

# **Evaluation of translation and cultural adaptation in global clinical trials included in Cochrane reviews**

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and**

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# **After this session, you will be able to:**

- **Define different methods for developing measures for use cross-culturally**
- **Specify the steps involved**
- **Identify and evaluate methods used in global clinical trials in Cochrane reviews**
- **Identify strategies for evaluating poolability of data from PROs in global clinical trials**

# The Context

Growing Interest in PROs



Development of PRO instruments...  
in only one language (UK/US English)



Adaptation for use in global clinical trials



Translation &  
Cultural adaptation

# The Context

## Official guidelines for Drug Approval

- EMEA (2005): No specification

- FDA (2006 – draft):

### Changed Culture or Language of Application

- An instrument developed in one language or culture is adapted or translated for use in another language or culture.
- The FDA recommends that sponsors provide evidence that the methods and results of the translation process were adequate to ensure that the validity of the responses is not affected.
- Some examples include the following:
  - PRO instruments are developed initially in one language, culture, or ethnic group and are used subsequently in another
  - PRO instruments developed and validated outside the United States are applied to the U.S. population

# The Context

## FDA (2006 – draft): continued

- Sponsors should consider whether generally accepted standards for translation and cultural adaptation have been used to support the validity of data from a translated/adapted PRO instrument, including but not restricted to the following:
  - The background and experience of the persons involved in the translation/adaptation
  - The translation/adaptation methodology used
  - The harmonization of different versions
  - The evidence that measurement properties for translated versions are comparable

# The Context

- UN/WHO guidelines and practice
- Recommendations from international groups (ISOQOL, ISPOR, ERIQA)
- Literature on translation and cultural adaptation
- Move toward certification of translations

 All recommend a multi-step procedure with little evidence to support approach

# Three Routes to Cross-Cultural Instruments

- **Translation only.** An instrument is developed in one language, usually English, within one country and the instrument is translated into one or several other languages.
- **Cultural adaptation.** An instrument is developed in a source language and the intercultural relevance and conceptual equivalence have been considered prior to the development in the source language. **Translation to other languages is still needed.**
- **Simultaneous development.** An instrument is developed simultaneously in different countries and languages and the source language needs only to track the items contributed from all countries. New versions follow the process in (1) or (2) as, after development, it is almost always impossible to change the items in other languages.

# Definitions

Cultural Adaptation



Two phases



I

Linguistic Validation  
(translation)

II

Psychometric Validation  
(reliability, validity,  
responsiveness to change)

# Definitions: Equivalence

- **6 types of Equivalence\***
  1. **Conceptual**
  2. **Semantic**
  3. **Operational**
  4. **Psychometric**
  5. **Item**
  6. **Criterion**
  
- **The Linguistic Validation covers the first three**

*\*Stewart AL, Napoles-Springer A. Health-Related Quality of Life Assessments in Diverse Population Groups in the United States. Medical Care 2000; 38 (9) suppl II:102-124.*

# Definitions: Equivalence

- **Conceptual equivalence of constructs and items**

Achieved when the constructs exist, are relevant and are acceptable in all cultures. The items should also represent the definition of the constructs.

- **Semantic equivalence**

Obtained when items mean the same thing to people from different groups and in the target and source language.

# Definitions: Equivalence

- **Operational equivalence**

Ensures that standardized methods of survey administration are appropriate for the target culture.

- **Psychometric or measurement equivalence**

Achieved when comparable psychometric properties are observed in the source and target measures.

# Definitions: Equivalence

## ■ **Item equivalence**

Observed when a) items are not differentially more difficult (e.g. biased) in the target culture than in the original, b) item weights reflect comparative importance of items in all groups and c) the meaning of and distance between response choices is similar across cultures.

## ■ **Criterion equivalence**

Is obtained when the interpretation of scores is the same across groups, and when compared with norms for each group. Translated versions should also demonstrate similar associations with any previously set independent criterion established during the validation of the original version.

# Types of Translation Difficulties

Problems arising from the translation process fall into four categories.

