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A Review of Major Quality of Life (QOL) Activities in Europe and in the USA

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Uses of QOL evaluation

- Quality of Life can be assessed in different settings.
- For instance:
  - Epidemiological Studies
  - Clinical Trials
  - Clinical Practice
- The examples of Clinical Trials and Clinical Practice will be presented

Evolution of QOL assessment in Clinical Trials since 1966

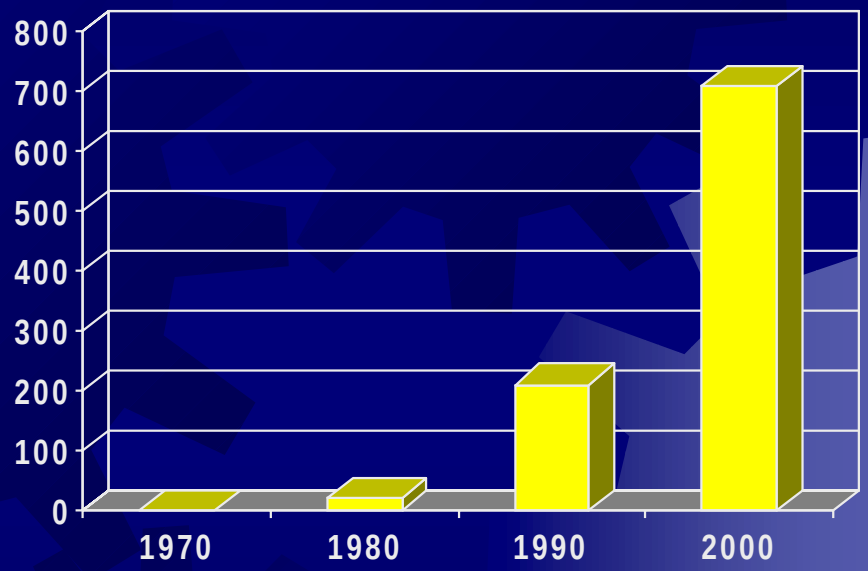
- **Literature search (Medline)**

"Quality of Life" Matched with

"Clinical Trials":

Results: number of references

- 1966 to 1970: 0
- 1966 to 1980: 20
- 1966 to 1990: 210
- 1966 to 2000: 708



Considerable increase of QOL assessment in Clinical Trials

Impact on Health Authorities

- Health Authorities involved in Drug Evaluation have to take this phenomenon (increase in QOL Assessment) into consideration
- Presentation of the situation in:
  - USA: **FDA** (Food and Drug Administration)
  - Europe:
    - **EMEA** (European Agency for the Evaluation of Medicinal Products)
    - Country-specific Agencies

Does FDA care about QOL? Recommendations from FDA

- **Examples**
  - **FDA - Oncologic Drugs Advisory Committee:**

    Quality of life and survival are recommended primary efficacy parameters as a basis for approval of anticancer drugs
  - **FDA - Obstetrics and Gynecology Advisory Panel:**

    Quality of life improvements can outweigh less-than-optimal clinical effectiveness results in the approval of thermal endometrial ablation devices
  - **FDA Guidance for Industry**

    Non-Small Cell Lung Cancer: “improvement in quality of life may be a sufficient end-point for drug approval under certain circumstances”

Does FDA care about QOL?

- There is **no General Guidance** on the use of QOL evaluation in Clinical Trials
- Hesitations because of potential misuses of QOL claims in medicinal products marketing

Review of Products with QOL Labeling in USA

- **19 products**
  - 7 in oncology
  - 2 in immunology,
  - 2 in cardiology,
  - 2 in CNS,
  - 2 in metabolic diseases
  - 1 in endocrinology,
  - 1 in genito-urinary diseases
  - 1 in respiratory diseases
  - 1 in sleep disorders

Products with QOL claims

- Accupril
- Aredia
- Atrovent
- Camptosar
- Casodex
- Coreg
- Enbrel
- Epogen
- Felbatol
- Gemzar
- Humatrope
- Muse
- Navelbine
- Nutropin AQ
- Oxycontin
- Procrit
- Provigil
- Remicade
- Thyrogen

Does EMEA care about QOL? Recommendations from EMEA

- Notes for Guidance produced by the Efficacy Working Party (EWP)
- Review of (EWP) documents:
  - **Guidelines**
    - Adopted, and Drafts
  - **Points to Consider**
  - **Concepts Papers**

➡ **To identify diseases where QOL evaluation is recommended**

Results: Review of EWP Guidelines adopted and drafts

QOL is:

- **Recommended as a potential efficacy criteria in 7 diseases**

  Anti-Cancer Drugs in Man, Alzheimer's Disease, Stable Angina Pectoris, Cardiac Failure, Chronic Peripheral Arterial Occlusive Disease, Multiple Sclerosis, Weight Control

- **And as secondary end-point in 3**
- **Mentioned, but not to be recommended: 1**
  (Parkison's Disease)
- **Only quoted («qol of patients is impaired»): 1**
  (antiarrythmics)

Review of products with QOL labeling in Europe

- QoL assessed in 37 Products out of 171 products with a European Marketing Authorisation (July 2001)
- Only 2 products with QoL labeling:
  - **Caelyx** (Doxorubicin Hydrochloride)
  - **Thyrogen** (Thyrotropin alfa)

Where are we headed?

Positive Issues

- Methods are becoming more rigorous
- More recent claims have validated instruments
- Statistical approach is becoming more sophisticated
  - This will result in fewer claims at a higher quality
- Currently expanding to other claims
  - Bother, Discomfort, Patient Satisfaction, Pain, etc.
  - Manuscripts forthcoming

Where are we headed?

Health Authorities Problematic Issues

- Handling of Missing data
- Interpretation of the differences
- Meaningfulness / clinical significance?
- Cross-Cultural Adaptation and Validity
  (use in different countries and cultures)

➡ **Authorities need Guidance and Training for better decision-making**

How to provide guidance to Health Authorities ?

3 initiatives have been launched:

- **ERIQA project**
- **Patient Reported Outcomes (PRO) Harmonization Group**
- **Cochrane Collaboration QOL Methods Group**

ERIQA Project: Overview (1)

Members

Academics
Ph. Industry
Health Authorities

2 Objectives

1. To provide European Regulators with guidance on:

- how to assess the quality of QOL studies in Clinical Trials,
- how to evaluate the validity of QOL claims

2. To convince European Regulators that HRQL is a relevant key outcome, *i.e. a credible criterion of evaluation*

ERIQA Project: Overview (2)

- **Phase I**
  - **Step 1**: Review of existing guidelines *(published)*
  - **Step 2**: Guidance document *(accepted)*
  - **Step 3**: Pilots
  - **Step 4**: Harmonization meetings

- **Phase II**

  Development of Consensus Guidelines in specific Diseases

Checklist for Designing, Conducting and Reporting Hrql / Pro in Clinical Trials

*Patient Reported Outcomes and Regulatory Issues : 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.*

O. Chassany et al for the European Regulatory Issues On Quality of Life Assessment (ERIQA) group. Drug Information Journal 2002, under press.

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 content of 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, MCID
- Comparison with other scores
- Comparison with external criteria
- Number needed to treat…

Perspectives for the Future

ERIQA Group:

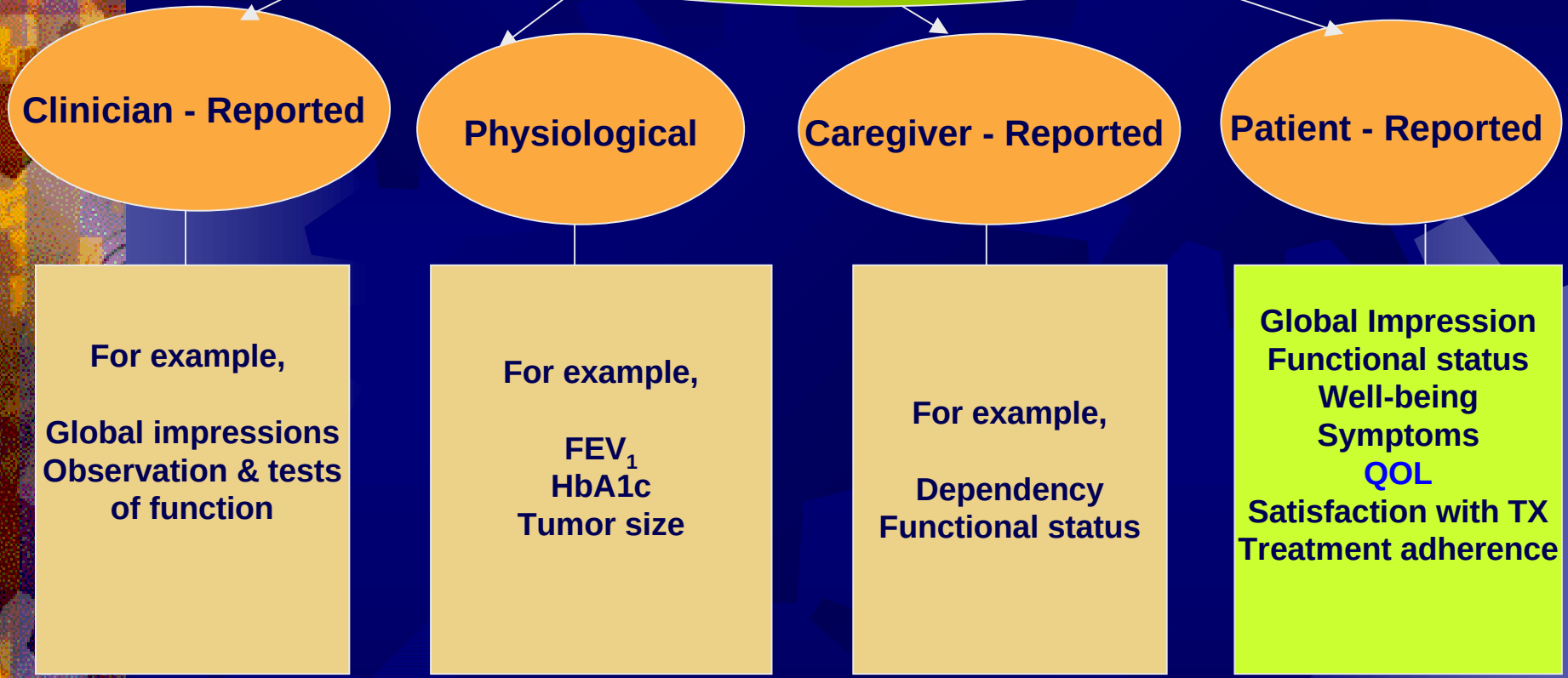
- Listed in EMEA EWP Interested Parties
- Invited to review EWP Papers

Patient Reported Outcomes Harmonization Team

- **What is its mission?**

To harmonize Patient Reported Outcome issues used in drug development and Evaluation

Patient Outcomes Assessment Sources and Examples



QOL is ONE of the Patient-Reported Outcomes

Who started the PRO Harmonization Group?

- European Regulatory Issues on Quality-of-Life Assessment (ERIQA)
- International Society of Pharmacoeconomic and Outcomes Research (ISPOR)
- International Society of Quality of Life (ISOQOL)
- Pharmaceutical Research and Manufacturers of America (PhRMA) Health Outcomes Committee (HOC)

What are its objectives?

- Clarify areas of concern or confusion about PRO evaluation
- Explain the added value of PRO outcomes among all key players, i.e., academics, regulators, industry researchers, prescribers and patients
- Open and maintain communication between key players
- Disseminate meeting outcomes, i.e., to publish papers, to participate in conferences

Forums

- 3 Harmonization Forums held
  - March 31, 2000
  - Sept. 14, 2000
  - February 16, 2001
- Representatives from ERIQA, ISOQOL, ISPOR, PhRMA HOC **and FDA observers**

Areas of agreement

- Patient Reported Outcomes (PRO) evaluation is a **valid concept**
- PRO can be **operationalized**
- PRO claims should **conform with the evidence and be pre-specified**
- PRO should be **reported with fair balance** in labeling and promotional claims

The Cochrane Collaboration

- It is an international organization that aims to help people make well-informed decisions about healthcare by preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions.
- It is a not-for-profit organization, established as a company, limited by guarantee, and registered as a charity in the UK (number 1045921).

Cochrane Collaboration Quality of Life Methods Group

- **Objective**: to advise Cochrane reviewers about when and how to incorporate QOL data into systematic reviews of health care interventions.
- **The CC QOL MG intends:**
  - refining methods of literature search on HRQL studies
  - developing methods for systematically reviewing HRQL studies
  - refining methods for meta-analysis of HRQL studies (in collaboration with the Statistics MG)
  - giving advice on software development

QoL MG Structure

- 3 Convenors
- 1 Coordinator
- 30 Members, representing 11countries, collaborating within Working Sub Groups
  (Australia, Belgium, Canada, France, Ireland, New Zealand, Russia, Spain, Sweden, UK, USA)
- 4 Working Sub Groups under the responsibility of Subgroup Chairs

QoL in Clinical Practice

A Survey of Health Care Professionals' Views in Massassuchetts, USA

OBJECTIVES

Assess the views of health care professional regarding the utilisation of patient-based health status instruments in clinical practice, and describe the rational for using these measures in their practices, their perceived benefits and barriers to the use of these measures.

Results

- **Completed questionnaires: 9.7%** (n= **553**)
- **Response rates :**
  - Physicians : **6.5%** (n=**223**)
  - Nurses : **12.0%** (n= **275**)

Results

PHYSICIANS

- Internal Medicine
- Pediatrics
- Psychiatry
- Geriatrics

Largest percentage of NON-USERS, whereas Obstetrics/ Gynecology are USERS

NURSES

Psychiatry → highest percentage of NON-USERS

Cardiology and Surgery → highest percentage of USERS

- Believe these instruments may help communicate and share a patient's health status;
- No particular profile evident for the Nurses, i.e., USERS and NON-USERS are found evenly spread throughout Specialties

PHYSICIANS and NURSES agree that a Health Status Questionnaire is USEFUL to facilitate the contact and help monitoring patient's therapy;

Conclusions

- NURSES' response rate
  = twice PHYSICIANS'
- **Half** of the Health Care Professionals **of our sample** USE Health Status Questionnaires

Take Away Points

Patient has a unique voice and valuable perspective that should play a role in medical decision making

Next steps in China

- Can we use Western Countries QOL measures ?

Or

- Should we develop specific measures adapted to China ?