



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Development and Trends in the Pharmaceutical Sector and the Future of the Regulatory Network in EU

MEB-day 2 June 2010

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An agency of the European Union 

Agenda

- **The European Regulatory System up to now**
- **The changing environment in the pharmaceutical field**
- **How do we respond to the changing environment**

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The European Regulatory System

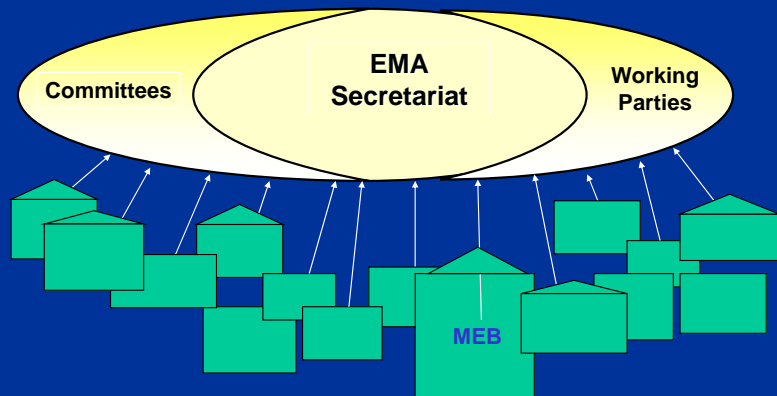
- “One European system: two procedures”
 - Centralised
 - Mutual and decentralised procedure
- 30 EU and EEA-EFTA countries
- Some 45 national competent authorities
- EMA and the European Commission
- Over 4,500 European experts
- 500 million users of medicinal product



The EU regulatory system up to now

- 2001: Orphan medicines
- 2004 – Part of new legislation into force and enlargement of EU 10 new Member states
- 2005 New legislation into force (extended scope)
- 2005: ‘Biosimilar’ and generic medicines
- 2005: Herbal medicines
- 2007: Paediatric medicines
- 2008/2009: Advanced therapies

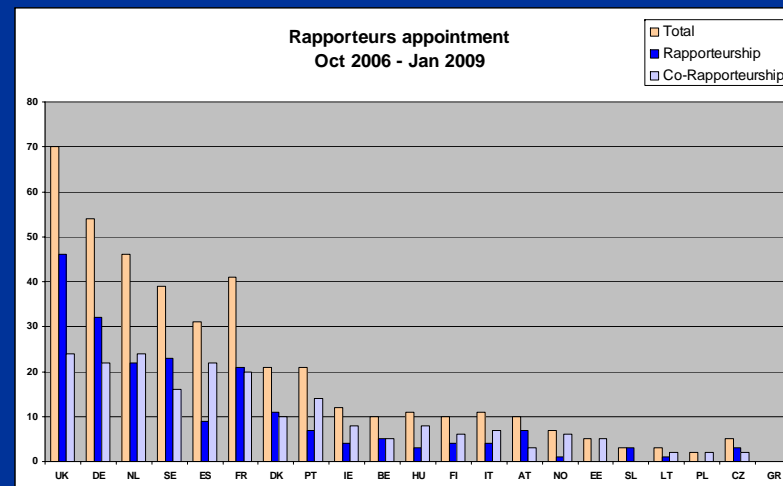
EMA and the European Regulatory Network



National Competent Authorities (NCAs)

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Rapporteurship appointment MEB



What our stakeholders think about us – evaluation of the Agency and the EU system of authorisation

- “EMA Secretariat together with 44 NCAs represents the archetype of an **effective and efficient** Community method.”
- “Since its creation in 1993, the EMA has made considerable progress in maintaining an **effective** European authorisation system for human and veterinary medicinal products”
- “In a quite limited timeframe, the EMA has gained **great consideration from all stakeholders**, at European as well as at international level.”
- “EMA opinions are undoubtedly considered of a **very high quality** from a scientific point of view and the Agency has become a leading actor in establishing international standards”

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The changing environment in the pharmaceutical field

- **Globalisation**
- Public health needs
- Scientific development
- Drug development
- Governments' responses to controlling drug budgets

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Globalisation

- Manufacturing of medicines is moving from classical sites in EU and US to new territories
- Clinical research is also moving to new parts of the world
- The world is becoming a 'supermarket' for pharmaceuticals
- Changing role for regulators
- Call for more international harmonisation and cooperation
- Counterfeit is an increasing problem
-

