The EXACT-PRO “Expedition”: Mapping the PRO Instrument Qualification Trail

Nancy Kline Leidy PhD
United BioSource Corporation (UBC)

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Acknowledgements

• Sponsors and sponsor representatives
  – 10+ sponsors and 20+ individuals
• Patients & clinical sites
  – 490 patients and 70 clinical sites
• Experts
  – 15 international, multi-disciplinary
• UBC Research Staff
  – 35+ international, multi-disciplinary
The EXACT-PRO “Expedition”: Mapping the PRO Instrument Qualification Trail
The “Expedition”

• Why did Lewis & Clark make this trip?
• How good a guide was Sacagawea?
• Did Lewis & Clark intend to discover the Pacific Ocean?
• Did other people accompany Lewis & Clark?
• How many people survived the trip?
• Who paid for the expedition?
• How can anyone say Lewis & Clark “discovered” anything, since Native Americans living along their route already knew the places & creatures?
• Can I follow their exact route today?

http://www.lewisandclark.com
The EXACT-PRO “Expedition”

• Why?
  – Background
• How?
  – Journey
• Now?
  – Current location
• Summary
Why?

• The EXACT-PRO Initiative
  – EXAcerbations of Chronic Pulmonary Disease Tool – Patient-Reported Outcome

• Purpose
  – Standardize measurement of frequency, severity, & duration of exacerbations of COPD

• Rationale
  – The initial detection of an exacerbation originates with symptoms known directly by the patient and clinical assessments are based on patient report to the clinician.
  – No standardized method for evaluating exacerbations in clinical trials.
Why?

• The presence of a PRO assessment problem
• Clearly named and described
• Sponsor & FDA interest & priority
• Timelines & resources
How?

- Identify a leader
- Clarify the concept
- Discuss concept with the Agency
- Identify sponsors
- Engage experts
- Assemble the research team

Experience
- Therapeutic area
- Instrument development
- Clinical trials
Reach Agreement

- Players
  - Sponsors, agency involvement, experts

- Purpose
  - Concept is important
  - There is a measurement issue that needs to be addressed

- Method
  - Scientific process & timelines

- Decision-making process
  - Responsible Principal Investigator
A Phased Approach

• Phase I
  – Literature review
  – Focus groups & interviews, item pool development
  – Cognitive debriefing
  – Expert participation

• Phase II
  – Validation study design, execution, SAP development
  – Analyses, interpretation
  – Expert participation

• Phase III
  – User manual, dossier development, dissemination, user guidance

• Phase IV
  – Translation, user guidance, instrument protection
Timelines (EXACT-PRO)

• Phase I - **7 months**
  – Literature review
  – Focus groups & interviews, Item pool development
  – Cognitive debriefing
  – Expert participation

• Phase II - **17 months**
  – Validation study design, execution, SAP development
  – Analyses, interpretation
  – Expert participation

• Phase III - **12 months**
  – User manual, dossier development, dissemination, user guidance

• Phase IV – **12 months**
  – Translation, user guidance, instrument protection
Milestones

- Concept & target claims
- Proposed approach
- Literature review
- Qualitative protocol
- Qualitative results with draft instrument
- Cognitive interviews with final items
- Validation study protocol
- Validation study results
- Dossier submission
- Qualification
Research Staff

Principal Investigator & Director
Co-Investigators

Types of Staff
• Project Managers, Associates, Research Assistants
• Data Managers
• Statisticians
  – IRT, Rasch; Biostatistics
• Statistical Programmers
• Production Assistants
• Meeting planning/logistics
• Information Technology
• Legal and finance

Expertise & Experience
• Therapeutic Area
• Regulatory Requirements
• Qualitative Methods
  – Interviews, Focus Groups
  – Analyses
• Quantitative Methods
  – Study Design
  – Statistical Analysis Plans
  – Analyses
  – Interpretation
• Report Preparation
  – Dossier
Experts & Expert Panels

• 2 clinical research/therapeutic experts
  – Consultation, document review, reality check
  – Telephone, in-person meetings
  – Small group expert-based decision making
• Additional experts*
  – Clinical area, clinical research
  – Instrument development
  – Regulatory issues
  – Sponsors
  – International considerations

*EXACT-PRO: Expert Panel Meetings
EXACT Expert Panel Meetings*

• #1 Concept, methods, qualitative results
  – Context of use, target sample, data

• #2 Qualitative results, draft items, validation protocol
  – Content validity, validation protocol designs

• #3 Quantitative results
  – Reliability, validity, responsiveness

• #4 Special issues
  – Scoring & interpretation, follow-up validation study

*Corresponding to milestones
Expert Panel Meetings

• Purpose & agenda
• Expert panel
  – Expertise-based exchange
  – Sponsor representation
• Observers
  – Additional FDA
  – Sponsors (2/company)
  – Opportunity for participation
FDA Involvement

• Informal
  – SEALD & review division input
  – Participation in expert panel meetings
    • At the table, regulatory considerations, exchange
    • Observer participants
  – Intervening agency dialogue
    • Focused - Specific purpose, agenda, slides, outcome

• Formal
  – Dossier submission and qualification review

• Recommendation
  – Formal milestones with review and feedback
Communication

• Sponsors, experts, FDA
  – Expert panel meetings
  – Web-site document access
  – E-mail updates

• Sponsors
  – E-mail newsletters
  – Conference calls
  – “1:1” conference calls – experts, sponsors

• Scientific community
  – National & international meetings

• Recommendation
  – Formal feedback from the FDA at milestones
Dissemination

- Subject the work to scientific review
- Open communication about the work
- Presentation -> publication
- Sponsor acknowledgment
- Authorship – Intellectual Work
  - PIs, experts, study group
Sponsorship

Scope of “Work”

Contracting & Timelines

# Sponsors

Budget

Continuous Funding Stream
Maintenance

• User support
  – Sponsors, new pharma, academics

• New context/purpose
  – Adjustments in target population or setting

• Translations
  – Standardized translated versions

• Mode of administration
  – Changing electronic platforms
  – Equivalence testing

• Ongoing validation testing
  – Clinical studies, clinical trials, target populations
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• Now?
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• Summary
Now?

- Dossier Submitted to the FDA
  - December 2009
  - Contents:
    - Concept
      - Definition, conceptual framework, example endpoint models
    - Qualitative methods & results
    - Quantitative methods & results
    - Supportive documentation

- Awaiting Feedback
Current Location

Click a dot to learn about each national park along the Lewis and Clark Trail.
The EXACT-PRO “Expedition”

- Why?
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- Summary
Summary

- Problem identification
  - Clarity & agreement
- Phased approach
  - Development, validation with milestones
- Research staff with dedicated time & broad expertise
  - Therapeutic, qualitative, quantitative
- Expert participation
  - Consultation & FDA feedback
- Communication
  - Sponsors, FDA, experts, community
- Dissemination
  - Presentations, publications
- Sponsorship
  - Continuous funding stream
- Maintenance
  - Use & ongoing validation work
- Dossier for qualification
  - Feedback & persistence
The “Expedition”

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With Time Comes Clarity