



Health Outcomes Scientific, Strategic & Regulatory Consultation

United BioSource Corporation’s (UBC) scientific staff **provides strategic scientific consultation on health outcomes strategy and regulatory requirements for the use of health outcomes measures**, including patient-reported outcomes (PROs), in clinical trials.

Creating and implementing a health outcomes research program, or evaluating an ongoing program, requires the ability to understand and navigate changes in regulatory and reimbursement policies and requirements. This requires a thoughtfully designed strategy that can withstand stakeholder scrutiny and effectively address the key issues across each stage of product development.

Exploratory Pre-clinical, Phase I	Registration Phase II, III	Commercialization Phase IIIb/IV
Limited knowledge of product and marketplace	Successful proof of concept	Label expansion, comparative assessment
<p>What are the differentiating factors of the product, and what will consumers, payers and clinicians view as most important?</p> <p>How can product attributes best be measured, and what is the best health outcomes measurement strategy?</p>	<p>How can requirements for FDA, EMEA and other regulatory agencies be met within the product development timeframe?</p> <p>Is there a clear focus or strategic plan in place for measurement of health outcomes?</p>	<p>What is the information that payers, clinicians and consumers will require to evaluate the value of the treatment and enable decision making?</p> <p>Is a health outcomes measurement strategy in place to capture this information?</p>

UBC accelerates the generation, analysis and communication of real-world evidence.

UBC scientists have years of experience partnering with, and working within, pharmaceutical companies to design and implement health outcomes strategies that meet FDA and global regulatory requirements for health outcomes endpoints.

UBC’s Health Outcomes Strategic and Regulatory Consultation provides:

- Expertise and Insight*
 - PRO and clinical endpoint development and psychometric evaluation, in accordance with FDA and EMEA standards
 - Synthesis and collection of all information required for PRO Evidence Dossiers
 - Strategic review of Phase II, III and post-approval study designs
 - Consultation on PRO-related label claims language
 - Authoritative communication with regulatory authorities on the health outcomes plan
- Comprehensive Guidance and Planning*
 - Outcomes measure selection
 - Review and synthesis of evidence for specific measures
 - Study design and analysis plans
 - Communication strategy for health outcomes endpoints
- Development and Implementation*
 - When new measure development is indicated, UBC scientists have the expertise to create measures that work as successful trial endpoints

UBC is a Valuable Strategic Partner

Industry Leaders

- Scientific experts with pharmaceutical industry experience and perspective
- Developed multiple health outcomes measures across a variety of therapeutic areas
- Extensive publication record in peer-reviewed journals
- Currently leading multi-sponsor consortia to address the need for better health outcomes endpoint measures (see www.exactproinitiative.com; www.cognitioninitiative.com)
- Instrumental in PRO harmonization efforts over the past 20+ years
 - Recommendations for the measurement and reporting of health-related quality of life to support labeling and promotional claims in the U.S. (Leidy et al., 1999; Revicki et al., 2000)
 - Contributed responses to the FDA on the Draft PRO Guidance through ISOQOL, ISPOR and major pharma
 - Co-chaired conferences and workshops to teach industry colleagues about the FDA Guidance and its requirements
 - UBC scientists have led the way in preparing PRO Evidence Dossiers to support PRO endpoint use

Demonstrated Results

Obtaining Regulatory Approval and Compliance

All research activities from methodology to documentation are consistent with best practices and the FDA draft guidance on optimal PRO instrument development (Revicki, 2007a; Leidy and Vernon, 2008).

UBC's PRO Evidence Dossiers have been successfully reviewed by the FDA and EMEA.

UBC-developed PRO measures have been used successfully as trial endpoints.

Selected UBC Health Outcomes Publications

Acquadro C, Conway K, *Hareendran A*, Aaronson N; European Regulatory Issues and Quality of Life Assessment (ERIQA) Group. Literature Review of Methods to Translate Health-Related Quality of Life Questionnaires for Use in Multinational Clinical Trials. *Value in Health* 2008 May-Jun; 11(3):509-21.

Wyrwich KW, Metz SM, Kroenke K, Tierney WM, Babu AN, Wolinsky FD. Triangulating Patient and Clinician Perspectives on Clinically Important Differences in Health-Related Quality of Life Among Patients with Heart Disease. *Health Serv Res* 2007; 42(6 Pt 1):2257-2274.

Leidy NK, *Vernon M*. Perspectives on Patient-Reported Outcomes: Content Validity and Qualitative Research in a Changing Clinical Trial Environment. *Pharmaco-Economics* 2008; 26(5):363-70.

Leidy NK, *Revicki DA*, Geneste B. Recommendations for Evaluating the Validity of Quality of Life Claims for Labeling and Promotion. *Value in Health* 1999; 2:113-127.

Revicki DA, Erickson PA, Sloan JA, Dueck A, Guess H, Santanello NC. Interpreting and Reporting Results Based on Patient-Reported Outcomes. *Value in Health* 2007a Nov-Dec; 10 Suppl 2:S116-24.

Revicki DA, Gnanasakthy A, Weinfurt K. Documenting the Rationale and Psychometric Characteristics of Patient-Reported Outcomes for Labeling and Promotional Claims: The PRO Evidence Dossier. *Qual Life Res* 2007b May; 16(4):717-723.

Revicki DA. Regulatory Issues and Patient-Reported Outcomes Task Force for the International Society for Quality of Life Research. FDA Draft Guidance and Health-Outcomes Research. *Lancet* 2007c Feb 17; 369(9561):540-2.

Revicki DA, Osoba D, Fairclough D, Barofsky I, Berzon R, *Leidy NK*, Rothman M. Recommendations on Health-Related Quality of Life Research to Support Labeling and Promotional Claims in the United States. *Qual of Life Res* 2000; 9:887-900.

Wild D, *Eremenco S*, Mear I, Martin M, Houchin C, Gawlicki M, *Hareendran A*, *Wiklund I*, Chong LY, von Maltzahn R, Cohen L, Molsen E. Multinational Trials – Recommendations on the Translations Required, Approaches to Using the Same Language in Different Countries, and the Approaches to Support Pooling the Data: The ISPOR Patient-Reported Outcomes Translation and Linguistic Validation Good Research Practices Task Force Report. *Value in Health* 2008 Nov 12.

Selected PROs Developed by UBC Scientists

Brief Male Sexual Function Inventory (BMSFI)

O'Leary MP, Fowler FJ, *Lenderking WR*, Barber B, Sagnier PP, Guess HA, Barry MJ. A Brief Male Sexual Function Inventory for Urology. *Urology* 1995; 46:697-706.

Overactive Bladder Questionnaire (OAB-q)

(www.oabq.com)

Coyne KS, *Revicki DA*, Hunt T, Corey R, Stewart W, Bentkover J, Kurth H, Abrams P. Psychometric Validation of an Over-active Bladder Symptom and Health-Related Quality of Life Questionnaire: the OAB-q. *Qual of Life Res* 2002; 11:563-574.

Treatment Satisfaction Questionnaire for Gastroesophageal Reflux Disease (TSQ-G)

Coyne KS, *Wiklund I*, Schmier J, Halling K, degl' Innocenti A, *Revicki DA*. Development and Validation of a Disease-Specific Treatment Satisfaction Questionnaire for Gastroesophageal Reflux Disease (TSQ-G). *Alimentary Pharma-cology and Therapeutics* 2003; 18(9):907-15.

Patient-Reported Outcomes in Cognitive Impairment (PROCOG)

Frank L, Flynn J, *Kleinman L*, *Margolis MK*, *Matza L*, Beck C, Bowman L. Validation of a New Symptom Impact Questionnaire for Mild to Moderate Cognitive Impairment. *International Psychogeriatrics* 2006; 18(1):135-149.

Gastroparesis Cardinal Symptom Index (GCSI)

Revicki DA, *Rentz AM*, Dubois D, Kahrilas P, Stanghellini V, Talley NJ, Tack J. Development and Validation of a Patient Reported Assessment of Severity of Gastroparesis Symptoms. *Qual Life Res* 2004 May; 13(4):833-844.

UFS-QOL: The Uterine Fibroid Symptom and Quality of Life Questionnaire

Spies JB, *Coyne K*, Guaou Guaou N, Boyle D, Skyrnarz-Murphy K, Gonzalves SM. The UFS-QOL, a New Disease-Specific Symptom and Health-Related Quality of Life Questionnaire for Leiomyomata. *Obstet Gynecol* 2002 Feb; 99(2):290-300.

The Infant Gastroesophageal Reflux Questionnaire

Kleinman L, Rothman M, Strauss R, Orenstein SR, Nelson S, Vandenplas Y, Cucchiara S, *Revicki DA*. The Infant Gastroesophageal Reflux Questionnaire Revised: Development and Validation as an Evaluative Instrument. *Clinical Gastroenterology and Hepatology* 2006; 4:588-596.

Schizophrenia Objective Functioning Instrument (SOFI)

Kleinman L, Lieberman J, Dube S, Mohs R, Zhao Y, Kinon B, Carpenter W, Harvey PD, Green MF, Keefe RSE, *Frank L*, Bowman L, *Revicki DA*. Development and Psychometric Performance of the Schizophrenia Objective Functioning Instrument: An Interviewer Administered Measure of Function. *Schizophrenia Research* 2009; 107:275-285.

PPMQ-R: Patient Perception of Migraine Questionnaire-Revised

Revicki DA, *Kimel M*, Beusterien K, Kwong JW, Varner JA, Ames MH, Mahajan S, Cady RK. Validation of the Revised Patient Perception of Migraine Questionnaire: Measuring Satisfaction with Acute Migraine Treatment. *Headache* 2006; 46:1-13.

PAGI-SYM: Patient Assessment of Upper Gastrointestinal Symptom Severity Index

Rentz AM, Kahrilas P, Stanghellini V, Tack J, Talley NJ, de la Loge C, Trudeau E, Dubois D, *Revicki DA*. Development and Psychometric Evaluation of the Patient Assessment of Upper Gastrointestinal Symptom Severity Index in Patients with Functional Gastrointestinal Disorders. *Qual Life Res* 2004; 13(10):1737-1749.

ASUI: Asthma Symptom Utility Index

Revicki DA, *Leidy NK*, Brennan-Diemer F, *Sorensen S*, Togias, A. Integrating Patient Preferences into Health Outcomes Assessment: The Multiattribute Asthma Symptom Utility Index. *Chest* 1998; 114:998-1007.

Rhinitis Symptom Utility Index (RSUI)

Revicki DA, *Leidy NK*, Brennan-Diemer F, *Thompson C*, Togias A. Development and Preliminary Validation of the Multiattribute Rhinitis Symptom Utility Index. *Qual Life Res* 1998 Dec; 7(8):693-702.

Breast Evaluation Questionnaire (BEQ)

Anderson RC, Cunningham B, Whiteley S, Tafesse E, *Lenderking WR*. Validation of the Breast Evaluation Questionnaire for Use with Breast Surgery Patients. *Plastic and Reconstructive Surgery* 2006; 118(3):597-602.

General Health Self-Assessment (for HIV)

Lenderking WR, Testa MA, Katzenstein D, Hammer S. Measuring Quality of Life in Early HIV Disease: The Modular Approach. *Qual Life Res* 1997; 6(6):515-530.