- ***Cultural difficulties:*** include the proper or improper usage of certain words, phrases based on the culture of a given society, as well as the specifics of the society itself such as the education system, health care system, societal or religious taboos, etc.
- ***Conceptual / Semantic Difficulties:*** are those that arise in conveying the meaning of a statement in a foreign language.
- ***Idiomatic Difficulties:*** correspond to the use of certain phrases, or the means of conveying ideas that are unique to a particular region, country, or society.
- ***Grammatical difficulties:*** include difficulties linked for instance to the grammar of a given language.



# Richard W. Brislin's Guidelines

1. use short, simple sentences;
2. employ the active rather than the passive voice;
3. repeat nouns instead of using pronouns;
4. avoid metaphors and colloquialisms;
5. avoid the subjunctive;
6. add sentences to provide context for key ideas;
7. avoid adverbs and prepositions telling "where" or "when";
8. avoid possessive forms where possible;
9. use specific rather than general terms;
10. avoid words indicating vagueness regarding some event or thing;
11. use wording familiar to the translators;
12. avoid sentences with two different verbs if the verbs suggest two different actions.



# Research Results

<b>Total n° of examples</b>	<b>78</b>
● N° of original instruments:	<b>25</b>
● N° of disease areas:	<b>12</b>
● N° of original languages:	<b>6*</b>
● N° of originals which language is not English:	<b>3</b>
● N° of translation difficulties (Multiple answers were possible)	
– Cultural differences:	<b>20</b>
– Semantic/conceptual differences:	<b>26</b>
– Idiomatic differences:	<b>3</b>
– Grammatical/script differences:	<b>7</b>
– Different use of questionnaire:	<b>0</b>
– Ambiguous original:	<b>15</b>
● N° of reformulations according to Brislin:	<b>24</b>

\*UK, US and Australian English are counted as different languages



# Example

**Name of questionnaire:** Diabetic Foot Ulcer (DFS) **Language of the original:** UK English

**Original item:** How much have your foot ulcer problems made you choose a different kind of holiday or short break that you would have preferred?

**Response scale:** 1 =Not at all; 2 =A little bit; 3 =Moderately; 4 = Quite a bit; 5 = A great deal

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**Nature of translation difficulty:** ambiguous original

**Issue 1:** unclear focus (2 different verbs)

**Issue 2:** use of 2 words (“holiday” and “short break”) with different semantic fields to describe one overall (undefined) concept

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**Solution 1:** Rewrite item according to Richard W. Brislin

**Solution 2:** Define the overall concept to facilitate choice of most appropriate term.

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**Reformulated item:** “How much has your foot ulcer determined your choice of holiday?”



# Conclusions

- ➔ Confirmation of Richard W. Brislin's Guidelines
- ➔ Definition of concepts is key to comprehension of original and development of translations



# Recommendations for Developers

- 1. Use Brislin's Guidelines when developing an instrument**
- 2. Create a list of concepts for each item, domain, or overall score**
- 3. Assess translatability of the original before its finalization**
- 4. For international use: think about developing an English version if original language is not English**

