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## Pharmaceutical R&D, innovation, HTA and policy: Some industry perspectives

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Sheffield, January 2010

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Answers That Matter.

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## Disclaimer

The views expressed in this presentation are those of the presenter and not necessarily representative of the industry as a whole

## Eli Lilly and Company



Headquartered in Indianapolis, Indiana since 1876, when it was established by Colonel Eli Lilly

- Over 40,000 employees worldwide
- Nearly 8,000 in R&D
- Clinical research conducted in more than 50 countries
- R&D facilities in seven countries
- Manufacturing plants in 13 countries



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## The pharmaceutical industry is facing some challenges!



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## Observations

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R&D productivity has diminished as “new science” proves harder to convert into medicines and cost of development of new medicines has risen dramatically

Payers are not seeing much additional benefit or value

Industry is working leverage “new science” and to reduce the costs of drug development (but still requires dramatic change to business models)

“Innovation” (real incremental benefits) need to be better recognised and rewarded

Industry is starting to learn what payers want

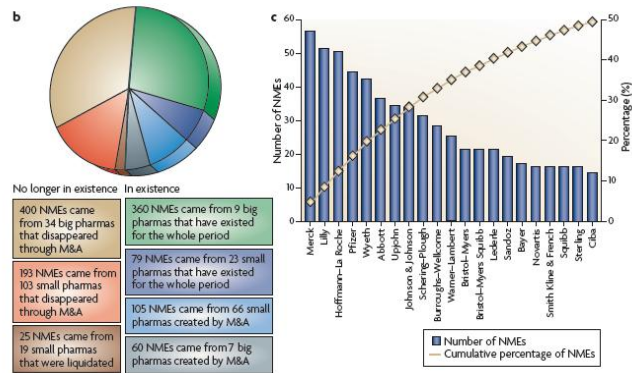
Tailored therapeutics bring opportunities and challenges

Further evolution of HTA is occurring but needs real partnership

## Part 1. Innovation, R&D Productivity, Cost

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## Where does industry innovation come from?



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## The cost of innovation

Estimate	Value of item (US\$ millions)
<b>DiMasi estimate in 2000 dollars</b>	802
• Adjustment for post-approval R&D	95
• Adjustment for new indications and non-US approvals (20%)	160
• Adjustment for success rate (11.5% versus 21.5%)	697
<b>Adjusted DiMasi estimate in 2000 dollars</b>	1,754
• Adjustment for inflation (3.7% per year)	592
• Adjustment for other cost increases, such as regulation (8.3% per year)	1,565
<b>Adjusted DiMasi estimate in 2008 dollars</b>	3,911

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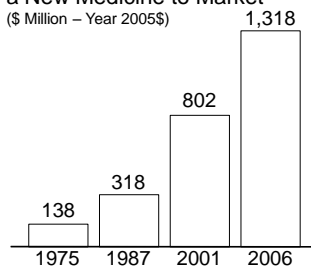
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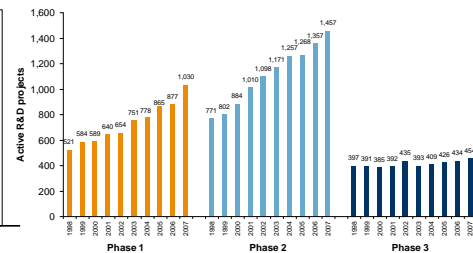
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## Bringing a new medicine to market: no more “low hanging fruit”

Estimated Full Cost of Bringing  
a New Medicine to Market  
(\$ Million – Year 2005\$)



Trends in Total Number of Global R&D  
Projects by Stage of Development



Source: DiMasi and Grabowski, “The cost of Biopharmaceutical R&D: Is Biotech Different?”, Managerial and Decision Economics 28(2007): 469-479; PharmaProjects as reported in Parexel’s Biopharmaceutical R&D Sourcebook 2007-08

## What is industry doing to change?

A number of radical and successful experiments that can be used as building blocks:

- *Innocentive*
- *Chorus*
- Public-private partnerships
- *open-source R&D*
- *X Prize*
- Innovation networks
- FIPNet
- consortia and various combinations of these and other initiatives

Also working with regulators on novel approaches to bringing the science forward

And with payers to develop more meaningful data, including exploration of evidence development pre and post marketing authorisation

## Part 2. Assessment and valuing of innovation

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## Variation in Valuation and Pricing Approaches Across Europe

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### OECD Report on Pharmaceutical Pricing 2008

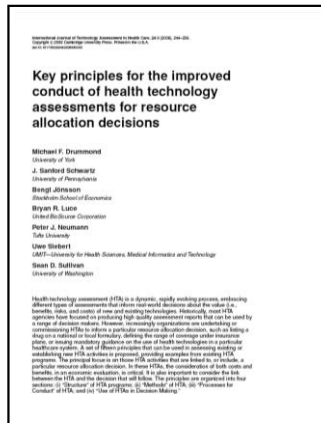
“In the interest of encouraging valuable innovation, efforts to link the level of expenditure for a given pharmaceutical product to **the value of the benefits offered by the new product** are attractive in that they can be used by manufacturers to assess willingness to pay for future innovations and should thus provide incentives for investment in R&D leading to valued innovation.”

