Geografic Distribution

- Presidency/Central Administration
- Technological Development & Production Units - Bio-Manguinhos and Farmanguinhos
- Biomedical Research Units - Oswaldo Cruz Institute, Laboratory Animals Breeding Centre, Araguaia Magalhães Research Centre (PE), René Rachou Research Centre (MG), Lencinas and Maria Deane Research Centre (AM), Gonçalo Moniz Research Centre (BA) and Institute of Molecular Biology (PR)
- Clinical Research and Mother/Child Care Units - Fernandes Figueira Institute and Evandro Chagas Institute
- Post-graduation and Technical Schools - National School of Public Health and Josepino Venancio Health Technological School
- Documentation, Information & Historical Units - Technological & Scientific Information Centre and Oswaldo Cruz’ House
- Specialized Technical Services - National Institute for Quality Control for Health
- International Office of Mozambique - Masters, PhD and expertise in Health

*In 2008 opened an Office in Mozambique, Africa, for training courses in Master, Doctoral and Post Graduation.

Fonte: CCS Fiocruz

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Bio-Manguinhos’ Figures

- Vaccines
- Diagnostic kits
- Biopharmaceuticals
- Technological development & production

1,300 employees ~ 31% of Fiocruz workforce
31% - Production
21% Quality Control and Assurance
11% R&D
6% Maintenance & Engineering
31% Management

Only one federal immunobiological laboratory

Main vaccines, IVD reagents and biopharmaceuticals producer for the Brazilian MOH programs

4 post-doctors
46 doctors
136 masters
225 post-graduated

www.bio.fiocruz.br
BM Portfolio

Vaccines
- DTP + Hib
- DTP/HBV + Hib
- Hib
- Meningitis Polysaccharides A+C
- OPV
- Triple Viral MMR
- Rotavirus
- Pneumococcal conjugate 10 valent (1 dose)

IVD Reagents
- HIV-1 IFI
- HIV-1/2 Rapid Test
- DPP HIV 1/2 Rapid Test and DPP confirmatory
- Chagas Disease ELISA and IFA
- Canine Leishmaniasis ELISA, IFA and DPP Rapid Test
- Human Leishmaniasis IFA
- Human Leptospirosis ELISA and DPP Rapid Test
- Schistosomiasis Helm Test

Biopharmaceuticals
- Interferon Alpha 2b Human Recombinant
- Erythropoietin Human Recombinant
- Interferon Alpha 2b Human Recombinant
- Erythropoietin Human Recombinant

Pre-Qualified by WHO

Yellow Fever 05, 10, 50 doses
Meningitis A and C 10 doses

Bio-Manguinhos’ Mission

Contribute to the improvement of the Brazilian Public Health standards through technological research and production of immunobiologics to meet the demand generated by the epidemiological scenario of the country.

Fulfill the demand of the NIP and others governmental programs - IYD for neglected disease and biopharmaceuticals

Population 190 millions
3.2 millions newborn
Innovation Strategies

- Endogenous Technological Development projects
- Partnerships with local and global institutions for TD&I
- Technological transfer partnerships
- Development of new presentations and improvement of already existing products

Pipeline

<table>
<thead>
<tr>
<th>Product Type</th>
<th>Quantity</th>
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<tbody>
<tr>
<td>Bacterial vaccines</td>
<td>5</td>
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<tr>
<td>Viral Vaccines</td>
<td>10</td>
</tr>
<tr>
<td>Biopharmaceuticals</td>
<td>10</td>
</tr>
<tr>
<td>Reagents for Diagnosis</td>
<td>8</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>33</strong></td>
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### Projects Development Level

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<th>Category</th>
<th>Pre Clinical</th>
<th>Clinical Trials</th>
<th>Non inferiority</th>
<th>Post-Marketing</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Clinical Trials</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ph1</td>
<td>Ph2</td>
<td>Ph3</td>
<td></td>
</tr>
<tr>
<td>Bacterial Vaccines</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td></td>
<td>7</td>
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<tr>
<td>Viral Vaccines</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>14</td>
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<tr>
<td>Biopharmaceuticals</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>IVD reagents</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>TOTAL</td>
<td>17</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>8</td>
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<tr>
<td>TOTAL</td>
<td>35</td>
<td></td>
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</tr>
</tbody>
</table>

### Technological Transfers / Partnerships

- **Rapid Test HIV diagnostic:** Chembio
- **Interferon Alpha 2b human recombinant:** Heber Biotec
- **Erythropoietin human Recombinant:** Cimab
- **Rotavirus:** GSK
- **DPP Leishmaniasis, Leptospirosis and HIV:** Chembio
- **Yellow Fever Vaccine Inactivated:** Fraunhofer

