INSTRUMENT DEVELOPMENT

from an industry perspective

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Development of PRO instruments: yesterday *vs* today

Yesterday

- Investigator compiled ad hoc tools
- No patient input
- Often use of medical terms
- No documentation of the steps in the development

A changing environment

- Increased safety concerns by regulators
- Increased regulatory awareness and requirements for PROs
- Patient’s voice is getting stronger

”It’s all about the patients”

- Ultimately the patients are our customers
- Patients are asking for information about how their life will be impacted by a new treatment

Draft vers 2006
Final vers 2009

Guidance for Industry

Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

February 2006
Clinical/Medical

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1/19/2006

Definition of Patient Reported Outcome (PRO)

Any report coming directly from patients, without interpretation of others, about a health condition and its treatment

Why use PROs?

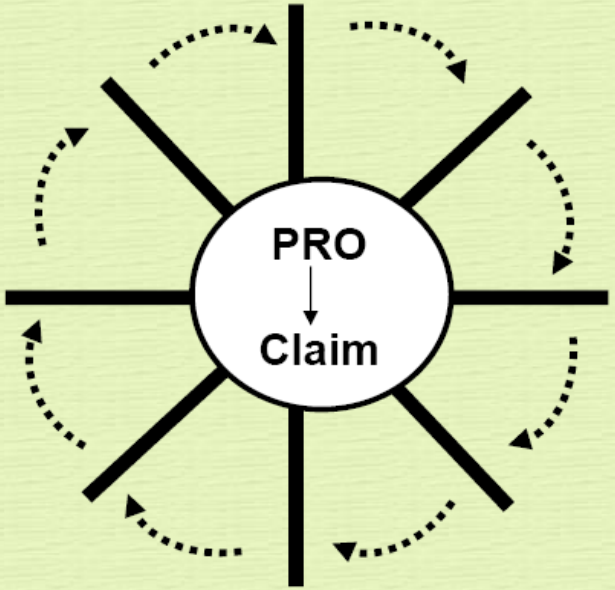
- Desire to know the patient perspective about the effectiveness of treatment
- Some treatment effects are known only by the patient, can be lost when filtered through clinician evaluation
- Formal assessment more reliable than informal interview

Instrument Development / Modification Process

i. Hypothesize Conceptual Framework

- Outline hypothesized concepts & potential claims
- Determine intended population
- Perform literature/expert review
- Develop hypothesized conceptual framework
- Place PROs within preliminary endpoint model
- Document preliminary instrument development

Content validity



ii. Adjust Conceptual Framework & Draft Instrument

- Generate new items
- Create instrument
- Select administration mode, recall period & response options
- Format instrument
- Conduct cognitive debriefing
- Pilot test draft instrument
- Document content validity

iii. Confirm Conceptual Framework & Assess Other Measurement Properties

- Confirm conceptual framework with scoring rule
- Assess score reliability, construct validity, & ability to detect change

iv. Collect, Analyze, & Interpret Data

- Prepare protocol & statistical analysis plan
- Collect & analyze data
- Evaluate treatment response using cumulative distribution & responder definition

v. Modify Instrument

- Change wording of items, populations, response options, recall period, or method of administration
- Translate & culturally adapt to other languages
- Evaluate as appropriate
- Document all changes

Content Validity

- Determine intended patient population
  - GERD / GERD partial response / GERD sleep problems
- Identify concepts and domains
  - Symptoms / HRQoL / Mental health / Sleep

PATIENT INPUT

- Interviews – individual / focus groups
- Interview guide – semi-structured / open-ended
- Analysis of data
  - incl saturation

