Health Innovation Project
Subproject: VACCINES

Coordination: Presidency of FIOCRUZ
An Agreement between FIOCRUZ/FIOTEC – Ministry of Health
FINAL REPORT

PROPOSALS STEMMING FROM VACCINE STUDIES AND WORKSHOPS
Background

• For the Vaccines Subproject, both Brazilian and foreign specialized consultants were hired, which in turn developed diagnostic studies and studies of propositions following the terms of reference established by the project coordinators.

• Every finished study was debated in Technical Groups at Workshops with the participation of the main public vaccine producers (Biomanguinhos/FIOCRUZ, Instituto Butantan, the Technology Institute of Paraná – TECPAR –, Fundação Ataulpho de Paiva); several branches of the Ministry of Health (the Secretariat for Health Surveillance – SVS –, the Secretariat of Science, Technology and Strategical Products – SCTIE –, the National Sanitary Surveillance Agency – ANVISA –, FIOCRUZ); the Ministry of Science and Technology (the Studies and Projects Financing Entity – FINEP –, the National Council for Scientific and Technological Development – CNPq), the Ministry of National Integration - MI - and the Ministry of Development, Industry and Foreign Trade - MDIC - (including the National Bank for the Economic and Social Development – BNDES), besides research Institutes and Universities.

• Around 200 administrators, researchers and technologists were involved in the process and made a series of propositions, which are detailed in the Final Report.
Studies presented and discussed during the Vaccine Workshops in 2003:

- “Desenvolvimento Tecnológico de Vacinas: projeções para 2015” (Technological Development of Vaccines: Projections for 2015) developed by the consultant Julie Milstien (University of Maryland School of Medicine, Center for Vaccine Development). 1st Vaccine Workshop (10/06/03), Sérgio Arouca National School of Public Health at the Oswaldo Cruz Foundation, Rio de Janeiro.

- “Avaliação Tecnológica da Produção Envolvendo os Produtores Públicos de Vacinas e Definição de Nichos de Atuação” (Technological Evaluation of Production Involving the Public Vaccine Producers and Identification of Market Niches) developed by consultant Manuel Limonta (Biotechnology of the Institute of Hematology and Immunology of Havana, Cuba). 2nd Vaccine Workshop (11/08/03), Novo Mundo Hotel, Flamengo, Rio de Janeiro.

- “Potencialidades para o Desenvolvimento de Vacinas no Brasil” (Potentialities of Vaccine Development in Brasil) developed by consultant José Vítor (Chemistry School of the Federal University of Rio de Janeiro - UFRJ, Rio de Janeiro). 3rd Vaccine Workshop (12/09/03), Biomanguinhos, Oswaldo Cruz Foundation, Rio de Janeiro.

- “Avaliação Gerencial dos Produtores de Vacinas do País” (Managerial Evaluation of Vaccine Producers of the Country) developed by consultant José Castañar (Getúlio Vargas Foundation – FGV, Rio de Janeiro). 4th Vaccine Workshop (29/12/03), Biomanguinhos, Oswaldo Cruz Foundation, Rio de Janeiro.
Background

The report of the main results of the studies and workshops was divided in two different parts complemented by appendixes that basically detail the major outcomes in the area of vaccines:

Part 1 – **Summary of the Propositions from the Workshops**

   Appendix I – Executive Summaries of the Studies

Part 2 - **Initial Developments**

   Appendix II – Guidelines of INOVACINA

   Appendix III – Immunobiologicals Chamber. Chart.

   Appendix IV – List of Priority Vaccines
Major Proposals

Political Sphere

- To incorporate the discussion into the Mercosul agenda.
- To map both national and international groups interested in the area.
- To promote biotechnology in Brazil for more visibility of this activity in the country and to aid in the cooperation with other countries and with the private industry (to promote an international event/to reactivate the Latin-American Society of Biotechnology).
- To define a policy for vaccine exportation and the necessary reforms to make it possible.
Major Proposals

Political Sphere

- Creation of the National Program of Competitiveness in Vaccines (INOVACINA) in order to implement the Brazilian Policy on Vaccines. It would be part of a process of retaking the active part of the State and the difference between this program and the previous one, the Program for National Self-sufficiency in Immunobiologials (PASNI), should be made clear.

