THE R&D PROCESS

AND THE CURRENT STATE OF PLAY VIS A VIS NEW VACCINES
Forces impacting the pharmaceutical industry

- Increased visibility of global health issues
- Pressure from pharmaceutical parents company to meet financial targets
- Emerging competitors
- Changes in regulation
- Emergence of many combination products
- Increased range of new and complex technologies
- Bio tech “revolution”
  - More products
  - New technologies
Emerging competitors

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- **India**: Serum Institute of India, Bhara Biotech
- **Indonesia**: Bio Farma
- **Cuba**: CIGB, and the Finlay Institute
- **Brazil**: Biomanguinhos
- **Others**: ?
Regulation (safety, biological, increasingly complex science)

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One manufacturer estimates that costs/sq m have risen 3 fold in the past 5 years because of increased regulatory requirements
Regulatory Issues

Regulatory requirements are increasing for all products:

One manufacturer estimates cost/sq m has risen 3 fold in past 5 years because of this

NRAs (National Regulatory Authorities) in developing countries have been weak historically:

NRAs in 32/51 producing countries are achieving required six regulatory functions

Only 73% of DTwP vaccine supply is of assured quality

Regulation requirements in industrialized countries are changing:

EU only licensing products used within EU

(DTwP = DIPHTHERIA TOXOID, TETANUS TOXOID, and whole-cell PERTUSSIS VACCINE. The vaccine protects against diphtheria, tetanus, and whooping cough).
Combination products

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• Pressure from pharmaceutical parents company to meet financial targets

• Emerging competitors

• Changes in regulation

• Emergence of many combination products

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• DTP-Hep B
• DT-IPV
• DTP-IPV-Hib
• DTPa-IPV
• DTPwHB+Hib
• DTwP-Hep B-Hib
Costs of new products

- Clinical trials
- Factory production costs
- Licensing fees
- Production costs
- Quality Control

Fully-loaded Costs

- All baseline costs
- Incremental opportunity costs/risk
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Risk shifts from public to private sector. How are the rewards shared?

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Decision gates

- Cumulative investment (US$ Millions)
- Elapsed years

- Basic, pre-clinical research
- Identify candidate
- Efficacy trials
- Scaling up manufacturing capacity
- Commercialization in target population

- High cost, low probability
- A disincentive to invest in early stage work
Large scale economies (illustrative)

Capital costs are highly scale sensitive

- Fixed capital per course ($)
- 65% scale curve

Incremental cost of global production capacity

- OECD base demand capital
- LDC based demand
- OECD plus LDC base demand capital

- $50
- $180
- $130m
Marginal cost pricing for poorer markets

Average price

- Overhead and R & D 47%
- Utilities 7%
- Depreciation 13%
- QC staff 10%
- Production staff 14%
- Raw materials 10%

Other QC 1%

Other 12%

- Filling 64%
- Bulk mat 24%

‘Full costs’

‘Fully Marginal’
Risks

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Baseline
R&D
Capacity
Production
Licensing
Delivery
Sales
Fully-loaded Costs
Risks

- Clinical trials
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- Failure
- Site problems
  - mgmt time
  - delays
- Promised product after trial over
- Parallel trials
- Different data hurts licensing

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  - plans
  - facility
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  - validation
  - staff

- Degree of dedication
- Management over-runs

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• Mgmt problems
• Equipment overruns
• Poor forecasting
• Supply overruns
• Batch failures
• Scale-up failure
• Raw materials failure
• Supply problems

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- Absorbs management time
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- License denied
- Complaints/adverse event

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- Slow uptake
- Can’t reach infants
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- Quality Control
- Unwillingness to pay
- Expected decline in price (due to public sector reneging, etc.)
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Typical cash-flow for a product

*NB expenditure on clinical studies, manufacturing, marketing etc continues after launch but for simplicity has been netted out.
Science v Revenue

- **High** (LDC)
  - **Barriers:**
    - Opportunity costs
    - High development risk
    - High demand risk/non-existent demand
    - *Malaria*

- **Low** (Global)
  - **Barriers:**
    - Opportunity costs
    - Capacity constraints
    - Pricing Risk
    - *Pneumococcal conj*

- **High** (LDC)
  - **Barriers:**
    - Opportunity costs
    - Capacity constraints
    - High pricing risk
    - *HIV*

- **Low** (Global)
  - **Barriers:**
    - High development risk
    - Capacity constraints
    - High demand risk
    - *Yellow fever*
    - *Meningococcal A*

- Different vaccines face different barriers which may require different types of interventions.
INCENTIVES?
A range of ‘push’ and ‘pull’

**PUSH**
- Direct investment in specific product trials
- Investment in trial infrastructure
- R&D tax credits
- Investment in production capacity
- Harmonize regulatory requirements

**PULL**
- Increasing the uptake of existing vaccines
- Strengthen/ensure delivery system
- Prizes and tournaments
- Tax credits on vaccine sales
- Tiered pricing to increase total revenues
- Transferable Patents
- Co-payments
- Market guarantees
Where to put ‘push’ and ‘pull’?

- Direct investment in clinical trials for specific products
- Strengthen trial infrastructure
- Tax credits for R&D
- Investment in capacity
- Improve forecasting
- Guarantee offtake
- Harmonize regulatory delivery requirements
- Create demand earlier
- Assure today’s market’s
- Tax credits on sales
- Transferable patents
- Co-payments
- Guaranteed purchase fund
Investments needed

• Investment to ensure a delivery system capable of reaching infants and other target groups with priority vaccines

• Investment to rapidly develop priority vaccines targeting the diseases of the developing world

• Investment in production capacity to ensure the supply of global vaccines to the developing world

• Pricing which is affordable to the developing world

• Funding to purchase vaccines as soon as they are technically available
## Conundrum

<table>
<thead>
<tr>
<th><strong>Current model</strong></th>
<th><strong>Required HIV vaccine model</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Introduction:</strong></td>
<td>• LDCs 10 years plus after OECD</td>
</tr>
<tr>
<td></td>
<td>• At earliest scientific opportunity</td>
</tr>
<tr>
<td><strong>Target population:</strong></td>
<td>• OECD</td>
</tr>
<tr>
<td></td>
<td>• OECD + global</td>
</tr>
<tr>
<td><strong>LDC-specific development spend:</strong></td>
<td>• Limited/zero</td>
</tr>
<tr>
<td></td>
<td>• Significant spend probably necessary</td>
</tr>
<tr>
<td><strong>LDC testing:</strong></td>
<td>• Limited/late</td>
</tr>
<tr>
<td></td>
<td>• Significant/required early</td>
</tr>
<tr>
<td><strong>Capacity availability:</strong></td>
<td>• Limited to OECD until maturity</td>
</tr>
<tr>
<td></td>
<td>• Global early</td>
</tr>
</tbody>
</table>

- Very low (marginal) prices available to LDCs only available at cost of delayed introduction
- Prices or other incentives must justify full costs of accelerated LDC introduction