# Meeting between the Swedish MPA and the ERIQA Group

Uppsala, Sweden

September 11th, 2003

# AGENDA

- 9:30-9:45 **Welcome – Background**
  *Swedish MPA representative,*
  *Pr. Ingela Wiklund*

- 9:45-10-15 **The Swedish Agency view on the use of PROs, such as HRQL, in clinical trials**
  *Swedish MPA representative*

- 10:30-11:00 **EMEA Guidelines and PROs – Current status**
  *Dr Catherine Acquadro*

# AGENDA

- 11:15-11:45 **Scientific criteria in studies assessing PROs**
  Dr Olivier Chassany
- 11:45-12:15 **The industry perspective**
  Pr Ingela Wiklund
- 12:15-12:45 **Future (the Workmats)**
  Dr Olivier Chassany

# Background

Ingela Wiklund, PhD., Professor
Senior Principal Scientist
Global Director Outcomes Research
AstraZeneca

# European Regulatory Issues on Quality of Life Assessment (ERIQA) Group

## Mission Statement

***« Establishing principles and practices for the integration of Health-related Quality of Life outcomes in the drug regulatory process »***

# European Guidance for the Improved Integration of Quality of Life in the Drug Regulation Process (ERIQA)

How to increase the credibility of Quality of Life data in files submitted to regulatory authorities ?

*Chassany O, Sagnier P, Marquis P, Fulleton S, Aaronson N.*

*Patient Reported Outcomes and Regulatory Issues: the Example of Health-related Quality of Life – A European Guidance Document for the Improved Integration of HRQL Assessment in the Drug Regulatory Process. Drug Information Journal 2002;36(1):209-238.*

# Previous programs (2000-2002)

## February 16, 2001

## *Important Issues in PRO Research*

## *FDA Office, Rockville, MD,USA*

Volume 6 • Number 5 • 2003
VALUE IN HEALTH

**Incorporating the Patient's Perspective into Drug Development and Communication: An Ad Hoc Task Force Report of the Patient-Reported Outcomes (PRO) Harmonization Group Meeting at the Food and Drug Administration, February 16, 2001**

Catherine Acquadro, MD,[1] Rick Berzon, PH,[2] Dominique Dubois, MD,[3] Nancy Kline Leidy, PhD,[4] Patrick Marquis, MD,[5] Dennis Revicki, PhD,[4] Margaret Rothman, PhD,[6] for the PRO Harmonization Group

[1]MAPI Research Institute, Lyon, France; [2]Boehringer Ingelheim GmbH, Ridgefield, CT, USA; [3]Janssen Pharmaceutica, Beerse, Belgium; [4]MEDTAP, Bethesda, MD, USA; [5]MAPI Values, Boston, MA, USA; [6]Johnson & Johnson, Raritan, NJ, USA