PATIENT INPUT

Content Validity, cont

Data analysis / saturation grids

Domain: Symptom **Sub-Domain: Burping/Belching**	Number of **Symptom** Mentions of Concept	% of mentions **of total Sub-Domain** (=42)	% mentions of total Symptom Domain (=578)	% of total mentions for Impacts & Symptoms (=1238)	*Number of people reporting each code*
Concept Description: Burping/Belching					
Patient Language					
burping	20	48%	3.5%	1.6%	14
belching	8	19%	1.4%	0.6%	6
bubbling in back of throat	6	14%	1.0%	0.5%	4
gas coming from the stomach up in to the mouth	5	12%	0.9%	0.4%	5
[burping]	1	2%	0.2%	0.1%	1
hiccups	1	2%	0.2%	0.1%	1
vapor	1	2%	0.2%	0.1%	1
Total within concept:	42	100%	7.3%	3.4%	

PATIENT INPUT

Data analysis / saturation grids

- Analysis of data +
- Empirical evidence +
- Expert input

- Items and Concepts
- *Response alternatives*
- *Treatment goal*

Develop instrument

- Layout
- Administration mode
- Instructions
- Scoring
- Pilot testing (debriefing)
- Refine instrument

Importance of content validity

Support that the instrument

- measures the concept it is intended to measure
- measures the concept claimed

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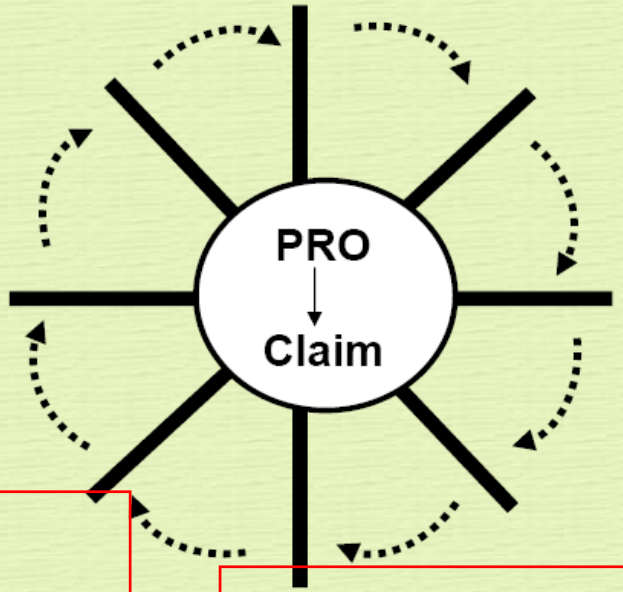

Instrument modifications

Examples of changes:

- Wording
- Population *(NB! Validated vs Fit for purpose)*
- Response options
- Recall period
- Method of administration
- Translation to other languages

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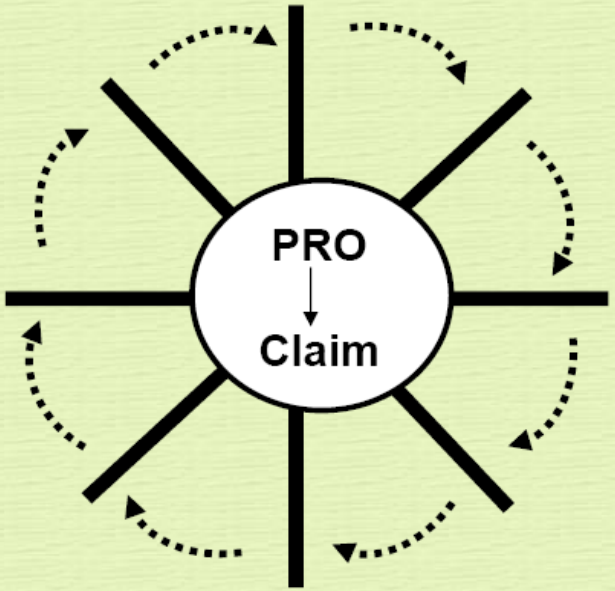