# Methodology: Steps

16 weeks



# Methodology: Players

Author



Coordinating Center



## Local team

Consultant

« Forward » translators

« Backward » translator

Clinician

Patients

## Local team

Consultant

« Forward » translators

« Backward » translator

Clinician

Patients

## Local team

Consultant

« Forward » translators

« Backward » translator

Clinician

Patients

15 participants per language version

# Forward Step

Source

Conceptual definition of each item

*Author*

1 "forward"  
translation

1 "forward"  
translation

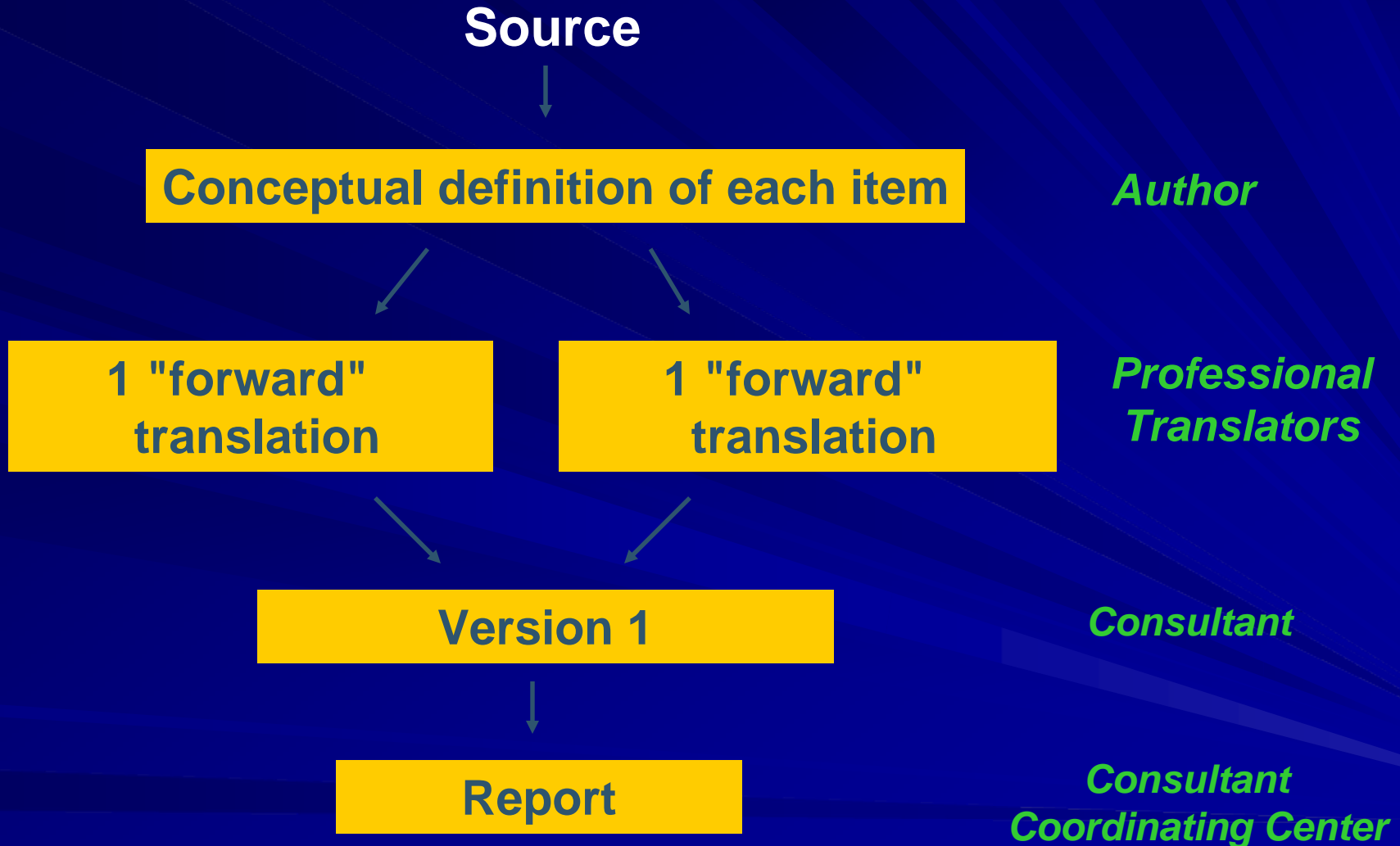
*Professional  
Translators*

Version 1

*Consultant*

Report

*Consultant  
Coordinating Center*



# Examples

*Swedish → UK English → For use in the US*

*Disease area: Angina Pectoris*

**Original**

En kortare promenad (ungefär 2 km)  
A short walk (about 2 km)

**Final UK version**

Short walk (about a mile)

**Test on  
American population**

One mile is not a short walk !!

**Problem**

What is important? "1 mile" or "short walk"?

# Examples

*Swedish → UK English → For use in the US*

*Disease area: Angina Pectoris*

**Original**

En kortare promenad (ungefär 2 km)  
A short walk (about 2 km)

**Final UK version**

Short walk (about a mile)

**Test on  
American population**

One mile is not a short walk !!

**Problem**

What is important? "1 mile" or "short walk"?

**Contact with  
author**



Concept = short walk

**Final American  
version**

Short walk (several blocks)

# Backward Step

Version 1

1/ 2 "backward"  
translation(s)

*Professional  
Translators*

Comparison with original questionnaire

*Consultant  
Coordinating Center*

Report

Version 2

*Consultant  
Coordinating Center*

# Examples

Danish → Finnish -- Existing UK version used to support

Questionnaire = Danish Prostate Symptom Score  
(DAN-PSS-1)

*Q2A: Do you consider your urinary stream as:  
Normal / Weak / Very weak / Dribbling*

**Problem** BT of response choices 2 & 3 =  
"slowly /very slowly" instead of "weakly/very weakly".

**Solution** "hitaasti" (slowly) and "hyvin hitaasti" (very slowly) were changed for "heikosti" (weakly) and "hyvin heikosti" (very weakly).

