REPORT OF THE AMERICAS DENGUE PREVENTION BOARD MEETING

Points for Consideration for First Introductions of Dengue Vaccines

BUCARAMANGA, COLOMBIA

JULY 16-17 2012
# CONTENTS

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>LETTER FROM THE DIRECTOR</td>
<td>3</td>
</tr>
<tr>
<td>SUMMARY</td>
<td>4</td>
</tr>
<tr>
<td>DENGUE PREVENTION BOARD MEETING OBJECTIVES</td>
<td>4</td>
</tr>
<tr>
<td>UPDATE ON DEVELOPMENT OF DENGUE VACCINES</td>
<td>5</td>
</tr>
<tr>
<td>UPDATE ON THE MATHEMATICAL MODELING OF THE IMPACT OF DENGUE VACCINATION</td>
<td>6</td>
</tr>
<tr>
<td>PREPARING FOR DENGUE VACCINE INTRODUCTION</td>
<td>7</td>
</tr>
<tr>
<td>POINTS FOR CONSIDERATION FOR FIRST-TO-INTRODUCE COUNTRIES</td>
<td>7</td>
</tr>
<tr>
<td>Regulatory</td>
<td>7</td>
</tr>
<tr>
<td>Evidence for Decision-Making</td>
<td>8</td>
</tr>
<tr>
<td>Impact Modeling</td>
<td>9</td>
</tr>
<tr>
<td>Immunization Systems</td>
<td>10</td>
</tr>
<tr>
<td>Demand and Financing</td>
<td>11</td>
</tr>
<tr>
<td>Post Licensure / Demonstration Projects</td>
<td>12</td>
</tr>
<tr>
<td>THE FUTURE</td>
<td>13</td>
</tr>
<tr>
<td>APPENDIX - SPEAKERS AND MEETING PARTICIPANTS</td>
<td>14</td>
</tr>
</tbody>
</table>
Dear Colleagues,

In this report we have captured the draft Points for Consideration as elaborated at the meeting of the Americas Dengue Prevention Board (AmDPB), held in Bucaramanga, Colombia, in July, 2012. One of the key lessons of the last several decades of vaccine development and introduction is that developing countries will not receive the benefits of a new vaccine if planning does not start early.

Over the last decade, very substantial progress has been made in the clinical development of several vaccines and dengue vaccine development has advanced to a point where it now seems likely that at least one vaccine will be available for use in developing countries, perhaps as early as 2014. The development of Points for Consideration is therefore particularly timely. In addition, primarily under the DVI, very important work has been completed and is still underway to create an enabling environment for the introduction and use of new dengue vaccines.

To make sure that developing countries have immediate access to new dengue vaccines, DVI has examined many issues of vaccine introduction and has sponsored a wide range of studies. A primary mechanism for conducting this work is the Dengue Prevention Boards (DPBs) in the Asia Pacific and Americas Regions. Reports of their deliberation are available at the DVI website.

In June, 2012, the Asia-Pacific Dengue Prevention Board (APDPB) meeting in Bangkok laid out a number of Points for Consideration to help countries determine if they wish to be first-to-introduce a dengue vaccine. The DVI is preparing a final set of Points for Consideration that will combine the issues raised from both the Asia-Pacific and Americas DPB meetings.

We hope these Points for Consideration will facilitate decision making by developing countries so that they can access the vaccine as soon as it is available.

Sincerely,

Luiz Jacintho da Silva
Director, Dengue Vaccine Initiative
SUMMARY

The Americas Dengue Prevention Board (AmDPB) meeting was held in Bucaramanga, Colombia, on 16-17 July, 2012, to consider and contribute to the draft Points for Consideration developed a month earlier at the Asia-Pacific Dengue Prevention Board (APDPB) meeting. The Points for Consideration, which are capabilities that countries should consider having in place to be ready for dengue vaccine introduction, will provide a framework for countries to decide if they are interested in and capable of undertaking introduction activities for the first dengue vaccine that is licensed.

The meeting was organized by the Dengue Vaccine Initiative (DVI), a consortium of the International Vaccine Institute (IVI), the International Vaccine Access Center (IVAC) at the Johns Hopkins School of Public Health, the Sabin Vaccine Institute, and the Initiative for Vaccine Research of the World Health Organization (IVR/WHO).

This was one of the largest DPB meetings held to date. Participants included representatives of Ministries of Health, and academic, research and health institutions in eight countries in the Americas (Argentina, Brazil, Colombia, Ecuador, Mexico, Nicaragua, Puerto Rico (USA), and Venezuela), as well as from the Pan American Health Organization (PAHO).

