How to accelerate approval of innovative drugs

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Created 26 January 1995

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Disclaimer

My presentation might not be the view of the of the CHMP/SAWP, the EMA, or the FAMHP.

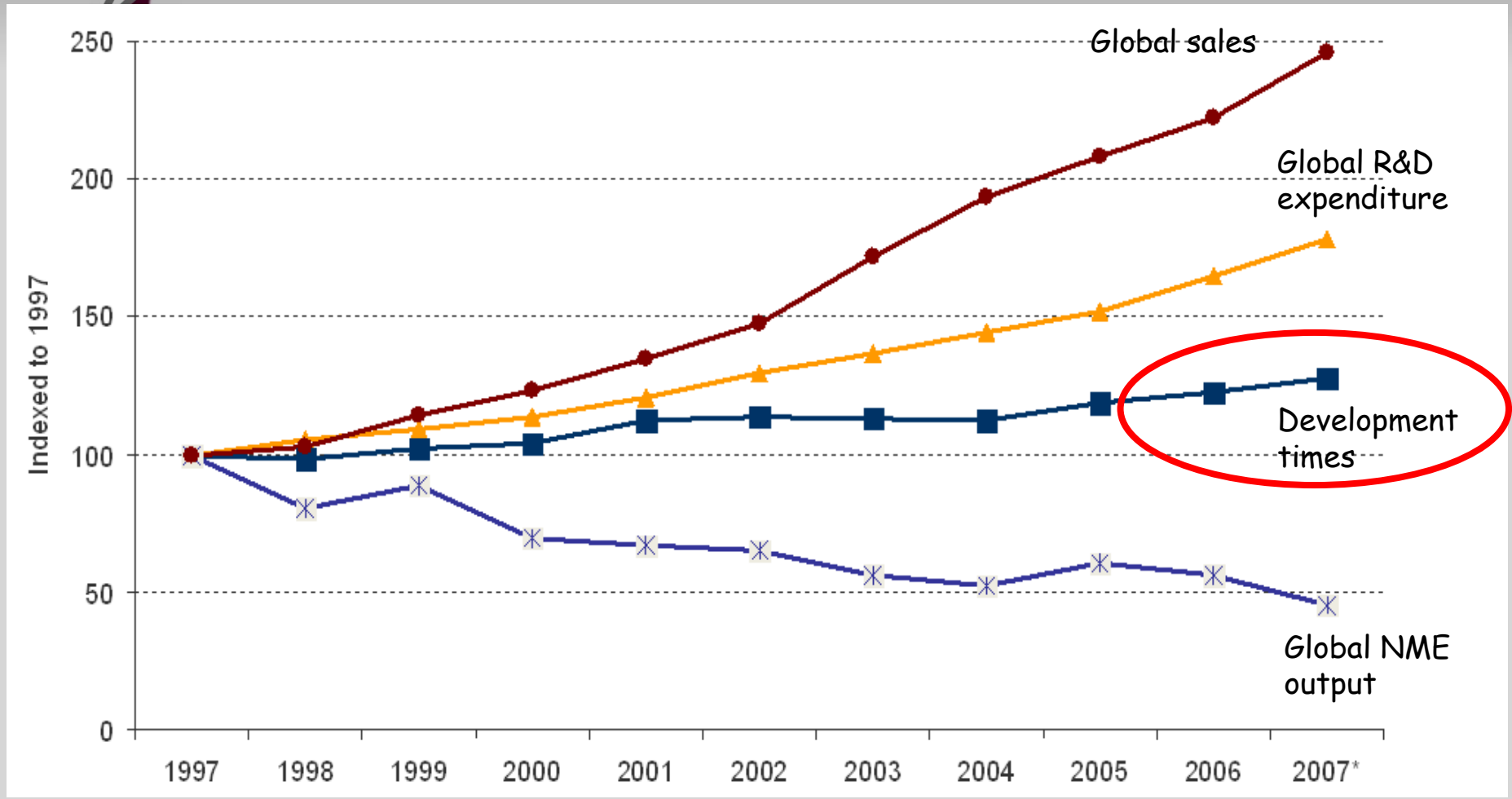
My presentation is a personal viewpoint and binds in no way the organisations mentioned above.

I have no financial interest to declare.

Acknowledgement

Prof. Hans-Georg Eichler, EMA

The drug development productivity gap



From: CMR International & IMS Health, 2008

Accelerated approval

- Is early access to the market the most appropriate solution to the productivity gap ?

Are regulatory agencies raising the entry bar?