# Test on Clinician and Patients

Version 2

Review by a clinician/expert in the field

*Clinician*

Version 3

Patient interviews/Cognitive Debriefing

- Filling out of the questionnaire
- Analysis of the interpretation of each item

*Consultant*

Report

Version 4

*Consultant  
Coordinating Center*

# Examples \*\*\*\*

Original: Canadian English -- Title: 'Parent/Guardian Asthma Questionnaire' (Asthma)

All translations of the word 'guardian' were checked during cognitive debriefing to ensure that they were easily understood and commonly used by respondents.

- *'Questionnaire for parent/guardian about asthma'* in Afrikaans
- *'Questionnaire for parents/tutors of children with asthma'* in Argentinean Spanish
- *'Questionnaire for parents or (persons) responsible of patients with asthma'* in Chilean Spanish
- *'Questionnaire about asthma for parent/guardian'* in Chinese for Hong-Kong
- *'Questionnaire for parents/substituted parents of patients with asthma'* in Colombian Spanish
- *'Questionnaire for parents/tutors of patients with asthma'* in Costa Rican Spanish
- *'Parent/guardian asthma questionnaire'* in Danish
- *'Questionnaire for parents/guardians of asthmatic patients'* in Mexican Spanish
- *'Questionnaire for parents/tutors of patients with asthma'* in Peruvian Spanish

# Examples

Original: **Canadian English**

Title: **'Parent/Guardian Asthma Questionnaire' (Asthma)**

- All translations of the word **'guardian'** were checked during cognitive debriefing to ensure that they were easily understood and commonly used by respondents.

*For example:*

- *'Questionnaire for parent/guardian about asthma' in Afrikaans*
- *'Questionnaire for parents or (persons) responsible of patients with asthma' in Chilean Spanish*
- *'Questionnaire about asthma for parent/guardian' in Chinese for Hong-Kong*
- *'Parent/guardian asthma questionnaire' in Danish*

# International Harmonization

Version 4

- IH Meeting:
- Comparison by group of languages
  - Checking of concepts

*Professional Translators  
Coordinating Center*

Control by Consultant

Report

*Consultant  
Coordinating Center*

Version 5

# Examples

## Quality of Life Questionnaire for Functional Digestive Disorders (FDDQL)

French → UK English, US English, Canadian English

**Original** Item 13: "La moindre aggravation de vos douleurs ou de votre transit intestinal vous a-t-elle angoissé(e) ?"

**Problem** Although very commonly used in France, the phrase "transit intestinal" (referring to the progression of food inside the intestines) was particularly difficult to render in all the languages.