Dengue costs over $2.1 billion a year in the Americas

Points for Consideration are designed to:

- Provide a framework to assist countries in determining if they wish to be a first-to-introduce country for the first dengue vaccine to be licensed; and
- Serve as a guide to other countries that may subsequently decide to adopt dengue vaccines.

MEETING OBJECTIVES

Unlike for previous vaccine introductions, the introduction of dengue vaccines is being discussed before a vaccine is available. The purpose of discussing introduction now is to shorten the time between licensing and use, by as much as is possible. The purpose of the AmDPB meeting was to refine, adapt and further develop Points for Consideration for first-to-introduce countries, in the context of the Americas.

Points for Consideration have been classified under six areas:

- Regulatory
- Evidence for Decision Making
- Impact Modeling
- Immunization Systems
- Demand and Financing
- Post-Licensure/Demonstration Projects
**UPDATE ON DEVELOPMENT OF DENGUE VACCINES**

In order to help countries in the Americas plan the timing of dengue vaccine introductions, vaccine manufacturers provided an update on the progress being made in the development of vaccines. The stages of development for each candidate vaccine are shown in Figure 1.

**PRECLINICAL**

**Live Attenuated Tetravalent Dengue Vaccine (licensed NIH vaccine)**
VA Biotech is in the process of making seed lots.

**Biological E** has made seed lots at scale and are reviewing their clinical development strategy.

**Panacea Biotech** has prepared lots and are proposing Phase I studies in early Fall 2012.

**Purified Inactivated Vaccine**

**GlaxoSmithKline Vaccines** is developing a tetravalent adjuvanted vaccine in partnership with the US Army and the Brazilian manufacturer Fiocruz. Two Phase I trials are planned in the US later in 2012.

**PHASE I**

**Recombinant Envelope Protein Vaccine**

An adjuvanted recombinant protein developed at Hawaii Biotech is being further clinically developed by **Merck**. Merck will conduct Phase I studies of Iscomatrix adjuvanted vaccine in Australia in 2012 to supplement previous Phase I testing with a monovalent alum adjuvanted vaccine.

**PHASE II**

**Live Attenuated Tetravalent Dengue Vaccine**

**US National Institutes of Health and Instituto Butantan** – First monovalents, then tetravalents were tested in Phase I. Phase II clinical trials are ongoing in the US and planned in flavivirus exposed subjects in Thailand and Brazil, later in 2012.

**Inviragen** has entered Phase II clinical trials in Puerto Rico, Colombia, Singapore and Thailand. In addition, rapid immunization strategies and needleless administration are being investigated.

**PHASE III**

**Live Attenuated Chimeric Tetravalent Dengue vaccine (using yellow fever virus as a backbone)**

**sanofi pasteur** is conducting several Phase III trials in Australia, and in countries in Asia and Latin America. To date, safety of the vaccine has been found to be comparable to control vaccines or NaCl placebo. The immunogenicity of the vaccine has been shown to be balanced and homogenous for all 4 serotypes. First results of an efficacy study conducted in 4,002 children aged 4 to 11 years, in Thailand, show the vaccine’s ability to protect against disease caused by three of the four circulating dengue virus serotypes.

**FIGURE 1. STATE OF DEVELOPMENT OF DENGUE VACCINE CANDIDATES**
Mathematical modelers provided an update on the models that they have developed for dengue. Given the complex epidemiology of dengue, modeling can help to inform careful decision making in order to optimize the impacts on the disease and minimize the risks of unintended consequences.

Modeling will be critical for determining appropriate immunization strategies, including appropriate age-targets, assessing the incremental value of vaccinating other segments of the population, and assessing the potential impact on disease transmission.

Further modeling will contribute to generating vaccine recommendations at both national and international levels.

The models presented were found to be useful for determining the appropriate immunization strategy for dengue. They suggest that routine vaccination at a young age can achieve a good level of disease control after several years but catch-up programs are likely to be required to obtain a rapid decline in disease incidence.

Mathematical models of disease transmission characterize the dynamics of interactions between humans and mosquitoes such that the size of the population, infectiousness, biting affinity, and death rates are all accounted for (Figure 2).

Both stochastic (non-deterministic) and deterministic models have been used to determine optimal vaccination strategies.

An agent-based dengue model, developed at the University of Florida and the Center for Statistical and Quantitative Infectious Diseases in Washington, shows that in Thailand routine immunization of 2 year-olds, and catch-up immunization rolled out to ages up to 44 years old, can approach elimination of outbreaks within 9 years (Figure 3).

