

Facilitate, Partnering for Vaccine Emerging Markets

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Brazil and Argentina—Profiling Vaccine Demand, Supply
and Aspirations

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Introduction

The conference was a true forum for the Emerging Markets global vaccine community. Close to 100 senior-level representatives from large and small vaccine-related private sector firms, from the UN system (World Health Organization -WHO and Pan American Health Organization—PAHO) as well as donors (The Global Alliance for Vaccines and Immunization—GAVI and the Gates Foundation), convened in Berlin in an atmosphere of open and helpful information exchange. The great challenges involved in working in Emerging Markets were discussed; the speakers repeatedly highlighted cultural awareness and close communication as key elements for success. Nonetheless an underlying optimism and can-do attitude permeated the discussions: many among the audience were directly responsible for the historically unprecedented success in vaccine delivery to third world countries occurring over the last decade.

Chairing this plenary session was by Dr Jon Kim Andrus, Pan American Health Organization's (PAHO) Deputy Director. He is a public health expert with over 25 y work experience in vaccines, immunization, and primary care in developing countries. The panelists were Dr Jorge Kalil, President of the Butantan Institute, in Sao Paulo, Brazil and Lic. Abel Di Gilio, President of Sinergium Biotech, in Buenos Aires, Argentina. Both speakers have extensive experience in the building of vaccine production factories in emerging market countries, and most importantly, in building, promoting and securing, at the national and international levels, the institutional and political support necessary for sustainability and growth.

Dr Andrus opened the session focusing on sustainability as a recurring theme throughout the conference. National vaccine legislation is the best guarantee, and three components, a

budget line in the national budget, a national program with an officer in charge, and a predictable demand forecast are crucial. PAHO's mission has benefited from the transfer of successful experience across countries. He gratefully acknowledged the Serum Institute of India and Dr Suresh Jadhav, as being great contributors to the success of PAHO's Rubella program in the Americas. Dr Andrus postulated that the work of PAHO is facilitated by a regional "culture of prevention", noting that in contrast with the resistance observed in other regions of the world, immunization is readily accepted in Latin America and the Caribbean. What follows are two different strategies in two countries with extraordinary technical capacity and solid government commitment.

Dr Jorge Kalil—President, Instituto Butantan

Overview of the Brazil vaccine market. Brazil is the largest and most populated country of South America (population 200 million), and likely one of the oldest public vaccine markets in the world. It started 120 y ago with the production of anti-plague serum, followed by anti-venoms, and now for over 40 y, by the production of vaccines. In the mid-1980s the Brazilian government decided Brazil would become self-sufficient in vaccines. The two largest facilities are FioCruz, owned by the Federal Government and Butantan, owned by the State of Sao Paulo (one of 27 Brazilian States, Sao Paulo generates 40% of Brazil's GDP). Together, the two factories produce 93% of the vaccine units provided to the national market, totaling over US\$ 1Billion.

The Ministry of Health purchases 85% of all vaccines produced for use by the National Immunization Program (PNI). Between 1970 and 2011 the PNI increased vaccine coverage from 20 to 95% of the Brazilian population.

The introduction of a vaccine in the PNI's vaccine schedule follows a careful assessment of cost effectiveness. Epidemiologically, it must be shown that morbidity and mortality is high. The immunological efficiency of the vaccine must be above 70% and lasting immunity must be demonstrated. In order to guarantee

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the supply and price, the PNI will only introduce locally produced vaccines. For this, an investment plan showing that the vaccine can be produced at an affordable price must be in place.

This sequence has resulted in a number of examples of vaccine successes. Smallpox, poliomyelitis and Measles have been eradicated, and neonatal and accidental tetanus, tuberculosis, diphtheria, pertussis, hepatitis B, influenza and pneumococcus are under control.

Butantan (<http://www.butantan.gov.br>). The Instituto Butantan was founded in 1901 for the production of the anti-plague serum needed to combat the epidemic coming from Porto dos Santos. Afterwards the focus was the production of antivenom sera specific to South American serpents. Things have changed much since those times, when the present norms of quality, safety and efficiency were not required. Today the Production Division concentrates in constant improvements to the production process, and the Biotechnology Center includes a modern facility with production capacity of one million doses/yr. Since 1990 the Center uses bioreactors for the large-scale production of monoclonal antibodies, and the production processes used in the tetanus and diphtheria vaccines include the latest closed system technology. Butantan collaborates closely with FioCruz, Brazilian Universities, research Institutes and hospitals. Technology transfer ventures with International partners, such as the anti-grippal vaccine with Aventis Pasteur are ongoing and under development.

Butantan's Future Plans. Part of maintaining sustainability is the ability to constantly innovate. Butantan is continually expanding and updating the facilities to make room for the new and more stringent requirements of innovative technologies.

