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

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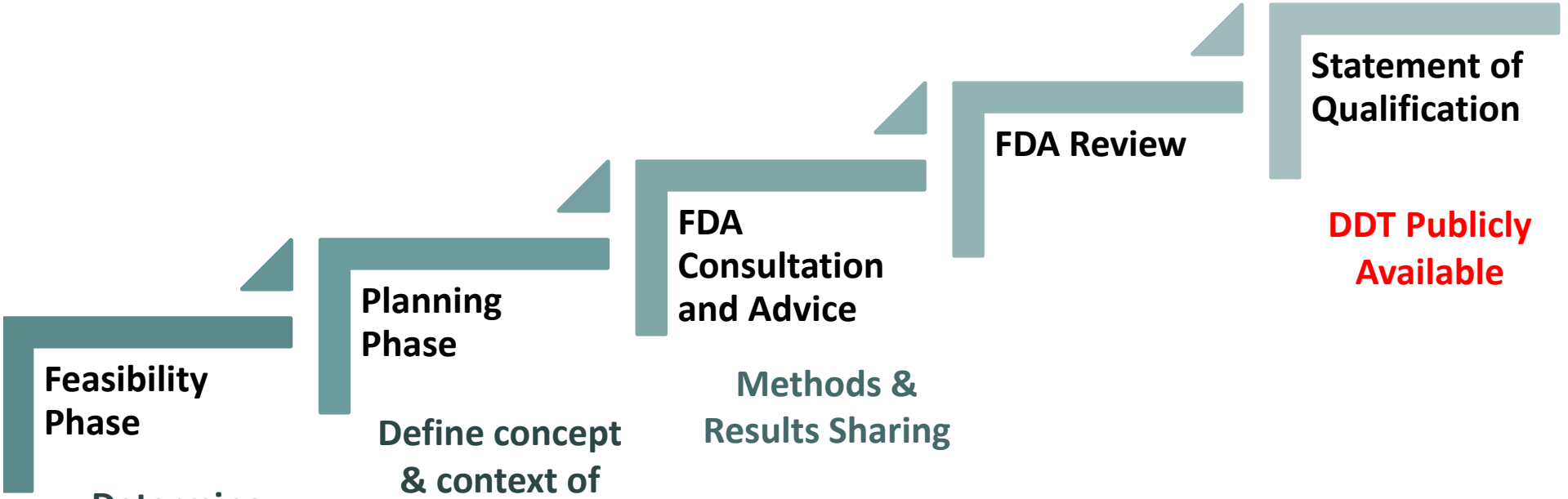
RA Working Group within the Qualification Process



Feasibility document (March 2010)

- Scoping stage summary document (Sep 2011)
- Stakeholders Workshop (Aug 2012)

Regulatory Agencies Guidance and Clinical - International Societies

PRO CONSORTIUM
CRITICAL PATH INSTITUTE

Guidance for Industry

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

Additional copies are available from:

emea
European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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

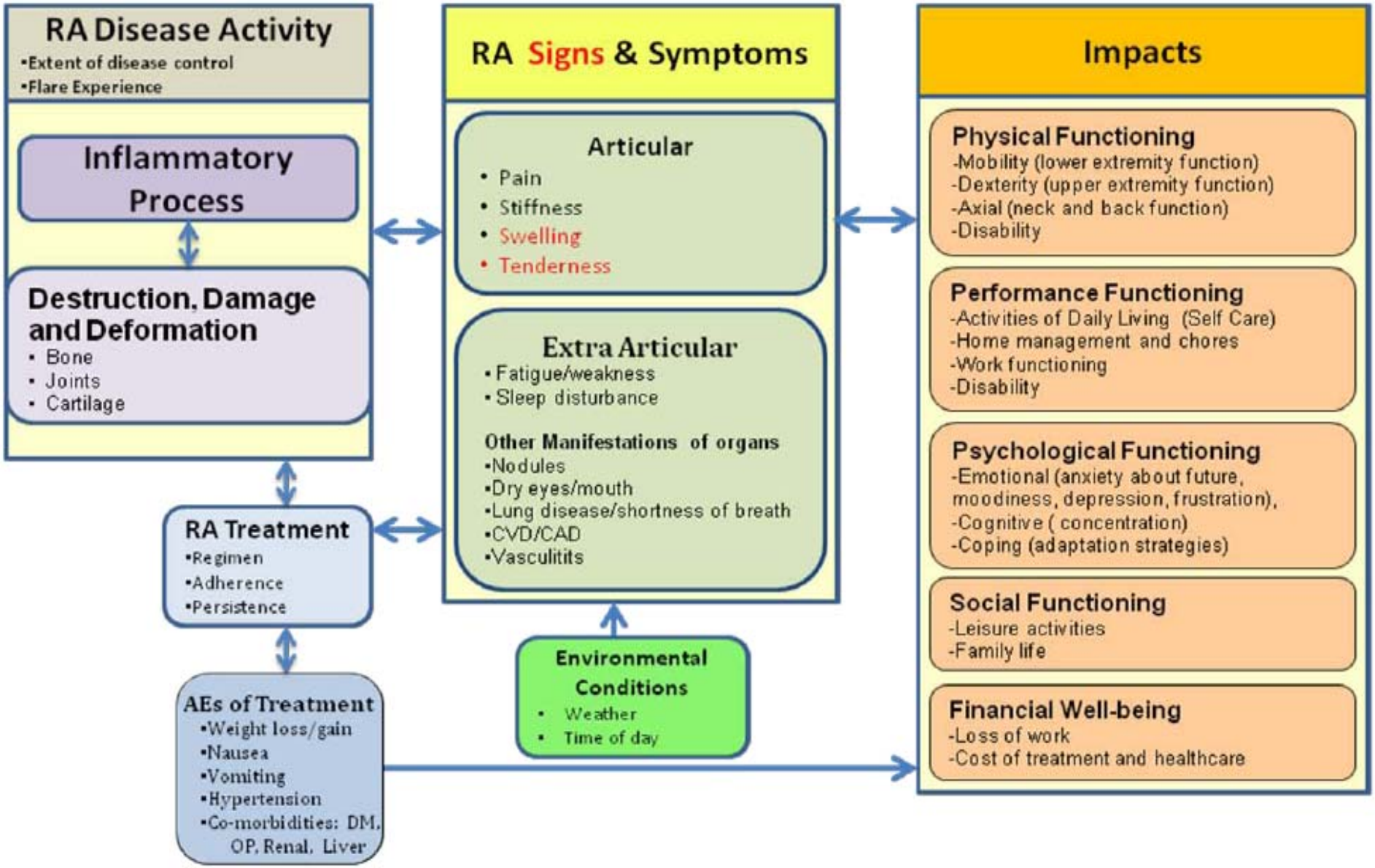
RA WG: Developing the Disease model - Supportive Evidence

- 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



Hypothesized Endpoint Model

Endpoint hierarchy	Proposed Concepts to document how a patient survives, feels or function	PRO, ClinRO, ObsRO/ Biomarker/ Survival
Primary 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 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?