### European markets may be “price takers” or “price makers”

UK: A “price taker”: Price is set by manufacturer at launch and assessment of value made by NICE.  
 France: A “price maker”: Price is negotiated following assessment of value by the Transparency Commission

**Discussion of potential to harmonise assessment of relative effectiveness, BUT agreement that decisions on reimbursement and pricing must remain the responsibility of Member States**  
 (European Observatory on Health Systems and Policies, 2008)

## What Does “Good” Look Like?



### The International Group for HTA Advancement International Journal of Technology Assessment in Health Care, 24:3 (2008), 1–15.

*15 principles in all, including:*

*transparent processes and decisions*

*consider a wide range of evidence*

*actively engage key stakeholder groups*

*HTA should be timely*

## “Innovation” or added benefit?

Such potential benefits can be structured in 3 main areas:

1. **“Therapeutic/Clinical” benefits** refer to those new medicinal products, which are able to treat or to prevent, in all patients or in specific patient groups, diseases lacking (adequate) treatments or diseases already treated with pre-existing medicinal products but with clinical or safety advantages.
  2. **“Quality of Life” benefits** refer to those new medicinal products, which, compared to the existing ones, are able, in all patients or in specific patient groups, to provide quality of life gains.
  3. **”Socio-economic” benefits** refer to those new medicinal products, which, compared to the existing ones, are (also) able to offer benefit on a higher-level for society (e.g. related to public health or public budgets).
- It is clear that the benefit brought by one medicine can cover more than one area. Furthermore, there is often interdependence between these three areas of benefit, one benefit influencing another. This is to be taken into account during assessments in order to avoid double-counting.

*EU High Level Pharmaceutical Forum final report, October 2008*

## SMC view of benefits

(data presented by Ken Patterson at Stockholm, December 2009)

- 61 cancer medicines reviewed
  - 36 for advanced/metastatic cancer
  - 25 for earlier/adjvant treatment
- Only 6 drugs (10%) offered  $\geq 1$  QALY
- 22 drugs (36%) offered  $\leq 0.2$  QALY  
= 3 months at 70% of normal QoL
- Some of the greatest health-gains are with really innovative drugs
  - Trastuzumab –2.4 QALYs
  - Nilotinib/Nilotinib –2.1 QALYs
  - Bortezomib –1.1 QALYs

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## Industry is listening to HTA agencies and payers

### Arzoxifene: Once-Promising SERM Fails Huge Phase III Trial

Monday, December 14, 2009 - Elsevier Global Medical News

*Eli Lilly (LLY) has finally admitted defeat in its long-running battle to make arzoxifene, a follow-on osteoporosis drug to its own blockbuster Evista, an approvable and commercially viable product. Although the results of a pivotal phase III trial met its primary endpoints, the drug failed on multiple secondary measures which would have provided an advantage over existing treatments, leaving Lilly with little option but to abandon plans to file for regulatory approval.*

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## Will “tailored therapeutics” and “personalised medicine” be the solution?

Lilly believes they will certainly help deliver better patient level outcomes and improve the value proposition

Most Lilly Phase III studies have biomarkers included

May include diagnostic associated with therapeutic (e.g. Herceptin) or may be tailored via other means (e.g. Alimta and NSCLC histology)

However, many challenges, not just in R&D...

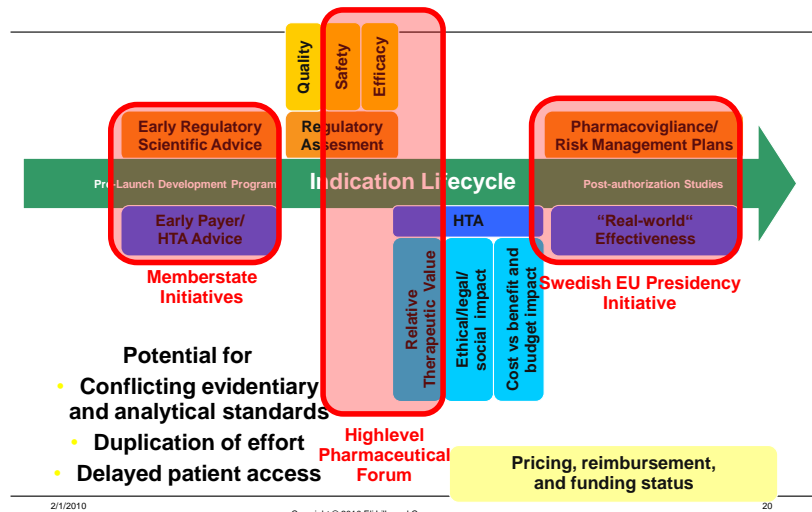
## Are personalised medicines like orphan drugs?