Likewise, in a deterministic model, Coudeville et al. (sanofi pasteur) found that in a Mexican setting, the impact of routine vaccination at 2 years of age on disease outbreaks could be accelerated by catch-up immunization in 3-14 year-olds (see Figure 4).
PREPARING FOR DENGUE VACCINE INTRODUCTION

By the time a new vaccine is available, countries should ideally have the capacity to conduct all necessary activities for successful vaccine introduction. These include the regulatory capacity to license and control quality and safety of the vaccine, evidence-based immunization strategies, logistical and delivery capacities, surveillance to monitor safety and the impact of the vaccine on disease, and communications capacities.

In this respect, the countries of the Americas will benefit from recent experiences with the introduction of other new vaccines.

POINTS FOR CONSIDERATION FOR FIRST-TO-INTRODUCE COUNTRIES

Regulatory

Introducing a new vaccine places specific demands on the regulatory authority. Therefore, first-to-introduce countries should consider:

WHO/PAHO recognition of their National Regulatory Authority (NRA) — It is essential for first-to-introduce countries to have a NRA that is recognized by the WHO and / or PAHO because the countries will need the capabilities shown in Figure 5.

Conducting a gap analysis of their NRA — WHO conducts assessment of NRAs for all countries, and identifies gaps and areas to be developed. First-to-introduce countries should ask for a WHO assessment of the country’s NRA.

To minimize the gaps, countries should then indicate where they need support, where they can obtain that assistance, and what the time frame and budget would be. The DVI’s role can be to assure a mechanism to handle these requests for support.

The willingness of the NRA to accord priority review for a dengue vaccine — NRAs in first-to-introduce countries should be prepared to provide priority review for dengue vaccine. This will ensure that the NRA is capable of licensing a dengue vaccine within the timeframe for planned early introductions.

The NRA’s thorough assessment of the manufacturers’ risk management plans — The regulatory process should include an assessment of manufacturers’ risk management plans, and may oblige the manufacturer to undertake specific Phase IV studies.

Demands on Regulatory Authority

- Experience in oversight of phase 3 and phase 4 trials
- Ability to make licensing decisions for innovative products, based on scientific file review, especially recombinant/chimeric products (GMO)
- Ability to evaluate data on target population and dosing schedules and set criteria on vaccine use for “Phase 4” studies, to avoid political pressure
- Needs to take into consideration trial protocols for upcoming dengue vaccines (WHO has clinical trial guidelines)
- Capacity to develop and validate lot release tests for innovative vaccines
- Ability to recognize and assure Good Manufacturing Practice
- Process and capacity to monitor and investigate adverse events (AEs) in context of Clinical trials, Routine immunisation, and Campaigns
- Long term safety monitoring
- Self-assessment process of performance

FIGURE 5. ESSENTIAL REQUIREMENTS OF AN NRA. (BLUE FONT INDICATES REVISIONS MADE IN ADBPB DRAFT POINTS FOR CONSIDERATION)
The NRA’s capacity to assess country specific issues — Some countries may have specific issues that they wish to address, and innovative vaccines may present specific challenges for NRAs, such as how to conduct an environmental impact assessment of Genetically Modified Organisms (GMOs). First-to-introduce countries should ensure that they are capable of addressing these issues.

The coordination between the National Immunization Technical Advisory Group (NITAG) and the NRA — First-to-introduce countries should ensure that there is good coordination between the NITAG and the NRA. This will ensure that both national institutions are working towards the same time frame for vaccine introduction.

Involving WHO recognized regulators to discuss needs for a licensing decision — Ideally an expert panel would be constituted and convened by DVI and there would be a joint review of the decision-making process involving the NRAs of first-to-introduce countries. This would support these NRAs in their decision-making process, which they would then carry out independently.

Box 1: Recommendations to DVI for regulatory capacity building.

Participants discussed the potential role of the DVI in supporting regulatory capacity building. They recommended that the DVI should:
- Avoid any conflict of interest (real or apparent) when providing technical support to countries;
- Develop a mechanism to monitor NRA processes during first vaccine introductions.

Evidence for Decision-Making

First-to-introduce countries should have the capacity both to generate evidence for the purpose of decision-making and to develop an evidence-based implementation framework. These Points for Consideration have been separated under these frameworks: decision-making, and implementation.

FRAMEWORK FOR DECISION-MAKING

First-to-introduce countries should consider:

Capacity for laboratory-confirmed epidemiological surveillance — In countries of the Americas, dengue surveillance is conducted in all at-risk countries, and is performing well in several countries. At a minimum, countries should have evidence of burden of disease including the incidence, the age distribution, the serotype circulation, cohort studies, and seroprevalence. Ideally these data should date back ten years, but at least cover two epidemic peaks.

Other important data include mortality and disease severity.