**Solution** UK English = bowel function  
US English = intestinal activity  
Canadian English = bowel activities

# Proof-reading & Final Report

Version 5



Proof-reading

*Natives in Target Language*



Control by Coordinating Center



Report



Final Version



Final Report

*Coordinating Center*

## Workshop Exercise:

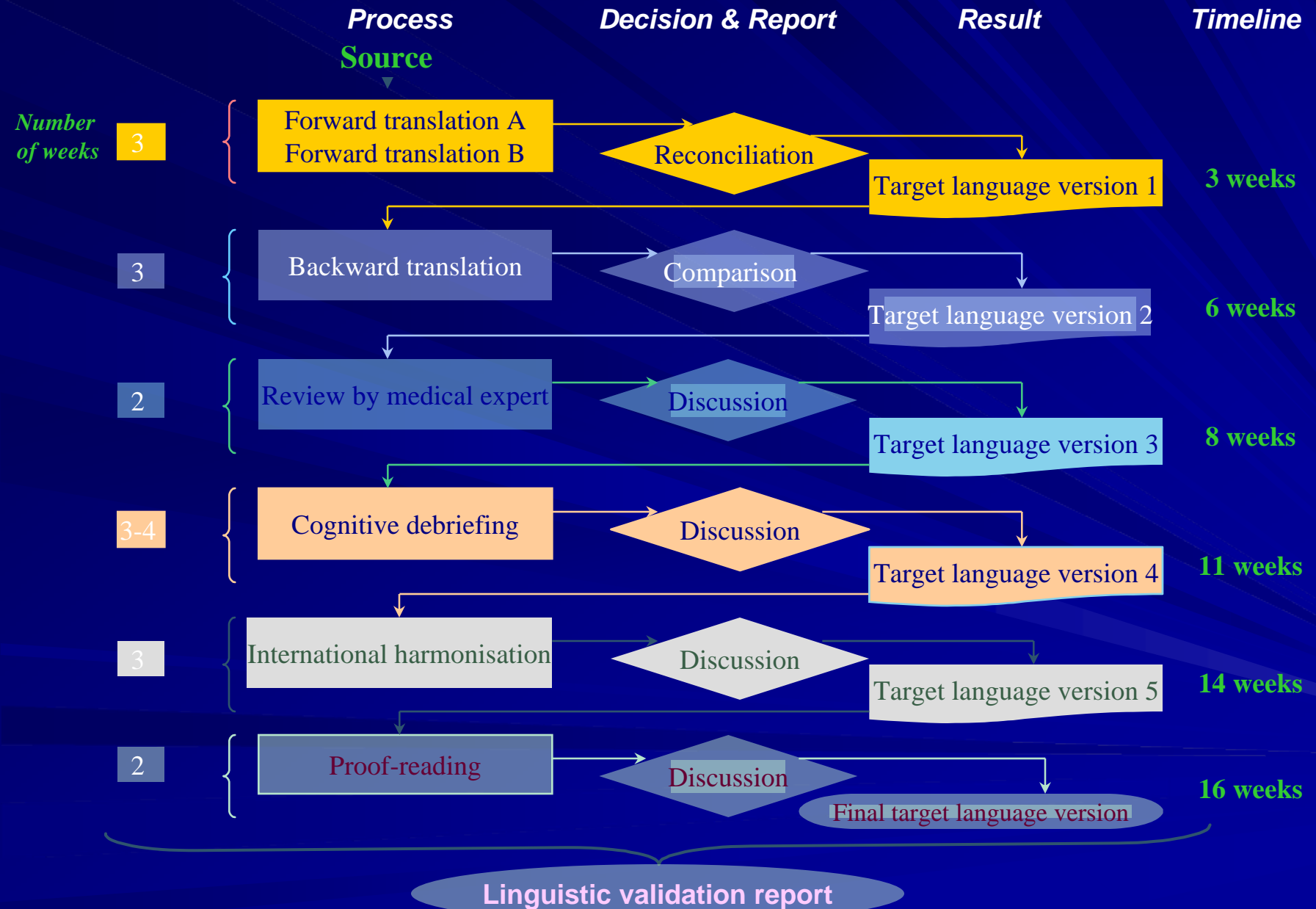
### Creation of Portuguese Brazilian translation of Urinary Incontinence Module for Neurogenic Bladder

- US-English I-QOL
- Brazil-Portuguese I-QOL
- US-English Neurogenic Bladder Module
- **REVIEW SHEET FOR BACK TRANSLATION OF BRAZIL-PORTUGUESE NB MODULE**
- Brazil-Portuguese Neurogenic Bladder Module

# Workshop Exercise

- Go through the REVIEW sheet and decide if the translation is OKAY by evaluating the back translation

# Timeline for Translation



# Conclusions

- Producing high quality translation is labor intensive and time consuming
- The availability of standardized guidelines and centralized review procedures can improve the quality of the translations and the efficiency with which those translations are produced
- The people involved in the translation process are critical in determining a questionnaire's performance in a new country or culture
- To ensure credibility of their methods, investigators need to specifically describe the process used and justify their recruitment criteria

# Take Home Messages

- Involve the questionnaire developer from the start
- Understand the concepts
- Work with local translators and patients
- Document each step

= **3Ts Rule**

- ⊠ **Thoroughness**
- ⊠ **Training**
- ⊠ **Transparency**



**Trust**



# **SUBGROUP 4**

**Caroline Anfray**, Mapi Research Trust, Lyon, France

**Objectives**

# Access to PRO instruments in cross-cultural research

- To identify and classify issues related to access to PRO translations,
- To provide recommendations and good practices on how to access, use and develop translations of PRO instruments.



