The EXACT-PRO "Expedition": Mapping the PRO Instrument Qualification Trail

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Presented at:

FIRST ANNUAL

PATIENT-REPORTED OUTCOMES (PRO) CONSORTIUM WORKSHOP

March 23, 2010 – Bethesda, MD

Co-sponsored by

CRITICAL PATH INSTITUTE

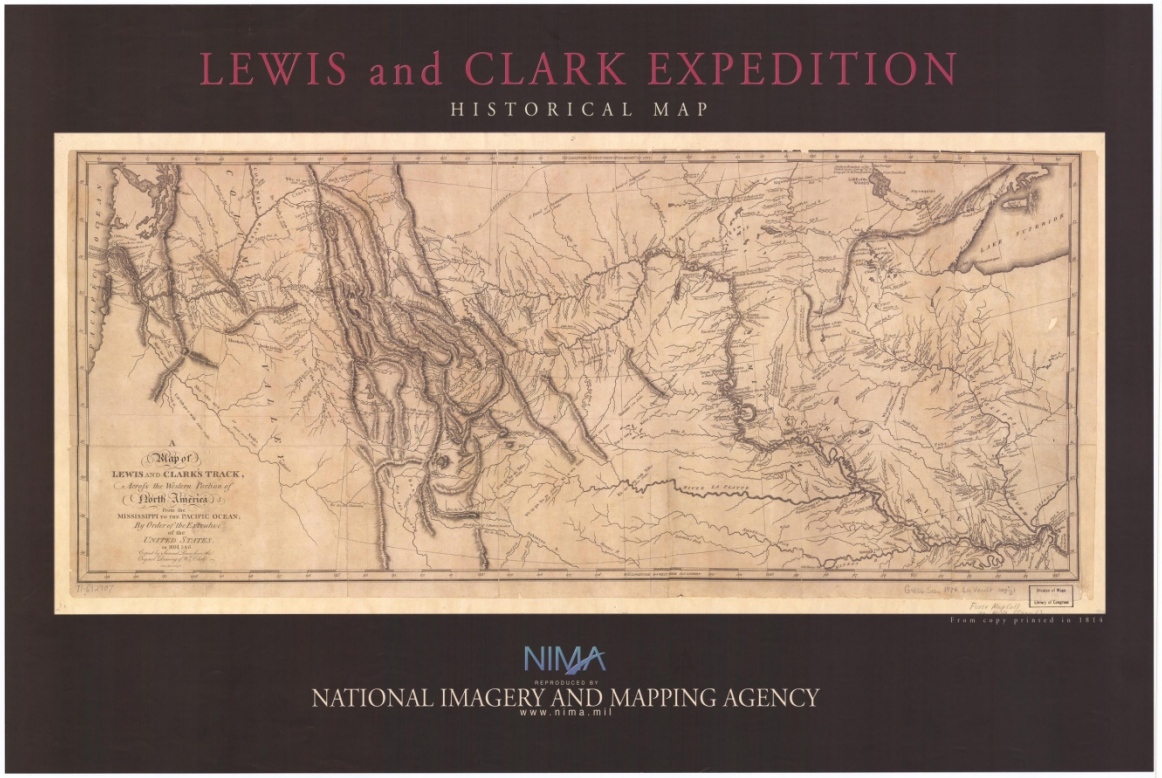
FDA

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

PRO CONSORTIUM



The "Expedition"

PRO CONSORTIUM

Why?

- Why did Lewis & Clark make this trip?

How?

- 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?

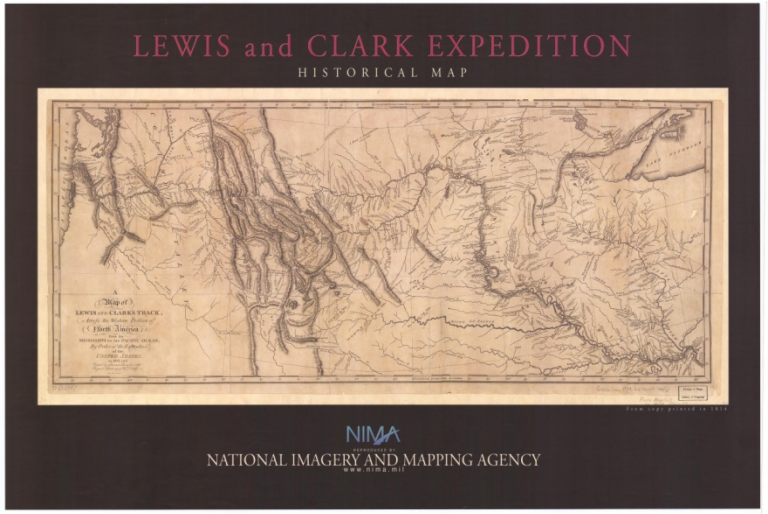
Now?