Yes

FROM THE ANALYST'S COUCH

New drug approval success rate in Europe in 2009

Hans-Georg Eichler, Bo Aronsson, Eric Abadie and Tomas Salmonson

Nature Rev Drug Discov May 2010

29/48 (**60%**) New Active Substances approved by CHMP in 2009

The regulator's dilemma

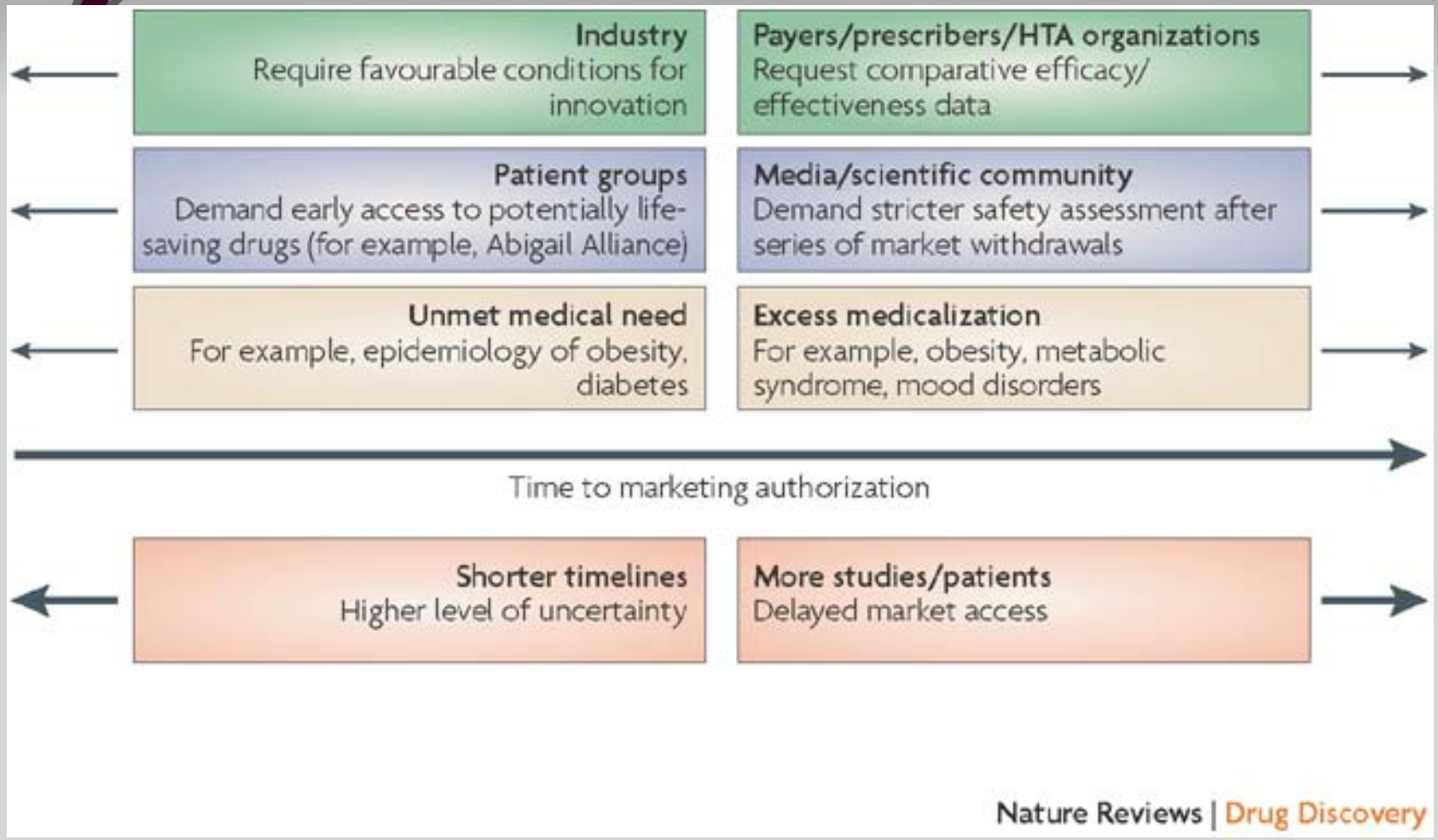
OPINION

Nature Rev Drug Discov Dec 2008

Balancing early market access to new drugs with the need for benefit/ risk data: a mounting dilemma

