Peer-Review process to improve the Quality of Linguistic Validation Process of COAs Instruments for Clinical Trials

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- The author and collaborators report conflicts of interests as were Cogstate employees at the time of the analysis.
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1. Challenges of Linguistic Validation (LV) Process

Type of COAs and Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Name</th>
<th>Reporter</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRO</td>
<td>Patient Reported Outcome</td>
<td>Patient</td>
<td>Scales, Inventories, etc..</td>
</tr>
<tr>
<td>ClinRO</td>
<td>Clinician Reported Outcome</td>
<td>Clinician</td>
<td>Assessment Scales, Interviews</td>
</tr>
<tr>
<td>ProxyRO</td>
<td>Proxy Reported Outcome</td>
<td>Relatives, Caregiver</td>
<td>Scales, Interviews</td>
</tr>
<tr>
<td>PerfRO</td>
<td>Performance Reported Outcome</td>
<td>Clinician</td>
<td>Cognitive Testing (paper&amp;pencil, computerized)</td>
</tr>
</tbody>
</table>
1. Challenges for LV

- Time Pressure
- Budget Limitations
- Availability of Local Experts
- Availability of Concept List
- Agreement on the steps to be done (i.e. debriefings, pilot testing, etc..)
- Different equivalence criteria
- Classification of primary vs secondary clinical endpoints

PROs, ClinPROs, ProxyPROs, PerfROs

COAs Local Versions

Precision Concerns on Measurement Validity
## 2. Usual LV Process – Concepts

### Linguistic versus Psychometric validation

<table>
<thead>
<tr>
<th>LV Steps</th>
<th>Linguistic Validation</th>
<th>Psychometric Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Translation &amp; Cultural Adaptation</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>• Cognitive Debriefing</td>
<td>Limited to PROs, ProxyRO</td>
<td>X</td>
</tr>
<tr>
<td>• Piot Testing</td>
<td>None</td>
<td>Depending on authors</td>
</tr>
<tr>
<td>• Psychometric Properties</td>
<td>None</td>
<td>X</td>
</tr>
<tr>
<td>Internal consistency, Test-Retest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reliability, External Validity, etc.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2. Usual LV Process

- Standard LV Process Diagram* usually from English to another language.
2. Usual LV Process

