

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

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# Disclosures

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- ▶ The author and collaborators report conflicts of interests as were Cogstate employees at the time of the analysis.



# Content

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1. Challenges of Linguistic Validation Process
2. Usual LV Review Process
3. Proposal of a Second Review
4. Steps for Auditing Translated COA Instruments
5. Applications
6. Concluding Remarks



# 1. Challenges of Linguistic Validation (LV) Process

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## Type of COAs and Abbreviations

| <b>Abbreviation</b> | <b>Name</b>                         | <b>Reporter</b>      | <b>Type</b>                                    |
|---------------------|-------------------------------------|----------------------|--|
| <b>PRO</b>          | <b>Patient Reported Outcome</b>     | Patient              | Scales, Inventories, etc..                     |
| <b>ClinRO</b>       | <b>Clinician Reported Outcome</b>   | Clinician            | Assessment Scales, Interviews                  |
| <b>ProxyRO</b>      | <b>Proxy Reported Outcome</b>       | Relatives, Caregiver | Scales, Interviews                             |
| <b>PerfRO</b>       | <b>Performance Reported Outcome</b> | Clinician            | Cognitive Testing (paper&pencil, computerized) |



# 1. Challenges for LV

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## PROs, ClinPROs, ProxyPROs, PerfROs

- ▶ 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

## COAs Local Versions



Precision Concerns on  
Measurement Validity



## 2. Usual LV Process – Concepts

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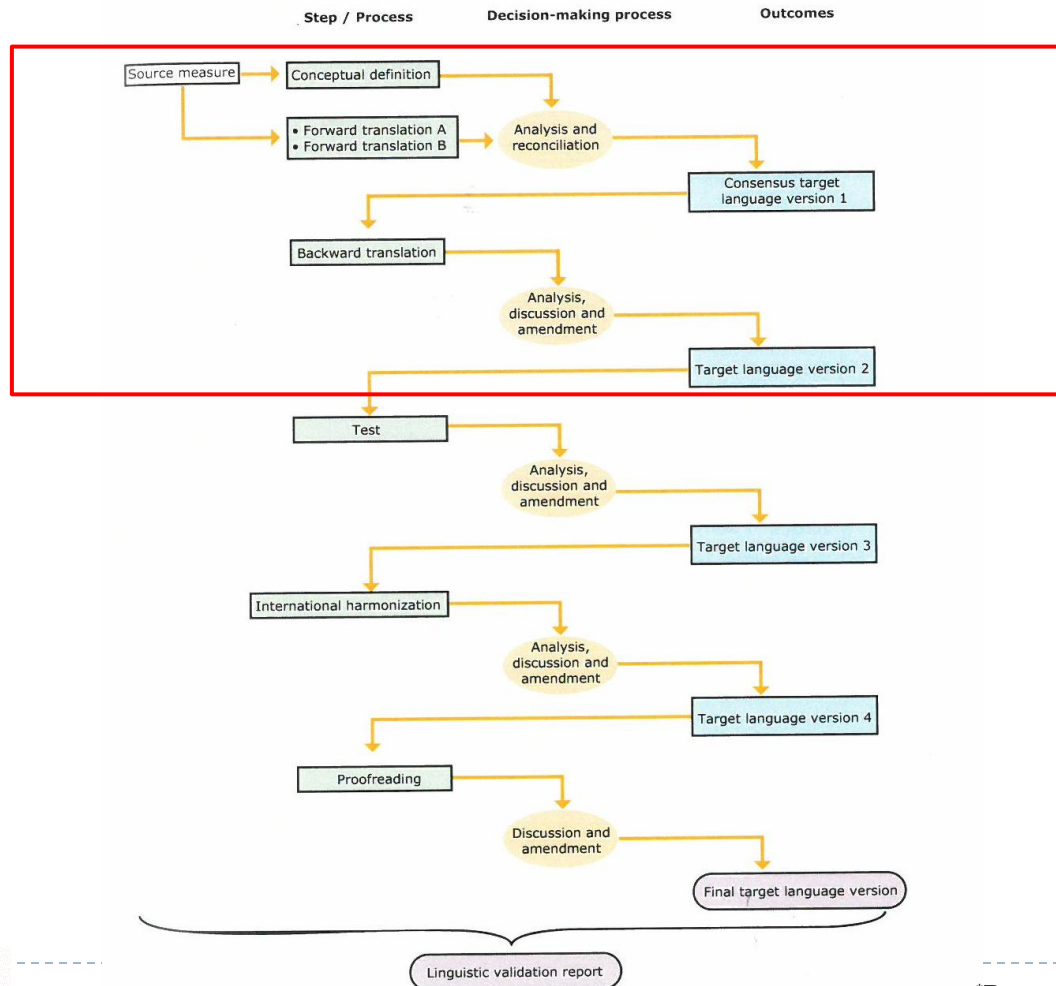
### ▶ **Linguistic** versus **Psychometric** validation