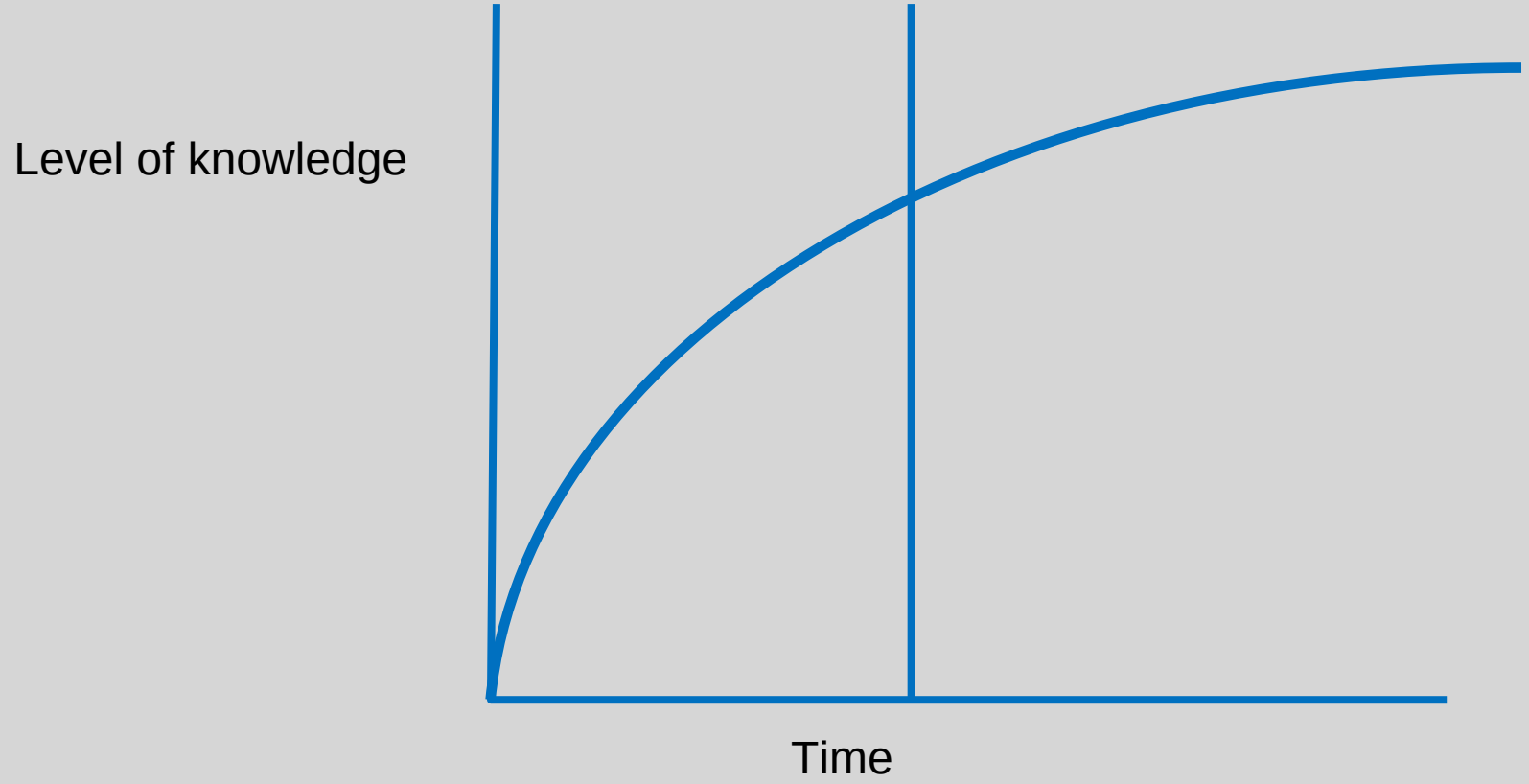
Hans-Georg Eichler, Francesco Pignatti, Bruno Flamion, Hubert Leufkens and Alasdair Breckenridge

The regulator's dilemma



Eichler HG, Pignatti F, Flamion B, Leufkens H, Breckenridge A. *Nature Rev Drug Discov* 2008