These data are essential for establishing priorities relative to other vaccine preventable diseases, for determining priority target groups where resources and/or vaccines are limited, for accurately forecasting the demand and logistical requirements for a vaccine, and for assessing the impact of the immunization program on the disease.

Capacity to conduct economic studies — At a minimum, countries should be able to collect data on the cost-benefits of vaccination, taking in to account the direct and indirect costs of the disease.

First-to-introduce countries should model the economic impacts of dengue, and the results should be shared.

Capacity to conduct policy studies — At a minimum a
policy review of the characteristics of the vaccine should be undertaken to ensure that the issues around vaccine safety, vaccine costs, program costs and financial sustainability are well understood.

Contingency strategies should also be developed to deal with unforeseen circumstances, such as if an epidemic occurs during vaccine introduction.

**FRAMEWORK FOR IMPLEMENTATION**

First-to-introduce countries should consider:

**Capacity to adequately address the specific needs for a dengue immunization program** — The National Immunization Programs in the region generally have good practices and infrastructure, but the specific programmatic requirements for dengue vaccine, including cold chain needs and necessary changes to immunization schedules, must all be adequately assessed and adjustments made where necessary.

**Capacity to monitor dengue immunization** — It will be critical to monitor dengue vaccination coverage and safety of the vaccine. (For vaccine safety surveillance, see ‘Regulatory’).

**Ability to integrate dengue immunization with vector control** — Immunization activities should not replace nor diminish good vector control programs and should instead be made fully complementary to vector control.

First-to introduce countries should ensure that resources for immunization are separate from those for vector control and do not reduce a country’s ability to maintain vector control initiatives.

**The framework for dengue immunization within the National Immunization Program** — A framework should be established within the national immunization program to ensure that appropriate clinical guidelines are developed and roles and responsibilities specific to dengue immunization are established.

**Ministerial and public awareness** — Government Ministers and the public should be sensitized to all aspects of the dengue immunization program. A Ministerial meeting should be considered to ensure adequate high-level awareness of the potential benefits and challenges of a dengue immunization program.

**Box 3: Recommendations to PAHO and DVI for adapting economic tools for dengue**

Participants discussed adapting existing economic tools for dengue vaccines and developing new tools where needed. They recommended:

- That PAHO consider adding dengue to the ProVac tools for estimating the cost-effectiveness of vaccination;
- That DVI consider developing additional health economic tools specific to dengue.

**Impact Modeling**

Impact modeling can help to answer important strategic and policy questions for new vaccine introductions. First-to-introduce countries should consider modeling for the development of optimal strategies for the best use of limited quantities of vaccine.

Mathematical models can be used for a number of purposes. First-to-introduce countries should consider the purpose specific applications of modeling, such as:

- Providing a transparent summary of the current dengue epidemiological situation by integrating information from multiple sources of data;
- Developing optimal immunization strategies;
- Determining the appropriate target groups for vaccination;
- Designing Phase IV studies;
- Forecasting demand for a vaccine;
- Assessing epidemiological effects of immunization (on infections, cases, deaths, hospitalizations);
- Informing vaccine target product profiles (for example, ideal vaccination schedules, target age groups and delivery strategies);
- Assessing the synergistic effects of other prevention/control strategies, notably vector control efforts.
However, modeling requires a minimum of data and design features. Therefore, first-to-introduce countries should carefully consider the data required for modeling. Data should be available from prospective cohort studies and from concurrent vector density studies.

Assumptions should be clearly stated, including those on the natural history of infections, and the transferability of data from a specific locale to other parts of the country.

Specific data required for modeling include:
- Vector density for the locale being modeled;
- Incidence of cases (both hospitalized and non-hospitalized) and deaths by age and gender;
- Serotype-specific susceptibility profile by age;
- Natural history of infection including incubation period, infectious period, and the interactions between different dengue serotypes;
- Historical distribution of each serotype by age;
- Corrective factors to ensure that under- or over-reporting of vaccination are accounted for in modeling (e.g. expansion factors);
- Interactions with other types of interventions, such as vector control activities including the use of Wolbachia bacteria to control mosquito populations;
- Vaccine-specific data, such as:
  - number of doses, duration of protection, vaccination schedule, vaccine efficacy (for susceptibility to infection, for susceptibility to disease, for infectiousness, for disease progression), and indirect effects,
  - assumed coverage rates by dose

**Immunization Systems**

In the Americas, immunization systems are generally quite strong. However, prior to making a decision about introducing a dengue vaccine, first-to-introduce countries must not only consider their regulatory and disease surveillance capacities (see ‘Regulatory’ and ‘Evidence for Decision-making’) but should also consider:

*Robustness of proposed vaccine introduction strategies* — Countries should consider in which geographic areas they will introduce the vaccine and in which age groups. Strategies can be assessed with good epidemiological data and mathematical modeling. In the development of dengue vaccine introduction strategies, countries should determine optimal strategies for the use of initially limited quantities of vaccine and assess whether vaccines should be used (first) in urban or rural areas, routine or mass campaigns.