| LV Steps   | Linguistic Validation    | Psychometric Validation |
|--|--------------------------|-------------------------|
| • Translation & Cultural Adaptation  | X                        | X                       |
| • Cognitive Debriefing   | Limited to PROs, ProxyRO | X                       |
| • Pilot Testing  | None                     | Depending on authors    |
| • Psychometric Properties<br>Internal consistency, Test-Retest Reliability, External Validity, etc.. | None                     | X                       |



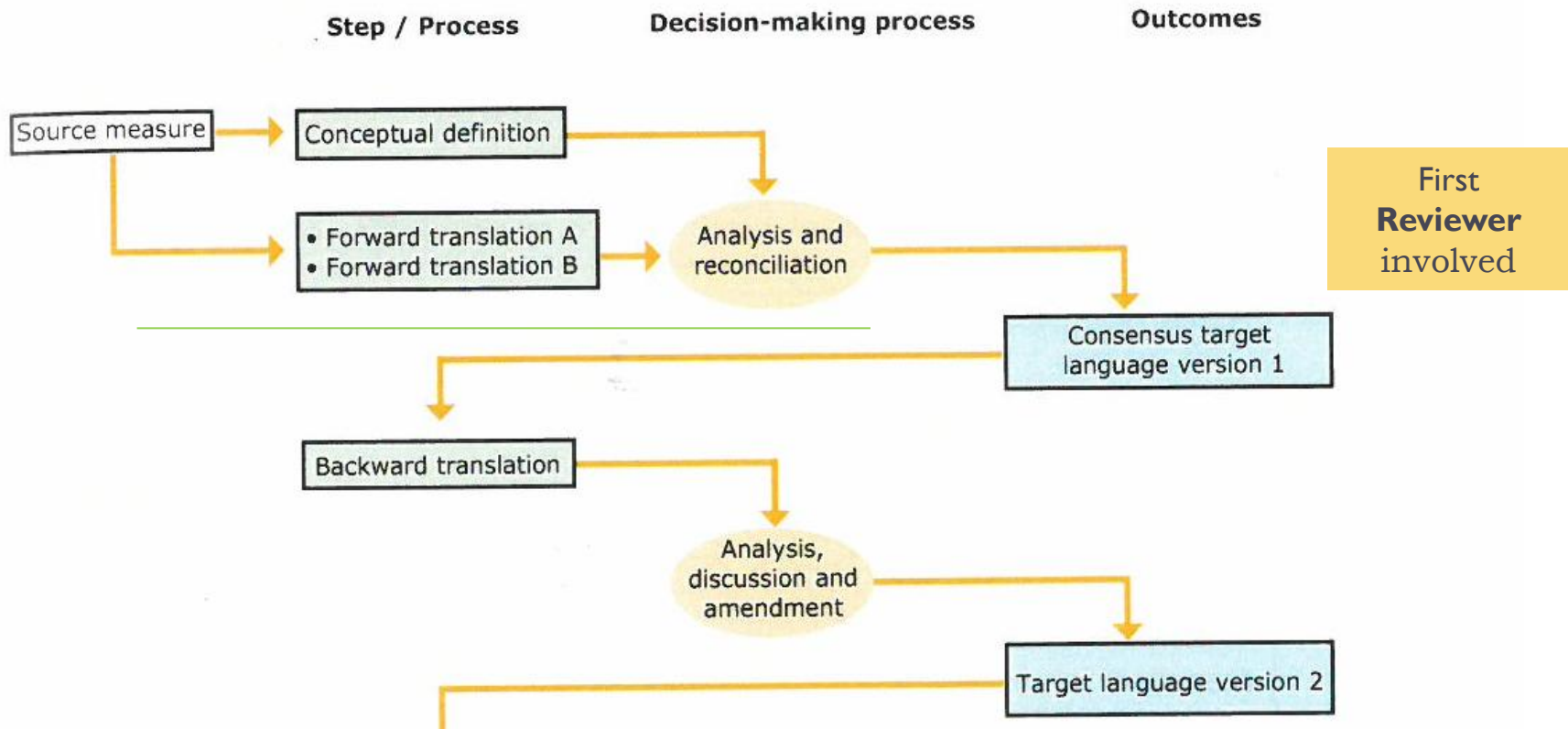
# 2. Usual LV Process

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



## 2. Usual LV Process

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



