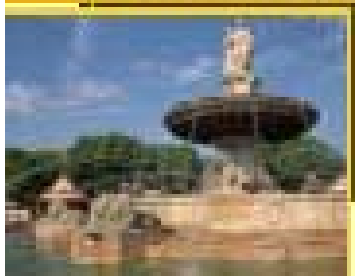
e-ternal medical progress?
March 5-7, 2003
Palazzo dei Congressi, Rome, Italy

DIA
Drug Information Association

Track 4



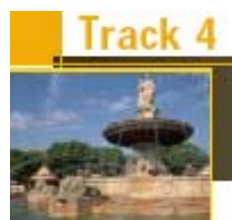
Do EMEA guidelines recommend the assessment of Quality of Life in clinical trials ?

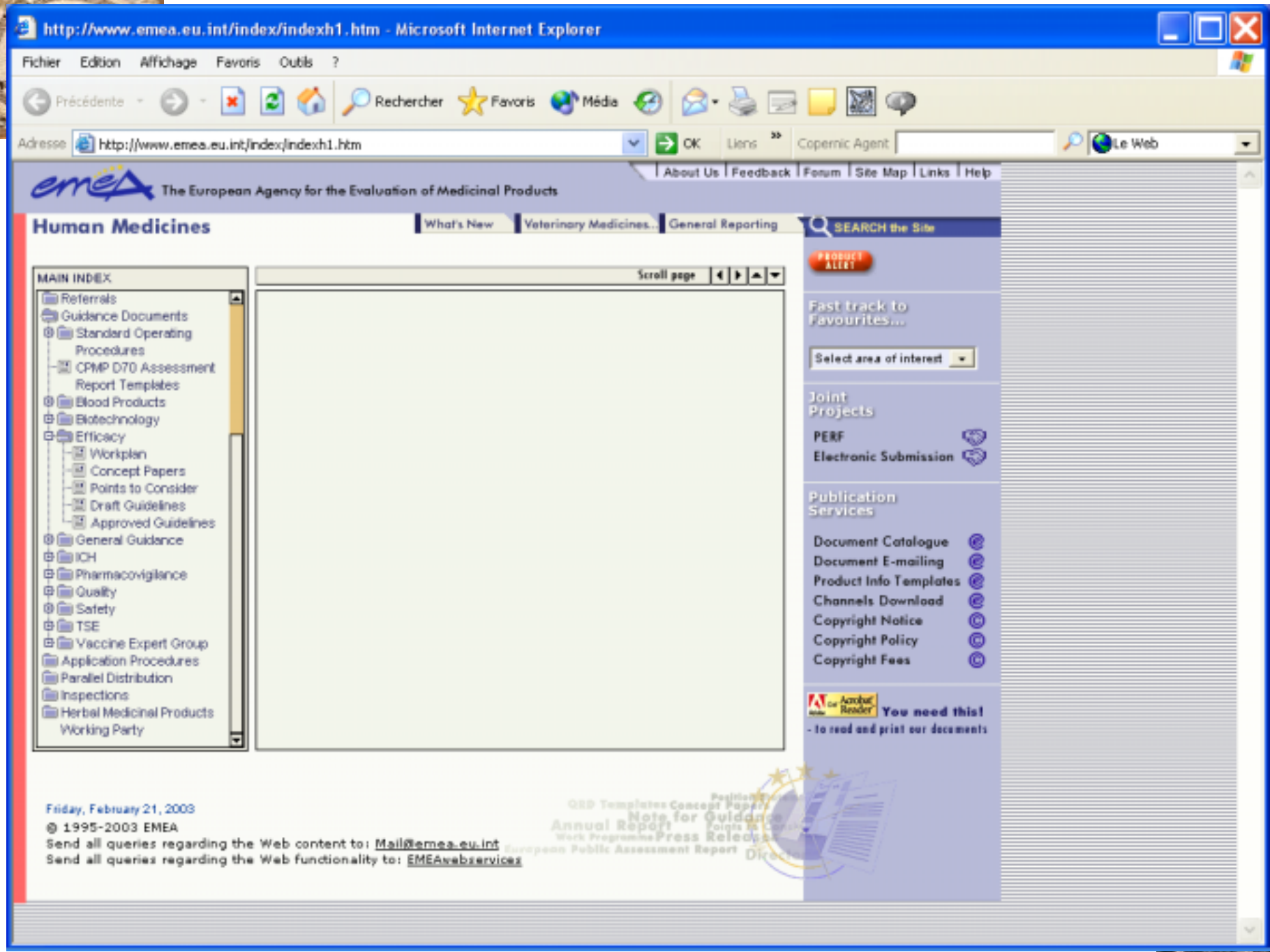
Catherine Acquadro, MD, Scientific Director,
Mapi Research Institute, France
For the ERIQA Group

Do EMEA guidelines recommend the assessment of Quality of Life in clinical trials ?

Which Guidelines ?

Efficacy? Safety? Quality ? ICH?

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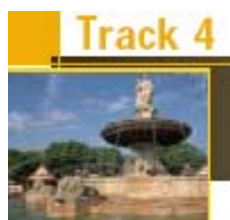
Notes for Guidance

- EMEA Documents available on: **www.emea.eu.int/index**
- Efficacy Working Party Notes for Guidance:
  - **Concept papers**
  - **Points to consider**
  - **Draft Guidelines**
  - **Approved Guidelines**

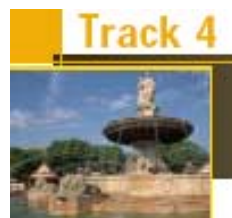


Objective

- **To identify diseases or drugs in which a formal HRQL evaluation is recommended (or not)**
- **To identify « recommended » measures**

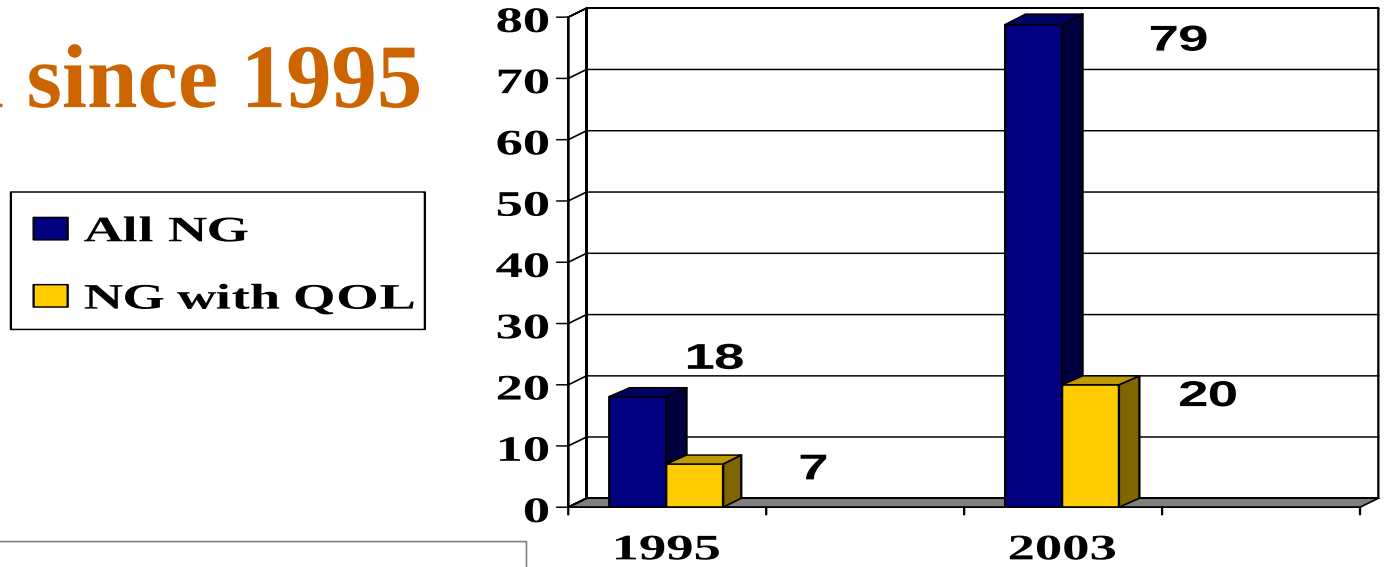
Results (02/27/2003)

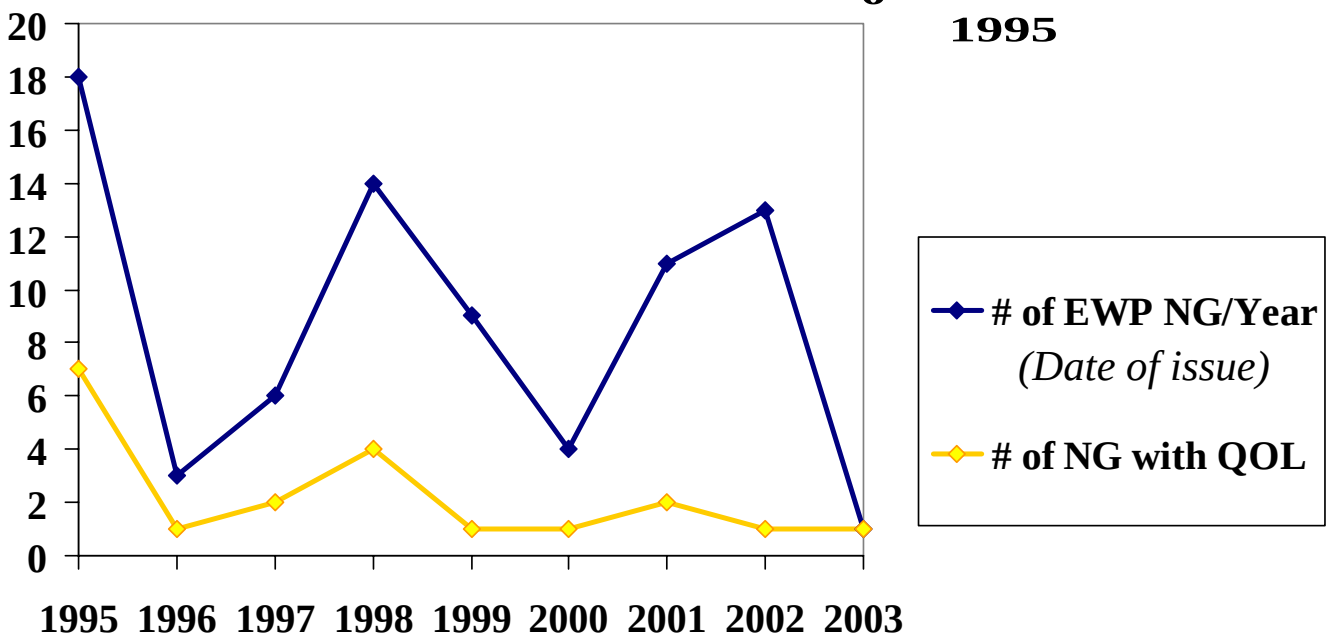
	# NG		Including QOL
Concept Papers	17		2
Points to consider	23		7
Draft Guidelines	4		1
Approved Guidelines	**35**		**9**
TOTAL	**79**		**20**

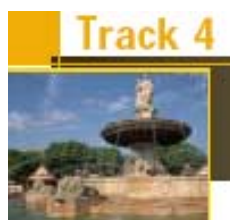


Review of EWP NG

Evolution since 1995



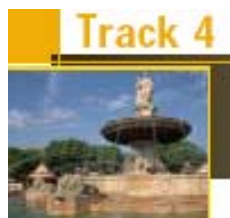




Review of EWP NG

20 Notes for Guidance including HRQL 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, Parkinson's Disease,
- Respiratory Diseases: Asthma, COPD
- Rheumatology: Osteoarthritis, Rheumatoid Arthritis
- Others: Anti-Cancer Drugs in Man, Neuropathic Pain Management, Psoriasis, Urinary Incontinence in women, Weight Control



4. Phase III Trials

4.1 Objectives and background

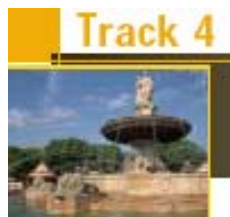
4.12. To study the effects of a new agent. Appropriate end-points of assessment include: progression-free/recurrence-free/relapse-free survival, overall survival, response rate, *symptom control/quality of life*

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.*



CPMP/EWP/714/98 final: PAOD

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.*

CPMP/EWP/714/98 rev 1: PAOD

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.

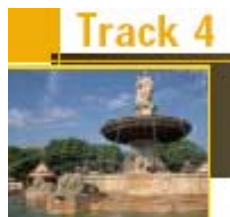
CPMP/EWP/235/95, Rev 1: Cardiac Failure

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.*



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

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

….

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

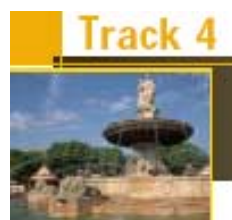
4. Supportive evidence for efficacy

…

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



5. Recommended primary/secondary efficacy endpoints

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. Psychosocial status and health-related quality of life must, however, be considered most important secondary endpoints

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.

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.

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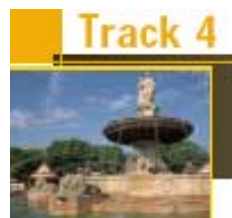
4.2. Quantification of symptoms

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)



CPMP/EWP/788/01: Migraine

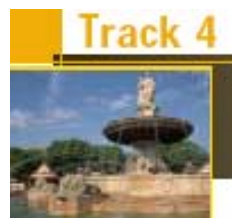
II. Method to assess efficacy

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



Review of EWP NG

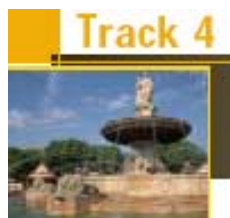
HRQL is:

- **Recommended as a secondary end-point: 13 NG**

  ALS, Asthma, Cancer, CHF, COPD, Crohn, IBS, Osteoarthitis, PAOD, RA, Stable Angina, Urinary Incontinence, Weight Control
- **As a potential efficacy endpoint**: Psoriasis, Neuropathic Pain Management (concept papers)

Development of scale encouraged in:

Stroke



Review of EWP NG

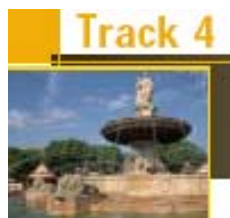
HRQL Questionnaires which might be used

- AIMS
- IBDQ
- Minnesota Living with Heart Failure

- « Generic » instruments
- Disease specific questionnaires

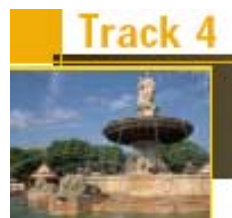
Do EMEA guidelines recommend the assessment of Quality of Life in clinical trials ?

YES!



Do EMEA guidelines recommend the assessment of Quality of Life in clinical trials ?

No...



Review of EWP NG

- Recommendation not possible because lack of info: 2

  Alzheimer, MS

- Not recommended as a primary endpoint: 2

  ALS, Parkinson Disease

- HRQL not established in: Migraine

Track 4

Conclusions

- **Recognition of:**
  - HRQL as a valuable endpoint (mainly secondary)
  - The value of the Patient's perspective in the evaluation of medicines
- **Update of guidelines**
  - Need to improve consistency between NG
  - Efforts are on-going