Butantan is very open to partnering for technology transfer with international companies. The pipeline includes a number of very interesting and innovative projects, including research and improvement of existing products, collaborative development, basic R&D and technology transfer. Dr Kalil specifically cited a cellular streptococcus pneumonia vaccine which will cover all serotypes.

Supplying the Brazilian public market is presently the main focus of Butantan. Export, however, is a new goal of the Government of Brazil for which Butantan now becomes increasingly ready.

Lic. Abel Di Gilio—President, Sinergium Biotech

Overview of the Argentine Vaccine Market. Argentina is situated in the Southern-most point of South America. It is the second largest country in South America (population 41 million) and home to the biggest Spanish-speaking population. The Government has long been committed to public health and the protection of the population from preventable diseases. In the past 10 y the National Immunization Program has made great strides, and the vaccination schedule has increased from 8 to 16 vaccines. These are offered to the population free of charge, although the system is not really completely a public market. Rather it covers five different levels of reimbursement: people without coverage, coverage by private insurance, retired and

pensioners, the national social health care system and the public administration employees.

Nevertheless in 2009, a flu (H1N1 influenza A) pandemic reached 11,931 thousand confirmed cases, 626 deaths, and close to one and a half million people presenting flu-like symptoms. The Government mobilized an intensive control program which at present covers almost 100% of the high-risk population. When the whole of the country is considered, in several provinces the coverage remains low, a failure due to a combination of lack of awareness relative the needs of prevention by some medical associations and the general population, thus inadequate and insufficient demand and access to the available vaccine supply.

The government had traditionally purchased most of the required vaccines for the National Immunization Program from PAHO and occasionally directly from pharmaceutical companies. Even though the market is open to competition (mostly coming from Argentine producers, Brazil, and Mexico, and including multinational companies such as Pfizer and Novartis) the Program has often required more vaccines than can be provided.

Until 2009, there had been no attempt to negotiate technology transfer in exchange for the purchase of vaccines. In that year, two Argentine companies decided to present the Government with their vision and a mission to replace the imports of vaccines by national production and to create a private consortium to finance the construction of a world-class vaccine manufacturing facility in Argentina.

Sinergium Biotech (<http://www.sinergiumbiotech.com>). Lic. Di Gilio described Sinergium as an “innovative strategic alliance of national and international laboratories to develop and produce vaccines and biological products in Argentina.” This private cooperative consortium was founded on the vision of two Argentine companies with very successful global operations. Biogenesis Bago and ELEA Laboratories decided to establish a world-class vaccine facility in Argentina capable of supplying the national market and future exports goals. They contacted Novartis, who agreed to train the personnel and initiate technology transfer, and together they won a public tender which included, under very strict penalty rules, the supply of anti-flu vaccines to the Argentine government for 10 y (at PAHO yearly prices), and the required building of one of the largest and most modern vaccine factories in the world. By December 2012 the first part of the facility was finished ahead of schedule, three technology transfers had been completed and validated, and a team of over 250 employees had been recruited and trained. In addition to these remarkable achievements, another tender was secured for the production of the pneumococcal vaccine Prevenar13 for 5 y.

A sequential five-year plan is underway: start of technology transfer, complete local packaging, local filling, formulation and production, and regulatory approval for antigen production. Sinergium is additionally sponsoring a mayor public awareness campaign aimed at increasing knowledge of and demand for vaccination. The President of Argentina has personally cooperated and images of her receiving vaccination are ubiquitous in the campaign materials.

As Sinergium continues to carry on its vision, a new formidable partner has joined the company: the INSUD Group, which brings its expertise in the production of global raw materials for biological products and in the building of pharmaceutical manufacturing and facilities. Lic. Di Gilio closed with a strong expression of interest in further collaborative ventures and detailing the advantages to potential partners such as the exclusive 5 to 10 y terms for sale (flu vaccine) to the Argentine government, the tax-free market access to Latin America provided by the MercoSur treaty, the regional counter-season market and the favorable disposition of the Argentine government to favor alliances between international and local companies.

Discussion and Question Session

The audience was enthusiastic about the advantages of local production evidenced by the two examples presented, and there were many questions to the panelists about how to encourage the government to prioritize vaccine production in the national

budget, how to target technology transfer to address country needs, and what would be the minimum size requirement of a plant to undertake technology transfer. A note of caution was introduced by Dr Samuel Ang (Abbot) about the sustainability of the model when every country wishes to initiate production. Dr Andrus noted that PAHO generally discourages small, low population countries from local production, favoring instead a regional approach. Both panelists stressed the need to be sensitive to the differences between cultures in the collaborating companies. Dr Kalil said that this is crucial even in their experience in collaborations inside Brazil. Lic. Di Gilio added that company cultures may also differ when working at different levels e.g., management vs. production. This discussion echoed the comments made by many of the presenters in other sessions about the crucial importance of understanding cultural differences and the need for constant and intensive communication.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.