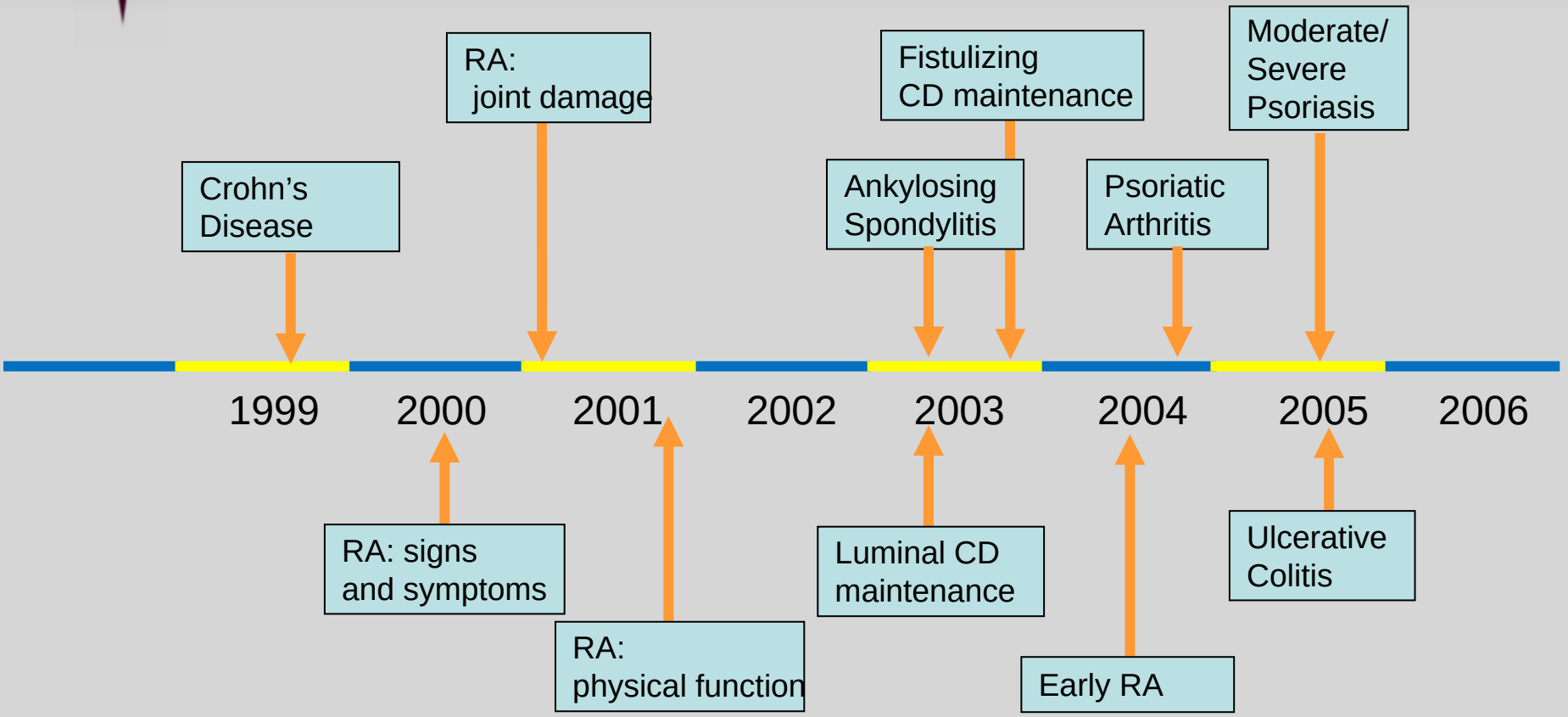
Timing of market authorisation?



