How to accelerate approval of innovative drugs

Bruno FLAMION, MD, PhD
Chair, Scientific Advice Working Party (SAWP) of the CHMP (EMA)
Federal Agency for Medicinal and Health Products (FAMHP), Belgium
Chair, Belgian Committee for Reimbursement of Medicines (CTG-CRM)
Professor of Physiology & Pharmacology, FUNDP Namur, Belgium

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Disclaimer

My presentation might not be the view 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
• 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
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.  
Timing of market authorisation?

Level of knowledge vs. Time
Accelerated approval

- Accelerating approval of innovative drugs is a risky business for regulators
Evolution of Remicade® (infliximab) at EMA

1999
- Crohn's Disease
- RA: joint damage
- RA: signs and symptoms

2000
- RA: physical function

2001
- Ankylosing Spondylitis
- Luminal CD maintenance

2002
- Fistulizing CD maintenance
- Early RA

2003
- Psoriatic Arthritis

2004
- Moderate/Severe Psoriasis
- Ulcerative Colitis

2005

2006
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

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
Scientific Advice on future studies required for qualification purposes

OR

CHMP Public Opinion on the Qualification
Example of a successful BMQ process

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

Example of a successful BMQ process

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 Vaidya¹, Josef S Ozer²,⁸, Frank Dieterle³, Fitz B Collings¹, Victoria Ramirez¹, Sean Troth⁴, Nagaraja Muniappa⁴, Douglas Thudium², David Gerhold², Daniel J Holder⁵, Norma A Bobadilla⁶, Estelle Marrer³, Elias Perentes³, André Cordier³, Jacky Vonderscher³, Gérard Maurer³, Peter L Goering⁷, Frank D Sistare² & Joseph V Bonventre¹
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

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<thead>
<tr>
<th>Pillar</th>
<th>Project Description</th>
<th>EMA Role/Participation</th>
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<tbody>
<tr>
<td><strong>IMI Safety Pillar</strong></td>
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<td>1. Improve Predictivity of Immunogenicity</td>
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<td>2. Non-genotoxic Carcinogenesis</td>
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<td>3. Expert Systems for in silico Toxicity Prediction</td>
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<td>4. Improved Predictivity of non-clinical Safety Evaluation</td>
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<td>5. Qualification of Translational Safety Biomarkers</td>
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<td>6. Strengthening the Monitoring of Benefit/Risk</td>
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<td>Consortium Leader</td>
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<td><strong>IMI Efficacy Pillar</strong></td>
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<td>7. Islet Cell Research</td>
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<td>8. Surrogate Markers for Vascular Endpoints</td>
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<td>9. Pain Research</td>
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<td>11. Neurodegenerative Disorders</td>
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<td>12. Understanding Severe Asthma</td>
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<td>13. COPD Patient Reported Outcomes</td>
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<td><strong>IMI Education &amp; Training Pillar</strong></td>
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<td>14. European Medicines Research Training Network</td>
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<td>15. Safety Sciences for Medicines Training Programme</td>
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<td>16. Pharmaceutical Medicine Training Programme</td>
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<td>17. Integrated Medicines Development Programme</td>
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<td>18. Pharmacovigilance Training Programme</td>
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<td>Consortium Member</td>
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“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
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.”
• 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
• 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!!