





Issue Panel 4
MCDA: A COMMON ROAD MAP FROM DRUG DEVELOPMENT TO REGULATORY AND REIMBURSEMENT DECISIONS?

MCDA at the EMA:
the benefit-risk (B/R) assessment


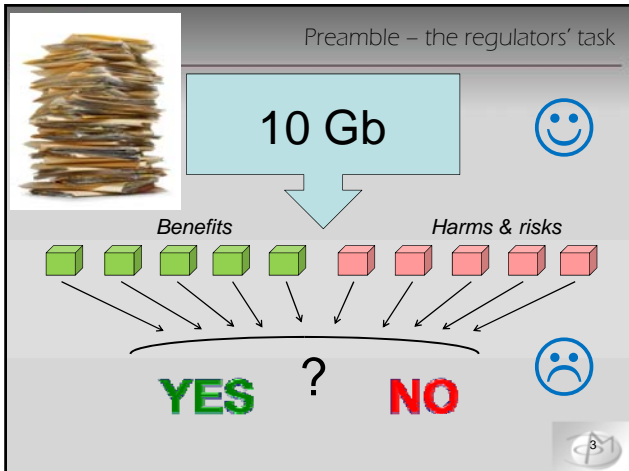


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Disclaimer

My presentation might not be the view of the organisations I am working for.
 My presentation is a personal viewpoint and binds in no way the organisations mentioned above.
 I have no financial interest to disclose.

The 2008 CHMP Reflection




2008 European Medicines Agency
 London, 19 March 2008
 Doc. Ref. EMEA/CHMP/15404/2007

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

REFLECTION PAPER ON **BENEFIT-RISK ASSESSMENT METHODS** IN THE CONTEXT OF THE EVALUATION OF MARKETING AUTHORISATION APPLICATIONS OF MEDICINAL PRODUCTS FOR HUMAN USE

2009

- Start of the **BR Methodology Project** (EMA sponsor: Xavier Luria):
 - London School of Economics (**Prof. Larry Phillips**) & University of Groningen (**Prof. Andrea Beyer**)
 - CHMP/EMA Steering Group



The EMA report on Work Package 1 (1)

March 2010



Work Package 1

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

30 March 2010
EMA/213482/2010
Human Medicines Development and Evaluation

European Medicines Agency Benefit-Risk methodology project

Description of the current practice of benefit-risk assessment for centralised procedure products in the EU regulatory network

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The EMA report on Work Package 1 (2)

6 participating agencies:

- FR
- NL
- SE
- ES
- UK
- DE (PEI)

Figure 1. The EMA's four-fold model of 'benefits' and 'risks'

Favourable effects (or beneficial)	Uncertainty of favourable effects
Unfavourable effects	Uncertainty of unfavourable effects

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The EMA report on Work Package 2 (1)

August 2010



WP 2

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

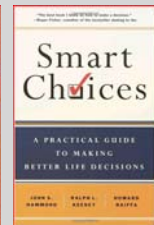
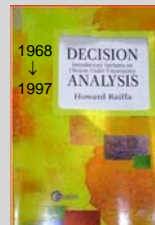
31 August 2010
EMA/549682/2010 - Revision 1
Human Medicines Development and Evaluation

Benefit-risk methodology project
Work package 2 report: Applicability of current tools and processes for regulatory benefit-risk assessment

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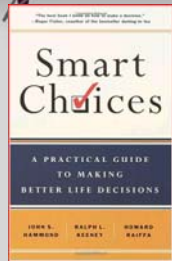
The EMA report on Work Package 2 (2)

1. Any quantitative method **requires a qualitative framework** within which the model can be effectively developed. The qualitative approach may be sufficient for simpler B/R decisions.
2. The EMA favours the 8-step **ProACT-URL** framework (Hammond et al., 1999; Hunink et al., 2001)



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The ProACT-URL framework



1. **PrOBLEM** formulation
2. **OBJECTIVES** (establish criteria)
3. **ALTERNATIVES** (options to be evaluated)
4. **CONSEQUENCES** (of all effects)
5. **TRADE-OFFS** (= balance)
6. **UNCERTAINTY** (of all effects)
7. **RISK ATTITUDE** (of the participants or the decision makers)
8. **LINKED DECISIONS**

→ Similar frameworks presented by, e.g., Felli et al. (Eli Lilly, 2009), Prof. Stuart Walker (CMR/CIRS CASS study, 2010), FDA BRF (2010), PhRMA's BRAT group (2011)...

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The EMA report on Work Package 2 (3)

3. **18 quantitative approaches** were analysed.
Only 3 are sufficiently comprehensive for a numerical representation of the B/R (as a difference or as a ratio) along with its uncertainties:
 - Bayesian statistics
 - Decision trees and influence/relevance diagrams
 - **Multi-criteria decision analysis (MCDA)**

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The EMA report on Work Package 2 (4)

4. Five other approaches, while more restricted in scope, **may well prove useful** for particular cases:
 - **Probabilistic simulation**
 - **Markov processes**
 - **Kaplan-Meier estimates**
(both for estimating changes in health states over time)
 - **QALYs** (for modelling multiple health outcomes)
 - **Conjoint analysis**
(to explicate trade-offs among effects, especially for eliciting patient preferences)
5. **Combination of approaches will prove useful in some situations**

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The EMA report on Work Package 3 (1)

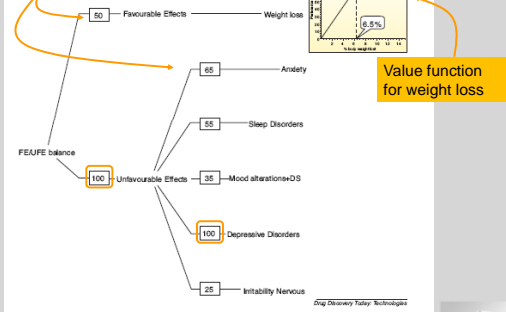


- 5 agencies → each chose a drug under review by the CHMP, at different stages
- Sessions were conducted as a 1-day « decision conference » (facilitated workshop)

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The EMA report on Work Package 3 (2)

Weights indicating relative clinical relevance



A value tree for rimonabant (Acompli®)

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The EMA report on Work Package 3 (3)



Added Value bar graph based on the original clinical trial data

Difference Display if weight reducing effect of rimonabant was halved

Graphical representations of the B/R balance for rimonabant (Acompli®)

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The ongoing Work Package 4

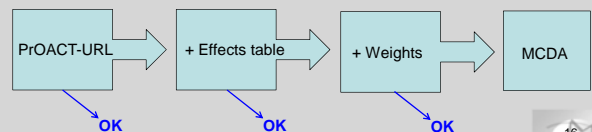
WP 4 deliverables:

- Operational decision aid / framework approved by the CHMP (end 2011 or later). This framework should be flexible to accommodate increasing degrees of B/R modelling
- Draft CHMP reflection paper
- Public consultation and workshop (early 2012)

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The future of MCDA at EMA/CHMP

- The ongoing B/R Methodology Project shows that quantitative B/R modelling of (new) drugs for the purpose of Marketing Authorisation is possible
- Is it desirable ?
The added value of this exercise (especially MCDA) for the national assessors and for the CHMP decision makers remains to be demonstrated
- A flexible framework allowing increasingly complex approaches may be an efficient way forward



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