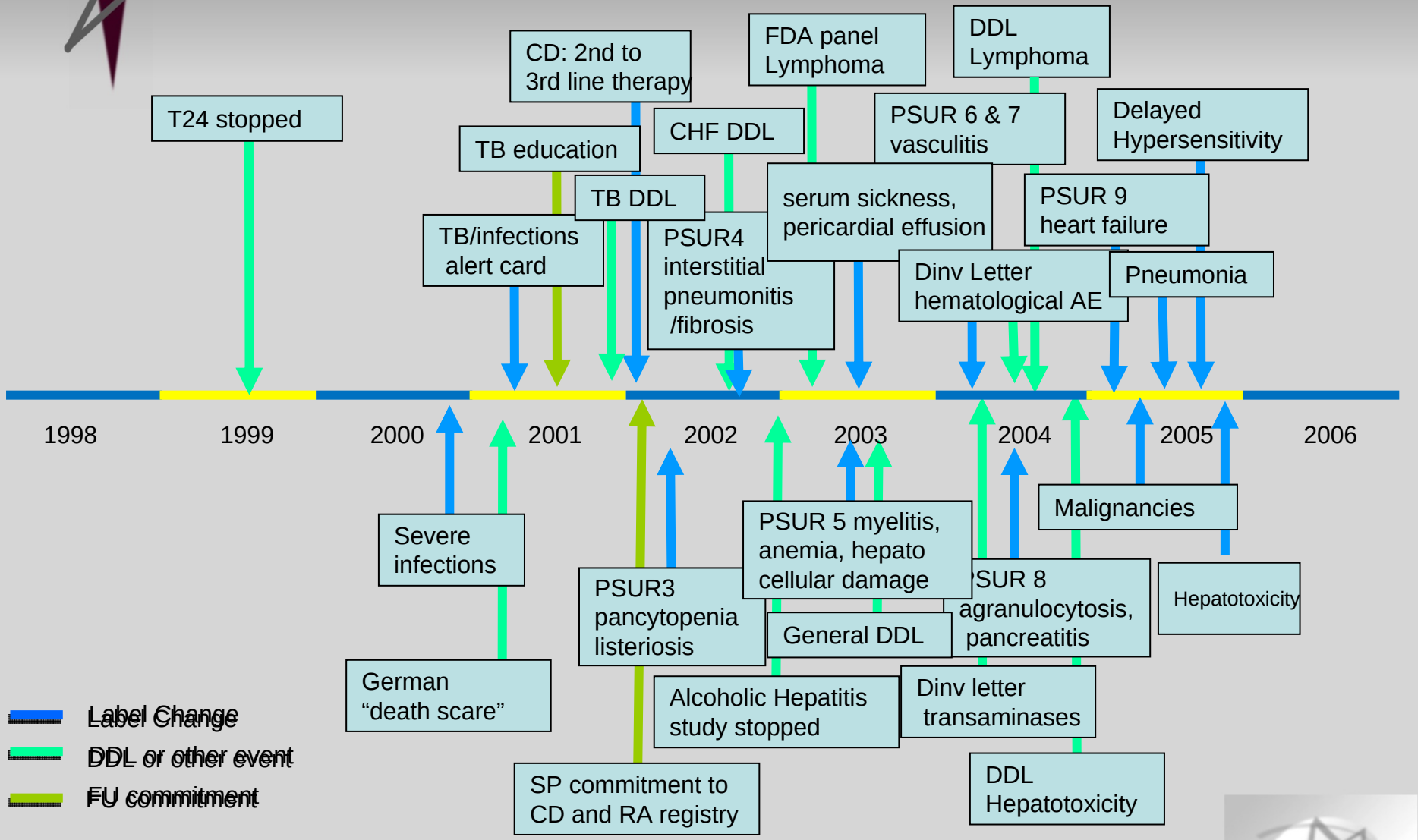
Accelerated approval

- Accelerating approval of innovative drugs is a risky business for regulators

Evolution of Remicade® (infliximab) at EMA



Evolution of Remicade® (EU): Safety



Evolution of Acomplia® (rimonabant)

Selective CB1 antagonist

Approved April 2006

European Medicines Agency

London 30 January 2009
EMEA/39457/2009

PUBLIC STATEMENT ON

Acomplia
(rimonabant)

WITHDRAWAL OF THE MARKETING AUTHORISATION IN THE EUROPEAN UNION

Enabling rapid access to market

Legal instrument in place since 2006:

Conditional Marketing Authorisation

Several requirements, including:

"...The benefit/risk balance is positive."

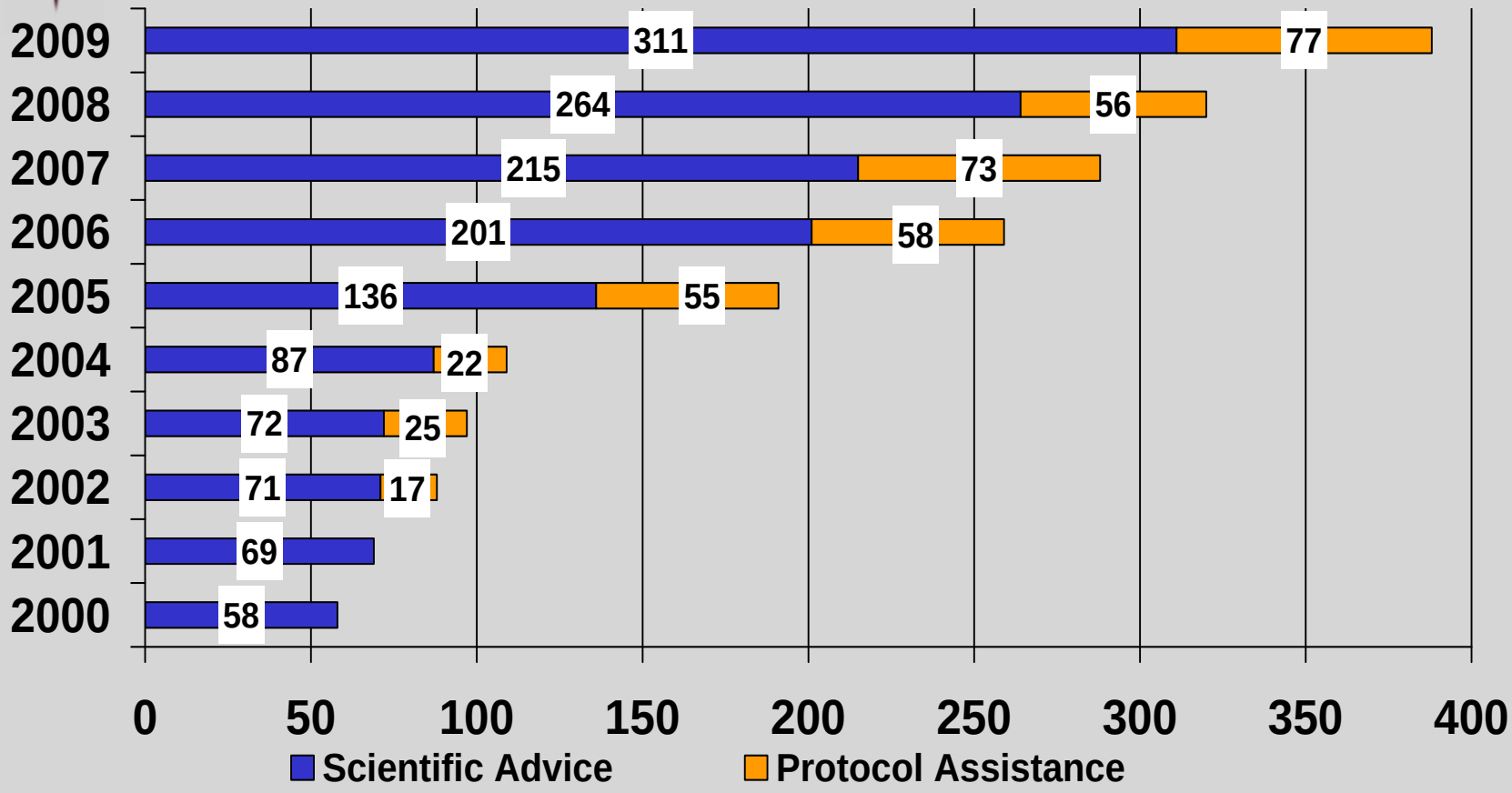
"...Benefits to public health of the immediate availability outweigh the risks inherent in the fact that additional data are still required."

