

# Ministry of Health – Brazil

## Oswaldo Cruz Foundation



**“PAHO Meeting for Preparedness Planning for Influenza  
Pandemic Vaccine Suppliers”**

**Washington, D.C, 21 November 2005**



Instituto de Tecnologia  
em Imunobiológicos

**Bio-Manguinhos**

# The Institute of Technology on Immunobiologicals – Bio-Manguinhos

## MISSION

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

# Bio-Manguinhos' Staff

<b>Directory</b>	
Director	1
Clinical & Medical Group	7
Planning & Organization	6
Projects Management	4
Communication Group	4
Others	11
<b>Sub-total</b>	<b>33</b>
<b>Technological Development Deputy Directory</b>	
Deputy Director	1
Development	84
<b>Sub-total</b>	<b>85</b>
<b>Management &amp; Market Deputy Directory</b>	
Deputy Director	1
Work Safety & Environment	7
Administration	67
Information Technology	13
Human Resources	11
Market Relations	15
Maintenance & Engineering	53
<b>Sub-total</b>	<b>167</b>

<b>Production Deputy Directory</b>	
Deputy Director	1
Planning & Control	3
Final Processing	93
Viral Vaccines	74
Bacterial Vaccines	33
Reagents	35
<b>Sub-total</b>	<b>239</b>
<b>Quality Deputy Directory</b>	
Quality Control	74
Quality Assurance	55
<b>Sub-total</b>	<b>129</b>
<b>TOTAL STAFF</b>	<b>653</b>

\* Does not include 171 employees from Cooprest

# Bio-Manguinhos' Portfolio

## Vaccines



Vaccine	Presentation
DTP + Hib	05 doses
Hib	01 dose
	05 doses
Yellow Fever	05 doses
	50 doses
Meningitis Polysacharides A + C	50 doses
TOPV	25 doses
Measles	05 doses
Triple Viral	10 doses

## Biopharmaceuticals



Drug	Presentation
Interferon Alpha 2b Human Recombinant	03 MUI
	05 MUI
	10 MUI
Eritropoyetine Human Recombinant	2000 UI
	4000 UI

# Bio-Manguinhos' Portfolio

## Reagents for Laboratory Diagnosis



### Others

- Anti Ig Human Conjugate
- Monoclonal Antibodies
- Reference Panel and Sera for Quality Control

Disease/Pathology	Methodology	Presentation (reactions per kit)
Dengue Human Leptospirosis	EIE IgM	384
HIV-1	IFI	500
HIV-1 e 2	Rapid test	20
Viral Diarrhea	EIE	80
Chagas Disease	EIE	384
	EIE Recombinant	384
	IFI	600
Canine Leishmaniasis	EIE	384
	IFI	2,000
Human Leishmaniasis	IFI	600
Human Leptospirosis	EIE	192
	Macroagglutination	100

# Vaccine Delivery - MOH

1,000 doses

Vaccine	Presentation	2000	2001	2002	2003	2004	2005
DTP+Hib	05 doses	-	-	22.174	8.007	16.487	12.000
Hib	01 dose	-	-	-	-	-	33,35
	05 doses	14.577	7.867	2.066	1	20	1,75
Measles	05 doses	7.500	10.000	3.694	-	-	-
Meningitis	50 doses	500	-	488	-	-	-
Poliomyelitis	25 doses	18.968	24.117	64.194	32.163	40.532	35.000
Triple Viral	10 doses	-	-	-	-	20,000	20.000
Yellow Fever	05 doses	6.051	1.173	19.141	29.120	15.880	-
	50 doses	32.387	9.284	2.884	-	-	-
<b>Total</b>		<b>79.983</b>	<b>52.441</b>	<b>114.641</b>	<b>69.291</b>	<b>92.919</b>	<b>67.035</b>



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# Exports – Yellow Fever Vaccine

Year	2002	2003	2004	2005	Total
Quantity	5.360.600	8.956.150	26.460.100	<b>28.000.000</b>	68.776.850



