A Method for Auditing the Quality of COAs Translations in Clinical Trials (TransQualiMetrics)

S. Zaragoza Domingo[1], V. Krishna,[2] O. Royuela[1]

[1] Neuropsychological Research Organization s.l, Barcelona, Spain.

[2] MedAvante, Inc.,Hamilton, NJ, USA

Methodological Question Being Addressed: Are translations based on Linguistic Validation process good enough for clinical research?

Background: Multicenter International Clinical Trials in Neurosciences must cope with a methodological challenge related to Linguistic Validation of PROs, ClinROs, ProxyROs and PerfROs into other languages. Specific guidelines exist for cultural adaptation of Clinical Outcomes Assessment (COA) instruments [1] and, Pharma industry and clinical researchers use existing standard processes as recommended by regulatory authorities [2][3]. Time and budget limitations, jeopardize translation-cultural adaptation quality, with potential negative impact on the validity of the outcomes assessment. In spite of adherence to available cultural adaptation guidelines, inaccuracies in the translated versions of the instruments are often reported by study staff in multicenter clinical trials; too literal translation difficulting understanding or unacuracies in cultural adaptation of items or stimuli, among others.. Efforts are needed to further improve the validity of international and cross-cultural endpoint measurement in clinical research.

Aims: With the aim to improve cultural adaptation accuracy, we propose to add to the standard process an extra step, consisting in an independent review of the reconciliation reports. The standard process itself, includes an expert review, but in our proposed method this review step will be then done in pairs. For this additional review, we propose a specific metric to evaluate and report the quality of the final local version.

Methods: A sample of 200 Reconciliation Reports, corresponding to the translation of 10 COAs into 18 languages/dialects, was analyzed and findings by reviewers were categorized, which included, but were not limited to the following: (1)translation does not fully adhere to the COA concept lists, which were defined at the beginning of the process, (2)missing sentence segments or items, (3)inaccuracy on the use of local terminology, (4)translations were too literal resulting in an unnatural use of the language making the text more difficult to understand, (5)inadequacy of stimulus used in neuropsychological testing (verbal, visual, etc.), (6)insufficient language adaptation to study population age ranges or educational level (7)inaccurate translations of instructions to subjects/raters for neurocognitive testing.

Results: A resulting method is proposed consisting in two-steps i.e. an initial review of "reconciliation report" to proceed with a Qualitative Analysis of findings followed by a second step with an Evaluation of its Potential Impact on outcome measurement. Qualitative Analysis provides a description of the problem and classification according to one of the following subtypes: (A)Inadequate Formatting, (B)Grammar Error, (C)Change of Word/Sentence, (D)Omission or word addition (E)Inadequate Cultural Adaptation. Evaluation of the expected Impact of the issue, on outcome measurement, made by an expert is then assessed in a scale ranging from 1 to 5; 1=None or Low Impact Expected, 2=Mild or minor impact, 3=Moderate Impact, 4=Significant/high impact and 5=Critical or extreme impact. By definition findings scoring ≥3 on the Expected Impact evaluation, are the ones requiring special attention based on potential impact on measurement, and will need to be addressed/resolved. Non-relevant findings if not modified will be considered as internal noise, compromising the validity of the COAs instruments when used by study sites. Definitions and examples of findings for each category are presented. All 217 findings identified by the evaluators of the 200 Reconciliation Reports, could be classified using this method, and a 44% of findings showed a potential impact on the measurement from which a 27% were rated as significant requiring futher attention and actions before its use in the studies.
Conclusion: The proposed method is valid to resolve outstanding issues in translated materials and provides a common language to evaluate translations quality. This methodology can be applied either to audit COAs translations as well as to conduct the final Quality Check as final step or, when auditing existing translations before its use as those existing from past clinical trials or created by authors/publishers for clinical use. This methodology can be used to further improve validity of outcomes measurement in international clinical trials.

1 Wild, D., et al. "Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: report of the ISPOR Task Force for Translation and Cultural Adaptation." Value.Health 8.2 (2005): 94-104.

2 Committee for Medicinal Products for Human use (CHMP). Reflection Paper on the Regulatory Guidance for the use of Health Related Quality of Life (HRQL) Measures in the Evaluation of Medicinal Products, 2005, Doc. Ref. EMEA/CHMP/EWP/139391/2004

3 US Food and Drug Administration. Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. December 2009. Available from: http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm