PRE-SELECTION OF EMEA EFFICACY WORKING PARTY GUIDANCE DOCUMENTS FOR REVIEW AND COMMENTS

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BACKGROUND

- Although the European Agency for the Evaluation of Medicinal Products (EMEA) recognizes the fact that there is a need for guidance on how to evaluate Health-related Quality of Life (HRQL) and acknowledges the importance of this area of research[1], there is no guidance document on Patient-Reported Outcomes (PRO) or Health-related Quality of Life assessments to support regulators when evaluating human medicinal products. The Efficacy Working Party (EWP), which is one of the working party collaborating with the Committee for Proprietary Medicinal Products (CPMP), develops Notes for Guidance. There are 4 types of documents: Concept Papers, which state the relevance of the problem, Points to Consider, with an in-depth approach to the problem, Draft Guidelines and finally, Adopted Guidelines.
- The ERIQA Group was created in 1998 with the following mission statement: "establishing principles and practices for the integration of Health-related Quality of Life outcomes in the drug regulatory process". In August 1999, a first review of the documents produced by EWP was performed by Giovanni Apolone et al.[2]. As part of its activities of year 2001, the ERIQA Group performed an update of this review and presented it at the DIA meeting in Philadelphia (October 2001).
- On August 2001, Mapi Research Institute, as a member of the ERIQA group, was added to the list of EMEA Interested Parties and invited to comment on the EWP Regulatory Guidance Documents.

OBJECTIVES

- The objective of this research is to screen the Efficacy Working Party Notes for Guidance documents focusing on HRQL evaluation: citation and appropriateness. Review and comments on each document would eventually be performed according to pre-selection results.

METHODS

- Two independent researchers performed the pre-selection: 68 documents produced by the EWP have been downloaded from the EMEA website (www.eudra.org/emea.html), on April 12, 2002: 13 concept papers (CP), 21 points to consider (PC), 7 draft guidelines (DG), 27 adopted guidelines (AG).
- Documents were classified according to 5 criteria:
  - . Their type (CP, PC, DG or AG): a code has been given to each document according to their order of appearance in the EMEA website (i.e. chronological order).
  - . The category covered by the guidance (i.e. pathology, pharmacological or methodological issues).
  - . Whether or not Health-related Quality of Life has been addressed in the guidance. If so, researchers have also indicated if the need for updating exists. Any other Patient-Reported Outcomes addressed in the guidance are also mentioned.
  - . Whether or not Health-related Quality of Life should be addressed in the guidance.
  - . The date when the CPMP has adopted the guidance or the guidance has come to operation, when the CPMP plans to either release documents for comments or create/update/finalise guidance.

RESULTS

- Results were analysed by the ERIQA EWP Guidelines working group: C. Acquadro, D. Dubois, L. Lobo-Luppi, A. Novak, M. Tomas and I. Wiklund, and are illustrated in TABLES 1 and 2.
- HRQL is addressed in 16 NG (see Table 1). Four documents address both HRQL and other PRO: DG 2, 3 and PC 18, 19 (see Table 1).

Type of EWP NG	# including HRQL outcomes
Concept Papers(CP)	none
Points to Consider (PC)	6, 8, 10, 17, 18, 19
Draft Guidelines (DG)	2, 3, 7
Adopted Guidelines (AG)	2, 4, 9, 16, 18, 20, 25

- These 16 documents should be updated concerning the HRQL issues.
- There are other 16 guidance documents where HRQL evaluation should be addressed (see Table 2 also sorted by category in order to facilitate classification).

➢ In total, 32 documents were selected for review and comments.

[1] van Zwieten-Boot, B. Letter from the CPMP/EWP Doc Ref.: EMEA/18291/01, dated July 5th, 2001.

[2] Apolone G, De Carli G, Brunetti M, Garattini S. Heath-Related Quality of Life and (HR-QOL) and Regulatory Issues. *Pharmacoeconomics* 2001; 19(2):187-195.

- Table 1: EMEA Efficacy Working Party Guidance -- HRQL addressed

CPMP Reference	Our code (*)	Abridged Title of Guidance	Category	QoL addressed /mentioned Yes/No	QoL to be addressed or updated	CPMP Deadline	Selection YES/NO
CPMP/EWP/2922/00	DG 3	Asthma	Respiratory Disease	Y, & PRO	to be updated	plan 2002/05	Y
CPMP/EWP/556/95	PC 18	Rheumatoid Arthritis	Rheumatology	Y, & PRO	to be updated	operation 1999/06	Y
CPMP/EWP/784/97	PC 19	Osteoarthritis	Rheumatology	Y, & PRO	to be updated	adopted 1998/07	Y
CPMP/EWP/18/01	DG 2	Urinary incontinence in women	Urology	Y, & PRO	to be updated	plan 2002/05	Y
CPMP/EWP/560/98	PC 6	Acute stroke	CNS	Y	to be updated	adopted 2001/09	Y
CPMP/EWP/565/98	PC 10	Amyotrophic Lateral Sclerosis (neuro)	CNS	Y	to be updated	adopted 2000/10	Y
CPMP/EWP/561/98	AG 2	Multiple Sclerosis	CNS	Y	to be updated	operation 2002/01	Y
CPMP/EWP/553/95	AG 18	Alzheimer Disease	CNS	Y	to be updated	operation 1998/01	Y
CPMP/EWP/714/98	DG 7	PAOD	CVD	Y	to be updated	plan 2001/05	Y
CPMP/EWP/235/95 Revision 1	AG 9	Cardiac Failure	CVD	Y	to be updated	operation 2000/06	Y
CPMP/EWP/234/95	AG 20	Angine pectoris	CVD	Y	to be updated	operation 1997/05	Y
CPMP/EWP/233/95	AG 25	CPAOD	CVD	Y	to be updated replaced by DG7	operation 1996/06	see DG 7
CPMP/EWP/2284/99	PC 8	Crohn's disease	GID	Y	to be updated	adopted 2001/06	Y
CPMP/EWP/281/96	AG 16	Weight control	Miscellaneous	Y	to be updated	operation 1998/06	Y
CPMP/EWP/205/95 Revision 1	AG 4	Anti-Cancer Products	Oncology	Y	to be updated	operation 2001/11	Y
CPMP/EWP/562/98	PC 17	COPD	Respiratory Disease	Y	to be updated	adopted 1999/05	Y

- Table 2: EMEA Efficacy Working Party Guidance -- HRQL to be updated or addressed

CPMP Reference	Our code (*)	Abridged Title of Guidance	Category	QoL addressed /mentioned Yes/No	QoL to be addressed or updated	CPMP Deadline	Selection YES/NO
CPMP/EWP/1776/99	PC 4	Missing data	Biostatistics	N	to be addressed	adopted 2001/11	Y
CPMP/EWP/788/01	CP 8	Migraine	CNS	N	to be addressed	plan 2002Q1	Y
CPMP/EWP/612/00	DG 4	Pain	CNS	N, PRO Yes	to be addressed	plan 1998/07	Y
CPMP/EWP/566/98 Revision 1	AG 7	Epileptic Disorders	CNS	N, PRO Yes	to be addressed	operation 2002/05	Y
CPMP/EWP/563/95	AG 13	Parkinson's Disease	CNS	N, PRO Yes	to be addressed	operation 2001/09	Y
CPMP/EWP/1533/01	CP 5	Acute Cardiac Failure	CVD	N	to be addressed	plan 2000/10	Y
CPMP/EWP/238/95 Revision 1	AG 14	Hypertension	CVD	N	to be addressed	operation 2002/01	Y
CPMP/EWP/1080/00	DG 5	Diabetes Mellitus	Endocrinology	N	to be addressed	plan 1998/01	Y
CPMP/EWP/785/97	CP 12	IDS	GID	N	to be addressed	plan 2001/05	Y
CPMP/EWP/021/97	PC 20	HRT	Gyn Ob	N	to be addressed	adopted 2000/06	Y
CPMP/EWP/552/95 Revision 1	AG 6	Post-menopausal osteoporosis	Gyn Ob	N	to be addressed	operation 1997/05	Y
CPMP/EWP/519/98	AG 8	Steroid Contraceptive	Gyn Ob	N	to be addressed	operation 1996/06	Y
CPMP/602/95	PC 1	Anti-HIV	Infectious Diseases	N	to be addressed	adopted 2001/06	Y
CPMP/EWP/462/95	AG 22	Evaluation of MP in Children	Pediatry	N	to be addressed	operation 1998/06	Y
CPMP/EWP/518/97	DG 6	Depression	Psychiatry	N, PRO Yes	to be addressed	plan2001/11	Y
CPMP/EWP/567/98	AG 5	Bipolar Disorders	Psychiatry	N, PRO Yes	to be addressed	operation 1999/05	Y

DISCUSSION / CONCLUSION

Instead of reviewing and commenting each of the 32 guidelines, members found more appropriate to write a generic template for creating a Note for Guidance for PRO & HRQL Evaluation in Clinical Trials. When an Interested Party submits a topic that might lead to the creation of a NG, the CPMP appoints an expert who will be in charge of developing a Concept Paper (CP). This CP has to be reviewed, then modified and adopted by the CPMP. Then it may evolve either to a Points to Consider (PC) if the field investigated is still in development (e.g. HRQL assessment) or to a Draft Guideline if the field is well known (e.g. CHF). This is a long process, which may take from 3 to 5 years.

A Concept Paper on the development of a CPMP Points to Consider on regulatory guidance for the use of PRO in clinical trials will be submitted to the Efficacy Working Party in the near future. This document will be based on the ERIQA checklist.