- Articulation with the Forum of Competitiveness in the Pharmaceutical Industry and with the Forum of Competitiveness on Biotechnology, both in the Brazilian Ministry of Development, Industry and Foreign Trade and with the Ministry of Health and other Ministries and specially with the Policy for the Industry, for INOVACINA to have a better chance of being implemented.

- Active participation of the instances of the Ministry of Health (the SVS, the Secretariat of Health Assistance – SAS –, the ANVISA, the National Institute for Quality Control in Health – INCQS –, etc.) aiming at more integration between the institutions.
Major Proposals

Political Sphere

➢ To guide the states’ commitment process, taking into account the purchasing capacity of the Ministry of Health.

➢ To change the price policy established by the Government in order to obtain a surplus for investments and to aid self-sufficiency.

➢ To stimulate the execution of studies on sera.

➢ To stimulate the creation of biotechnology companies.

➢ To stimulate/ provide more investment in R&D by the producers.

➢ To include the final vaccine report in the discussions of the National Conference of Science and Technology in Health (2004).
Major Proposals

Political Sphere

Criteria for Prioritization and Decision Making

➢ To develop studies (cost-benefit, disease burden, the existence of alternatives for intervention, technological evaluation, technical and economical viability, etc.) that can serve as a guide for the establishment of research and development priorities and as a background for decisions taken by the National Immunization Program (PNI), taking into account the effectiveness of the programs.

➢ To use post-licensing epidemiological studies (adverse reaction and delivery problems) to define innovation priorities.
Major Proposals

Physical and Organizational Structure

- Alternative models for laboratory management.

In the macrosectorial ambit, a larger articulation with other areas if the Ministry of Health, other Ministries, other production institutes and financing agents;

In the microsectorial ambit, to improve the inside management with the creation of cooperation networks between and inside institutions.

- To establish a Consortium (strategical alliance/ integrated network/ cooperation) between public laboratories that produce immunobiologials. This Consortium would be able to compete in the world market and would start from the restructuring of strategical integration policies of manufacturers and the definition of technological niches for the specialization of each laboratory, without superimposition.
Major Proposals

Physical and Organizational Structure

- To mold the legal and institutional structure of the sector in order to give it more flexibility, autonomy, integration and cooperation (i.e. the Support Foundations at FIOCRUZ and at the Butantan Institute).

- To place innovation into organizations’ strategies.

- To manage the business activity and the development process so that it aims at exportation, having been trained in leadership, group work and monitoring.

- To strengthen the contact between producers and the Ministry of Health while the Ministry writes its budget.
Major Proposals

*Physical and Organizational Structure*

- To have efficiency as the main goal of a model of organization and management that may include partnerships (to reach the level of competitors) and ways other than the customary Invitation for Bids to reach government buys.

- To seek the managerial dynamics of the private sector in order to be more competitive and to obtain financing more easily, since the demands of some of the financiers such as the National Bank for Economic and Social Development (BNDES) are the same either for the private sector or the public sector.
Major Proposals

Physical and Organizational Structure

Human Resources

- Education and Vocational Training of Strategic Human Resources in Vaccines – involving the National Council for Scientific and Technological Development (CNPq) and the Coordination for the Improvement of Higher Education Personnel (CAPES):
  - Technicians and researchers in basic research, technological development of immunobiologics, vaccine production, management of projects involving biotechnology and industrial production, management of the market of immunobiologics.
  - Program for maintaining PhDs and Post-docs in the country.
  - Regular training, specially in production institutions.
  - Training in languages (English) to develop comprehension of international regulation, project management and intellectual property.
  - Specific investment to stimulate Science & Technology in vaccines, offering grants that are specific for the Science and Technology system (the grants of the Human Resources in Strategic Areas – RHAEN – program).
Major Proposals

*Physical and Organizational Structure*

- To improve the hiring of human resources. The fact that a great part of the HR is outsourced contributes for the weakness of the system and harms the continuity and the preservation of groups.

- To lead the management of human resources to innovation and the formation of the “public entrepreneur” (multidisciplinary, including high-level engineering and partnerships that change at each developmental step).

- To improve training of human resources specially for the final steps of the development of vaccines (scale-up and clinical trials).
Major Proposals

Physical and Organizational Structure

Certification of Production Plants

➢ To consider as an “anchor producer”, he whose plant has been certified (either by the WHO or by the National Agency of Sanitary Surveillance – ANVISA), has the appropriate know how and is capable of transferring to other producers the experience obtained in the process of certification.
**Major Proposals**

*Evaluation and Regulation*

Clinical Trials

- To strengthen phase I, II, III and IV clinical trials in public institutions.
- To hold a seminar on the subject.
- To establish a national infra-structure (network) for clinical trials that follows the Good Clinical Research Practices.
- To involve the ANVISA, the Department of Science and Technology (DECIT) and the universities in the establishment of a Brazilian Clinical Trial Platform.
- To define specific financing sources.
**Major Proposals**

**Evaluation and Regulation**

**Intellectual Property**

- To add Intellectual Property to the strategies for development, management and production of vaccines.
- To carry out a survey on patents that are to expire in the next few years (mostly regarding biopharmaceuticals).
- To use intellectual property as an index to evaluate if the objectives are being achieved through R&D infra-structure or not and to evaluate the efficiency of the management of the production.
- To work with patented vaccines that are the result of commercial or licensing agreements.
- To train human resources, from investigation to marketing.
Major Proposals

Evaluation and Regulation

Regulation

- To discuss the adjustment of the regulation performed by the ANVISA and the ethics commissions in relation to clinical trials, pre-clinical trials and the registry of new vaccines suitable to the reality of the country.

- To strengthen the role of the ANVISA, not only its role as an inspection agency, but as a regulator/advisor, which would make possible the increase in competitiveness of the public producers since they would have to follow Good Manufacturing Practices (GMP), something that demands high investments today.
Major Proposals

Production and Commercialization

- To strengthen the national production capacity and the national vaccine quality control system through the National Institute for Quality Control in Health (INCQS).
- To use full installed capacity and all human resources available to reduce fixed costs of production.
- To make the existing technology in the present installed capacity adequate to international standards.
- To assure that every single product manufactured in each of the institutions are certified by the ANVISA and the WHO in order to increase competition, to enhance quality and to make possible the exportation of the production to other countries, thus overcoming technical barriers.
Major Proposals

Production and Commercialization

- To establish the quality warranty system in all producers.
- To modernize facilities and to replace old equipment to attain a high technological standard, to follow Good Manufacturing Practices, to obtain certification and to develop vaccines that are adequate for international standards.
- To use the exploration of the foreign trade as a means of seeking economical and technological competitiveness.
Major Proposals

*Production and Commercialization*

Financing and Commercialization

- To develop alternative methods of financing production in order to assure the transfer of financial resources, for example, through a management agreement.

- To seek for the BNDES and other development agencies to follow more closely the discussion of the changes that are necessary for public producers to capture resources with these agencies.

- To designate that resources from the Sectorial Health Fund (Fundo Setorial da Saúde) and from other sources (the Inter-American Development Bank and state foundations) should be used on priority projects on R&D in vaccines.
Major Proposals

Production and Commercialization

- To create the Working Capital Fund (Fundo de Capital de Giro), capitalized by the government and used in the case of a lack of regularity in the flow of resources.
- To use resources from the RHAE program (CNPq) in grants for vaccine producers to incorporate young PhDs.
- To restructure prices of vaccines produced by public manufacturers since they are obliged to produce taking into account the prices used by the PAHO Rotating Fund, to which multinational companies sell their products at marginal values, since they are compensated by the profit they make in the private market.
- The financing (BNDES, FINEP) should be taken into account and the costs be considered before the setting of the price (which should be defined before the budget is written).
Major Proposals