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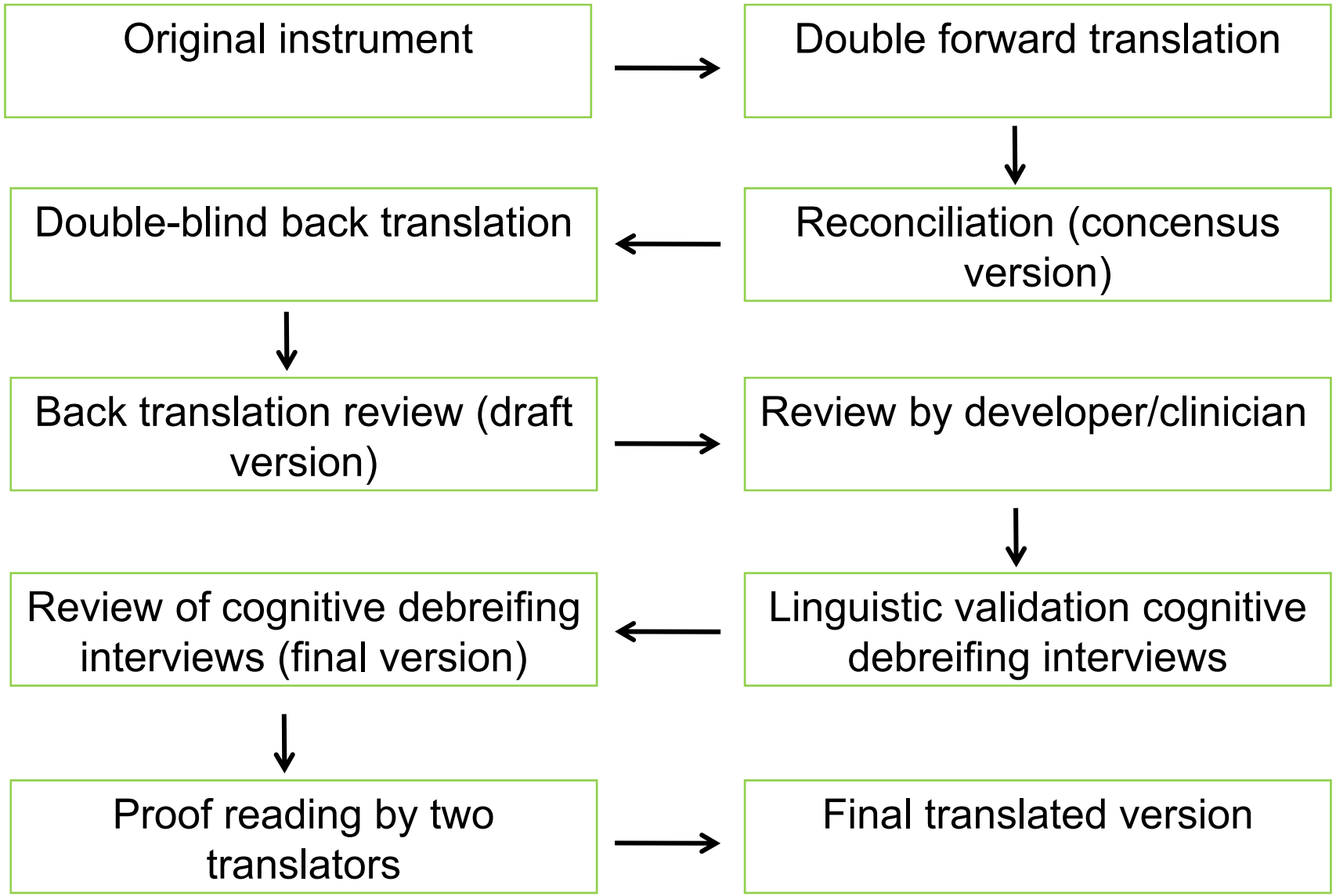
Translation process



Translation process

English → Japanese → English

Heartburn *A bone in the chest*

Short walk, eg a block → *Not short (US)*