*Cold chain and logistics management capacity* — Before initiating introduction it should be determined if the vaccine will be delivered through the routine program or in mass campaigns. Based on the introduction strategy, the capacity of the cold chain should be assessed to determine if additional storage and transport capacity will be required, and whether the infrastructure is capable of delivering the vaccine. The stability of the vaccine under field conditions should also be assessed to consider any other impacts on the cold chain capacity.

*Assessing training needs for related personnel and agencies* — Adequate training, including on the disease, vaccine administration, disease surveillance, surveillance of adverse events following immunization (AEFIs), vaccine characteristics, vaccine wastage and storage needs, will be required. First-to-introduce countries should serve as models for other countries, for example in devising vaccine access strategies and in developing vaccine registries, including for high risk groups. Therefore, they should determine whether sufficient training has been given in critical areas, or identify additional required training assistance.

*Robustness of the information system* — Several data collection mechanisms should be in place. These include immunization registries to record administered doses, including for high risk groups such as pregnant women and the HIV+, and systems to record and report adverse events.

*Capacity for communications* — Several forms of communication strategies need to be developed,
starting with clear messages on the rationale for the target population, including where (geographically) immunization will occur if a vaccine is introduced in a phased basis. Countries should develop risk communication plans to be prepared to deal with adverse events, and to counter groups opposed to vaccination.

Communications should be developed with the help of experts in mass communications.

**Intersectoral collaboration** — Both intrasectoral and intersectoral collaboration should be established to define and integrate the role of the national immunization program. Collaborations should occur for dengue control activities, for communications on dengue and dengue immunization, and for the development of public policy on dengue and dengue immunization. Discussions should involve actors from a range of initiatives, especially with vector control departments, NGOs, the DVI, the Sabin Vaccine Institute, WHO and PAHO, clinicians, politicians, and others.

**Plans and capacity for monitoring and evaluation** — There needs to be a permanent system to monitor the impact of the dengue immunization program on disease burden and to assess the vaccine’s effectiveness. First-to-introduce countries should ensure that, at a minimum, they have these capacities.

---

**Demand and Financing**

First-to-introduce countries should have met the minimum requirements noted under the other areas, including having up to date dengue surveillance data (see ‘Evidence for Decision-Making’), and robust vaccine introduction strategies (see ‘Immunization Systems’) in order to be capable of assessing their demand and finance requirements. These countries will have determined dengue to be a priority disease, based on the health and economic burdens, and on public demand.

**DEMAND**

Note: assumptions for demand are subject to variations in supply, price, and efficacy.

First-to-introduce countries should consider:

*Previous experiences with modeling and/or new vaccine introductions* — Modeling should be available to inform decision-making with respect to best vaccination strategies. Countries will benefit from previous experience in new vaccine rollouts, and lessons learned and previously collected data on demand and costs of these vaccine introductions will inform plans for dengue vaccine introduction.

*Rollout plans* — Rollout plans should include phased introductions, development of appropriate logistics, provision of training, and so forth. The rollout plan will determine how much vaccine is to be utilized at any given time and ensure good coordination with the vaccine supplier to ensure sufficient supply.

*Prior experience with mass immunization campaigns or with delivery of a vaccine outside of the EPI schedule* — First-to-introduce countries should have prior experience with successful implementation of mass vaccination campaigns (measles or rubella), or vaccines outside EPI schedules, such as pandemic flu, yellow fever, or HPV vaccines. In addition, campaigns or routine immunization programs should be functioning well. Previous experience with mass campaigns and other immunization program activities will help to inform strategies for managing vaccine demand in relation to the available supply.

*The functioning of immunization management and delivery systems* — First-to-introduce countries should have well-functioning vaccine management and delivery systems, measured by such indicators as a lack of supply interruptions, high immunization coverage rates, a lack of vaccine-preventable disease outbreaks, and good EPI infrastructure (such as strong cold chain and surveillance systems). The lack of supply interruptions can serve as a proxy for capacity to adequately forecast vaccine demand, but programs should be closely coordinated with the supplier to ensure that the demand can be met.

**FINANCING**

First-to-introduce countries should consider:

*The budget line-item for dengue vaccine* — Countries
should have a line item for dengue immunization in the budget for its National Immunization Program. This will help prevent a lack of funding that could disrupt implementation of dengue vaccination.