Illustrates the growing need for **post-marketing benefit-risk assessment**

Accelerated approval

- How to deal with the uncertainty of earlier approvals?

Scientific Advice (SA) and Protocol Assistance



* Protocol Assistance = Scientific Advice for Orphan Medicinal Products

Benefits of SA

Eur J Clin Pharmacol
2010 Jan; 66(1): 39-48

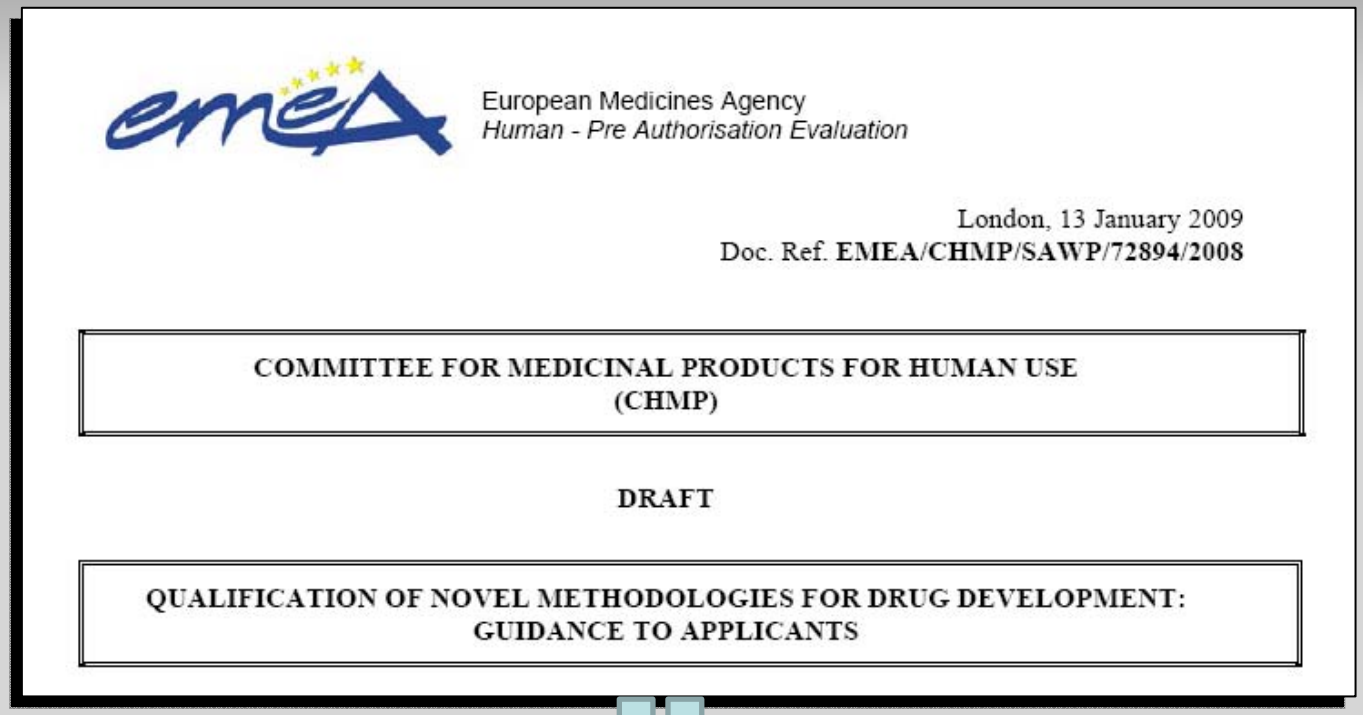
SPECIAL ARTICLE

Factors associated with success of market authorisation applications for pharmaceutical drugs submitted to the European Medicines Agency