## 2. Usual Review Process – Deliverables LV

### Documentation Related to the LV Process



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

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- ▶ Are translations good enough for clinical research?



From: Franz Xaver Messerschmidt—Character Heads



## 2. Usual LV Process - Issues

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### 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.



# 3. Proposal of a Second Review – Justification

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## 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.



# 3. Proposal of a Second Review – Justification

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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.

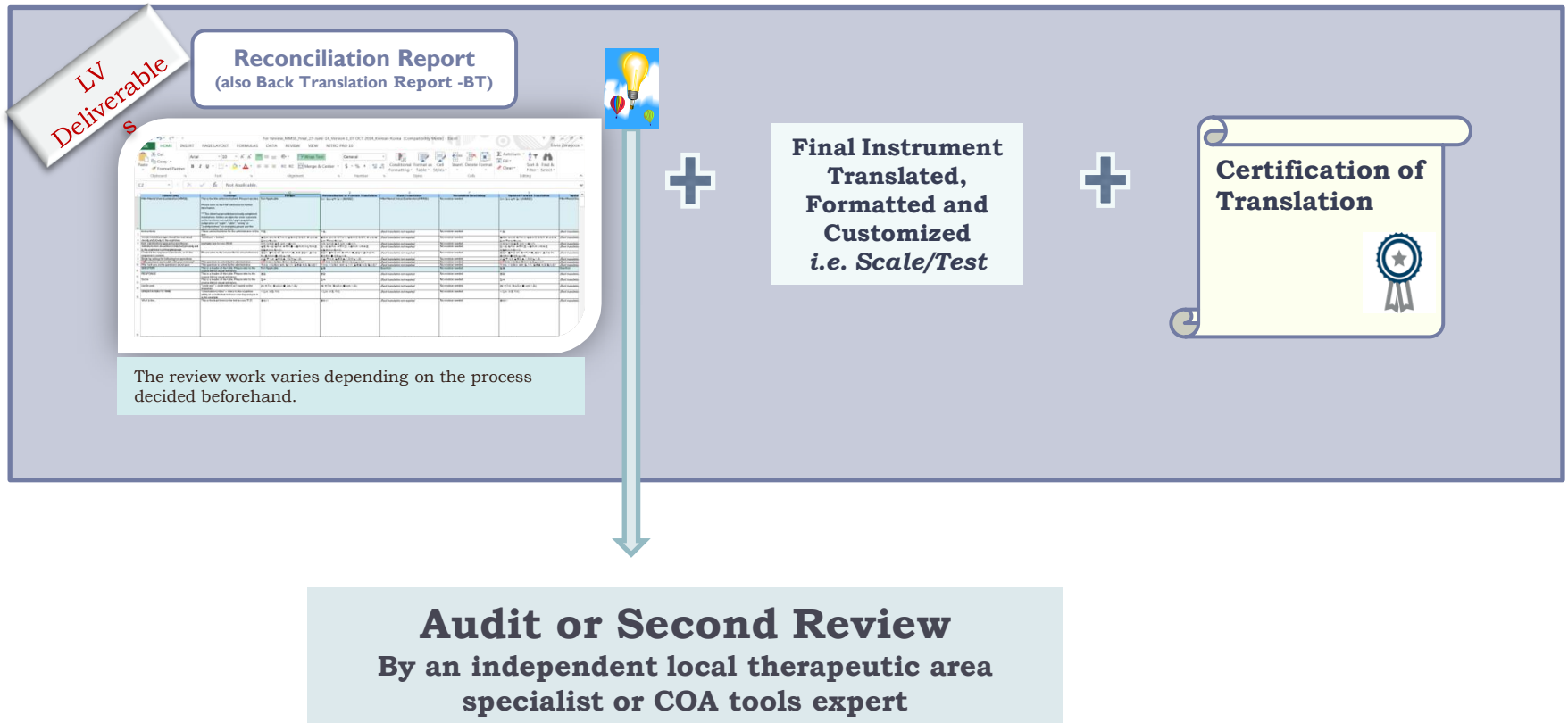
Overall a more systematic method is needed ....

