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**ISPOR PRO Mixed Modes Task Force**  
([www.ispor.org/sigs/mixedmodes.asp](http://www.ispor.org/sigs/mixedmodes.asp))

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**Mixing Modes of Patient-Reported Outcomes Data Collection in Clinical Trials: Recommendations**

**Moderator:**  
Sonya Eremenco, MA, ePRO Manager  
United BioSource Corporation

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**Workshop Objectives**

To discuss the Task Force's preliminary findings regarding

- ⊙ mixing modes of PRO data collection in clinical trials used for regulatory purposes

*and*

- ⊙ issues related to the analysis of data from trials involving mixed modes

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**Workshop Faculty**

**Study Design Issues**  
**Sonya Eremenco, MA**, ePRO Manager, United BioSource Corporation, Bethesda, MD, USA  
**Chair, ISPOR PRO Mixed Modes Task Force**

**Operational Issues**  
**Jean Paty, PhD**, Founder & Senior Vice President, Scientific, Quality & Regulatory Affairs, invivodata, inc., Pittsburgh, PA, USA

**Statistical Issues**  
**Andrew Lloyd, DPhil**, Vice President & Practice Lead, Oxford Outcomes Ltd., an ICON PLC company, Oxford, UK



## Background

- ISPOR ePRO Task Force Report (Coons et al. 2009)
  - Migrating from paper to electronic data capture
  - Mixing modes not explicitly addressed
- FDA PRO Guidance
  - “We intend to review the comparability of data obtained when using multiple data collection methods or administration modes within a single clinical trial to determine whether the treatment effect varies by methods or modes.” (FDA, 2009)
- In this workshop, “mode” refers to all means of administration and methods of data capture
- Mixing modes is most challenging when one of the modes is paper



## Issues to Consider

Technology makes mixed modes data collection feasible operationally, however...

- Clinical trial designs should avoid as many sources of error variance in the PRO data as possible.
- Measurement error can be introduced into the trial design by different PRO data capture modes that are not providing comparable data (i.e., the modes lack sufficient measurement equivalence.)
- Measurement error reduces statistical power and attenuates the ability of the trial to detect real change (i.e., treatment effect) in the PRO-based trial endpoint.



## Important Note about “Validation”

- *Measurement equivalence* should not be equated with “validation.”
- In fact, the term “validation” should be avoided in most cases in which it is used in the context of PRO measurement instruments.
- The term is best used with a qualifier, such as in “systems validation,” which is the focus of an ISPOR ePRO Systems Validation Task Force report that is nearing completion.



## Study Designs to Evaluate Multiple Modes of Administration and Data Capture

Sonya Eremenco, MA  
ePRO Manager  
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## Mode to Mode Migration

- ⊙ Patients comprehend questions the same way regardless of mode of data capture
- ⊙ Patients answer in a similar way
- ⊙ Demonstrate this comprehension by hearing from patients and/or demonstrating equivalence in responses
- ⊙ It is important that the migration does not introduce changes to the measurement properties
  - ⊙ Reliability, validity, ability to detect change

Adapted from Jean Paty, ISPOR Forum, May 24, 2011

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## Modes and Sources of Variability

Mode of administration	Method of data capture	Sources of variability between methods	Sources of variability between modes
1. Self-administered Direct patient report considered PRO	Paper Handheld Tablet /Netbook IVRS Web via computer Web via phone	Variation due to: -items being seen or heard; -how they appear on page or screen; -number of items visible on page or screen at one time. -how responses are presented, and -how patients are to input answer <b>-edit /validity checks</b> <b>-completion windows</b>	Patient may alter response due to presence of interviewer (e.g. social desirability); and variation across interviewers (e.g. age, gender, personality); <b>Interviewer performs "edit check" and enforces completion window</b>