Jan Regnstrom · Franz Koenig · Bo Aronsson ·
Tatiana Reimer · Kristian Svendsen · Stelios Tsigkos ·
Bruno Flamion · Hans-Georg Eichler · Spiros Vamvakas

Compliance with SA (vs no advice) gives an odds ratio of 14.71 (1.95 – 111.15) for a successful approval

Qualification of novel methodologies



European Medicines Agency
Human - Pre Authorisation Evaluation

London, 13 January 2009
Doc. Ref. **EMEA/CHMP/SAWP/72894/2008**

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

DRAFT

QUALIFICATION OF NOVEL METHODOLOGIES FOR DRUG DEVELOPMENT: GUIDANCE TO APPLICANTS

Scientific Advice on future studies required for qualification purposes

OR

CHMP Public Opinion on the Qualification

Example of a successful BMQ process

PERSPECTIVE

nature biotechnology

Renal biomarker qualification submission: a dialog between the FDA-EMEA and Predictive Safety Testing Consortium

Frank Dieterle[1], Frank Sistare[2], Federico Goodsaid[3], Marisa Papaluca[4], Josef S Ozer[2,28], Craig P Webb[5,6], William Baer[5,7], Anthony Senagore[5,8], Matthew J Schipper[5,9], Jacky Vonderscher[10], Stefan Sultana[5], David L Gerhold[2], Jonathan A Phillips[11], Gérard Maurer[1], Kevin Carl[1], David Laurie[1], Ernie Harpur[12], Manisha Sonee[13], Daniela Ennulat[14], Dan Holder[15], Dina Andrews-Cleavenger[16], Yi-Zhong Gu[17,29], Karol L Thompson[3], Peter L Goering[3], Jean-Marc Vidal[4], Eric Abadie[4], Romaldas Maciulaitis[4,18], David Jacobson-Kram[3], Albert F Defelice[3], Elizabeth A Hausner[3], Melanie Blank[3], Aliza Thompson[3], Patricia Harlow[3], Douglas Throckmorton[3], Shen Xiao[3], Nancy Xu[3], William Taylor[3], Spiros Vamvakas[4], Bruno Flamion[4], Beatriz Silva Lima[4], Peter Kasper[4], Markku Pasanen[4,19], Krishna Prasad[4], Sean Troth[20], Denise Bounous[21], Denise Robinson-Gravatt[22], Graham Betton[23], Myrtle A Davis[24], Jackie Akunda[25], James Eric McDuffie[13], Laura Suter[10], Leslie Obert[22], Magalie Guffroy[12], Mark Pinches[23], Supriya Jayadev[11], Eric A Blomme[26], Sven A Beushausen[22], Valérie G Barlow[12], Nathaniel Collins[17,29], Jeff Waring[26], David Honor[26], Sandra Snook[13], Jinhe Lee[26], Phil Rossi[27], Elizabeth Walker[27] & William Mattes[27]

Example of a successful BMQ process

nature biotechnology

ARTICLES

Urinary clusterin, cystatin C, β2-microglobulin and total protein as markers to detect drug-induced kidney injury

Frank Dieterle, Elias Perentes, André Cordier, Daniel R Roth, Pablo Verdes, Olivier Grenet, Serafino Pantano, Pierre Moulin, Daniel Wahl, Andreas Mahl, Peter End, Frank Staedtler, François Legay, Kevin Carl, David Laurie, Salah-Dine Chibout, Jacky Vonderscher & Gérard Maurer

Kidney injury molecule-1 outperforms traditional biomarkers of kidney injury in preclinical biomarker qualification studies

Vishal S Vaidya[1], Josef S Ozer[2,8], Frank Dieterle[3], Fitz B Collings[1], Victoria Ramirez[1], Sean Troth[4], Nagaraja Muniappa[4], Douglas Thudium[2], David Gerhold[2], Daniel J Holder[5], Norma A Bobadilla[6], Estelle Marrer[3], Elias Perentes[3], André Cordier[3], Jacky Vonderscher[3], Gérard Maurer[3], Peter L Goering[7], Frank D Sistare[2] & Joseph V Bonventre[1]

EMA and precompetitive research

- Qualification of novel methodologies
- Early dialog between industry with regulators:

  e.g., non-binding “Briefing Meetings” on pharmacogenomics, personalised medicines, drug-diagnostic combinations, etc.
- EMA participation in Public-Private-Partnerships (e.g. IMI)