**Previous programs (2000-2002)**

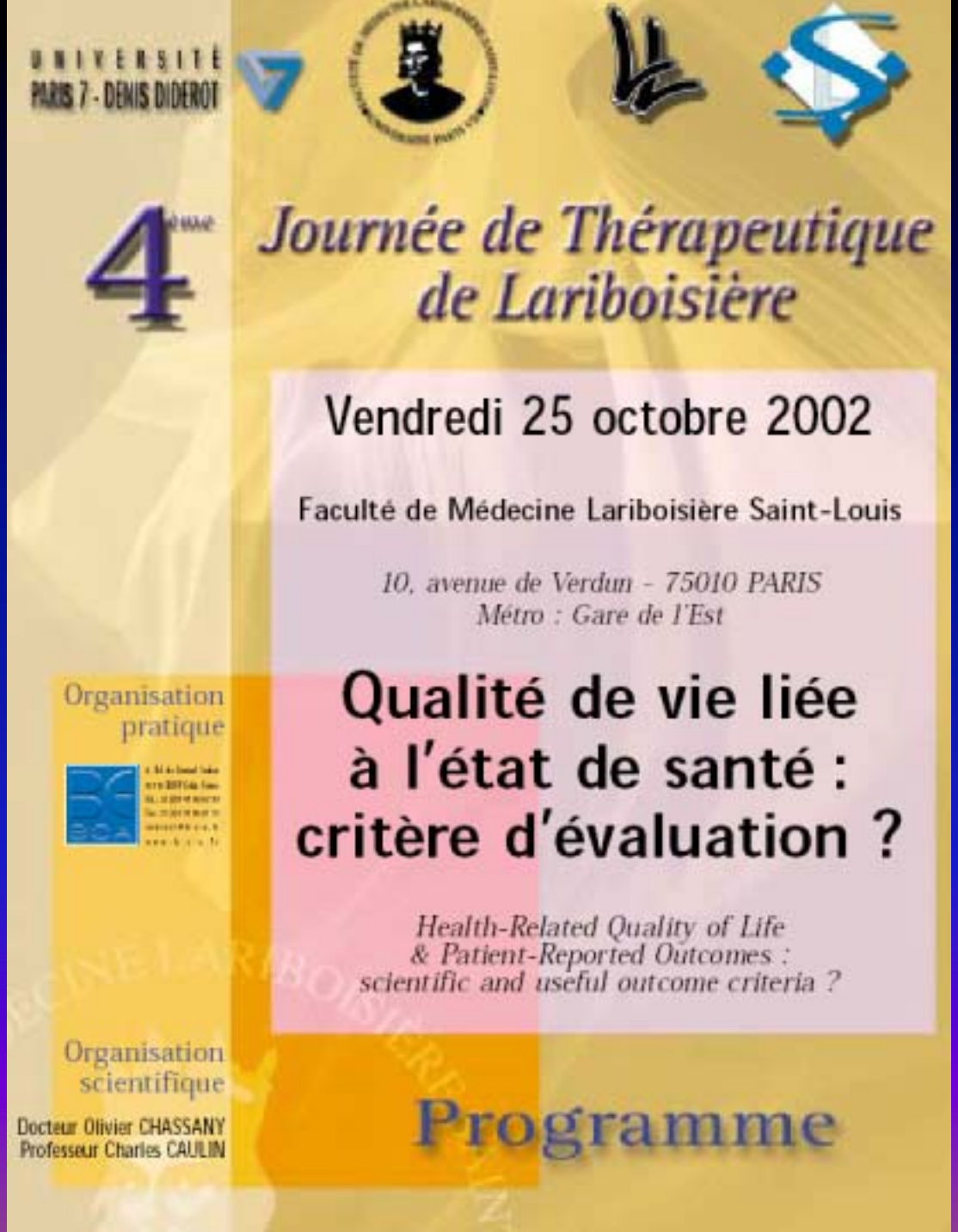
***March 1, 2002***

***Important Issues in PRO Research***

***Continued Discussions***

***FDA Office, Rockville, MD,USA***

# Previous programs (2000-2002)



**Future Program (2004)**

**May 10-11, 2004 -- Paris**

# Assessing Treatment Impact Using PROs : Challenges in Study Design, Conduct and Analysis

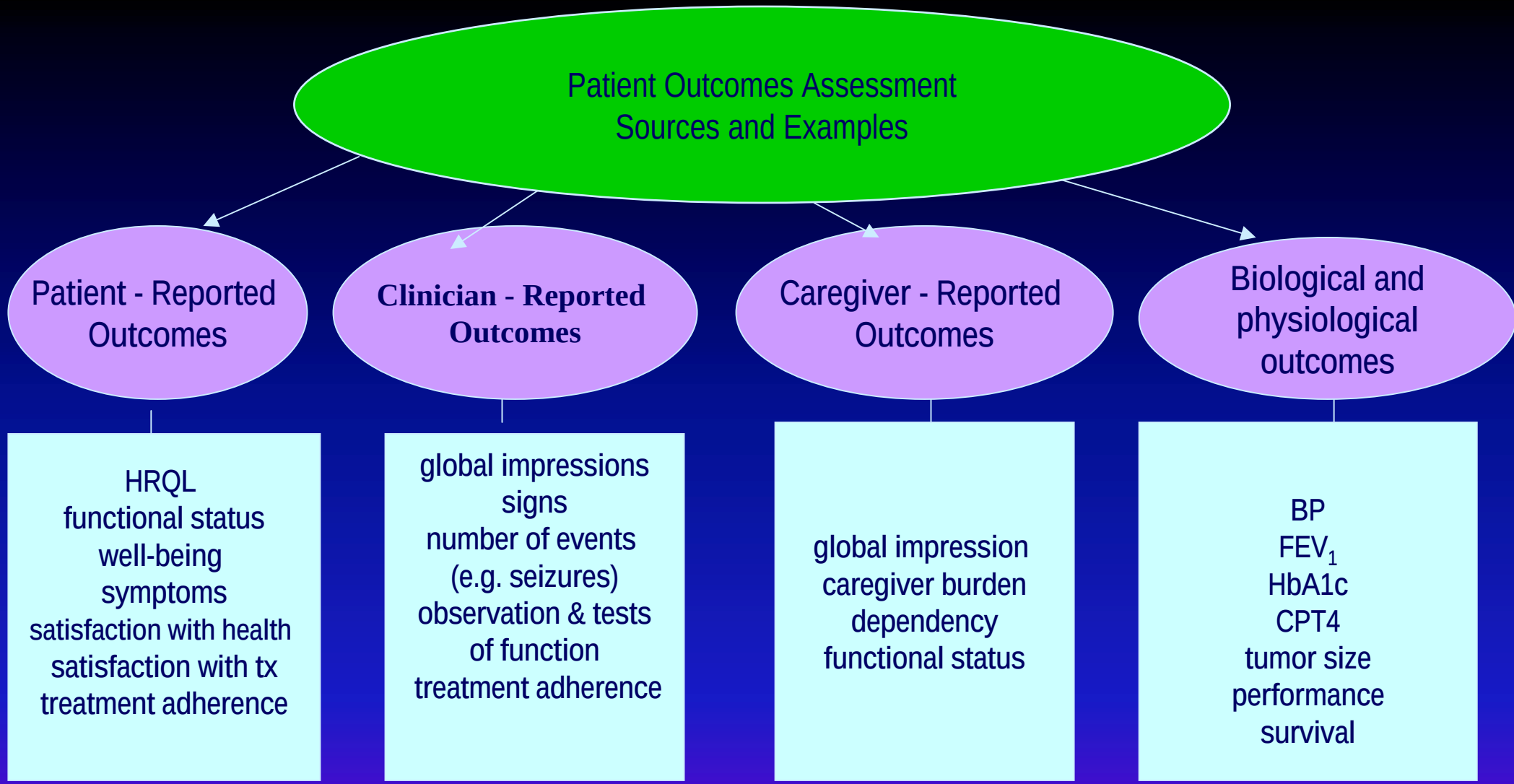
A DIA & ERIQA Group Meeting

*QUALITY OF LIFE*

**Health related quality of life**

**Health outcomes**

***PATIENT REPORTED OUTCOMES (PROs)***

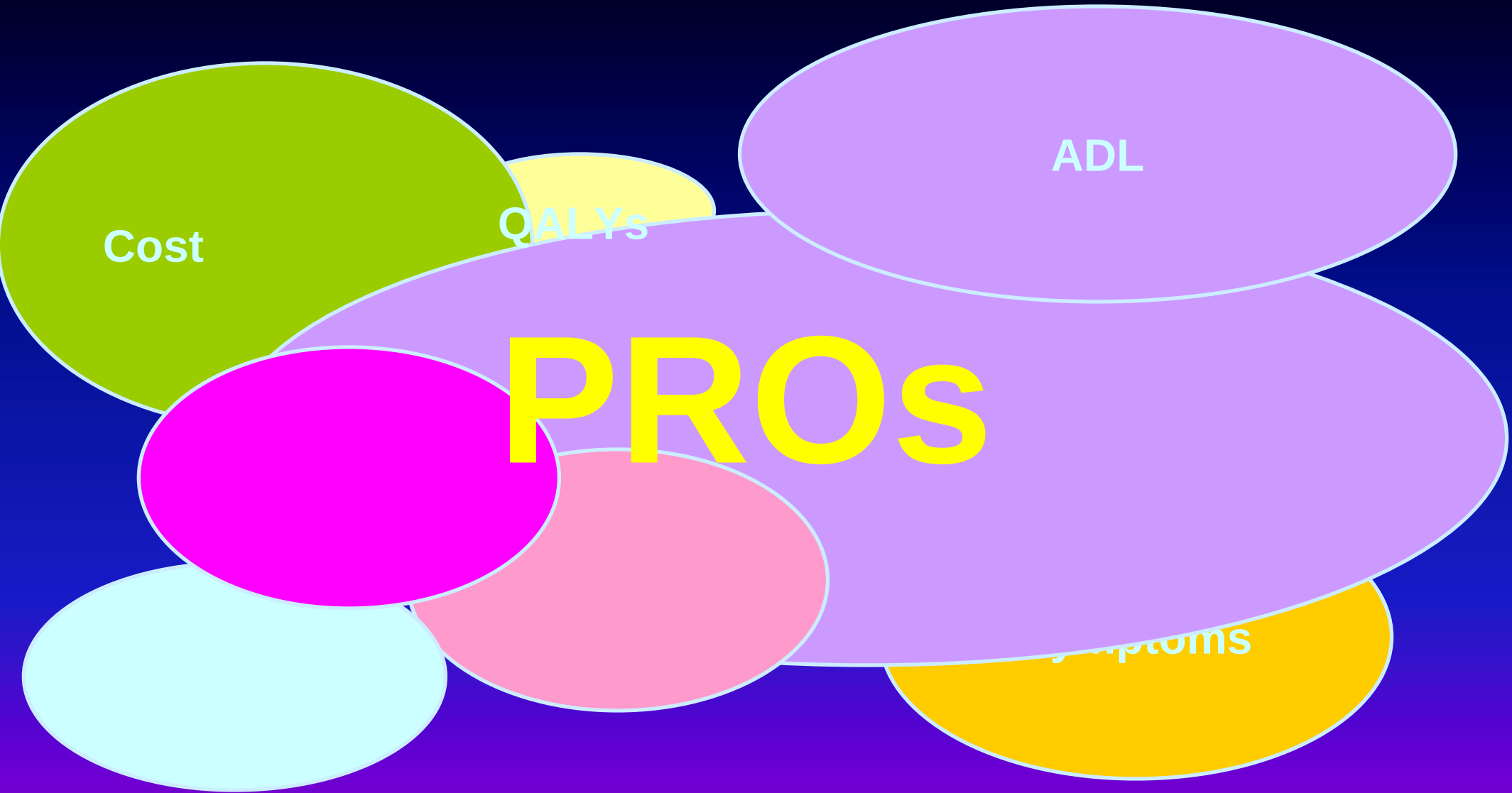

Patient Outcomes Assessment
Sources and Examples
Patient - Reported Outcomes
Clinician - Reported Outcomes
Caregiver - Reported Outcomes
Biological and physiological outcomes
HRQL
functional status
well-being
symptoms
satisfaction with health
satisfaction with tx
treatment adherence
global impressions
signs
number of events
(e.g. seizures)
observation & tests
of function
treatment adherence
global impression
caregiver burden
dependency
functional status
BP
FEV1
HbA1c
CPT4
tumor size
performance
survival

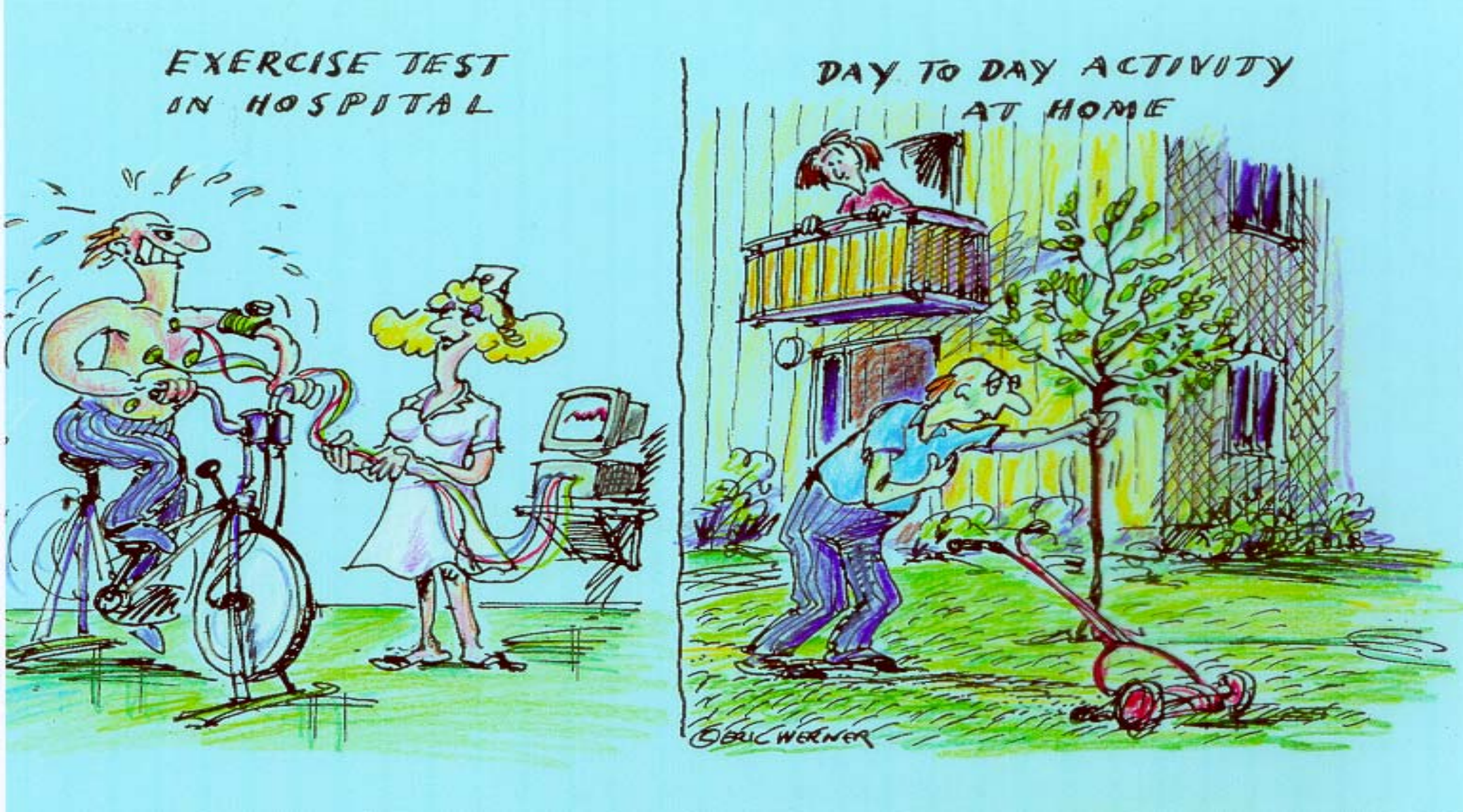
# Patient Outcomes Assessment

- Umbrella term to describe four types of endpoints for measuring the end results of health interventions:
  - patient reported
  - clinician reported
  - caregiver reported
  - biological and physiological
- All four endpoints use standardized measurement
- All four types endpoints yield potentially valuable information to informing decision making

Recently, the FDA suggested the use of **Patient Reported Outcomes (PROs) in place of Health-Related Quality of Life (HRQL)** as an umbrella term to capture the patient´s perspective and subjective perception. In fact, the FDA´s advertsiement division suggested that the term PROs more accurately reflects the goal of measuring the impact of treatment from the patient´s perspective. The agency found **the term QL unsatisfactory because it is too broad and unspecific to describe treatment outcome.**

# FDA view on Outcomes claims classification






OBJECTIVE

SUBJECTIVE

# Patient-Reported Outcomes

- Assess patient perspective according to science of measurement
- Clear specification of hypotheses is required for claim
- Data collection methods are similar
- Standard methods of analysis and interpretation apply

# Patient-reported Outcomes: Similarities

- Data represents patient perspective
- Data collection methods are similar
- Data usually collected in clinical trials using scales or questionnaires
- Clear specification of hypotheses is required

# Benefits of Patient Reported Outcomes - FDA perspective

- May provide better information about the actual impact (both positive and negative) of drug therapy
- Many HRQL instruments are better developed and validated than traditional measures of effectiveness
- May detect less obvious or unexpected effects
- May provide more relevant information to decision-makers

# Regulatory Situation

- Despite wide differences across diseases, PRO claims for label and/or promotion are gaining momentum.
- For pricing & reimbursement claims, PRO measures have long been included in assessment of added value by pricing-reimbursement authorities.
- **FDA appoints Laurie Burke to head a new program ”Study Outcomes and Labeling Claims” across all review divisions starting August 2002.**
- **Increased interest at EMEA and other regulatory agencies mark a turning point in the development of PRO measures.**

**Recent & ongoing regulatory developments will boost the acceptability of PRO endpoints**

# EMEA guidelines and Patient-Reported Outcomes

## Current Status

**Catherine Acquadro, MD**
Coordinator of the ERIQA Group
HRQL Methods Group Convenor
Scientific Director,
Mapi Reasearch Institute, France

Secure IE

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Back http://www.emea.eu.int/index/indexh1.htm



emea The European Agency for the Evaluation of Medicinal Products

## Human Medicines



PRODUCT ALERT

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Monday, May 26, 2003



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Send all queries regarding the Web functionality to: EMEAwebservices

# Notes for Guidance (NfG)

- EMEA Documents available on:

  **www.emea.eu.int/index/indexh1.htm**

- Efficacy Working Party Notes for Guidance:
  - **Concept papers (CP)**
  - **Points to consider (PC)**
  - **Draft Guidelines (DG)**
  - **Approved Guidelines (AG)**

# Review of EWP NfG

## Today's Objective

- To identify diseases or drugs in which a formal Patient-Reported Outcomes (PROs) evaluation is recommended
- To identify recommended measures

# Review of EWP NfG

*Results (09/01/2003)*

| | # NfG | With PROs | Incl. HRQOL |
|---|---|---|---|
| Concept Papers | 16 | 4 | 2 |
| Points to consider | 24 | 7 | 7 |
| Draft Guidelines | 7 | 1 | 1 |
| Approved Guidelines | **36** | **12** | **11** |
| **TOTAL** | **83** | **24** | **21** |

# Review of EWP NfG

## 24 Notes for Guidance including PRO evaluation

- **CVD**

  Stable Angina Pectoris, Cardiac Failure, Chronic Peripheral Arterial Occlusive Disease
- **Gastroenterology**: Crohn's Disease, IBS
- **Neurology**

  Acute Ischemic Stroke, Alzheimer's Disease, Amyotrophic Lateral Sclerosis, Migraine, Multiple Sclerosis, Neuropathic Pain Management, Nociceptive Pain*, Parkinson's Disease
- **Psychiatry**: Panic Disorder*, OCD*
- **Respiratory Diseases**: Asthma, COPD
- **Rheumatology**: Osteoarthritis, Rheumatoid Arthritis
- **Others**: Anti-Cancer Drugs in Man, HIV, Psoriasis, Urinary Incontinence in women, Weight Control

***not including HRQL**

# CPMP/EWP/205/95 Rev 2- corr: Anticancer MP in Man

AG

## 4. Phase III Trials

## 4.1 Objectives and background

4.12. To study the effects of a new agent. Appropriate end-points of assessment include: progression-free/recurrence-free/relapse-free survival, overall survival, response rate, *symptom control/quality of life*

## 4.5 Evaluation of Efficacy

4.5.4. Symptom control and quality of life: *The choice of scales should be justified and the validity of the scale for the specific study population and its reliability should be documented. Cultural aspects should be taken into account, especially in the case of multinational studies.*

## 5. Requirements for authorisation

5.3.2.Quality of Life Studies: *QOL studies may be used to support symptom control data provided that established quality of life questionnaires (including for example level of hospitalisation) are used, which are relevant to the study population treated.*

3.1.2. & 3.2.4. Other clinical parameters: *In long-term therapeutic studies with an appropriate sample size of patients, the assessment of QoL should also be performed by using general or disease specific questionnaires. However, at present not fully validated scales are available for this purpose.*

**3.3, 4.3, 5.3 Criteria of Efficacy**

**3.3.2, 4.3.2, 5.3.2 Secondary end-points**

**3.3.2.4, 4.3.2.4, 5.3.2.5 Quality of Life**

*In trials with adequate sample size an assessment of Quality of life may be performed by using properly validated general and disease specific questionnaires.*

# *CPMP/EWP/234/95: Stable Angina Pectoris*



## 2. Criteria of Efficacy

2.2. Anginal pain: Frequency, intensity and duration of anginal pain… should be documented. It is highly relevant as a secondary end-point.

2.3. Quality of life: *QoL measurement can provide valuable information about the effect of therapy on the general health status*

## 3. Methods to assess efficacy

3.2. Anginal Pain: The patient's experience of anginal pain should be recorded in a patient diary. The daily frequency of anginal pain should whenever possible be registered by patients using available log books.

3.3. Quality of life: *A QoL assessment may be considered, provided the questionnaire is validated in the context of the proposed target group.*

# *CPMP/EWP/235/95, Rev 1: Cardiac Failure*



**3.4. Quality of Life:** *A broadly based assessment of the quality of life scales is recommended in Heart Failure studies because almost all components of the life quality may be influenced by an intervention for heart failure. Various QOL questionnaires have been used in the past and new ones devised. Unless these have been fully validated, evidence of efficacy derived from QoL questionnaires must be viewed as supportive only.*

*It is particularly important to consider whether (a) the scale is linear over the range of measurements, (b) is sensitive to the changes anticipated, (c) it is valid and useful to adjust results using the baseline scores, (d) there is any correlation between the score and the objective responses, (e) the observer and the patients should be blinded and (f) training of both the observer and the patient is necessary.*

*Rating scales to assess QoL should also be considered and should have been validated beforehand in the context of the proposed trial and its aims.*

**The Minnesota Living with Heart Failure Questionnaire is one of the many systems used in cardiac failure.** *Translations of questionnaires used should also have been thoroughly validated beforehand.*

## 2. Study design and methods

## 2.2 Choice of tools

2.2.5. Quality of Life:

*Although QOL is an important dimension of the consequences of diseases the lack of validation of its assessment in AD does not allow specific recommendations to be made as yet. When adequate instruments to assess this dimension in patients and their care givers become available, QOL assessment may be justified in AD trials*

## 5. Supportive evidence for efficacy

…

e) quality of life:

*Of the above list only d) and e) are established as useful additional secondary endpoints.*

# *CPMP/EWP/556/95 rev 1: Rheumatoid Arthritis*

PC

## 3. Tools to measure efficacy (primary or secondary endpoints)

…

*d) patient's global assessment of disease activity (VAS)*

*e) pain score (patient's assessment of pain, VAS, Likert Scale)*

…

*g) physical function (assessed by patient, e.g. HAQ, AIMS (function and quality of life)*

