 Activity of ampoule contents

The main function of preparation 81/565 is to serve as a primary reference reagent against which secondary standards for immunoassay of TSH are calibrated. On the basis of the immunoassay results from the collaborative study, 81/565 was established by the ECBS of WHO as the 3rd International Standard for TSH, Human, for Immunoassay with a defined content of 11.5 mIU per ampoule. This preparation replaces the 2nd IRP for TSH, 80/558. All attempts have been made to ensure the continuity of the unit as evidenced by the results from the majority of assay systems in the study. However, this cannot be guaranteed for all assay systems and recalibration may be necessary.
SO FOR TSH...

- Traceability is possible because:
  - All assays are calibrated against the same IRP (80/558)
  - The measurand is stable in serum, and keeps the main structure of the pituitary hormone, with which all antibodies are assumed to be raised.
### PTH Standards

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Assay Code</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABBOTT</td>
<td>79/500</td>
<td></td>
</tr>
<tr>
<td>CENTAUR</td>
<td>79/500</td>
<td>73% mean WHO standard recovery in the assay whole range</td>
</tr>
<tr>
<td>ROCHE</td>
<td>95/646</td>
<td></td>
</tr>
<tr>
<td>IMMULITE</td>
<td></td>
<td>Assay is traceable to an internal standard manufactured using qualified materials and measurement procedures</td>
</tr>
<tr>
<td>LIAISON</td>
<td></td>
<td>standarized /calibrated with Bachem PTH</td>
</tr>
</tbody>
</table>

Information provided by manufacturers inserts
<table>
<thead>
<tr>
<th></th>
<th>CAPTURE Ab</th>
<th>SIGNAL Ab</th>
<th>hPTH CROSS REACTIVITY %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABBOTT</td>
<td>No details provided</td>
<td></td>
<td>0 % to 1-34, 39-68, 53-84, 44-68, 39-84 fragments</td>
</tr>
<tr>
<td>CENTAUR Intact</td>
<td>Biotynilated goat polyclonal Ab</td>
<td>Acridinium labelled goat polyclonal Ab</td>
<td>0.74 % 1–34; 0.005 39–68; 0.024% 39–84; 0.007 44–68; 0.003% 53–84 fragments; 0.0004 % Calcitonin</td>
</tr>
<tr>
<td></td>
<td>PTH 39–84</td>
<td>PTH 1–34</td>
<td></td>
</tr>
<tr>
<td>IMMULITE</td>
<td>murine monoclonal Ab</td>
<td>goat polyclonal Ab</td>
<td>ND: 1-34; 1-44; 44-68; 53-84; Calcitonin 48.3 % to 7-84 fragment</td>
</tr>
<tr>
<td></td>
<td>PTH 44-84</td>
<td>PTH 1-34</td>
<td></td>
</tr>
<tr>
<td>LIAISON N-TACT</td>
<td>Solid phase Ab</td>
<td>Isoluminol Ab</td>
<td>0.1% hPTH: 39-84; 53-84; 39-68; 44-68; 1-34; 13-34 fragments; 52%: 7-84; 100% 1-84 fragments</td>
</tr>
<tr>
<td></td>
<td>PTH 39-84</td>
<td>PTH 1-34</td>
<td></td>
</tr>
<tr>
<td>ROCHE</td>
<td>Biotinilated Ab</td>
<td>Ruttenium labeled Ab</td>
<td>0 % to osteocalcin; 1-37 fragment, protein associated to PTH 1-86, Alcaline phosphatase bone-specific, β-CrossLaps.</td>
</tr>
<tr>
<td></td>
<td>PTH 1-37</td>
<td>PTH 38-84</td>
<td></td>
</tr>
</tbody>
</table>

*Information provided by manufacturers inserts*
<table>
<thead>
<tr>
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<th>CAPTURE Ab</th>
<th>SIGNAL Ab</th>
<th>hPTH CROSS REACTIVITY %</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIAISON 1-84</td>
<td>Solid phase purified polyclonal goat antibodies for capture with C-terminal specificity</td>
<td>Isoluminol detection with extreme N-terminal specificity</td>
<td>0% cross reactivity to 7-84 ; 1-34; 13-34; 39-68 ; 44-68; 39-84; 53-84</td>
</tr>
<tr>
<td>ROCHE 1-84</td>
<td>Biotinilated Monoclonal Ab Reacts N-terminal 1-37</td>
<td>Rutenium labeled Monoclonal Ab Reacts C-terminal 38-84</td>
<td>≤ 0.1 %: Osteocalcina, β-CrossLaps and Alcaline phosphatase bone-specific ≤ 0.1 %: PTH 1-34, PTH 7-84 by epitope analysis no cross reactivity with N-terminal PTH related peptide, PTH-Rp in the N-terminal fragment</td>
</tr>
</tbody>
</table>

*Information provided by manufacturers inserts*
SO FOR PTH...

• Traceability is difficult to demonstrate because:
  • Reagents are calibrated against different preparations, not all of them certified standards
  • Antibodies in the immunoassays designs recognize different fragments, active or not
  • EQAS show method differences
STRESS ITS IMPORTANCE TO USERS
TRACEABILITY, PRESENTATIONS IN CONGRESSES AND WORKSHOPS

• IX Congreso Argentino de Calidad en el Laboratorio Clínico CALILAB. Symposium Traceability in Clinical Chemistry. November 30th, 2016
  • The JCTLM: Its implication on patient safety by improving laboratory results. Silvia Quiroga. Marta Torres

• XXIII Congreso Latinoamericano de Bioquímica Clínica 2017 (COLABIOCLI). Symposium: Trazabilidad en el laboratorio clínico: qué es y cuál es su importancia. On behalf of JCTLM. Punta del Este, Uruguay September 14th, 2017
  • Biological Standardization in Laboratory Medicine: Influencing Quality of the Patient care. Jean-Claude Forest
  • Traceability and Harmonization: a powerful tool for laboratory results trueness. Marta Torres
  • Traceability in Clinical Laboratory: what each laboratorist should know. Silvia Quiroga

Information provided by manufacturers inserts
Workshop Final Report XXXI Round EQAS ProgBA participants, Buenos Aires November 24th, 2017
Traceability in laboratory medicine: a global driver for accurate results for patient care. Beastall GH, Brouwer N, Quiroga S, Myers GL; prepared on behalf of the Joint Committee for Traceability in Laboratory Medicine.

Spanish translation, Marta Torres and Silvia Quiroga
BUENOS AIRES EQAS

• DIRECTOR: Marta Torres
• Silvia Quiroga
• Margarita Porta
• Lorena Del Vechio
• Zulema Farinati
• Carlos Nagle
• Cristina Videla
• Veronica Montero
• Karina Castiñeira
• Karina delli Carpini
• Graciela González
• Guillermo Gette

Hospital Universitario Sede Saavedra
Buenos Aires - Argentina