*Ability to increase the vaccine budget to add a dengue vaccine* — Having the fiscal space to add an additional vaccine to the immunization budget is an indication of political support and an assurance that dengue vaccine introduction will not harm other immunization or vector control initiatives. This ability should also be corroborated by the Ministry of Finance or National Planning Departments.

*Ability to fund the implementation and delivery of a dengue immunization program* — In addition to having sufficient funds to purchase vaccine, countries should ensure they have sufficient funding to cover the operational costs of introducing and delivering a dengue vaccine. This could include school-based delivery, which could represent a significant cost.

*Ability to maintain financing for existing vector control* — The country should understand the importance of maintaining financing for existing control measures (e.g., vector control) and should not divert funds away from current control programs.

*Ability to finance monitoring and evaluation* — In addition to vaccine delivery, countries should have the ability to finance the evaluation and monitoring of vaccine impact, such as vaccine effectiveness and cost-effectiveness, and to finance post-licensure studies to evaluate the long term safety of the vaccine.

*Experience in the coordination of financing across Ministries* — Countries should ideally have past experience with coordinating budgets and financing of vaccine programs across Ministries (e.g. with the Ministries of Education, of Health, of Tourism, etc), and across public and private sectors (e.g. insurance).

**Post Licensure / Demonstration Projects**

Because of the novelty of dengue vaccines, and the potential for the vaccine to cause more severe disease (by antibody-dependent enhancement), some Phase IV trials may be requested by licensing authorities. Beyond requirements for Phase IV studies, there will be questions the countries will want to answer through pilot introduction studies, such as how to introduce a vaccine to have the most impact on disease as quickly as possible. Therefore, first-to-introduce countries should consider whether or not they have the capacity to conduct post-licensure demonstration projects or Phase IV trials.

All of the other Points for Consideration, including safety surveillance (see ‘Regulatory’), are critical for enabling successful demonstration projects and must be met before demonstration projects can be considered (Figure 6).

Additionally, first-to-introduce countries must consider:

*Inter-country collaboration* — Inter-country institutions (e.g. international technical agencies such as WHO, PAHO, UNICEF, DVI, and others) should cooperate in the development of common guidelines, case definitions, manuals, sharing of post-licensure data, etc.

*Capacity to enhance disease surveillance* — Countries should develop a manual for dengue surveillance and develop criteria for successful surveillance based on country capacity.

First-to-introduce countries should build upon existing integrated country surveillance systems. Disease surveillance should start before the vaccine is available (such as was the case for rotavirus surveillance which
started three years before rotavirus vaccine became available). The country should have serotype specific surveillance, and strengthen laboratory capacity, data management and analysis capacities.

**Capacity to conduct vaccine effectiveness studies** — While select first-to-introduce countries (e.g. Brazil, Mexico, and Colombia) will likely consider conducting cohort studies to evaluate vaccine effectiveness, other countries may also want to consider conducting such studies which follow cohorts of vaccinated and unvaccinated people over time. Based on country capacity and needs, these studies could examine disease severity following immunization, length of immunity, and herd protection, among other outcomes. Countries should also have the capacity to investigate vaccine failures.

**The Future**

Now that the Asia-Pacific and Americas Dengue Prevention Board meetings have been held to develop the draft Points of Consideration for countries in their region, the points from both meetings will be compiled and made available to all dengue-endemic countries.

Between July and September, 2012, Ministries of Health will use these Points of Consideration to determine their interest and capability to be among the first-to-introduce a dengue vaccine. Once countries have determined an introduction timeframe, the DVI is prepared to organize discussions among the countries to determine vaccine needs and needs for partner assistance.

During 2013, the first-to-introduce countries will complete a final design of the introduction activities to be able to introduce the vaccine soon after it is licensed and available in countries.

Specific assistance that the DVI is prepared to offer first-to-introduce countries include:

- Management of a coordination center for Phase IV and other introductory activities;
- Incorporation of mathematical modeling in country plans;
- Assistance in the preparation of demand forecasts;
- Dissemination of information about the self-selection of first-to-introduce countries;
- Facilitation of collaboration amongst NRAs.