Innovation and Technological Development

- To use present vaccines as a platform for the development of new vaccines.
- To prioritize research as a consequence of explicit public priorities of the national health policy.
- To transfer technology as a development platform and to seek self-sustainability.
- To give support to the program of technological development for official laboratories, creating, thus, a means of ensuring a minimum R&D budget for these laboratories.
Major Proposals

Innovation and Technological Development

- To define which vaccines are priorities for technological development and innovation in the short, mid, and long terms.
- To invest in coordination processes and in the development of networks between and inside institutions to unite the different steps of the process of developing vaccine projects.
- To hold a meeting to integrate all vaccine researchers.
- To promote the development of the steps to select adjuvants and studies necessary to define pre-clinical studies.
- To add a percentage in the price offered to the Ministry of Health destined for innovation projects.
First Outcomes

1. National Program of Competitiveness in Vaccines INOVACINA

Major role: To help define policies in this area and to serve as an instrument for scientific, technological, industrial and sanitary policies in vaccines and in immunizations, setting goals for the next 15 years.

The strategic guidelines of the INOVACINA will approach political, organizational, regulatory, scientific, technological, industrial and economical dimensions.

The analytical matrix presents, in an objective way, the dimensions and spaces of intervention, the major proposals, goals, instruments and institutional partnerships involved and financing needs.
First Outcomes

1. National Program of Competitiveness in Vaccines
   INOVACINA

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<td>I- Implementation of Policies</td>
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<td>II- Sectorial Redesign towards Cooperation</td>
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<td>2- Physical Structure</td>
<td>III- Modernization of the Production Capacity</td>
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<td>IV- Certification of Production Plants</td>
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<td>3- Organization</td>
<td>V- Organizational and Managerial Model</td>
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<td>4- Activities Related to Evaluation and Regulation</td>
<td>VII- Clinical Trials</td>
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<td>VIII- Intellectual Property</td>
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<td>IX- Regulation</td>
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<td>5- Production and Commercialization</td>
<td>X- Production</td>
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<td>XI- Pricing Policy</td>
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<td>XII- Quality</td>
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<td>6- Innovation and Development</td>
<td>XIII- Innovation and Development of Products and Processes</td>
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<td>XIV- Prioritary Vaccines</td>
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</tbody>
</table>
First Outcomes

2. Development of a Chamber of Immunobiologicals

A multisectorial Chamber of Immunobiologicals has been proposed so that problems can be permanently discussed and so that priorities and policies are constantly reevaluated. The objectives of this measure would be the acceleration of the improvement and the competitiveness in that sphere and the increase of the technological capacity and the synergy between producers.

The chamber would be under the Ministry of Health.

It would be an instance of decision making regarding policies and would count on Technical Chambers for advisement in the decisions and one Executive Secretariat for the implementation and coordination of its actions.
First Outcomes

National Program for Competitiveness in Vaccines
INOVACINA

Strategic Definitions

MULTISECTORIAL CHAMBER
OF IMMUNOBIOLOGICALS
Political decision making

Executive Secretariat

Technical Chambers
(technical advisory)

Management and HR
(Institutional Judicial Model)

Production and Quality Control
(Certification and Exportation)

R&D
(Technology Transfer, Self development)
First Outcomes

3. List of Priority Vaccines

The development of a matrix to serve as background for the decision making regarding priority vaccines for the short (5 years), mid (10 years) and long (15 years) terms was proposed and should be based on the identification of the major economic, technological and structural opportunities and difficulties in R&D and Production.

A priority vaccine matrix is being developed by Bio-Manguinhos / FIOCRUZ and the Butantan Institute.
Investment on Technological Innovation of Priority Vaccines

Criteria for the definition of priorities (arranged in order of relevance):

(1) – Epidemiological Impact (to consider the existence of alternative technology for control and prevention);
(2) – The need it represents for the National Immunization Program. If imported, its cost should be then considered;
(3) – The existence of an appropriate technological base and the mastering of the technology involved in the process inside or outside the country;
   - The level of development of the product in the country;
   - The existence of Research, Development & Innovation groups in the country;
(4) – A study of the technical and economical viability;
(5) – The existence of alternative technology for control and prevention of the disease (for example, the control and/or eradication of vectors).
(6) – In the case that the vaccine is required for the National Immunization Program and there are no groups involved in the country, the following should be considered:
   - The level of urgency for the product;
   - The cost-benefit of the vaccine;
   - The technological and economical evaluation and the establishment of the bases for technology transfer.
# Investment in Production, Technological Development and Innovation of Priority Vaccines

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Relation to the PNI (Nat. Immun. Prog.)</th>
<th>Product perfectioning, Existence of components and technological base, others</th>
<th>Justification</th>
<th>1) Bottle needs 2) actions</th>
<th>Anchor Institutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Pentavalent (DTP/HB+Hib)</td>
<td>Lowering of operational cost and number of injections</td>
<td>Existence of national vaccine components being produced and supplied regularly to the PNI</td>
<td>1) Study adverse effects of DTP/Hib; difteric and hepatitis B component. Develop pre clinical and clinical studies 2) Projects in progress;</td>
<td>Butantan Institute will produce DTP + Hepatitis B and Bio-Manguinhos will develop the DTP + Hib vaccine all together</td>
<td></td>
</tr>
<tr>
<td>2) Cell culture Rabies</td>
<td>Increase in safety and efficacy. Available in the CRIES</td>
<td>Existence of technological base and interest in making national due to high price of imported product. Increase in the technological capacity in viral vaccines</td>
<td>1) Finalization of Clinical Studies (Butantan) and standardization of initial production parameters (Tecpar) 2) Production scaling (Butantan). Production of experimental batch, clinical studies (Tecpar)</td>
<td>Butantan Inst. Is developing phase II clinical tests; Tecpar is still in earlier stage</td>
<td></td>
</tr>
<tr>
<td>3) Meningococcal Meningitis type B</td>
<td>Control and Prevention of outbreaks. Strategic Stock in the PNI</td>
<td>The current vaccine (Cuban) does not protect children under 4 years of age. Existence of a multi-institutional project being developed over for 10 years (IAL, Butantan, BioManguinhos)</td>
<td>1) Phase I and II Clinical Trials 2) Financial support for the studies</td>
<td>Bio-Manguinhos will coordinate clinical trials</td>
<td></td>
</tr>
<tr>
<td>4) Conjugates Meningococ. Meningitis Type B</td>
<td>Possible inclusion in the vaccination calendar. Available in the CRIES</td>
<td>The current polissacharide vaccine does not protect children under 4 years of age. The protein/polissacharide chem. conjugation technology is mastered by national laboratories</td>
<td>1) Study of production scaling; pre-clinical studies; clinical studies; 2) Financial support for clinical studies</td>
<td>Bio-Manguinhos will coordinate clinical trials</td>
<td></td>
</tr>
<tr>
<td>5) Hepatitis A</td>
<td>Conta of outbreaks and inclusion in basic calendar. Available in the CRIES</td>
<td>Vaccine made from inactivated virus’. Development project in progress, if adequately supported will take 5 years for final development. Production technology mastered by multinationals; discuss technology transfer.</td>
<td>1) Still in early phases of development in the country 2) Support to find technology abroad</td>
<td>IOC and Bio-Manguinhos have a joint development project; Butantan also has a development project</td>
<td></td>
</tr>
<tr>
<td>6) Canine Leishmaniasis</td>
<td>Control of Human Visceral Leishmaniasis.</td>
<td>Existence of RD&amp;I that identify proteins with a protective capacity in dogs.</td>
<td>1) Definition of technological routes 2) Strengthening of RD&amp;I</td>
<td>Protozoology Department of the IOC, CPqGM</td>
<td></td>
</tr>
<tr>
<td>7) DNA Vaccine for use in therapy</td>
<td>Therapy for drug resistant tuberculosis.</td>
<td>Projects in Phase I with satisfactory results in tests. Phase I assays for the treatment of head and neck cancer. Study being organized on the efficacy in drug resistant TB patients</td>
<td>1) Development of a P3 infirmary for the treatment of drug resistant disease 2) BNDES financing of US$ 1.6 million</td>
<td>Lab of Genetic Vaccines/Parasitology Dept., Microbiology and Immunology/University of Sào Paulo – Ribeirão Preto</td>
<td></td>
</tr>
</tbody>
</table>
### Investment in Production, Technological Development and Innovation of Priority Vaccines

#### Justification

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Relation to the PNI (Nat. Immun. Prog.)</th>
<th>Product Perfectioning, Existence of Components and a technological base, others</th>
<th>1) Bottle necks 2) actions</th>
<th>Anchor Institutions</th>
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<tbody>
<tr>
<td><strong>UPTO 5 YEARS - EXISTENCE OF THE TECHNOLOGY, PROJECTS IN INITIAL STAGES OF DEVELOPMENT AND WITH INCIPIENT FINANCIAL SUPPORT</strong></td>
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<tr>
<td>3) Conjugated Meningococcal Meningococcal vaccine B + C</td>
<td>Control and prevention. Possible inclusion in the vaccination calendar</td>
<td>If clinical trial results for meningitis B and C conjugates are approved, this combined vaccine will be developed</td>
<td>1) The study of scaling parameters, pre-clinical trials and clinical trials. 2) Financial support in order to carry out clinical trials</td>
<td>Results from clinical trials and of production output will define which labs will participate in the production.</td>
</tr>
<tr>
<td>3) Rabies vaccine produced in tissue culture for canine use</td>
<td>Higher efficacy and safety of vaccine</td>
<td>Vaccines against canine rabies produced in tissue culture in the national market already exist. Public labs need this vaccine in tissue culture in order to maintain production. Know-how already exists in the country</td>
<td>1) Production scaling, pre-clinical and clinical trials 2) Financial support in order to carry out scaling and clinical trials. Adjust laboratories for the new technology</td>
<td>Tecpar and Butantan have been developing projects of production in SHK cells.</td>
</tr>
<tr>
<td>10) Inactivated Yellow Fever vaccine</td>
<td>Higher vaccine security</td>
<td>Harsh adverse effects associated to the vaccine, including deaths, compels the search for alternative technologies</td>
<td>1) High density virus production in cell culture, scaling, inactivation, pre-clinical and clinical trials. 2) Financial support in order to accelerate project activities;</td>
<td>Bio-Manguinhos and COPPE/UFRJ have been developing a in this area</td>
</tr>
<tr>
<td>11) Streptococcus pneumoniae</td>
<td>Important for inclusion in the PNI</td>
<td>Data exists on the more important serotypes. The polysaccharide and protein conjugation technology is mastered. There are currently groups developing projects in this field</td>
<td>1) Necessary strengthening of teams and lab infra-structure, search for alternative technological approaches. 2) Financial support for project development</td>
<td>The Adolfo Lutz Institute is responsible for epidemiological surveillance. Bio-manguinhos and Butantan develop their own projects</td>
</tr>
<tr>
<td>12) HPV</td>
<td>Not yet discussed at the PNI level</td>
<td>Little epidemiological and viral type prevalence information available; little data on the impact of the disease in the country. The vaccine is in the final phase of development and no offer exists for combined development and technology transfer.</td>
<td>1) Little epidemiological and prevalence information available. 2) Define the vaccine necessity and identify users. Support projects to better understand the problem.</td>
<td>National Cancer Institute/RJ. - Butantan and Bio-manguinhos are interested in discussing a national producto.</td>
</tr>
<tr>
<td>13) Inactivated Polio</td>
<td>Necessary for the 2015 Global Polio Eradication report and for formation of strategic stock. Diminish adverse effects</td>
<td>This oral attenuated live virus vaccine may no longer be used following the global eradication of poliomyelitis, October 2005. There are groups developing projects in this field</td>
<td>1) High density production in cell culture, scaling, inactivation, pre-clinical and clinical trials. 2) Define the SVS/PNI demand. Financial support to accelerate project development</td>
<td>Bio-Manguinhos is involved in the production of the OPV vaccine. This group could produce the inactivated vaccine.</td>
</tr>
<tr>
<td>14) DTPA (diphtheria tetanus and pertussis) Combined vaccine is identified</td>
<td>Severe effects caused by B. pertussis, such as whooping cough and Hypotonic Syndrome, have limited the development of combined DTP vaccines. There has been a global increase in the use of the bacteria's components. There are groups developing this product.</td>
<td>1) Identify technological strategy and appropriate vaccine components and/or antigen expression; pre-clinical and clinical trials. 2) Define technological routes. Financial support to increase number of projects.</td>
<td>Butantan develops acellular pertussis via components of the antigen and by Molecular Biology. Bio-Manguinhos also has projects focused on Molecular Biology.</td>
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</tr>
<tr>
<td>15) WHO/Cholera</td>
<td>Although in the vaccination calendar</td>
<td>Unfolding and broadening of the triple viral vaccine (measles, mumps and rubella). Possible cloning of the vaccine virus or technology transfer.</td>
<td>1) Nationalize the triple viral vaccine 2) Clinical trials</td>
<td>Bio-Manguinhos is constructing a new pland for viral vaccines to produce the triple viral vaccine and possibly the varicella component.</td>
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</tbody>
</table>
## List of Priority Vaccines

### Main opportunities and difficulties in the stages of development

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<th>VACCINE</th>
<th>Justification</th>
<th>R&amp;D</th>
<th>PRODUCTION</th>
<th>PNI</th>
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<tr>
<td>Inactivated Yellow Fever*</td>
<td>AE</td>
<td>Technological</td>
<td>Economic</td>
<td>Structural</td>
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<tr>
<td>Influenza (H1N1)*</td>
<td>New Production Technologies</td>
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<tr>
<td>DTPa*</td>
<td>AE</td>
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<tr>
<td>MMR (Mumps from Jeryl Lynn)</td>
<td>AE</td>
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<td>7-valente pneumococcal conjugate</td>
<td>EI</td>
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<tr>
<td>Meningitis C conjugate</td>
<td>EI</td>
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<tr>
<td>DT/HBV+Hib*</td>
<td>New Combination</td>
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<td>Cell culture Rabies</td>
<td>Lessen doses and AE</td>
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<td>Meningitis B/C conjugate</td>
<td>EI and high aggregate value</td>
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<td>Hepatitis A</td>
<td>EI</td>
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<td>Polio (injected)*</td>
<td>EI and AE</td>
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<tr>
<td>Hib*</td>
<td>Lessen number of doses</td>
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<tr>
<td>Meningitis B/C conj + Hib*</td>
<td>New Combination</td>
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<tr>
<td>DTPa/ HVB + Hib</td>
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<td>HBV/NAV</td>
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<td>MMR + chicken-pox</td>
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<td>Rabies</td>
<td>EI</td>
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<tr>
<td>Meningitis A/IM conjugate</td>
<td>EI</td>
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</tr>
<tr>
<td>Measles*</td>
<td>EI</td>
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</tr>
<tr>
<td>Dengue Fever**</td>
<td>EI</td>
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<tr>
<td>Lymphomaosis*</td>
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<tr>
<td>HIV*</td>
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<tr>
<td>Tuberculosis*</td>
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<tr>
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<tr>
<td>Sclerodermatosis</td>
<td>EI</td>
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<td>Shigellosis</td>
<td>Bio-defense</td>
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</table>

AE = Adverse effects / EI = epidemiological interest / * defined as a priority by national sanitation authorities
4. Production of the PENTABRASIL Vaccine

Initiatives have now been restarted, including the production of the pentavalent vaccine (DTP + Hepatitis B + Hib), a joint development project between the Butantan Institute and Bio-Manguinhos/FIOCRUZ. The PENTABRASIL, produced entirely in Brasil, should be available for the PNI by the year 2006, considering the pre-clinical and clinical trials, data analysis and completion of the work.
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