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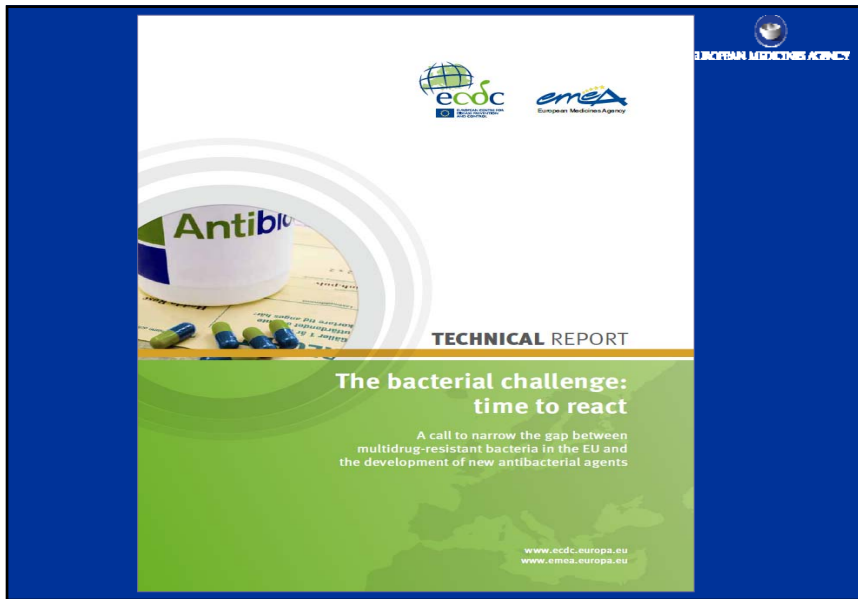
The changing environment in the pharmaceutical field

- Globalisation
- **Public health needs**
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The public health needs

- Demographics and disease patterns
- Geriatrics
- The needs of developing countries
- Rational use of medicines
- **Gaps in pipeline**
- In emerging situations
 - Pandemic



Gaps in pipeline

- The pharmaceutical industry are steered by commercial considerations when to decide on research strategy
- This does not always match the need for new treatment from a public health perspective
- How big is the gap?
- What to do about it?
- Who is doing something about it?

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The changing environment in the pharmaceutical field

- Globalisation
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- **Scientific development**
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Scientific Development

- The mapping of the human genome
- **Personal medicine**
- Regenerative medicine
- Preventive medicine
- Nanotechnology and delivery systems
- Integration of different science and sectors of the healthcare industry

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Stratified medicine: Herceptin®

Patients with HER2 positive ... breast cancer

	With HER2 neu	Without
Response rate	50%	10%
# of patients in trials	470	2200
Years of follow-up	1.6	10

- Savings in clinical trial costs ~ \$35 million
- Income from 8 year acceleration of product ~ \$2.5 billion
- Access to drug from acceleration ~ 120,000 patients

Modified from Press and Seelig, Targeted Medicine 2004, New York, November 2004

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The changing environment in the pharmaceutical field

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The drug development productivity gap



* The development time data point for 2007 includes data from 2006 and 2007 only
Source: CMR International & IMS Health

© CMR International, a Thomson Reuters business

What will be left?

- 50% decline in 10 years
- Regulators don't approve 20% of applications
- Study suggests that only 30% of approved medicines demonstrated a therapeutic innovation
- HTA adding cost effectiveness criteria and further reduce the number of products that will reach the patient

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Drug development

- Why do we have a productivity decline?
- Are the requirements too high ?
- Is the model for drug development wrong ?
- Is mother nature too difficult ?
- Is the business model of pharma industry wrong?

The changing environment in the pharmaceutical field

- Globalisation
- Public health needs
- Scientific development
- Drug development
- **Governments' responses to controlling the drug budgets**

Governments' responses to controlling the drug budgets

- 10-15 years ago health care system could absorb the cost of new drugs and drug treatments.
- Over time health budgets have got more stretched and focus is on pharmaceutical spending
- The few new medicines coming on the market are extremely expensive
- Governments starting to introduce economic evaluation of the value of medicines.
- Regulatory approval is not anymore the same as market access to new and old medicine in EU

The EU dilemma

- *One* central set of standards for drug approval
- *One* scientific advice
- *One* application *one* assessment and *one* opinion
- *One* decision valid in 27 EU MS and 3 EFTA countries
- *One* system for following the medicine on the market
- But *30* independent decision about if the medicine should be made available to patients or not
- Based on different methodologies and interpretations