_The mission of the Dengue Vaccine Initiative is to encourage the development and use of vaccines to prevent dengue. As a consortium of organizations committed to a world without dengue, DVI is working to lay the groundwork for dengue vaccine introduction in endemic areas so that, once licensed, vaccines to prevent dengue will be swiftly adopted._
## APPENDIX ONE — SPEAKERS AND MEETING PARTICIPANTS

<table>
<thead>
<tr>
<th>Update on DVI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overview and Objectives for the meeting: The need for development of points for consideration for adoption of dengue vaccine. Roles of the DPBs. Relationship to SAGE and PAHO Immunization TAG</td>
<td>Luiz da Silva</td>
</tr>
<tr>
<td>Updates on vaccine development:</td>
<td></td>
</tr>
<tr>
<td>Butantan</td>
<td>Ricardo Palacios</td>
</tr>
<tr>
<td>Developing country manufacturers</td>
<td>Julie Milstien</td>
</tr>
<tr>
<td>GSK Vaccines</td>
<td>Suely Tubois</td>
</tr>
<tr>
<td>Inviragen</td>
<td>Jorge Osorio</td>
</tr>
<tr>
<td>Merck</td>
<td>Lois Lockledge</td>
</tr>
<tr>
<td>sanofi pasteur</td>
<td>Fernando Noriega</td>
</tr>
<tr>
<td>Historical review of the experience with early adoption of new vaccines. Review of the deliberations of the AmDPB meetings on vaccine introduction in Panama and Brasilia. Implications for points for consideration for first introducers.</td>
<td>Richard Mahoney</td>
</tr>
<tr>
<td>Evidence for Decision Making: What data are needed to support vaccine adoption?</td>
<td>Jorge F. Mendez-Galvan</td>
</tr>
<tr>
<td>Strategic Demand Forecasting and Financing considerations for first introducers</td>
<td>Dagna Constenla</td>
</tr>
<tr>
<td>Impact modeling considerations for first introducers</td>
<td>Jonathan Sugimoto</td>
</tr>
<tr>
<td>Immunization systems considerations for first introducers</td>
<td>Andrea Vicari</td>
</tr>
<tr>
<td>Regulatory considerations for first introducers</td>
<td>Julie Milstien</td>
</tr>
<tr>
<td>Phase IV/Demonstration project considerations for first introducers</td>
<td>Tom Wierzba</td>
</tr>
<tr>
<td>Discussion and agreement on further development, refinement and publication of the points for consideration</td>
<td>Roberto Tapia Conyer</td>
</tr>
<tr>
<td>Next steps</td>
<td>Richard Mahoney</td>
</tr>
</tbody>
</table>

## BOARD MEMBERS

**Dr. Aracely Alava Alprecht**  
Coordinator, Investigation and Microbiological Diagnosis  
Leopoldo Izquieta Perez National Institute of Hygiene and Tropical Medicine  
Chair, Virology, Guayaquil University  
Ecuador  

**Dr. Juan Jose Amador**  
PATH  
Nicaragua  

**Dr. Jorge Boshell**  
Director Biosafety Committee  
Bioseguridad, Banco de Huesos y Tejidos Fundación Cosme y Damián  
Colombia  

**Dr. Iris Villalobos de Chacon**  
Chief of Epidemiological Services  
Hospital Central de Maracay  
Venezuela  

**Dr. José F. Cordero**  
Dean, Graduate School of Public Health  
University of Puerto Rico  
Puerto Rico  

**Dr. Delia A. Enria**  
Director, INEVH (Instituto Nacional de Enfermedades Virales Humanas)  
Argentina  

**Dr. Eduardo Fernandez**  
Adjunct Professor  
Community Health Sciences  
Brock University  
Canada
BOARD MEMBERS

Dr. Maria Guadalupe Guzman
Head Virology Department
Director
PAHO/WHO
WHO Collaborating Center for Viral Diseases
Pedro Kouri Tropical Medicine Institute
Cuba

Dr. Harold Margolis
Branch Chief, CDC (Centers for Disease Control and Prevention) Dengue Branch,
Puerto Rico

Dr. Jorge F. Mendez-Galvan
Investigador National
Hospital Infantil de México “Federico Gómez”
Mexico

Dr. Steve Waterman
Lead, US Mexico Unit
Division of Global Migration and Quarantine, CDC Senior Medical Epidemiologist
USA

MINISTRY OF HEALTH GUESTS

Dr. Gonzalo Lopez Casas
Director
Instituto Nacional de Salud de Colombia
Colombia

Dr. Guillermo Comach
Coordinador General
Laboratorio Regional de Diagnostico e Investigacion del Dengue y otras Enfermedades Virales (LARDIDEV)
Instituto de Investigaciones Biomedicas de la Universidad de Carabobo (BIOMED-UC).
Venezuela

Dr. Juan I. Arredondo Jimenez
Direccion del Programa de Enfermedades Transmitadas por Vectores
Programa de endereços doenças transmitidas por vetores
Brazil

Dr. Jaime Lazovski
General Director
Ministry of Health
Editorial Committee

Argentina

Dr. Beatriz Londoño
Ministra de Salud y Protección Social
Colombia

Dr. Carlos Eduardo Mosquera Martínez
Research and Diagnostic Coordinator
National Institute of Hygiene and Tropical Medicine
Ecuador