- **Meningitis polysaccharides A + C:** Merieux Institute
- **Attenuated poliomyelitis, Oral:** J PRI
- **DTP + Hib:** Butantan Institute
- **Erythropoietin human Recombinant:** Cimab
- **Meningitis polysaccharide A and C:** Finlay Institute

#### Dates

- **1976**
- **1980**
- **2002**
- **2004**
- **2008**
- **2010**

#### Vaccines

- **1937** Yellow Fever Vaccine: Rockefeller Foundation
- **1980** Measles: Biken Institute
- **1999** Haemophilus influenzae, type b: GSK
- **2003** Triple viral (MMR): GSK
- **2007** Meningitis polysaccharide A and C: Finlay Institute
- **2009** Pneumococcus, Dengue: GSK
Why Transfer Technology to BM/ Fiocruz?

- Government’s policy:
  - Whenever a new vaccine is introduced into NIP the local production and TT must be considered
  - Use of buyer power

- Long term policy and multi-year forecast
- Brazilian Public Market
- Guarantee of the market and competitive price
- Financial support for new facilities
- Existence of NRA Pre Qualified by WHO

The Hib Vaccine Technology Transfer

Bio- Manguinhos features

- Technological capability – Pre existing knowledges: production of Meng A/C polysaccharides vaccine; Coupling skillfull group; clinical studies experience
- Adequate facilities and equipments – large freeze-drying facility
- Structure, organization and budget for long term implementation – team organized to receive technology
- Selection of the most adequate technology and proposal

GSK features

Updated technology

- Scientific and technolgy knowledge
- Operational and functional production operation
- Compromise to make full technology transfer: entire organization must agree and cooperate
- Organization of a specific group dedicated to TT

WIN-WIN Model
**Win Win Model**

The TT provider (according to BM view)
- Expansion of market
- Guarantee of market while the technology transfer is in process
- Economic benefit and revenue assurance for long term
- Long term planning for production operation
- Production facility - use of BM freeze-drying capacity
- Perception on social awareness and international recognition
- Brand Marketing
- Royalty up to 5% with a full local production of Hib Vaccine

**Bio-Manguinhos/ Fiocruz**
- Accelerate incorporation of technology for production
- Guarantee of vaccine supply - avoid shortage
- Incorporation of modern technology platforms;

**BRAZIL**
- The cost per dose drops as the steps of TT is performed and further price drops whenever the TT is fully accomplished

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**Hib Technology Transfer - Step wise transfer**

<table>
<thead>
<tr>
<th>1st step</th>
<th>2nd step</th>
<th>3rd step</th>
</tr>
</thead>
<tbody>
<tr>
<td>Importation of bulk material and formulation, filling, freeze-drying,</td>
<td>Conjugation of polysaccharides and tetanus toxoid using imported</td>
<td>Production of polysaccharides and conjugation using locally produced</td>
</tr>
<tr>
<td>training in quality control and assurance training;</td>
<td>• local conjugated vaccine production</td>
<td>• Local produced tetanus toxoid: validation of facilities,</td>
</tr>
<tr>
<td>modernization of facilities and new equipments;</td>
<td>• training in polysaccharides production; up and down stream</td>
<td>methodologies and production;</td>
</tr>
<tr>
<td>training in production:</td>
<td>• QC training for PS step validation of new facilities</td>
<td>• Production of three consecutive lots for clinical uses;</td>
</tr>
<tr>
<td>conjugation step at GSK</td>
<td></td>
<td>• Development of protocol for non-inferiority clinical study</td>
</tr>
</tbody>
</table>

---
Hib Technology Transfer - Step wise transfer

4th step
Noninferiority study using the 2nd step vaccine as control 2005-2007
Protocol approval by Ethical Committee;
Preparation of the site of study - 1000 volunteers;
Organization and implementation of the clinical study;
Preparation of the documentation for licensing by ANVISA

5th step
License at ANVISA in October 2007

6th step
Pharmacovigilance
- Organization and implementation of pharmacovigilance

Bio-Manguinhos & TT- Tangible and Intangible benefits

Institutional strengthen
- Administration and managerial capacity
- Knowledge underlying the technology - Quality system, engineering standards
- Better visibility
- Social benefits - availability of the vaccine at better price

Capability strengthen
- Accelerate the incorporation of new technology of production
- Increase of specialized professionals
- New laboratories, new equipments
- Strengthen the infrastructure and the technological capability

New products & developments
- Tetravalent (DTP + Hib)
- Pentavalent (DTP/HB+Hib)
- Development of heptavalent (DTP/HB/IPV/MenC + Hib)
Haemophylus influenza B Meningitis after the implementation of mass vaccination

Figura 5 - Meningite por Haemophylus influenza b: coeficiente de incidência e cobertura vacinal em crianças menores de um ano, RS, 1995-2001


Thank you!

Photos by Anne Geddes

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