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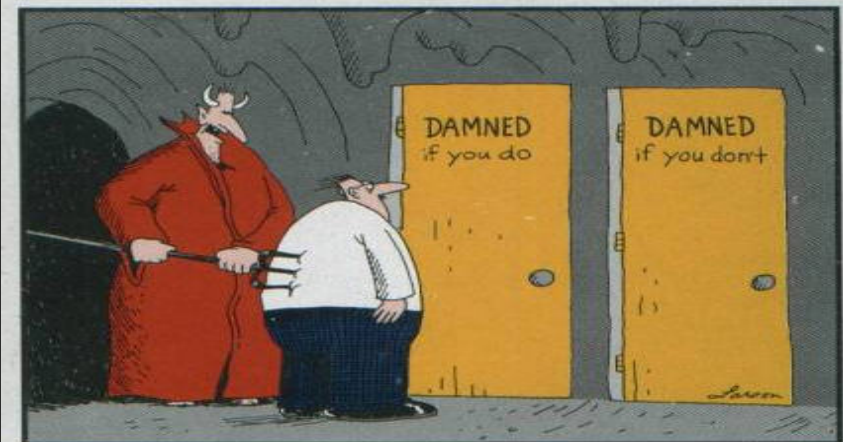
How do we respond to the changing environment

- **Is the current regulatory model fit for purpose?**
- Heads of medicine Agency response
- EMA response
- EU Commissions response

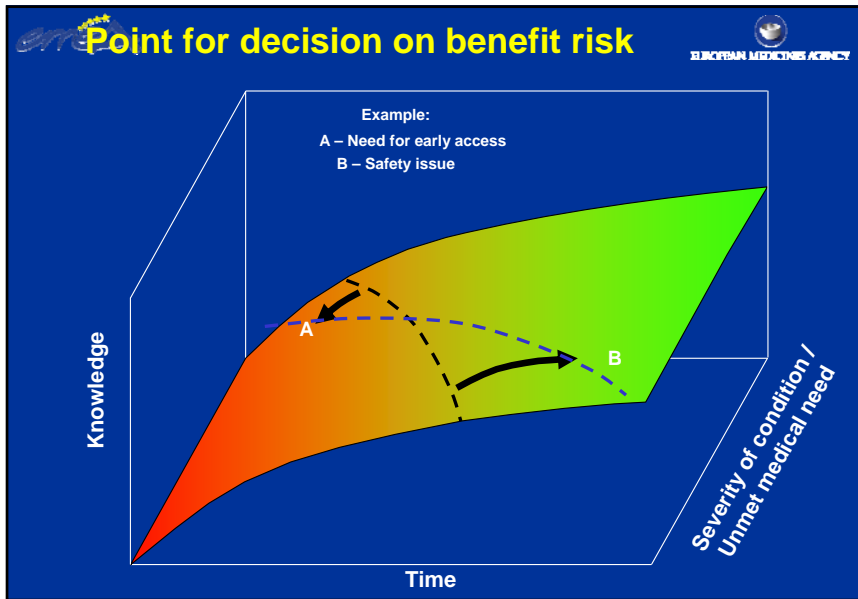
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Is the current regulatory model fit for purpose?

- Is the model for drug development up to date ? (clinical trials)
- **Are the requirement to high or to low?**
- Do we need a model for benefit-risk assessment ?
- Are we consistent in balancing the benefit-risk post authorisation or are we to risk averse ?
- How do we interact with health-technology bodies ?
- How do we develop the International harmonisation and cooperation?
- Will we be more transparent and informative ?²⁷



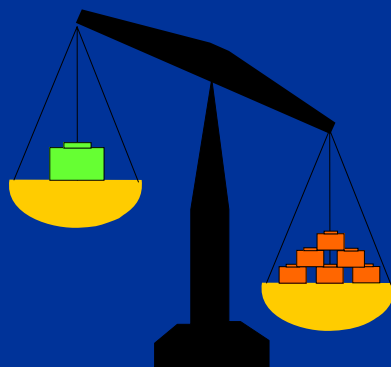
"C'mon, c'mon — it's either one or the other."



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Benefit-Risk balance is key



Risks

Benefits

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Do we need a model for benefit-risk assessment ?

- Benefit-risk assessment: the regulator's core business
- Challenges:
 - Avoid false positive and false negative regulatory decisions
 - Ensure consistency & predictability
 - Provide proper explanation
 - Be fully transparent

Do we need a model for benefit-risk assessment ?