## 4. Supportive evidence for efficacy

…

*d) emotional and social function (e.g. AIMS-1)*

*e) quality of life (RA-specific, e.g. AIMS, or generic tests)*

*Of the above list only d) and e) are established as useful additional secondary endpoints*

## 4. Methods to assess efficacy

*The use of indirect efficacy variables as primary efficacy variable in pivotal studies, such as an improvement in the clinical global impression, quality of life or L-dopa+ savings is not recommended unless the association between these variables and improvement in core symptoms or motor fluctuations or handicap has been proven.*

## 2. Assessment of Efficacy Criteria

2.2. Secondary (supportive) Efficacy Endpoints:

*Choice of secondary variables should be justified by the applicant and could include variables such as quality of life parameters, biochemical parameters of lipid and glucose metabolism as well as blood pressure, cardiac function and sleep apnoea episodes.*

# *CPMP/EWP/784/97: Osteoarthritis*

PC

## II. Recommended primary/secondary efficacy endpoints

a) Symptom modifying drugs

**Pain** attributable to the target joint is recommended as primary endpoint. Functional disability is an important additional primary endpoint.

Pain should be measured by self-assessment with validated methods, such as visual analogue or Likert scales.

**Functional disability**

A disease-specific and joint specific instrument such as the WOMAC ...is recommended…

*Secondary endpoints include:*

*Global rating, Flares, Physical signs including range of motion, Quality of Life, Consumption of medications for pain relief*

# 5. Recommended primary/secondary efficacy endpoints

Primary: The patient's global assessment of symptoms and abdominal discomfort/pain should be used as the two primary endpoints. Statistically significant changes must be found in both parameters.

Secondary (supportive): choice of secondary efficacy variables should be justified by the applicant and should include variables such as bloating/distension, stool frequency and urgency, and quality of life parameters. Health-related quality of life must, however, be considered most important secondary endpoints

# 3. Methods to assess efficacy

Assessment scales for the measurement of stroke-related impairment, disability and handicap include neurological deficit scales, functional and global outcome scales as well as health-related quality of life scales (although the latter have not been developed specifically for stroke and have yet to be validated)

## 3.4. Health-related Quality of Life scales

At present, QOL scales are not among the primarily focussed end-points in stroke. If these scales are used, they should be validated for stroke. **Development of validated scales is encouraged for future trials.**

In case QOL scales are used as additional evidence, special attention should be paid to possible confounding factors such as post-stroke depression or change in the environment that might interfere with the specific treatment effects.

## 4. Methods to assess efficacy

4.4. Quality of Life: *Few data are available on validation of specific instruments for QoL in patients suffering multiple sclerosis.*

***If a claim with respect to QoL in MS is considered, reliable and valid scales should be used.***

## VI. Recommended Primary and secondary endpoints:

In the major efficacy studies of symptomatic benefit the primary endpoint should reflect the clinical benefit the applicant wishes to claim in the future SPC.

*The Primary symptomatic benefit endpoint should be justified by referencing published data which support its validity; one example is the St George's Respiratory Questionnaire.*

***There are a number of secondary endpoints which may provide useful information. These measure different aspects of the disease but they should be justified by referencing published data which support their validity; examples include…..symptom scales, exacerbation rates and QoL assessment.***

*Which are chosen will depend upon the claims being made in the SPC.*

*Care should be taken with respect to statistical multiplicity if secondary endpoints become the basis for specific claims.*

# *CPMP/EWP/565/98 draft: ALS*

PC

## VIII. Methods of Efficacy Variables Measurement

### VIII.4.Function Tests (Assessment of Disability)

Efficacy variables should include functional tests ofdisability. These maybe rating scales or functional scales. Rating scales should be validated for ALS. Examples include the ALS Functional Rating scale, the Baylor ALS Rating Scale**…**

### VIII.5. Assessment of Quality of Life:

***Measurement of QoL is a valuable and independent measure of therapeutic efficacy, which may be applied as a secondary end-point in ALS trials.***

*Use as a primary endpoint is not recommended.*

*Quality of Life scales specific to ALS have not been developed, and the use of a well-known general Quality of Life scale as an additional secondary end-point should be validated.*

## 2.2. Management of Crohn's disease and potential claims:

***Other end-points such as fistula healing, steroid sparing, treatment of abscess, treatment of obstruction and improvement in quality of life can be subsumed as response variables or outcomes measures of either the treatment of active disease or maintenance of remission****. Unless otherwise justified, they should not be mentioned in the indication.*

**EFFICACY**

2.2.1 Treatment of active disease/Induction of remission

2.2.1.3 Response variables

**Secondary endpoints may include:**

**Validated QOL measurement, e.g. IBDQ**

## 8. Recommended Primary and Secondary end-points

### 8.4. Selection of Secondary end-points

…**a number of secondary endpoints may provide useful information**. These measure different aspects of the condition and they should be justified by referencing published data that support their validity. **Examples in chronic asthma include symptom scores, use of rescue medication, nocturnal symptoms, exercise tolerance, exacerbation rates and quality of life.**

## 4. Clinical Outcome Measures

The primary aim for developing new drugs should be to obtain a subjective improvement or cure of symptoms for the patient.

### 4.1. Subjective outcome measure

The overall outcome of treatment as perceived by the patient should be recorded by simple scales.