- 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
  - **EXA**cerbations of **C**hronic Pulmonary Disease **T**ool – **P**atient-**R**eported **O**utcome
- 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

Trial Use

2+ Years

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

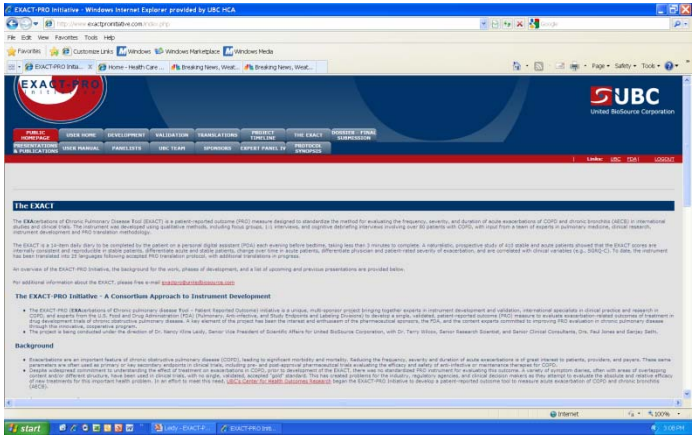
- Purpose & agenda
- Expert panel
  - Expertise-based exchange
  - Sponsor representation
- Observers
  - Additional FDA
  - Sponsors (2/company)
  - Opportunity for participation