- Opinion based on B-R are difficult
- Confronted with this complexity, regulators rely on value judgements given by experts
- Experts are good at valuing individual items of evidence but less good at synthesising multiple valuations
- Heuristic methods to simplify complex problems often lead to biases in judgement
- The need to be 'consistent' with prior decisions may lead to further distortion

How to improve benefit risk assessment



- Enhance methodology of Benefit-Risk assessment
- Goals:
 - Qualitative → Quantitative
 - Implicit criteria → Explicit criteria
 - Incorporate patients' valuations of beneficial/adverse outcomes

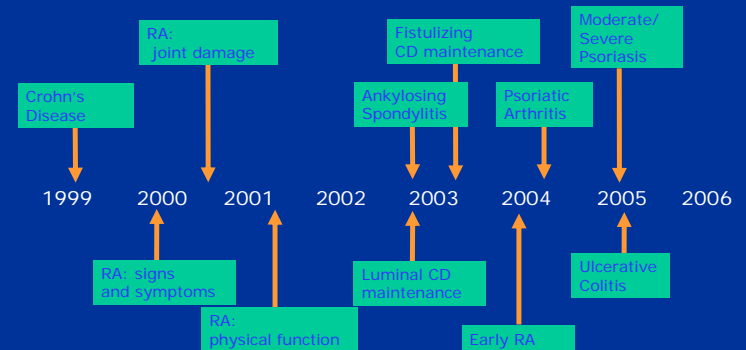
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Is the current regulatory model fit for purpose?



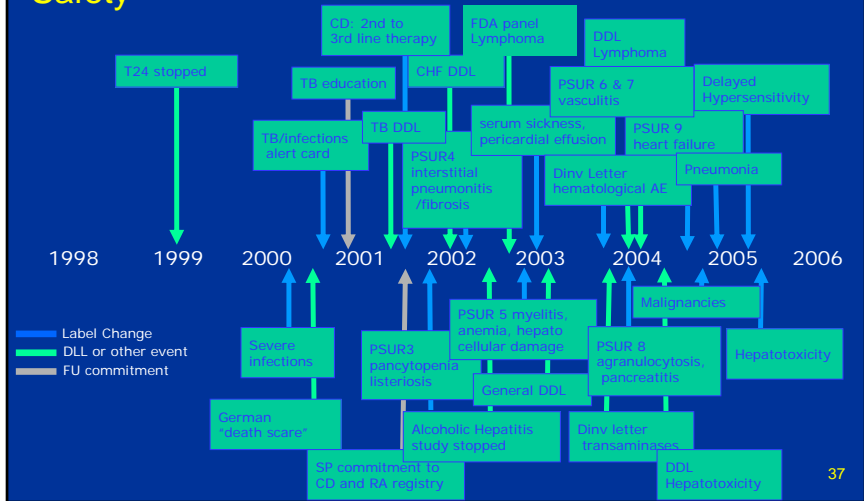
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Evolution of Remicade (EU): Efficacy



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Evolution of Remicade (EU): Safety



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Is the current regulatory model fit for purpose?

- Is the requirement and procedure for drug development and assessment up to date?
- Do we need a model for benefit-risk assessment ?
- Point for decision on benefit risk
- Are we consistent in balancing the benefit-risk during post authorisation?
- **How do we interact with health-technology bodies ?**
- How do we develop the International harmonisation and cooperation?
- Will we be more transparent and informative ? ³⁸