<i>Consideration</i>	<i>Orphan drugs</i>	<i>PM</i>	<i>However ...</i>
1. Held to same clinical evidence hurdles as larger population product?	Not fully, but becoming more stringent in some markets	Yes	High evidence threshold → lower innovation Low evidence threshold → poor value
2. Held to same economic evidence hurdles as larger population products?	As above	Yes	ICER-driven prices do not reward innovation (may miss patient-relevant benefits)
3. Individual financial impact may be small but payers are concerned about budget impact of multiple products	Yes	Yes	Some PGx products will reduce total government budgets Government budgets ≠ WTP
4. Pricing evaluated with greater scrutiny	Yes	Yes	Value-based pricing still evolving
5. Conventional health economic modelling approaches “fit”	Debatable	Yes (really??)	Economic models for PGx are far more complex than for drugs
6. Conventional large population HTA approach “fit”	Debatable	Debatable	HTA of PGx requires more than conventional HTA

Extension of E Faulkner et al. “Orphan Drug Funding: A Model for Personalized Medicine. Paris, ISPOR 25 October 2009

### Part 3: Evolution of European regulatory and HTA environment

### The Challenge



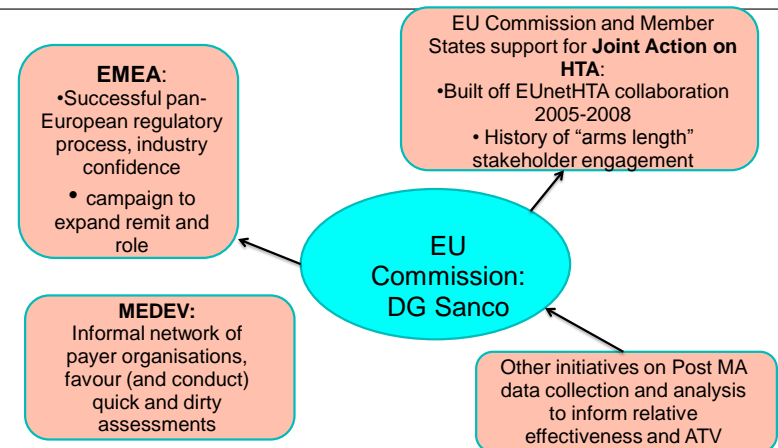
# “EU Terminology”

## Definitions by the High Level Pharmaceutical Forum

- Efficacy is the extent to which an intervention does more good than harm under ideal circumstances
- Relative Efficacy[...], compared to one or more alternative interventions
- Effectiveness is the extent [...] when provided under the usual circumstances of health care practice
- Relative Effectiveness[...] compared to one or more intervention alternatives

[http://ec.europa.eu/pharmaforum/docs/rea\\_principles\\_en.pdf](http://ec.europa.eu/pharmaforum/docs/rea_principles_en.pdf). (Oct 2008)

## Key Players



## What is being proposed by each player?

### EMA:

- Expansion of EPAR documents to include clearer and more detailed information on “relative efficacy” (based on regulatory dossier and other data already in possession of the EMA)
- Collaboration with HTA agencies (individually with major agencies and collectively via the Joint Action), industry and patients to:
  - Develop the “relative efficacy” statement to appropriately reflect relevant outcomes (including PROs)
  - Evolve the “relative efficacy” statement into one of “relative effectiveness” via sharing of further evidence

## What might the relative-efficacy, relative effectiveness statement look like?

EMA slide, DIA meeting Nov 2009, describing new document in Orphan process

The slide features the EMA logo in the top left corner. The main title is 'Transparency of "significant benefit" (SB) assessment'. Below the title, it states 'Solution: dedicated document on SB by COMP:'. A bulleted list follows, detailing the components of the solution. At the bottom, it says 'Effective Jan 2010' and has a small number '12' in the bottom right corner.

**Transparency of  
"significant benefit" (SB) assessment**

**Solution: dedicated document on SB by COMP:**

- **Nature of SB (endpoint, e.g. PFS)**
- **Comparator**
- **Magnitude of SB (Effect size, e.g. x months)**
- **Uncertainty around SB estimate (e.g. Conf. Interval)**

**Effective Jan 2010**

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## What is being proposed by each player?

### EU Joint Action on HTA

- Builds on 3 years of EUnetHTA work
- Proposed series of work packages, including relative effectiveness, pilot appraisals, dissemination of member agency appraisals, and database development
- Wide membership, level of commitment by all members is not clear
- Very “arms length” approach to stakeholder engagement and participation: “inform” rather than “consult”
- Pilots are unlikely to begin until 2011: not clear if “reassessments” or parallel assessments of new products

## Joint Action membership

### EUnetHTA Joint Action 2010-2

- A total of 33 government appointed organisations from 23 EU Member States and Norway (“Associated Partners”)
- Relevant non-for-profit organisations that produce or contribute to HTA and will be actively involved and provide scientific input (“Collaborating Partners”) --- huge interest

## Conclusions

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Industry is at a crossroads: real innovation will come, including targeted therapies, but business model and current industry structure must evolve

Evolution of HTA is:

- Desirable: need to balance scientific rigor with new approaches to understanding patient benefits and values
- Politically supported: Especially within the EU and US (CER)
- Broadening to overlap with regulatory processes and post-marketing evidence generation
- Supported by industry: Provided genuine stakeholder dialogue is possible (EMA model) and industry understands and fulfils its role and obligations

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Thank you for your  
attention.

Q&A?