# Translation and Cultural Adaptation Special Interest Group

## International Society for QoL Research

- I. Collection and classification of requests  
(examples of typical issues related to access to translations)
- II. Overview of existing copyright laws  
(international and country-specific)
- III. Overview of existing solutions to get access to translations (pros and cons)
- IV. List of preliminary recommendations



# Results I

## Collection and classification of requests

### Collection and classification of requests:

*n=2,679*

- Conditions to use selected items (1%)
- Conditions to use in e-application (5%)
- Conditions to modify (12%)
- Conditions to translate (19%)
- Practical information on the instrument and its translations (30%)
- Ownership and licensing of original version and derivative works (33%)



# Results I

## Collection and classification of requests

### Examples of typical issues related to instrument translations

- Who may claim copyright on a translation?
  - Original author?
  - Translator?
  - Translation agencies?
  - Sponsor?
- Who should be contacted to get permission to develop a new translation or to use an existing translation of a PRO questionnaire?
- The questionnaire is published in an article: do I have the right to translate it?
- The translation is available on the internet: can I use it?



# Results II

## Overview of existing copyright laws

### What is copyright:

- Copyright protection means that certain types of utilisation of a document are not permitted unless they are authorised by the holder of the copyright.
- It is a right which comes under the domain of intellectual property. It governs all works which are literary.
  - Berne Convention\* is the definitive convention concerning “international” copyright.
  - National copyright laws

\*Berne Convention for the Protection of Literary and Artistic Works  
"Paris Act of July 24, 1971, as amended on September 28, 1979."



# Results II

## Overview of existing copyright laws

By virtue of the Berne Convention, the holder of copyright has the following rights:

- Moral rights (article 6 bis)
  - Paternity
  - Integrity
- “Authorization” rights
  - Translation (article 8)
  - Reproduction (article 9)
  - Public performance (article 11)
  - Adaptation (article 12)



# Results II

## Overview of existing copyright laws

### Authorship and ownership issues

<b>Questionnaire's life</b>
<b>Development</b>
<b>Communication, publication</b>
<b>Derivative works</b> Translations Electronic PROs Adaptations - modifications



<b>Who may claim authorship/ copyright?</b>
Scientific Expert(s)? Sponsor, University? Joint authorship?
Publishers /Journals?
Translator? Translation agencies ? IT companies? Original copyright holder?



## Results II

### Overview of existing copyright laws

#### Example of conflicting laws re. authorship: Works made for hire

- In the US, “the author” is the person who pays for the development of an instrument/translation
- In France, the author of a questionnaire is the scientific developer, the author of a translation is the translator, etc.



# Results II

## Overview of existing copyright laws

- The copyright holder decides of the distribution rules which governs:

- Access
- Use
- Reproduction
- Adaptation
- Translation

- The distribution rules should be defined in writing

# Results III

## Overview of existing distribution process for translations

### Non-centralized distribution process

#### Issues :

- difficulty finding right contact information,
- multiplication of contacts,
- multiplication of paper work,
- difficulty obtaining reliable information,
- Potential risk of multiple translations for one county and language.

### Centralized distribution process

#### Advantages :

- one point of contact,
- quick and easy access to reliable information
- control and follow up on use



# Preliminary recommendations to facilitate access to PRO instruments in cross-cultural research

- The question of authorship of original and translation should be discussed in the beginning between all parties involved,
- Each step of the instrument's life should be anticipated for purpose of copyright (e.g. publication of the instrument/translation in journals),
- All agreements should be stated in writing,
- Copyright holder/author of original must be contacted prior to any use of instrument or its derivative work,
- Copyright holder should clearly define the distribution rules,
- Centralized distribution process seems to be best way to provide access to reliable translations and information about them,

## Further research still required :

- ➔ Country-specific laws,
- ➔ Levels of questionnaire protection (©, TM, ®),
- ➔ Distribution rules: what are the conditions of use that copyright holders may require ? (business model vs. public domain)

# Pooling of data

- To investigate methods for analyzing the ability to pool PRO data across all language versions and cultural groups in a clinical trial or PRO investigation
- To develop criteria for when pooling is not justified
- To publish a paper on methodologies and recommendations for analyzing the ability to pool data using classical and modern test theory

