Technology Transfer and Vaccines: The GSK Experience
WHO Workshop on Technology Transfer for Local Manufacturing Capacity of Vaccines
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Vaccine Manufacturing
TT Objectives
GSK Biologicals: Profile, Pipeline, Global Network, Partnerships
The « Right Partnership Balance »
4 TT concrete examples:
- Brazil
- Singapore
- China
- Japan
Conclusion
Vaccines Manufacturing (1/4)

- Bulk
  - QC/QA
  - Formulation
  - QC/QA
  - Filling/Freeze drying
  - QC/QA
  - Packaging
  - QA

Samples submission to NCL

Lead-times: 6 – 12 months

- Quality Control/Quality Assurance (QC/QA): 55%
- Manufacturing: 25%
- NRA: 20%
Vaccines Manufacturing (2/4)

- Consistent biological processes
  - detailed mfg method and documentation

- Handling of live organisms Biosafety + cGMP’s
  - containment through HVAC system
  - waste treatment

- Facilities dedicated to one mfg process
  - one product / group of products
  - capital intensive
• Formulation
  → adjuvantation / stabilization
  → removal of preservative

• Filling
  → liquid and freeze-dried products
  → presentation: single dose vials
  → multi dose vials
  → syringes
  → plastic tubes

→ move to isolator technology to increase Sterility Assurance level
Vaccines Manufacturing (4/4)

- Quality Control
  - at each stage of manufacturing process
  - assess - purity
    - sterility
    - activity
    - immunogenicity
    - innocuousness
  - long lead-time
- Final release of each lot by NRA
Strategic objectives and partnership models

- Quality of life
- Access to vaccines
- Develop biotech sector
- Sustainable supplies
- Improved vaccines quality
- Economic success

- Acquisition
- Equitization
- Joint Venture
- Technology Transfer Agreements
- Supply Agreements
- Collaborative R&D
R&D expenses = $600m / annum
= 15% of revenues
= 40% external

1,500 people for all development activities (scaling up, pre-clinical, clinical) of which 650 in pre-clinical

> 25 projects (20 in clinical)

Supply of 25% of the worldwide vaccines
## GSK Biologics: Examples of signed partnerships

<table>
<thead>
<tr>
<th>Type of Partnership</th>
<th>Bulk Antigen</th>
<th>Sterile Operations</th>
<th>Packing</th>
<th>R&amp;D</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil (1997)</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>OPV, Hib, MMR, Rotavirus, Strept. Pneumoniae, Dengue</td>
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<tr>
<td>Russia (1997)</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>Hep-B</td>
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<tr>
<td>India (2003)</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>Various vaccines</td>
</tr>
<tr>
<td>China 1 (1995)</td>
<td>JV</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>Various vaccines</td>
</tr>
<tr>
<td>China 2 (2009)</td>
<td>JV</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Flu</td>
</tr>
<tr>
<td>China 3 (2009)</td>
<td>JV</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>MMR, Rotavirus</td>
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<td>Taiwan</td>
<td>Collaborative R&amp;D</td>
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<td>✓</td>
<td>✓</td>
<td>Clinical trials</td>
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<tr>
<td>Japan</td>
<td>Licensing Out</td>
<td></td>
<td>✓</td>
<td></td>
<td>Flu</td>
</tr>
</tbody>
</table>
The Right Partnership Balance (1/2)
The Right Partnership Balance (2/2)

Hi

Business Potential

Med

Low

Governmental support

Hi

Conducive

Incentive

Med

Competitive

Attractive

P.R. China

India

Russia

Ukraine

Egypt

Japan

Brazil

Korea

Saudi Arabia

Singapore

Russia

Ukraine

Egypt

Japan

Brazil

Korea

Saudi Arabia

Singapore

Hi

Hi

Med

Med

Low

Low

« Everything is negotiable! »

« Our market is small but you can export from here! »

« Everyth ing is negotiable! »

GlaxoSmithKline
A history of successful technology transfers
Brazil: FIOCRUZ – GSK (2/5)
(201m population – 3.6m birth cohort)

- **Polio strategic alliance 1985-2010**
  - Signature 1998
  - Clin development completed in 2007
  - Licensed end 2007
  - Fiocruz full production
  - Eradication wild polio

- **Hib tech transfer**
  - Signature 1998

- **MMR tech transfer**
  - Signature 2003
  - Transfer completed
  - Clinical trials to start

- **Rotarix tech transfer**
  - Signature 2003
  - Transfer completed
  - Clinical trials to start