EMA participation in IMI first call projects

		EMA role/participation
	IMI Safety Pillar	
1	Improve Predictivity of Immunogenicity	None
2	Non-genotoxic Carcinogenesis	None
3	Expert Systems for in silico Toxicity Prediction	None
4	Improved Predictivity of non-clinical Safety Evaluation	Scientific Advisory Board Member
5	Qualification of Translational Safety Biomarkers	Scientific Advisory Board Member
6	Strengthening the Monitoring of Benefit/Risk	Consortium Leader
	IMI Efficacy Pillar	
7	Islet Cell Research	None
8	Surrogate Markers for Vascular Endpoints	None
9	Pain Research	None
10	New Tools for the Development of Novel Therapies in Psychiatric Disorders	None
11	Neurodegenerative Disorders	Scientific Advisory Board Member
12	Understanding Severe Asthma	Scientific Advisory Board Member
13	COPD Patient Reported Outcomes	Scientific Advisory Board Member
	IMI Education & Training Pillar	
14	European Medicines Research Training Network	None
14	European Medicines Research Training Network	None
15	Safety Sciences for Medicines Training Programme	None
16	Pharmaceutical Medicine Training Programme	Scientific Advisory Board Member
17	Integrated Medicines Development Programme	None
18	Pharmacovigilance Training Programme	Consortium Member

EMA could also mine and share data

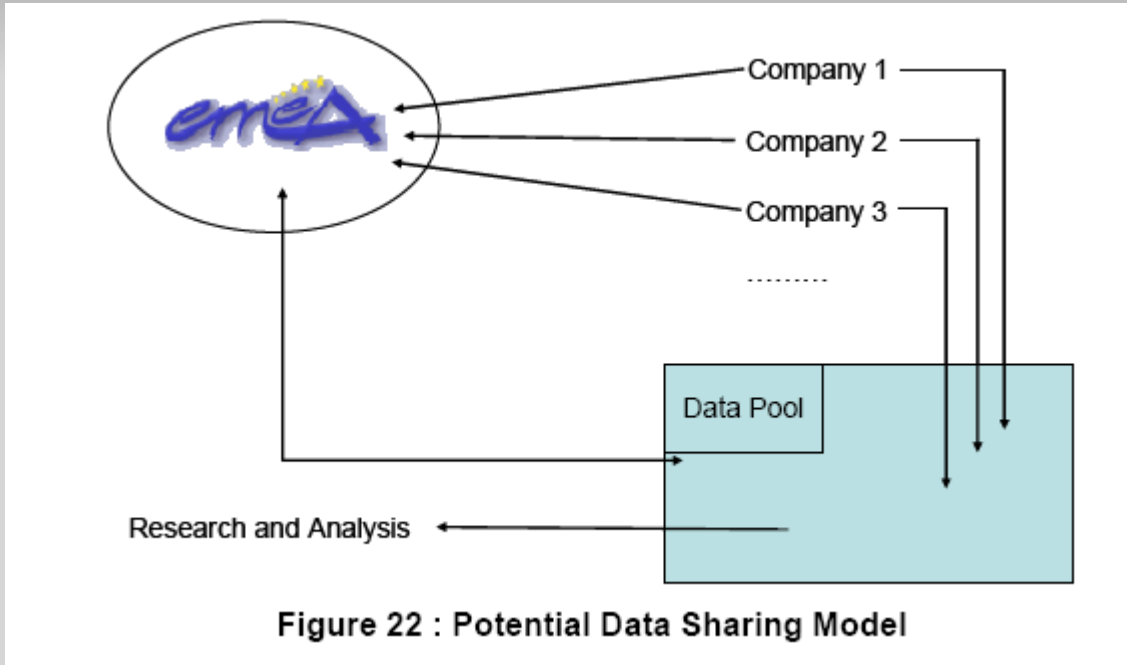


Figure 22 : Potential Data Sharing Model

"EMEA's proposal that it will undertake outcomes research using the vast data pool it has available is encouraging…"

From: The IMI Research Agenda 2009

Another type of incentive

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 May 2010
EMA/CAT/328191/2010
Press Office

Press release

Committee for Advanced Therapies gives first certification opinion for advanced therapies medicinal product

New certification procedure designed to help small and medium-sized enterprises developing innovative medicines

Finally, a critical question...

How to measure the level of innovation

- Relative efficacy
- Relative effectiveness
- What is the role of national pricing and reimbursement committees?
- What is the role of HTA bodies?
- What is the role of EMA?

(EMA RoadMap to 2015) "There is no reason why the EMA and the HTA bodies should take a different approach to the assessment of net health benefit (benefits minus risks) since the ultimate objective should be to achieve integrated medicine development satisfying the various needs."

Conclusions - 1

- Accelerating approval of innovative drugs is a risky business for regulators

- What we need is:
  - ✓ earlier, more focused knowledge
  - ✓ more understanding of the mechanism of action
  - ✓ personalised medicines
  - ✓ drug-device & drug-diagnostics developments

Conclusions - 2

- Companies and consortia are advised to consider early dialogs with regulatory bodies (informal contacts, Briefing Meetings, Qualification processes, Scientific Advices…)

- What incentive/benefit for innovative drugs ?

- (*Unavoidable*)
  How to measure the level of innovation ?

→ In the end, regulatory decisions must be appropriate, predictable and consistent

Thank you !!