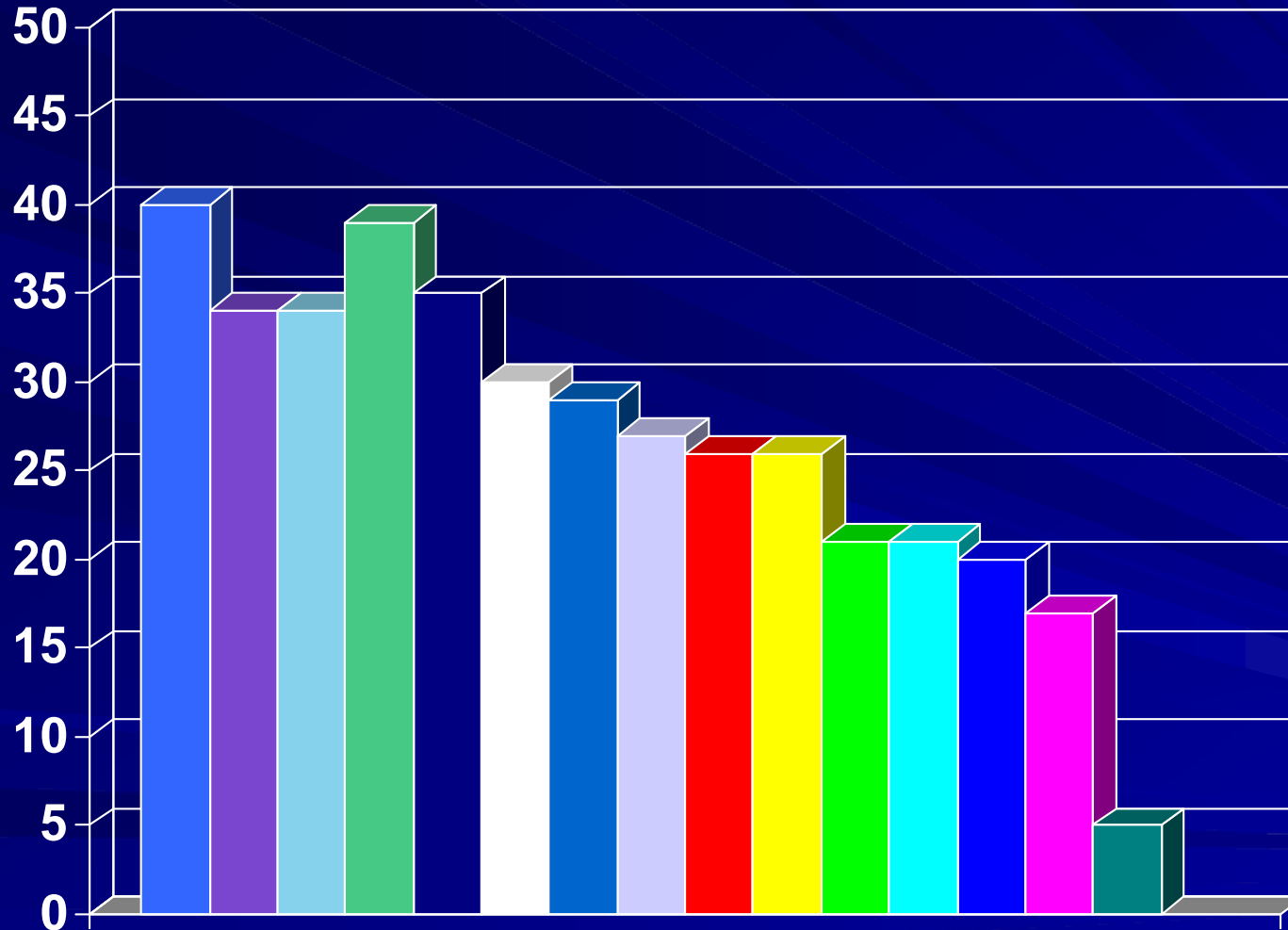


## Example: Participant countries in international clinical trials

Country	No. Pts	Country	No. Pts
U.S.A	258	Russia	28
France	141	Croatia	24
Argentina	98	Italy	23
U.K.	85	Peru	23
Poland	71	Hungary	22
Germany	61	Israel	14
Belgium	46	Netherlands	11
Spain	42	Canada	3