Ms. Sirlene de Fatima Pereira
Gerência de Incorporação Técnica-Científica e Normatização
Coordenação Geral do Programa Nacional de Imunizações
Departamento de Vigilância de Doenças Transmissíveis - DEVEP
Secretaria de Vigilância em Saúde – SVS, Ministério da Saúde - MS
Brazil

Dr. Carlos Saenz Torres
Director of Epidemiology and in charge of Dengue and the National Immunization Programme
MOH
Nicaragua

Dr. Rosa Patricia Vidal-Vázquez
Technical Subdirector Child Health
National Center for Child and Adolescents Health
Mexico

DVI STAFF & ADVISORS

Ms. Mabel Carabali
Consultant Epidemiologist
Dengue Vaccine Initiative Program
International Vaccine Institute
Colombia

Ms. Ana Carvalho
Associate Director
Vaccine Advocacy and Education
Sabin Vaccine Institute
USA

Dr. Dagna Constenla
International Vaccine Access Center
Associate Scientist
John Hopkins Bloomberg School of Public Health
USA
Ms. Denise DeRoeck  
Consultant  
USA

Dr. Shawn Gilchrist  
S Gilchrist Consulting Services Inc  
Canada

Dr. Scott Halstead  
Senior Scientific Advisor  
Dengue Vaccine Initiative  
International Vaccine Institute  
Korea

Ms. Hyo Jin Lee  
Administrative Assistant  
Dengue Vaccine Initiative  
International Vaccine Institute  
Korea

Ms. Jacqueline Lim  
Epidemiologist  
Dengue Vaccine Initiative  
International Vaccine Institute  
Korea

Dr. Richard Mahoney  
Coordinator  
Policy & Access Unit  
Dengue Vaccine Initiative  
International Vaccine Institute  
Korea

Dr. Brian Maskery  
Associate Research Scientist  
International Vaccine Institute  
Korea

Dr. Julie Milstien  
Adjunct Professor of Medicine  
University of Maryland School of Medicine  
International Vaccine Access Center  
USA

Dr. Luiz Jacinthe da Silva  
Director  
Dengue Vaccine Initiative  
International Vaccine Institute  
Korea

Dr. Jonathan Sugimoto  
Research Assistant Professor,  
Department of Epidemiology, School of Public Health and Community Medicine, University of Florida,  
Staff Scientist,  
Vaccine and Infectious Disease Division,  
Fred Hutchinson Cancer Research Center,  
Seattle WA  
USA

Dr. Thomas Wierza  
Deputy Director General  
Translational Research Division  
International Vaccine Institute  
Korea

**INVITED GUESTS**

**Butantan**  
Dr. Ricardo Palacios  
Clinical Research Manager  
Division of Clinical Trials and Pharmacovigilance  
Instituto Butantan  
Brazil

**Carlos Slim Health Institute**  
Dr. Roberto Tapia  
Director General,  
Carlos Slim Health Institute (Instituto Carlos Slim de la Salud)  
Mexico

**GAVI**  
Dr. Alan Brooks  
Senior Specialist, Policy | Policy & Performance  
GAVI Alliance Secretariat  
Switzerland

**GlaxoSmithKline Vaccines**  
Dr. Diana Caceres  
Medical Affairs Manager, Colombia & Venezuela  
GSK

Dr. Pilar Rubio  
Director  
Medical Affairs Latin America & Caribbean  
GSK

Dr. Suely Tubois  
Epidemiology Manager, Latin America & Caribbean  
GSK  
Brazil
**Inviragen, Inc.**
Dr. Matt Dreitz
Manager, Clinical Operations
Inviragen
USA

Dr. Aurelia Haller
Director, Vaccine Development and Regulatory Affairs
Inviragen
USA

Dr. Jorge Osorio
Co-founder and CSO
Associate Professor
Department of Pathobiological Sciences
University of Wisconsin
USA

**Merck**
Ms. Lois Lockledge
Director, New Vaccines
Global Vaccines Strategy & Innovation
Merck
USA

**Pan American Health Organization**
Dr. Andrea Vicari
Advisor,
Immunization Comprehensive Family Immunization
Regional Project
Pan American Health Organization
World Health Organization
Costa Rica

**sanofi pasteur**
Dr. Emmanuel Burckel
Dengue project Leader, Latin America
sanofi pasteur
Mexico

Dr. Maria de los Angeles Cortes
Director
LATAM Regulatory Affairs
sanofi pasteur
Mexico

Dr. Laurent Coudeville
sanofi pasteur
France

Dr. Carlos Espinal
Vaccination Policy and Advocacy