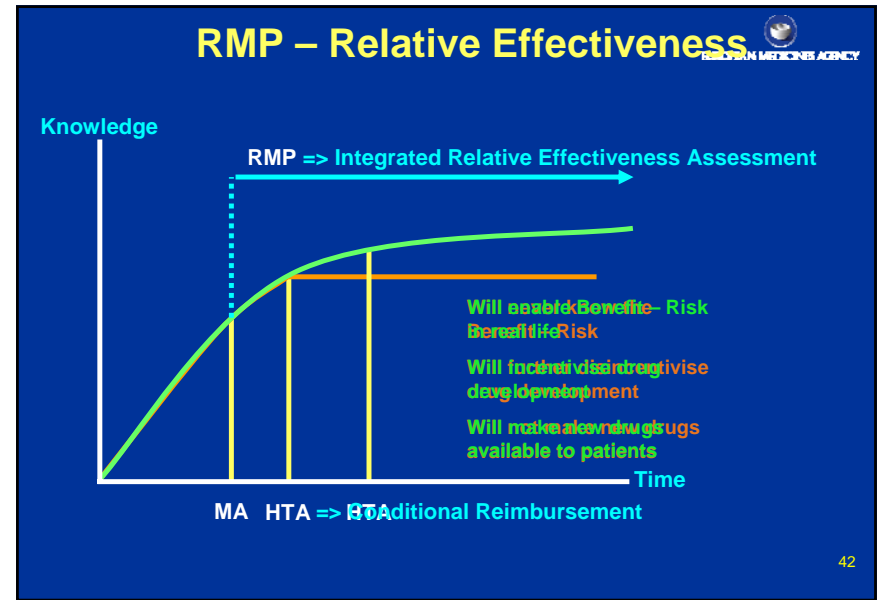
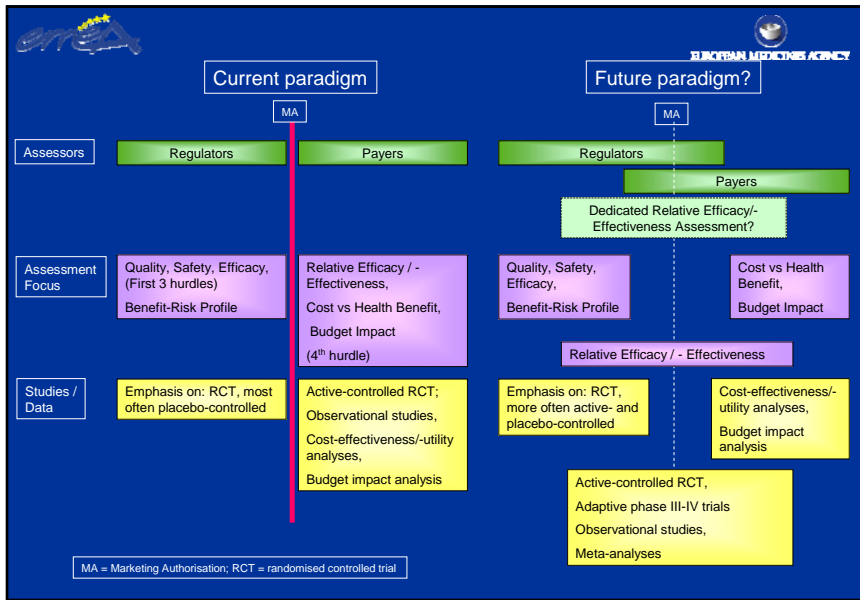
EMA interaction with Health Technology Assessment

- Differences
 - Endpoints
 - Efficacy vs. effectiveness
 - Relative efficacy vs. placebo-controlled studies
- Areas of possible interaction
 - Drafting of clinical guidelines
 - Scientific advice
 - Benefit-risk evaluation
 - Risk-management plans

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Speculating on a more distant future...

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A common approach

Licensing:
Benefits
and Risks

Relative
Efficacy
Assessment

HTA: Cost
and Health
consequences

- **HLPF report:** “distinction between [...] relative effectiveness of medicinal products and health-economic assessments.”

How do we respond to the changing environment

- HMA Strategy
- European Medicine Agency Road Map 2015
- The European Commission initiatives

The new Road Map 2015

- First priority for the next five years will still be on a successful delivery of the core business, further strengthening efficiency and reducing the administrative burden, but the focus will now more be on how to increase the quality of the outcome of the work
- Three strategic areas have been identified for the future

Roadmap 2015 – Three Strategic Areas

1. Addressing public health needs

- Gaps in drug development
- New and emerging science
- Public health threats

2. Facilitating access to medicines

- Drug development process, early assessment and continuing dialogue
- Benefit Risk assessment and communication
- Interaction with HTA bodies throughout the product lifecycle

3. Optimising the use of medicines

- Post-authorisation follow-up, patient safety
- Distribution of information to the EU regulatory network
- Outcomes research



The European Commission initiatives

- Proposal on information
- Revision of pharmacovigilance
- Proposal on counterfeit
- Reflection on the clinical trials directive
- Reflection on the future of medical devices

Conclusion

- The EU regulatory system have been successful up to now
- The environment surrounding the pharmaceutical field is rapidly changing
- Both industry and regulators need to change the way they operate
- Change in legislation will be necessary but much could be done without legislative interventions
- EMA way forward; the Road Map 2015 (now out for public consultation)