- Standard LV Process Diagram* usually from English to another language.

```
<table>
<thead>
<tr>
<th>Step / Process</th>
<th>Decision-making process</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source measure</td>
<td>Conceptual definition</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Forward translation A</td>
<td>Analysis and reconciliation</td>
</tr>
<tr>
<td></td>
<td>• Forward translation B</td>
<td>Consensus target language version 1</td>
</tr>
<tr>
<td></td>
<td>Backward translation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Analysis, discussion and amendment</td>
<td>Target language version 2</td>
</tr>
</tbody>
</table>
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First Reviewer involved

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2. Usual Review Process – Deliverables LV

Documentation Related to the LV Process

The review work varies depending on the process decided beforehand.

In addition, other materials to archive for future reference:

- Concept Lists
- List of generated stimuli (PerfRO)
- COA instrument Manual and instructions
- Background documentation as related published papers
- Cognitive Debriefing Related Materials
  - Scripts
  - Results
- Final LV report (may include part of the additional documentation)
2. Usual Review Process

- Are translations good enough for clinical research?

From: Franz Xaver Messerschmidt—Character Heads
Most common reported issues

- Translations are too literal, unnatural sentence structure,
- Translation does not fully adhere to the Concept Definition,
- Missing sentence segments or even items,
- Inaccuracy on the use of local terminology,
- Inadequacy of stimuli used in cognitive testing (verbal, visual, etc.),
- Insufficient language adaptation to study population (age ranges or educational level),
- Confusing translation of instructions to subjects/raters.

Limitations of the First Review

- Reviewers across countries can have different backgrounds depending on training nuances for every speciality.
  - Psychiatrists, Neurologists, Psychologists, Neuropsychologist, Speech Therapists....

- Some countries are broad enough to have language variations within the same linguistic area.
  - Language and terminology needs to be standard enough to be valid for all users within the country.

Actually ....

- Sometimes, an **additional review** is conducted once the translation is completed ...  
  - Not independent
    - Performed by the customer contracting the translation
    - Pharma companies or local sponsor affiliates
    - Substantial modifications can be suggested following this review while other not accepted by the translation specialist.
  - Non systematic

- “**Last minute**” reviews basically based on **linguistic equivalence** rather than impact over outcome measurement.

Overall a more systematic method is needed ....

The review work varies depending on the process decided beforehand.

LV Deliverable
Reconciliation Report (also Back Translation Report - BT)

Final Instrument Translated, Formatted and Customized i.e. Scale/Test

Certification of Translation

Audit or Second Review
By an independent local therapeutic area specialist or COA tools expert
3. Proposal of a Second Review – Metrics

- Created during the audit of “reconciliation reports” of 10 COAs instruments used in Clinical Trials, that were translated into 18 languages/dialects.

- Observations made by reviewers during:
  - Review of Back Translation by staff - native English US language,
  - Review of Forward and Back Translations by local bilingual consultants,
  - Findings from site raters at study start up,

- All observations were analyzed, *post hoc*, using the new proposed metrics.
4. Steps for Auditing Translated COAs

QUALITY ANALYSIS OF COAs INSTRUMENT TRANSLATION

1st Step
IDENTIFICATION & CATEGORIZATION
(A – E)

2nd Step
IMPACT EVALUATION
(1-5)

3rd Step
FINAL RESOLUTION

QUALITATIVE ANALYSIS
Categorization of findings observed at different steps of the LV process into a 5 level types.

EVALUATION OF IMPACT
Analysis of each finding regarding impact on endpoint measurement by allocating a score to range impact severity from 1 to 5.

RESOLUTION AND FINAL EDITING
Final decisions to edit or not the COA and issue the final version and certification.
4. Steps for Auditing Translated COAs

QUALITY ANALYSIS OF COAs INSTRUMENT TRANSLATION

1st Step
IDENTIFICATION & CATEGORIZATION
(A – E)

QUALITATIVE ANALYSIS

A. Inadequate Formatting: Error in the formatting of texts or sections.

B. Grammar Error: A word / sentence has a different meaning after an inadequate sentence composition. Inaccurate translations or too literal translations are included also in this category.

C. Word/Sentence Modified: One word is changed and it results in a different meaning of the sentence.

D. Omission or wrong word addition: Modifications that that results in some information lost in the local translation.

E. Inadequate Cultural Adaptation: Either full or partial sentence has to be further adapted to the local cultural context.
4. Steps for Auditing Translated COAs

**EXAMPLES FOR QUALITATIVE ANALYSIS STEP - TYPE OF FINDING**

A. **Inadequate Formatting:** WMS-Logical Memory (PerfRO) French-France version, some text to be memorize not in bold letter. Affecting results on memory performance.

B. **Grammar Error:** In the MCI Inventory (ClinPRO) in Spanish-Argentina, it is translated “diarios” as “diaries” which is a language false friend because “diarios” refers to a newspaper and not a memory aid tool.

C. **Word/Sentence Modified:** In the Digit Symbol Substitution (PerfRO) Polish-Poland version the sentence for instructions to score the test, has a different meaning because impacting the “number of errors” count. This kind of mistakes will have an impact how the performance is scored that will be different than in other countries.

D. **Omission or wrong word addition:** In the FAQ (ClinRO) Romanian Romania a word is missing in a question, erasing the component that will produce a Yes/No answer.

E. **Inadequate Cultural Adaptation:** In the RUD inventory (PRO and ProxyRO) Romanian from Romania, it is used a word similar to hospice (implies the patient is terminal) and in the source English US the item do not has this implication.

WMS Wescheler Memory Scale, MCI Mild Cognitive Impairement Inventory, FAQ Functional Assessment Questionnaire, RUD Resources Utilization in Demencia
4. Steps for Auditing Translated COAs

**QUALITY ANALYSIS OF COAs INSTRUMENT TRANSLATION**

**Evaluation of Impact**

1. **None or low impact:** Impact is not expected on measurement but in order to concur with other items, tests or evaluations, it needs to be changed.

2. **Minor or Mild Impact:** The item is almost equivalent as the source English, but changes can be introduced order to improve understanding or to be more specific.

3. **Moderate Impact:** Impact on measurement because, an important segment of the target population, can potentially make a wrong interpretation of the item.

4. **Significant or high impact:** Significant because the item is not clear so a half of the population can understand it in one way and the other half in the other.

5. **Critical or extreme impact:** The item has an important mistake (so everyone will answer it wrongly) or it is talking about another factor or about a factor not evaluated in the test.

**Scores 3 to 5 are considered to represent the most relevant impact levels requiring resolution.**
4. Steps for Auditing Translated COA Instruments - Results

A total of **200 Reconciliation Reports** were analyzed.

- **217** findings as commented by consultants.
  - **44%** with potential impact on COA measurement.
  - **27%** rated as **significant**.

All the findings were resolved for the final local versions.
4. Steps for Auditing Translated COA Instruments

**QUALITY ANALYSIS OF COAs INSTRUMENT TRANSLATION**

**Editing Resolution and Editing**

- **Final decision** on impact on COA measurement and define actions.

- Any *editing* involves:
  - *LV process* for the edit (i.e BT and reconciliation)
  - Authors/publishers must be *informed*
  - *Approval* for modifications must be obtained
  - A *new translation version* needs to be issued
  - Update of previous *Certification of Translation* (adding step and date)
4. Steps for Auditing Translated COA Instruments

Outcomes of COA Translation Audits:

When just **one** language is audited:
- Total number of observed issues by category (# A, # B, # C, # D, # E)
- Total number of issues with impact (impact score ≥ 3)
- Description of impacting issues and proposed solutions
- Appraisal with the instrument author/s or author of the translation

When **more than one language** are audited:
- Report per language as above
- # and % of issues over total segments one each translation
- Look up existing patterns of findings
  - Some languages can accumulate more issues than others
  - COAs length can be also a risk factor for issues on translation
  - Type of COAs (PerfRO, ClinRO, PRO&ProxyRO)
- Potential Impact summary i.e. # and percentage of issues per level of impact.
5. Applications

- **For new translations***
  - An audit can be useful to rate measurement precision and to prevent issues on clinical outcomes measurement.

- **For existing translations**
  - From past projects or obtained from publishers

- **For ongoing trials** when issues are reported
  - To confirm or identify issues that can impact on measurement

*Driven by any stakeholder like a pharma company, CRO, translation agency, publisher, research group, etc.
6. Concluding Remarks

- The proposed method offers a systematic way to review local versions of assessment instruments.

- It includes:
  - An independent audit/review
  - A method to categorize issues and to assess its expected impact on the evaluation.

- It provides a common language for adaptation quality, among involved stakeholders.

  - Specialized translation companies
  - Investigators
  - Raters
  - Sponsors and local affiliates
  - Health Agencies
  - Research Centers
És el destí de l’home, la seva mà no pot executar mai amb rigor màxim allò que idealment crea amb l’esperit. (...) Però l’home té molts recursos i pot determinar en quin grau la seva creació difereix de la perfecció.

Denis Guedj “La Mesura del Món” (“Le Mètre du Monde”)
References


Thank you!

Please cite this work as: