

Rheumatoid Arthritis Working Group: General Concepts of Measurements in RA Clinical Trials

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RA Working Group within the Qualification Process



FDA Review FDA Consultation **Planning** and Advice **Phase Feasibility** Methods & **Phase Results Sharing Define concept** & context of **Determine** use interest and resources availability Feasibility Scoping stage summary document document (Sep 2011) (March 2010) Stakeholders Workshop (Aug 2012)

Statement of **Qualification**

DDT Publicly Available

Regulatory Agencies Guidance and Clinical - International Societies



Guidance for Industry

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

Additional copies are available from:



London, 27 July 2005 Doc. Ref. EMEA/CHMP/EWP/139391/2004

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

REFLECTION PAPER ON THE REGULATORY GUIDANCE FOR THE USE OF HEALTH-RELATED QUALITY OF LIFE (HRQL) MEASURES IN THE EVALUATION OF MEDICINAL PRODUCTS

ISPOR TASK FORCE REPORTS

Content Validity—Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 1—Eliciting Concepts for a New PRO Instrument

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ACR, EULAR, OMERACT, PROMIS, International Classification of Function (ICF), etc.

Good Practices: Eliciting Concepts for a New PRO Instrument



- Good practice 1: **Determine the context of use:**
 - Understand the disease or condition in the target population,
 - Develop an endpoint model for the contact of use,
 - Consider target population-cultural/language groups,
 - Consider preliminary issues related to instrument content and structure,
 - Consider the theoretical conceptual framework,
 - Develop an hypothesized conceptual framework.
- Good practice 2: Develop the research protocol for qualitative concept elicitation and analysis
- Good practice 3. Conduct the concept elicitation interviews and focus groups
- Good practice 4. Analyze the qualitative data
- Good practice 5. Document concept development and elicitation methodology and results

RA WG: Developing the Disease model - Supportive Evidence



- Review of previously conducted qualitative research with RA patients and literature reviews with the objective to develop a disease model:
 - Identify concepts that are important to RA patients,
 - Identify existing PRO measures used in RA clinical trials,
 - review of RA labels (FDA and EMA),
- Consultations with several key opinion leaders (KOLs)
 in the field of RA and PRO,
- Review of the disease model by clinicians (RA WG member firms),

Hypothesized Disease Model

Co-morbidities: DM.
 OP. Renal, Liver



RA Disease Activity RA Signs & Symptoms Impacts *Extent of disease control •Flare Experience Physical Functioning Articular Inflammatory -Mobility (lower extremity function) · Pain -Dexterity (upper extremity function) Process Stiffness -Axial (neck and back function) -Disability Swelling Tenderness Performance Functioning Destruction, Damage -Activities of Daily Living (Self Care) and Deformation -Home management and chores Extra Articular Bone -Work functioning Fatique/weakness Joints -Disability · Sleep disturbance Cartilage Other Manifestations of organs Psychological Functioning Nodules -Emotional (anxiety about future, ·Dry eyes/mouth moodiness, depression, frustration), ·Lung disease/shortness of breath -Cognitive (concentration) RA Treatment ·CVD/CAD -Coping (adaptation strategies) Vasculitits •Regimen Adherence Social Functioning Persistence -Leisure activities -Family life Environmental Conditions **AEs of Treatment** Financial Well-being Weather ·Weight loss/gain -Loss of work Time of day •Nausea -Cost of treatment and healthcare .Vomiting *Hypertension

Hypothesized Endpoint Model



Endpoint hierarchy	Proposed Concepts to document how a patient survives, feels or function	PRO, ClinRO, ObsRO/ Biomarker/ Survival
Composite endpoint for indication of treatment of RA	 Symptom: Pain Symptom: Fatigue Symptom: morning Stiffness Sign: Swollen joint Sign: Tender joint Inflammation (CRP or ESR) Disease activity Impact: Disability/decrements in physical function 	 PRO PRO PRO ClinRO ClinRO Biomarker ClinRO/PRO PRO
Secondary Other treatment benefits	 RA-related symptoms RA-defining decrements in physical function 	•PRO •PRO

Feed-back from the FDA on the proposed PRO concepts from the RA WG



- Regulatory relevance: "We acknowledge that the PRO measures currently used in RA patients could be improved to meet current standards for measurement..."
- **Concept of measurement**: "In principle, the overall concepts you have proposed (i.e., RA symptoms and RA-defining decrements in physical function) appear relevant, but it is' premature to commit to specific items or domains (i.e., subconcepts of measurement) for labeling".
- **Context of use**: comments on early RA and the wide spectrum of RA population (from mild to severe)



General Discussion

Discuss Research Agenda



- Is there an unmet need to improve or develop new PRO measures in RA clinical trials?
- What RA-related symptoms should be measured in clinical trails to show treatment benefit?
 - Is fatigue one of the core symptoms of RA?
 - Is stiffness one of the core symptoms of RA?
 - Are there additional RA-related symptoms that should be measured?
- Is the current assessment of **physical function** adequately measured with HAQ-DI in RA?