- **Synflorix tech transfer & R&D collaborative agreement**
  - Signature 2009
  - Innovative agreement encompassing R+D on Dengue vaccine
  - Signature 2009
  - Innovative agreement encompassing R+D on Dengue vaccine

- **Fiocruz full production**
  - 2007
ENVIRONMENT AND CRITICAL SUCCESS FACTORS

- Clear long term procurement policy from the Brazilian MOH and clear industrial strategy to support the recipients of the technology transfers
- Coherence of Fiocruz development strategy and objectives of the technology transfer
- Set clear priorities for development and phased transfer from simple to complex processes
- Build-up technical expertise along the phases and maintain stability of manpower
DEFINITION AND IMPLEMENTATION OF THE TRANSFER

- Definition on clearly scope, content, roles and responsibilities of the partners
- Establishment of technology, technical, regulatory and commercial milestones
- Establishment of a steering committee, definition its role precisely and mechanism of resolution of conflicts
- Establishment of a long term plan of training
LESSONS LEARNED

- Build trust at all levels of workforce and management
- Emphasize on matrix organization and project team way of working
- Do not under-estimate Quality Control, QA and safety data management
- Develop people by training and empowerment
- Learning by doing and the learning curve: The recipient of technology must adapt a “do-it“ attitude
Singapore – GSK
(4.7m population – 40k birth cohort)

**Strategy**
PS center in GSK Bio’s global manufacturing network

**Activities**
- Site dedicated to the production of polysaccharides, conjugates, and r-EColi.
- Strep. pneumoniae, N. Meningitis and Hib
- Full technology transfer in wholly-owned plant
- 5 years investment program from construction to consistency lots

**Support of Singapore Government**
- Access to land
- Tax incentives
P.R. China - GSKNB
(1350 m population – 16.5m birth cohort)

**Strategy**
Building large-scale flu capacity to meet domestic demand and respond to potential pandemic threat

**Activities**
- Site dedicated to the production of egg-grown influenzae vaccines
- Full tecnology transfer in GSKNB, a joint-venture between GSK and NIBT (49/51)
- 5 years investment program from re-engineering to GMP license

**Support of Chinese Government**
- None
Japan : Kaketsusten – GSK
Common contribution to Japan’s pandemic plan

Strategy
Combining expertise of the Japanese leader in influenza market with GSK’s innovative technology and know-how, to make available as quickly as possible a cell-culture based, adjuvanted pandemic influenza vaccine.

Activities
- GSK licenses to Kaketsuken the necessary Intellectual Property, including GSK’s Adjuvant System, and sub-licenses EB66® cell line.
- Both companies collaborate closely for the vaccine development and the local clinical trials.
- Kaketsuken sets up the suitable manufacturing capacity.

Support of Japanese Government
- Japanese Government supports the project through funding the installation of local manufacturing facility.
Conclusions

- Stepwise Approach
- Which Steps for which Opportunity
### Phase 1

**Quality Management Systems & Packaging**

**Implementation of:**
- Quality Management Systems & GMP (1)
- Labeling
- Cold chain
- Warehousing
- Adverse event reporting
- Etc.

### Phase 2

**Phase 1 +**

**Filling of bulk antigen & QC**

**Implementation of:**
- Sterile filling unit
- Sterility assurance
- QC expertise
- Validated suppliers
- QMS and GMPs (2)
- Etc.

### Phase 3

**Phase 2 +**

**Production of antigens**

**Implementation of:**
- Engineering
- Bulk production expertise
- Sustainability
- Economic viability
- Etc.
Minimum volume requirements to maintain quality and to guarantee pay-back

- A few million doses / year
- > 10 million doses / year
- > 30 million doses / year
Which Steps for which Opportunity

- **Attractive**
  - Antigen Manufacturing
  - Sterile Operations & QC
  - Packing & QMS

- **Conducive**
  - Med

- **Competitive**
  - Med

- **Incentive**
  - Low

- **Governmental support**
  - Hi

- **Business Potential**
  - Hi

- **Med**
Conclusions: Based on GSK experience, Requirements for a successful partnership

- At least two committed partners
- Stable political climate
- Strong political will and commitment (demonstrated by prioritisation of immunisation in health budget)
- Balanced expectations w.r.t. vaccines prices and service
- At the minimum, 5 to 10 years commitment
- Money
- Skilled workers to carry out R&D and/or blue-chip manufacturing
- Independent albeit supportive and efficient regulatory environment
- Independent NRA
- Intellectual property (IP) protection
- Predictable commercial environment
Thank you