### 4.2. Quantification of symptoms

4.2.1 Diaries

4.2.3. **Quality of Life**

**Disease specific and generic instruments for measuring HRQL can be used in trials of products for urinary incontinence. The instruments used should be properly validated.**

## 4. Clinical Outcome Measures

## 4.2. Quantification of symptoms

### 4.2.3. Quality of Life

**Disease specific and generic instruments for measuring HRQL can be used in trials of products for urinary incontinence. The instruments used should be properly validated.**

**A clinically relevant change in pre-specified domains (dimensions) of QOL should be defined and justified in the protocol of the study. HRQL data should be considered an extension of an evaluation of efficacy, which can provide meaningful information to the prescriber and the patient. HRQL data can, however, never be the sole basis for efficacy claims. HRQL data usually do not contribute data to be included in section 4.1 [Subjective outcomes measures]. Indication of the SPC, may, if clinically relevant changes have been found, be included in other parts of the SPC (e.g. section 5.1 Pharmacodynamics)**

## II. Method to assess efficacy

### Acute migraine attack trials

HRQL measures are not established in migraine, and they should not be used until fully clinically validated

### Migraine Prophylaxis trials

The use of HRQL measures and Disability-adjusted life years (DALYs) is not established, and they should not be used until fully clinically validated

# Concept Paper

## 3. Discussion

**It is suggested that the following topics are addressed in the guideline:**

**...[...]...**

**Choice of endpoints (PASI, BSA, clinical outcomes measures, quality of life)**

## Concept Paper

### 3. Discussion

**Main topics to be addressed**

**1. Design of efficacy studies in adults**

**...[...]...**

**- Definition of secondary parameters: e.g. effect on social functioning**

# Concept Paper

## III. Discussion

Scales which have been used in patients with PD should be discussed, e.g. the Anxiety Sensitivity Index (16-item self-report questionnaire), the Mobility Inventory for Agoraphobia (self-report questionnaire), the Mastery of your Anxiety and Panic II (diary technique for recording of panic attacks)…

# Concept Paper

## 3. Discussion

**It is suggested that the following topics are to be addressed:**

**...[...]...**

**<u>Study design</u>**

**...[...]...**

**Primary and secondary endpoints (e.g. pain reduction, functional and social performance, quality of life)**

# *CPMP/EWP/633/02: Treatment of HIV Infection*



**Adopted March 2003**

**3. General aspects of study design**

**3.2. Measures of treatment outcome and supplementary investigation**

**3.2.7. Safety**

The use of justified Quality of Life Instruments in long term controlled and preferably double-blind studies may provide additional information of principal importance in the assessment of benefit risk, given the impact of poor tolerability on compliance and psychosocial well-being.

# Review of EWP NfG

PROs:

- **Recommended as primary end-point: 4 NfG**

  Osteoarthritis, IBS, Urinary Incontinence in women

  Nociceptive pain

  **➔PROs = Symptoms, pain, discomfort**

- **Also Recommended as a secondary end-point: 13 NfG**

  ALS, Asthma, Cancer, CHF, COPD, Crohn, IBS, Osteoarthitis, PAOD, RA, Stable Angina, Urinary Incontinence, Weight Control

# Review of EWP NfG

PROs:

- **Recommended as a potential efficacy endpoint**:

  **4 NfG** – OCD, Panic Disorder, Psoriasis, Neuropathic Pain Management (concept papers)

- **Useful in safety: 1 NfG** - HIV

Development of HRQL scale encouraged in:

**1 NfG**: Stroke

# Review of EWP NfG

PRO Questionnaires which might be used

- AIMS, HAQ
- IBDQ
- Minnesota Living with Heart Failure
- St Georges Respiratory Questionnaire

- Self assessed symptoms

- HRQL « Generic » instruments
- HRQL Disease specific questionnaires

# Do EMEA guidelines recommend the assessment of PROs in clinical trials ?

YES!

Often HRQL data

# Conclusion

- **Recognition of:**
  - The value of the Patient's perspective in the evaluation of medicines
  - HRQL as a valuable endpoint (mainly secondary)
- **Update of guidelines**
  - Need to improve consistency between NfG
  - Need to improve consistency between FDA and EMEA
  - Efforts are on-going (harmonization meetings, EMEA position paper, FDA guidelines)

# ERIQA Guidance Document

*Drug Information Journal*, Vol. 36, pp. 209–238, 2002
Printed in the USA. 

0092-8615/2002


# PATIENT-REPORTED OUTCOMES: THE EXAMPLE OF HEALTH-RELATED QUALITY OF LIFE—A EUROPEAN GUIDANCE DOCUMENT FOR THE IMPROVED INTEGRATION OF HEALTH-RELATED QUALITY OF LIFE ASSESSMENT IN THE DRUG REGULATORY PROCESS

OLIVIER CHASSANY, MD, PHD
Délégation Régionale à la Recherche Clinique Hôpital Saint-Louis, Paris, France
PIERRE SAGNIER, MD, MPH
Bayer, Medical Affairs, Health Economics and Outcomes Research, Buckinghamshire, United Kingdom
PATRICK MARQUIS, MD
Mapi Values, Boston, Massachusetts
STEVE FULLERTON
Zynx Health Incorporated, Cedars-Sinai Health System, Beverly Hills, California
NEIL AARONSON, PHD
The Netherlands Cancer Institute, Amsterdam, The Netherlands
FOR THE EUROPEAN REGULATORY ISSUES ON QUALITY OF LIFE ASSESSMENT GROUP*

# How to increase the credibility of PROs ?

## Checklist for designing, conducting and reporting HRQL - PRO in clinical trials

### HRQL / PRO objectives
- Added value of HRQL / PRO
- Choice of the questionnaires
- Hypotheses of HRQL / PRO changes

### Study design
- Basic principles of RCT fulfilled ?
- Timing and frequency of assessment
- Mode and site of administration...