Impact on Lifestyle Questionnaire (Acromgealy)

Lenderking WR, Zacker C, Katznelson L, Vance ML, Hossain S, Tafesse E, Guacaneme AO, Pashos CL. The Reliability and Validity of the Impact on Lifestyle Questionnaire in Patients with Acromegaly. Value in Health 2000; 3(4):261-269.

QIDS-SRD14 (Daily version of the QIDS-SR for Depression trials)

Lenderking WR, Hu M, Tennen H, Cappelleri JC, Petrie CD, Rush AJ. Daily Process Methodology for Measuring Earlier Antidepressant Response. Contemporary Clinical Trials 2008; (29):867-877.

Schwartz Outcomes Scale (SOS-10)

Blais M, Lenderking WR, Baer L, deLorell A, Peets K, Leahy L, Burns C. Development and Initial Validation of a Brief Mental Health Outcome Measure. Journal of Personality Assessment 1999; 73(3):359-373.

Haemophilia-Specific Health-Related Quality of Life Questionnaire for Adults (Haemo-QoL-A)

Rentz AM, Flood E, Altisent C, Bullinger M, Klamroth R, Garrido RP, Scharrer I, Schramm W, Gorina E; Members of the HAEMO-QoL-A Steering Committee. Cross-Cultural Development and Psychometric Evaluation of a Patient-Reported Health-Related Quality of Life Questionnaire for Adults with Haemophilia. Haemophilia 2008; 14(5):1023-34. [Epub 2008 Jul 28]

Gastrointestinal Symptom Rating Scale (GSRS)

Revicki DA, Wood M, Wiklund I, Crawley J. Reliability and Validity of the Gastrointestinal Symptom Rating Scale in Patients with Gastroesophageal Reflux Disease. Qual Life Res 1998; 7:75-83.

Quality of Life in Reflux and Dyspepsia (QOLRAD)

Wiklund I, Junghard O, Grace E, Talley NJ, Kamm M, Veldhuyzen van Zanten S, Paré P, Chiba N, Leddin DS, Bigard M-A, Colin R, Schoenfeld P. Quality of Life in Reflux and Dyspepsia Patients. Psychometric Documentation of a New Disease-Specific Questionnaire (QOLRAD). Eur J Surg 1998; 164 (Suppl 583):41-49.

Nocturia Quality-of-Life Questionnaire (N-QOL)

Abraham L, Hareendran A, Mills IW, Martin ML, Abrams P, Drake MJ, MacDonagh RP, Noble JG. Development and Validation of a Quality-of-Life Measure for Men with Nocturia. Urology 2004 Mar; 63(3):481-6.

Venous Leg Ulcer Quality of Life Questionnaire (VLU-QoL)

Hareendran A, Doll H, Wild DJ, Moffatt CJ, Musgrove E, Wheatley C, Franks PJ. The Venous Leg Ulcer Quality of Life (VLU-QoL) Questionnaire: Development and Psychometric Validation. Wound Repair Regen 2007 Jul-Aug; 15(4):465-73.

Work Productivity and Activity Impairment Questionnaire for Patients with Gastro-esophageal Reflux Disease (WPAI-GERD)

Wahlqvist P, Guyatt GH, Armstrong D, Degl'Innocenti A, Heels-Ansdell D, El-Dika S, Wiklund I, Fallone CA, Tanser L, Veldhuyzen van Zanten S, Austin P, Barkun AN, Chiba N, Schünemann HJ. The Work Productivity and Activity Impairment Questionnaire for Patients with Gastroesophageal Reflux Disease (WPAI-GERD): Responsiveness to Change and English Language Validation. Pharmacoeconomics 2007; 25:385-396.

Reflux Disease Questionnaire (RDQ)

Shaw M, Dent J, Beebe T, Junghard O, Wiklund I, Lind T, Johnsson F. The Reflux Disease Questionnaire: a Measure for Assessment of Treatment Response in Clinical Trials. Health Qual Life Outcomes 2008 Apr 30; 6:31.



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