Regulatory Science and the FDA

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An Existential Challenge

- **a**

  - Chart showing the number of NMEs or NBEs over time from 1950 to 2008.
  - Data categories: Small molecules (NMEs), Biopharmaceuticals (NBEs), Total.

- **b**

  - Pie chart indicating the proportion of NMEs that are no longer in existence.

- **c**

  - Bar chart showing the number of NMEs and cumulative percentage of NMEs.
  - Companies listed include: Merck, Lilly, Hoffmann-La Roche, Pfizer, Wyeth, Abbott, Upjohn, Johnson & Johnson, Schering-Plough, Warner-Lambert, Bristol-Myers Squibb, Merck KGaA, Bayer, Novartis, SmithKline & French, Squibb, Sterling, and Chia.

- **Additional Information**
  - 400 NMEs came from 34 big pharmas that disappeared through M&A.
  - 360 NMEs came from 9 big pharmas that have existed for the whole period.
  - 193 NMEs came from 103 small pharmas that disappeared through M&A.
  - 79 NMEs came from 23 small pharmas that have existed for the whole period.
  - 105 NMEs came from 66 small pharmas created by M&A.
  - 25 NMEs came from 19 small pharmas that were liquidated.
  - 60 NMEs came from 7 big pharmas created by M&A.

**Nature Reviews | Drug Discovery**
Munos B NRDD 2009; 8: 959-68.
Global drug market by treatment area

<table>
<thead>
<tr>
<th>Treatment Area</th>
<th>2006</th>
<th>2011 (forecast)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td></td>
<td></td>
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<tr>
<td>Statins</td>
<td></td>
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<tr>
<td>Acid suppressants</td>
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<tr>
<td>Respiratory</td>
<td></td>
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<tr>
<td>Diabetes</td>
<td></td>
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<tr>
<td>Blood pressure</td>
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<tr>
<td>Anti-psychotics</td>
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<tr>
<td>Anti-depressants</td>
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<tr>
<td>Anti-platelet</td>
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<tr>
<td>Anti-epileptics</td>
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</tbody>
</table>

Average annual treatment cost in the US

<table>
<thead>
<tr>
<th>Year</th>
<th>Cost</th>
<th>Product</th>
</tr>
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<tbody>
<tr>
<td>1990</td>
<td></td>
<td>Zoladex</td>
</tr>
<tr>
<td>1992</td>
<td></td>
<td>Taxol</td>
</tr>
<tr>
<td>1996</td>
<td></td>
<td>Arimidex</td>
</tr>
<tr>
<td>1998</td>
<td></td>
<td>Camptosar</td>
</tr>
<tr>
<td>1996</td>
<td></td>
<td>Gemzar</td>
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<tr>
<td>1997</td>
<td></td>
<td>Femara</td>
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<tr>
<td>1997</td>
<td></td>
<td>Rituxan</td>
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<tr>
<td>1998</td>
<td></td>
<td>Xeloda</td>
</tr>
<tr>
<td>1998</td>
<td></td>
<td>Herceptin</td>
</tr>
<tr>
<td>2001</td>
<td></td>
<td>Oleseve</td>
</tr>
<tr>
<td>2002</td>
<td></td>
<td>Zavolin</td>
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<tr>
<td>2003</td>
<td></td>
<td>Iressa</td>
</tr>
<tr>
<td>2004</td>
<td></td>
<td>Erbitux</td>
</tr>
<tr>
<td>2004</td>
<td></td>
<td>Avastin</td>
</tr>
<tr>
<td>2004</td>
<td></td>
<td>Tarceva</td>
</tr>
<tr>
<td>2008</td>
<td></td>
<td>Revlimid</td>
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<tr>
<td>2007</td>
<td></td>
<td>Sprycel</td>
</tr>
</tbody>
</table>

Source: IMS
An Appeal to Reason

“If we don’t change the business models, we’re not going to survive as an industry”.

Richard Clarke, Merck CEO
Financial Times, Oct 22nd 2008
Another Existential Challenge

Prescription drugs rose from 10% to 18% of health care costs from 1996 to 2006
Regulatory Science
Regulatory Science

The acquisition and analysis of data sufficient to inform decision making pertinent to the approval of safe and effective therapeutics, devices and cosmetics and ensuring the safety and nutritional value of the food supply.
What it’s not...

A new set of regulations
An approach to speed the approval process
An attempt to establish cutting edge biomedical science in the FDA
Why should we care?
Regulatory Science

• Provide purpose, focus and respect for the scientific mission of the agency
• Encourage and reward innovation
• Enhance risk detection and conserve value
• Leverage the resources of the academic sector to refine decision making at the FDA
Elements of Regulatory Science

• Exploit the lifecycle approach to approval and withdrawal of novel therapeutics and devices: graded introduction and graded withdrawal

• Incentivize innovation and early, unrestricted exploration of drug action and mechanisms of SAEs: a safe haven for systems pharmacology and physiology
Elements of Regulatory Science

• Broaden the approach to risk detection
  Lessons of Vioxx, Tegenero and Avandia: look beyond pharmacoepidemiology and meta-analyses
• Catalyze development of orphans; drugs and diseases. FDA as a unique repository of information
• FDA – Academia Centers of Excellence
FDA Centers of Excellence

Add value by leveraging academic expertise to Agency needs:

- Adaptation of trial design
- Informatics for collation, storage, interpretation and communication
- Translational Medicine and Therapeutics
- Emerging therapeutic modalities – stem cell biology, nanotechnology
FDA Centers of Excellence

• A source of incremental expertise in partnership with FDA investigators
• A neutral testing ground – a JPL for the FDA
• A bi-directional educational opportunity
• Lessons from CPI and CERTS – sufficient incremental resource to attract engagement and demand delivery
• Leverage NIH peer review system
A Parallel Initiative...
A coincident role for NIH, Academia and Industry; Rebuild Capacity in Human Pharmacology

Critical to the development of NMEs
The Prescribing Physician’s Primary Source of Drug Information
A coincident role for NIH, Academia and Industry; Rebuild Capacity in Human Pharmacology

• Critical to the role of the FDA in determining benefit and risk
• Critical to comparative effectiveness
• Critical to the education of doctors
• Deficient or absent in industry, academia and the FDA
Recapture the imagination of the Young(er)
LAUNCHING A NEW DISCIPLINE IN ACADEMIA: TRANSLATIONAL MEDICINE AND THERAPEUTICS

• Develop and project mechanism based quantitative biomarkers from model systems into humans.
• Evoking phenotypic responses in humans to guide individualization of rational dose selection
• Harness the unbiased technologies to select amongst molecules directed against a single target
• Complements the emergence of Regulatory Science
Steps in the right direction...

• A Joint NIH-FDA Leadership Council

• The NIH and the FDA will jointly make 2-3 awards of $450,000 - $675,000 per year, each for 3 years.
Final Message

- Academia and its funders, the Pharma and Biotech industries and the FDA face serious and integrated challenges
- How we address them will directly impact both the health and wealth of the US and the wider world
- Shared problems demand imaginative approaches to developing shared solutions
A word from Philadelphia.....

Let’s not hang together