### HRQL / PRO measure
- Description of the measure (items, domains...)
- Evidence of validity
- Evidence of cultural adaptation

### Statistical analysis plan
- Primary or secondary endpoint
- Superiority or equivalence trial
- Sample size
- ITT, type I error, missing data

### Reporting of results
- Participation rate, data completeness
- Distribution of HRQL / PRO scores

### Interpreting the results
- Effect size,
- Minimal Important Difference
- Number needed to treat…

**Patient Reported Outcomes (PRO) and Regulatory Issues : A European Guidance Document for the improved integration of health-related quality of life assessment in the drug regulatory process. Chassany O et al. Drug Information Journal 2002.**

# Future (Workmats)

Olivier Chassany, MD, PhD.
Catherine Acquadro, MD

# Objectives

- ✓ To help pharmaceutical companies, reviewers, and investigators of clinical trials acquire the skills needed to assess PRO included in regulatory files and publications
- ✓ To facilitate decisions made by health authorities and health-care providers
- ✓ To facilitate dialogue between regulators, members of pharmaceutical companies, and health-care providers through the same training

# Background

- ✓ 1st version developed by Adelphi and Mapi Values in 1995 on model from airline industry
- ✓ Adaptation and development for a Program on HRQL/PRO in Clinical Trials in 2002, collaboration between:
  - **Mapi Research Institute, Lyon, France**
    ***Catherine Acquadro, MD***
  - **The ERIQA Group**
    ***Olivier Chassany, MD, PhD***
  - **and the Cochrane HRQL Methods Group**
    ***Donald L. Patrick, MSPH, PhD***

# Methods: Workmats

- ✓ Interactive learning method
- ✓ Participants
  - Small ***group discussions*** and interactions
  - To understand the new information
  - To complete the assignments through group discussions
  - Group answers have to be discussed by all participants to reach a consensus

# Methods: Workmats

- ✓ Workmats (WM)
  - Large worksheets
  - Contain concise information: background
  - Present various assignments
- ✓ Workbook
  - Reference source
  - Additional information on PRO
  - Questionnaires and articles

# Content

| WM | |
|---|---|
| 1 | How do disease and treatment impact upon a patient – from the patient's perspective? |
| 2 | Deciding which PRO to assess the impact of disease and treatment |
| 3 | How is a new PRO questionnaire developed?<br>1st Steps: Development of items and item reduction |
| 4 | How is a new PRO questionnaire developed?<br>2nd Steps: Psychometric validation and cultural adaptation |
| 5 | Choosing an appropriate existing measure |
| 6 | Analysis of PRO data |
| 7 | Presentation and interpretation of PRO included in clinical trials |

# Pilot training: 2002

| Tests | Speakers |
|---|---|
| **Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS)**, May 15, 2002; Paris, France | Catherine Acquadro, MD; Olivier Chassany, MD, PhD; Juliette Longin, PhD |
| **Food and Drug Administration (FDA)**, May 23, 2002; Washington, D.C., USA | Catherine Acquadro, MD; Olivier Chassany, MD, PhD; Bruce Crawford, MA, MPH; Patrick Marquis, MD, MBA |
| **International Cochrane Colloquium**, July 31 to August 3, 2002 Stavanger, Norway | Catherine Acquadro, MD; Olivier Chassany, MD, PhD; Elaine McColl, Msc; Donald L. Patrick, MSPH, PhD |

**Finalization of workmats**

# 2003 Sessions

## Health Authorities

- Jan. 24: **AFSSAPS**, Faculté Lariboisière, Paris, France
- April 8: **ANAES**, Paris, France
- May 23: **INAMI**, Brussels, Belgium

# WORKMAT 1

How do disease and treatment impact upon a patient from the patient's perspective?

## Learning objectives

- To identify the impact of health conditions and treatment from a patient's perspective
- To distinguish the different ways diseases and treatment may affect a patient
- To create an awareness that treatments can affect patients

# WORKMAT 2

## Deciding which PRO to assess the impact of disease and treatment

Learning objective

To define the relevant domains and items depending on the conditions studied

# WORKMAT 3

## How is a PRO questionnaire developed?

## 1st Steps: Development of items and item reduction

### Learning objective

To describe the process of item generation and item reduction

# WORKMAT 4

## How is a PRO questionnaire developed?
## 2nd Steps: Psychometric and linguistic validation

### Learning objectives

- To describe the evaluation of psychometric properties: reliability, validity, and responsiveness
- To describe the process of linguistic validation

# WORKMAT 5

## Choosing an appropriate existing measure

### Learning objectives

- To explore the process for selecting appropriate health status instruments for use in specific clinical trial scenario
- To examine the trade-offs in the selection process
- To review the criteria necessary for appropriate evaluation of a PRO instrument
- To identify and evaluate established questionnaires for use in a specific patient group

# WORKMAT 6

## Analysis of PRO data

### Learning objectives

- To identify the issues and potential problems in designing a statistical analysis plan for PRO data
- To understand the different methods of treating missing data
- To gain the knowledge and skills needed to analyze differences in PRO between two or more treatments

# WORKMAT 7

## Presentation and interpretation of PRO included in clinical trials

## Learning objectives

- To critically evaluate published literature describing PRO surveys data
- To interpret PRO data that are reported in the published literature