# Kit for Laboratory Diagnostic – CGLAB e PN-DST/Aids

Disease/Pathology	Methodology	Delivery 2003 (Reactions)	Delivery 2004 (Reactions)	Forecast 2005 (Reactions)
Dengue	EIE IgM	166.272	97.920	307.200
Hepatitis B	EIE HBsAg	109.440	113.280	-
HIV-1	IFI	173.000	130.000	173.000
	Rapid Test	-	-	1.000.000
	Viral Load	-	-	248.400
Viral Diarrhea	EIARA-m	2.800	400	12.000
Human Leptospirosis	EIE	22.464	40.800	76.800
Chagas Disease	EIE	58.752	44.160	28.800
	EIE Recombinant	115.584	3.840	-
	IFI	318.600	39.000	150.000
Human Leishmaniasis	IFI	93.600	115.800	150.000
	Montenegro	18.910	70	-
Canine Leishmaniasis	EIE	95.232	243.840	576.000
	IFI	-	1.036.000	1.600.000
<b>Total</b>	-	<b>1.174.654</b>	<b>1.865.110</b>	<b>4.322.200</b>



# Bulk Production Installed Capacity

Vaccine	Bulk N. Doses x 1000/year	Source
Yellow Fever	100,000	Bio-Manguinhos
Poliomyelitis (TOPV)	-	GSK
Measles (CAM-70)	40,000	Bio-Manguinhos
Triple Viral (Measles, Mumps, Rubella)	-	GSK
<i>H. Influenzae</i> type b (Hib)	20,000	Bio-Manguinhos
Combined DTP/Hib	-	DTP – Butantan Inst.
Meningitis A/C	3,000*	Bio-Manguinhos

\*In the old facility

# Final Processing Installed Capacity

## 1. Filling and Freeze-drying

Year 2006

Product	Doses	Vials	Number of Lots
Yellow Fever 5 doses (export - CPFII)	20,000,000	4,000,000	57
Yellow Fever 5 doses (national)	5,000,000	1,000,000	14
Triple Viral 10 doses	20,000,000	2,000,000	53
Hib 5 doses	12,000,000	2,400,000	34
Interferon	600,000	600,000	10
Total	57,600,000	10,000,000	168

**Current capacity in lots:**

42 weeks >> 5 cycles/week >> **TOTAL = 210 lots/year**

# Final Processing Installed Capacity

## 1.1 Filling and Freeze-drying – LaLio\*

Year 2006

Product	Doses	Vials	Number of Lots
Yellow Fever 5 doses (export -LaLio)	28,000,000	5,600,000	140