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# 3. Proposal of a Second Review –Implementation

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### 3. Proposal of a Second Review – Metrics

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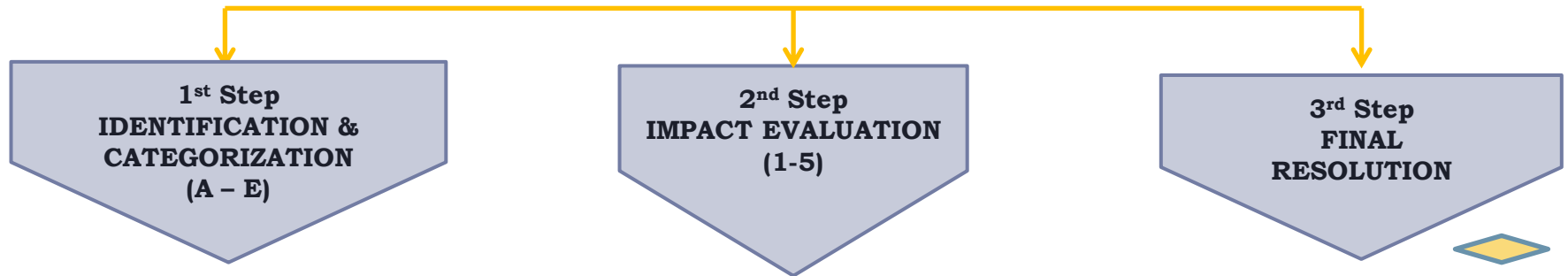
- ▶ Created during the audit of “**reconciliation reports**” of 10 COAs instruments used in Clinical Trials, that were translated into 18 languages/dialects.
- ▶ Observations made by reviewers during:
  - Review of Back Translation by staff - native English US language,
  - Review of Forward and Back 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

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## QUALITY ANALYSIS OF COAs INSTRUMENT TRANSLATION



### 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

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## QUALITY ANALYSIS OF COAs INSTRUMENT TRANSLATION



1<sup>st</sup> 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

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## 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.



# 4. Steps for Auditing Translated COAs

## QUALITY ANALYSIS OF COAs INSTRUMENT TRANSLATION

2<sup>nd</sup> Step  
IMPACT EVALUATION  
(1-5)

### 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

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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

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### 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

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### 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  $\geq 3$ )
- ▶ 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 on 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

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## ▶ 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

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- ▶ 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”)*



From: Franz Xaver Messerschmidt –Character Heads



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Thank you!

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