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

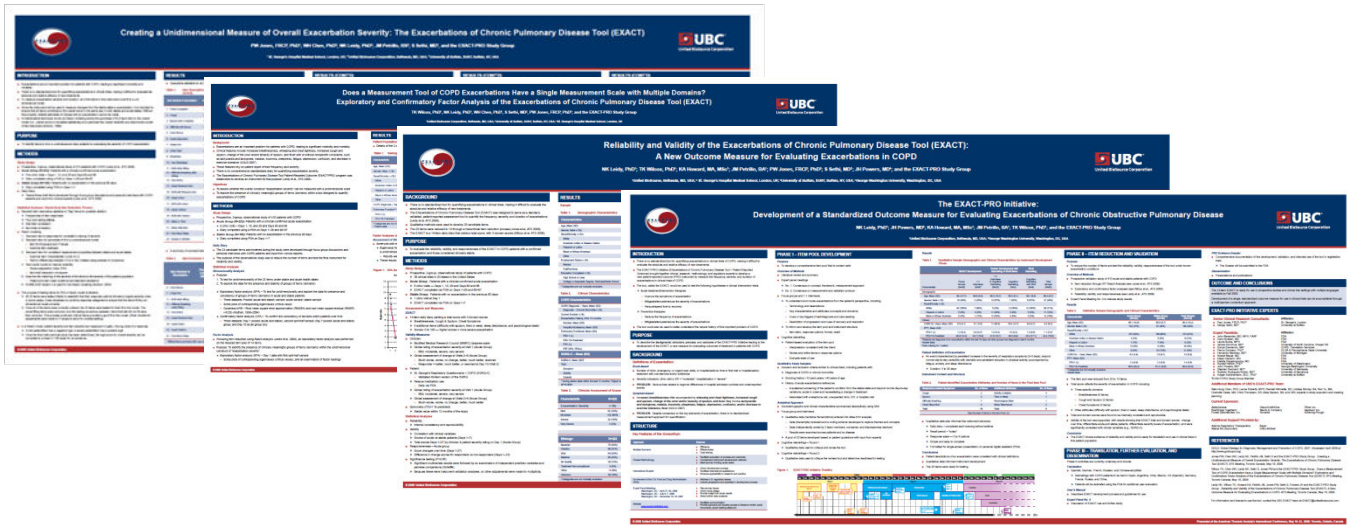
Communication

- 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

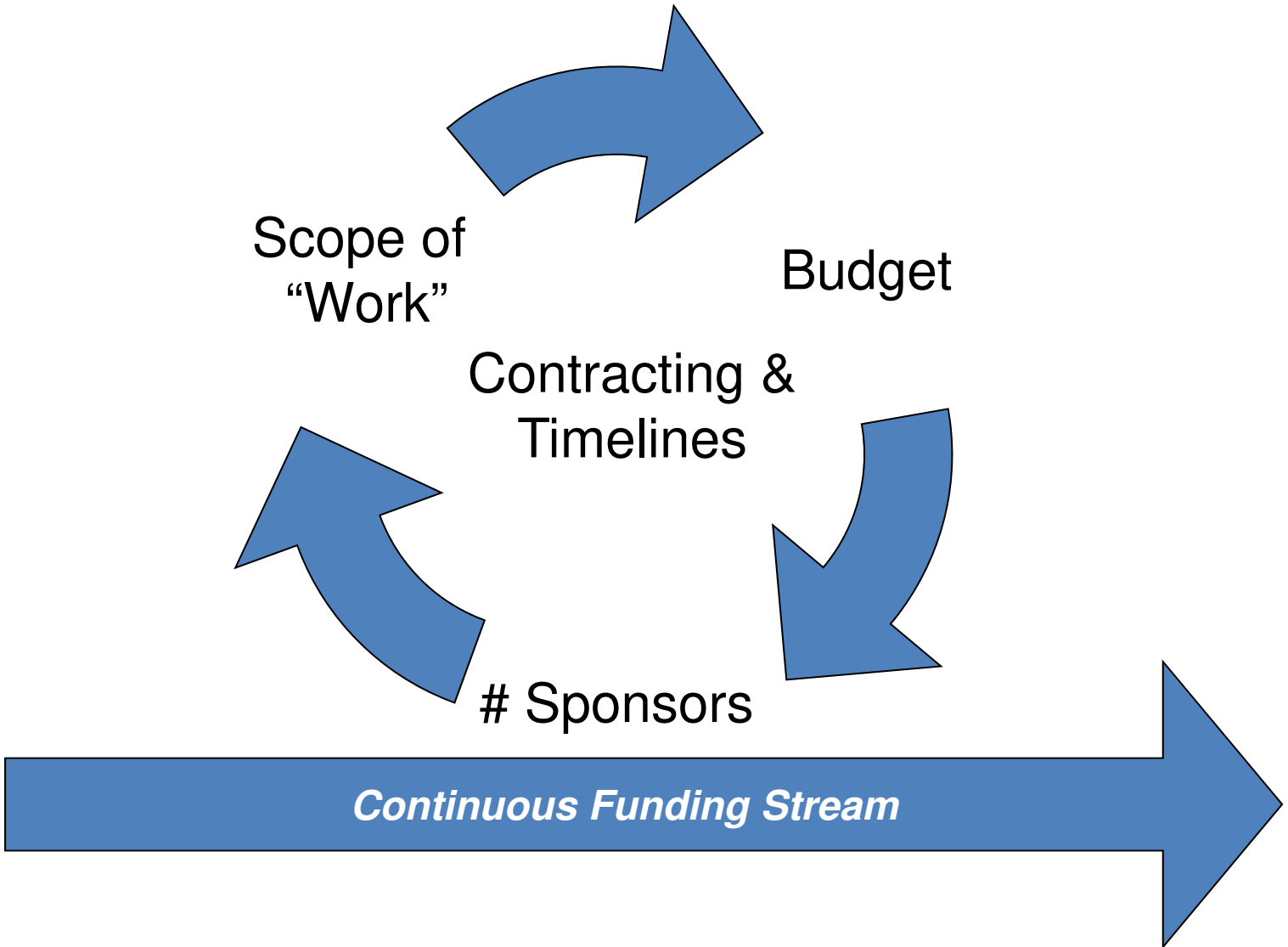


Dissemination

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



Sponsorship



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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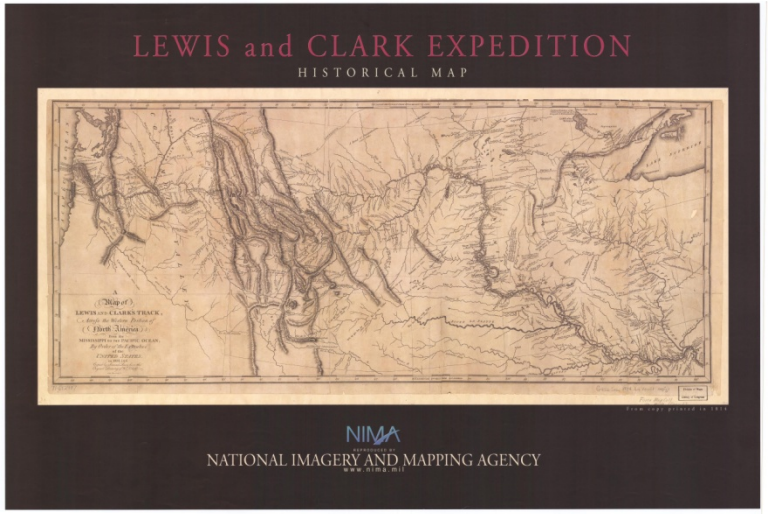

Now?

- 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

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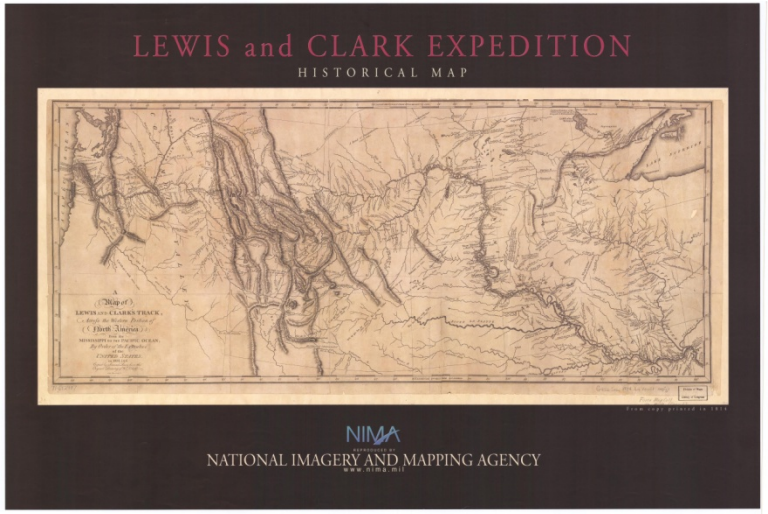

Summary

- 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

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With Time Comes Clarity