**Current capacity in lots:**

42 weeks >> 4 lots/week >> **TOTAL = 168 lots/year**

# Final Processing Installed Capacity

## 2 – Filling Liquid vaccines in vials (DTP/Eritropoyetine)

42 weeks >> 5 cycles/week >> 72.000 vials/cycle >>

TOTAL = 15,120,000 vials/year

## 3 – Filling Liquid vaccines in plastic tubes (TOPV)

42 weeks >> 5 cycles/week >> 42.000 tubes/cycle >>

TOTAL = 8,820,000 tubes/year

## 4 – Filling of diluents in ampoules

a) Bosch (open ampoules) 5 cycles/week >> 60,000

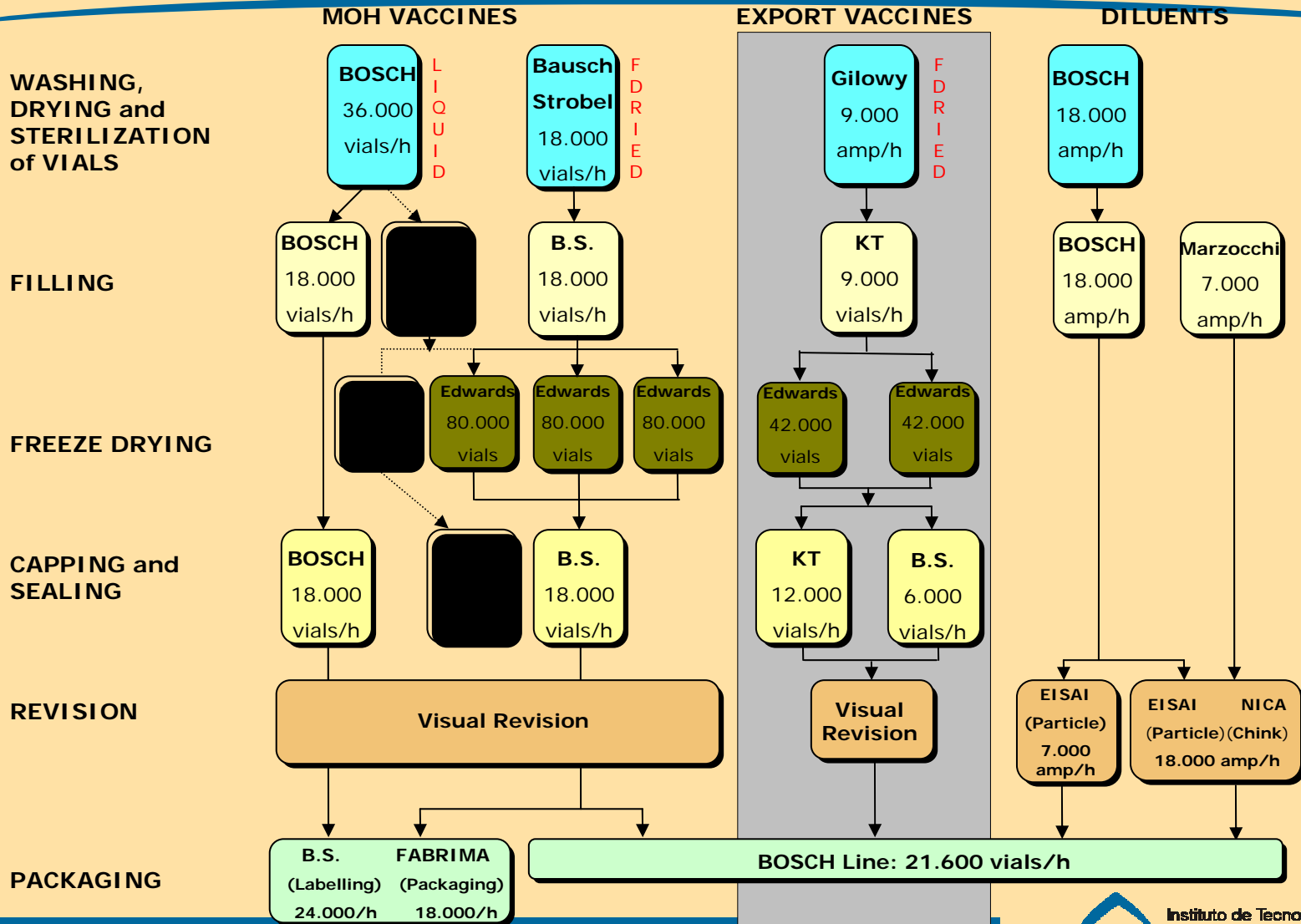
ampoules/cycle >> TOTAL = 12,600,000 ampoules/year

b) Marzocchi (closed ampoules) 5 cycles/week >> 35,000

ampoules/cycle >> TOTAL = 7,350,000 ampoules/year

TOTAL = 19,950,000 ampoules/year

# Filling and Freeze Drying Capacity



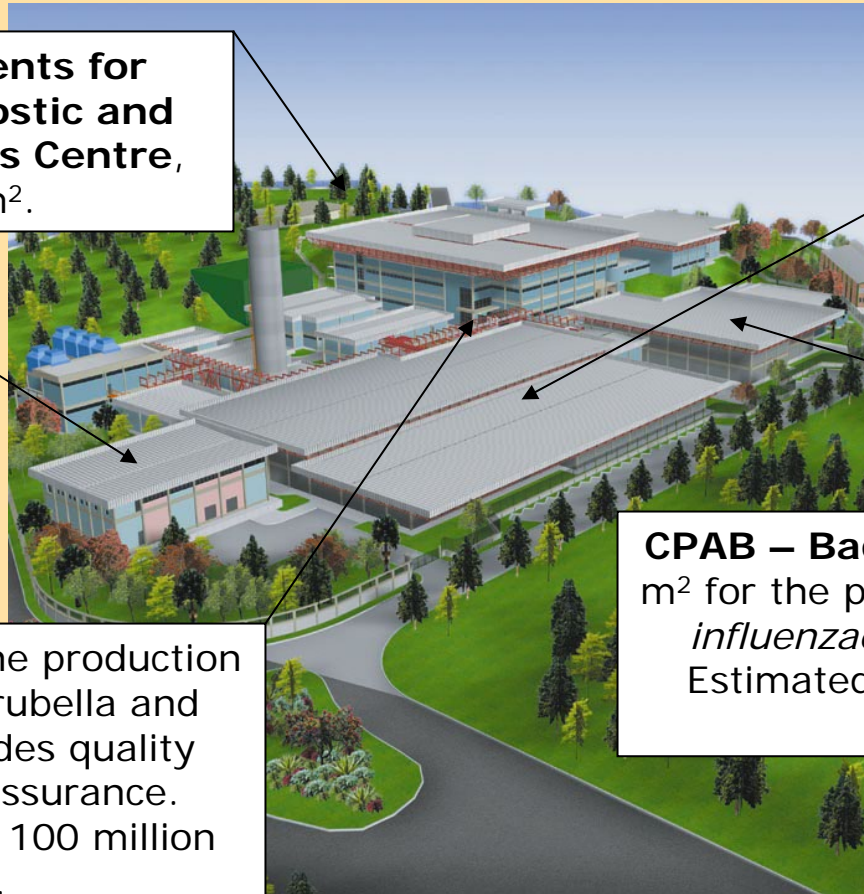
# Investments on Technology

## Technological Complex of Vaccines - 2005

**Prototype, Reagents for Laboratory Diagnostic and Biopharmaceuticals Centre**, with 8,000 m<sup>2</sup>.

**CAPA – Final Products Storage Center** – 600m<sup>2</sup>

**CPAV – 9,920 m<sup>2</sup>** for the production of measles, mumps, rubella and other antigens. Includes quality control and quality assurance. Estimated production: 100 million doses/year.



**CPFI – Immunobiologicals Final Processing Center** - 6.400m<sup>2</sup>.  
Production:

**CPAB – Bacterial Antigens** - 2,400 m<sup>2</sup> for the production of *Haemophilus influenzae b* and other antigens. Estimated production: 45 million doses/year.



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# GMP Certification

**NRA**

Bulk production- YF

**FORMULATION, FILLING, FREEZE-DRYING  
AND SECONDARY PACKAGING:**

DTP+Hib, Hib, OPV, Yellow Fever and diluents

**SECONDARY PACKAGING:**

Triple Viral Vaccine (measles, mumps and rubella)

**WHO**

Yellow Fever

New production area to be submitted still in 2005

**OTHER QUALIFICATIONS:**

- Certificate in Biosafety / Ministry of C&T

(for the manipulation of organisms genetically modified)

# Technological Development - Vaccines

## 1, 2 and 3 YEARS

- *N. Meningitidis* B (Outer Membran Vesicle) + C Conj.
- Pentavalent DTP/Hepatitis B + *Hib*

## 5 - 10 YEARS

- Rotavirus
- Pneumococos
- Triple Viral + Varicella
- *N. Meningitidis* B (OMV) + C Conj + A Conjugate
- Dengue
- Leishmaniasis
- Leptospirosis
- Inactivated Polio Vaccine
- Yellow Fever Inactivated
- Varicella

# Technological Development - Reagents

Disease/Pathology	Projects / Products
<b>Dengue</b>	IgG capture IFA for the identification of isolated viruses Expression of recombinant proteins of Dengue virus Molecular Tests for detection and identification of Dengue virus
<b>Viral Diarrhea</b>	Expression of recombinant proteins of the main Viral Diarrheas agents
<b>HIV/Aids</b>	Western Blot for HIV-1 Carga Viral CD4/CD8
<b>Viral Hepatitis</b>	IgM capture for Hepatitis A New HBsAg and anti-HBs kits using recombinant antigens
<b>Leishmaniasis</b>	EIA for canine leishmaniasis using recombinant antigens Rapid test for canine leishmaniasis
<b>Leptospirosis</b>	EIA using recombinant antigens Rapid test for antigens capture
<b>Anti IgG and Anti IgM</b>	Methodology for the production of recombinant antibodies
<b>Chagas Disease</b>	Biological model adaptation for the evaluation of the immune response Diagnosis Tests using biosensors

# Projects – Biodrugs

2005

- Humanized Monoclonal Antibody

- Factor IX

- Interferon Alpha Peguilated

2008

- Interferon Beta Recombinant



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# Planning for Influenza Pandemic

## The Oswaldo Cruz Foundation

- 1) IOC – National Reference Center for Influenza
  - Diagnosis
  - Virus Isolation
  - Virus characterization
- 2) ENSP – Training of personal for the Health System
- 3) Farmanguinhos – Antiviral medicines production

# Planning for Influenza Pandemic

## The Oswaldo Cruz Foundation

### 4) Bio-Manguinhos – Influenza Pandemic Diagnosis Reagents and Vaccine

- Production of diagnosis kits – Human and Avian Influenza
- Vaccine formulation and final processing
- Vaccine Quality Control
- Vaccine delivery – National and regional
- Master seeds production in SPF eggs in a P3 laboratory
- Vaccine bulk production by alternative technology: Cell Culture; recombinant virus