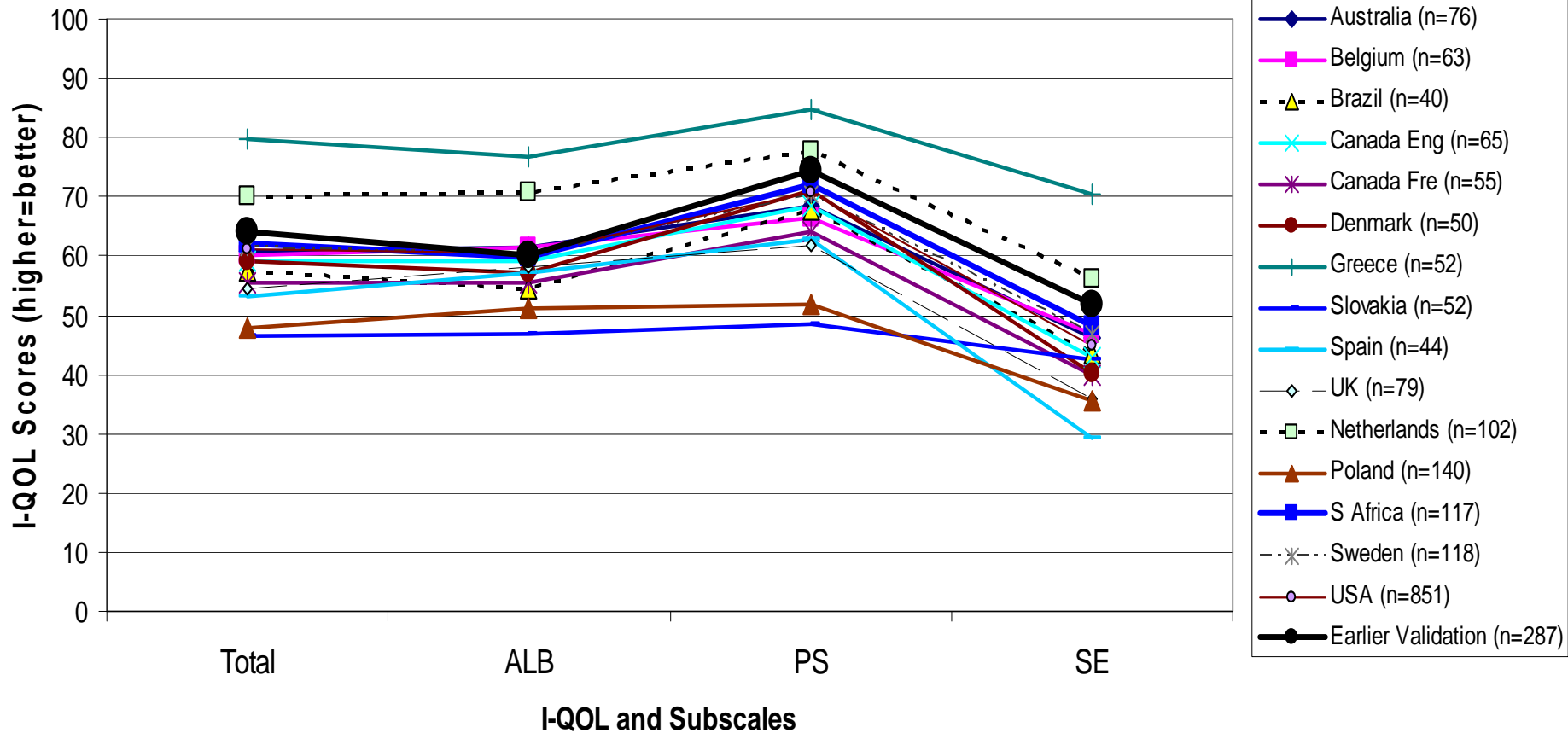
# Example: Pain and/or Analgesic progression



USA	258
France	141
Poland	71
Peru	23
UK	85
Argentina	98
Croatia	24
Netherlands	11
Italy	23
Germany	61
Russia	28
Israel	14
Belgium	46
Spain	42
Hungary	22

# Example: Urinary incontinence

## I-QOL Scores by Country



Legend: ALB = Avoidance and limiting behavior; PS = Psychosocial; SE = Social Embarrassment