Planning for the Introduction of Dengue Vaccines

Hanoi, Viet Nam
19-20 April 2011
The Asia-Pacific Dengue Prevention Board with the Dengue Vaccine Initiative organized a meeting in Hanoi on 19-20 April 2011 on planning for the introduction of dengue vaccines, an important and timely topic in view of the significant progress being made in developing vaccines and the promising results from clinical trials. The 50 participants included members of the Asia-Pacific Dengue Prevention Board and the Dengue Vaccine Initiative, representatives of the vaccine-manufacturing industry, medical researchers, clinicians and senior health ministry staff members from Cambodia, Cook Islands, Indonesia, Malaysia, Philippines, Singapore, Sri Lanka and Viet Nam.

The meeting was opened by the Deputy Minister of Health of Viet Nam, Professor Nguyen Thi Kim Tien, who stressed the need for good estimates of disease burden, a long-term strategy and effective control measures. She also emphasized the Government’s support for surveillance at the national level and the importance of vector control as part of community-based programs.

The meeting aimed to support the preparation of country-specific investment cases for the introduction of dengue vaccines, in particular for Thailand and Viet Nam, while providing information for other countries in the region. The participation of key decision-makers from health ministries was designed to help ensure practical outcomes, while the inclusion of vaccine manufacturers was intended to facilitate mutual understanding of the challenges ahead.

For dengue, the priority is global and national.
We need a vaccine; we need champions; we need a reinvention of public health.
~ Dr. Jacob John, Vellore, India

<table>
<thead>
<tr>
<th>DVI 4 “Focal” Countries</th>
<th>THAILAND</th>
<th>VIET NAM</th>
<th>COLOMBIA</th>
<th>BRAZIL</th>
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<tbody>
<tr>
<td>Population size</td>
<td>68 million</td>
<td>88 million</td>
<td>45 million</td>
<td>192 million</td>
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<tr>
<td>Study region</td>
<td>Ratchaburi (Bang Phae)</td>
<td>Nha Trang</td>
<td>Medellin</td>
<td>Salvador</td>
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<tr>
<td>Catchment area population</td>
<td>49,506</td>
<td>38,989</td>
<td>56,977</td>
<td>10,842</td>
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<tr>
<td>Documented incidence in national surveillance</td>
<td>0.6 - 1.8/1000</td>
<td>0.7 - 1.2/1000</td>
<td>2.1/1000</td>
<td>4.5/1000</td>
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Presented by Jacqueline Lim
On the first day of the meeting, Professor Jacob John, presented a wide-ranging comparative analysis of priority setting in public health and the implications for dengue. Professor John’s presentation, set the tone for the sessions that followed.

Looking at a number of public health initiatives over the last century, John noted that each time four key public health questions were posed:

- Is the problem real?
- If it is real, how big an issue is it?
- If it is a big issue, can something be done about it?
- If something can be done, how much will it cost?

John noted that the answers can never be absolute and their interpretation is subject to many biases, including the personal views of those doing the interpretation. However, without exception – regardless of number of deaths or other quantitative measures – a decision to accord high priority seemed to rest invariably on the existence of champions for the cause and an effective technology – vaccine or drug. John argued most strongly that the existence of an effective technology allows the attack on a disease to move from a case-by-case medical approach to a systematic public health assault, and that this is the prerequisite for success.

Professor John’s presentation puts dengue in the context of medical and public health interventions, and draws tight and actionable conclusions from a broad historical context. Both his presentations and those that followed helped to answer some of the very questions raised, and illustrated the growing case for dengue vaccines.

An examination of the investment-case study for the introduction of oral cholera vaccine in Bangladesh was presented. Following on from Prof. John’s presentation, it was argued that, in a world of competing resources, even the existence of an effective technology which allows the launch of the public health approach, success cannot be ensured. It is essential to put together well reasoned arguments based on sound data. The Dengue Vaccine Initiative, in collaboration with ministries of health, will assemble country-specific investment cases for this purpose.

* Advocacy

Advocacy is vital to changing perceptions, creating demand and influencing policies and budgeting decisions. Champions of causes have a valuable role to play in raising awareness at all levels. The Sabin Vaccine Institute brings to the DVI its expertise in advocating prevention and control of neglected tropical diseases and introduction of numerous vaccines. The Global Network for Neglected Tropical Diseases and the Pneumococcal Awareness Council of Experts (PACE) both projects of Sabin have notable successes against lymphatic filariasis, onchocerciasis, schistosomiasis and pneumococcal disease. DVI can build on these achievements in its fight against infectious diseases and learn from countries that already accord a high profile to dengue.

-- Dr. Ananda Amarasinghe, Colombo, Sri Lanka
**BURDEN OF DISEASE**

Responding to Prof. John’s first two questions (Is the problem real? If it is real, how big an issue is it?) speakers emphasized that epidemics are becoming more frequent, and that the rapidly increasing incidence of dengue fever and dengue haemorrhagic fever will certainly continue. Global warming is extending the habitat of the *Aedes aegypti* mosquito vector; rapid population growth increases the size of populations at risk; poverty and growing uncontrolled urbanization increase the likelihood of outbreaks in cities; and increasing travel exposes more people to the risk of infection, with imported cases triggering outbreaks in areas where the disease is not endemic. In less developed regions the urban population will exceed rural populations after 2020 and will continue to grow rapidly. These factors will continue to drive the rise in incidence being seen globally (the rate exceeded 300 per 100,000 population in the Americas in 2010). Through its field studies managed by the lead partner, the International Vaccine Institute (IVI), DVI is working to accumulate high quality data on incidence and burden of disease.

**ESTIMATING AND FORECASTING DEMAND**

Ministries of health and of finance want to know how much a dengue vaccination program will cost. Companies want to know how much vaccine they should plan to supply. Donors want to know what might be expected of them. In studies at the IVI, the potential vaccine demand has been estimated in 54 likely early-adopter dengue-endemic countries (excluding Africa). The estimates demonstrated large potential demand in both the public and private sector...
markets: the upper limit figures for early-adopter countries were about 1.5 billion doses for a three dose schedule over an initial five years after introduction. A detailed study of the potential demand in Brazil showed that the development of effective immunization strategies will be complicated because of the very great potential need associated with catch-up immunization. As a practical exercise, participants were asked to predict whether countries would introduce a dengue vaccine and what priority it would be given, what the likely possible coverage would be, and how long after a vaccine was licensed it would take for countries to introduce the vaccine. Interestingly, in this informal exercise, almost all ministry of health staff argued that dengue would be integrated very quickly and high levels of coverage would be achieved given sufficient supply.

Another DVI consortium partner, the International Vaccine Access Center (IVAC) at the Johns Hopkins University will lead activities related to the financing of dengue vaccine purchase including budget impact analysis and strategic demand forecasting. IVAC will also provide high level support to WHO on regulatory pathways.

The Dengue Vaccine Initiative’s field studies will be conducted in four countries likely to be early adopters of dengue vaccine: Brazil (Salvador), Colombia (Medellin), Thailand (Bang Phae) and Viet Nam (Nha Trang). In addition to undertaking surveillance and collecting serological survey data, studies of cost of illness, willingness to pay, and use of health services will be undertaken. The aim is to provide a complete package of evidence to contribute to the national investment case for dengue vaccine and thus answer Prof. John’s questions.

Another DVI initiative, undertaken by the Fred Hutchinson Cancer Center in Seattle, is to develop a model of the impact of dengue vaccination. This will provide a means to allow ministries of health to see the potential results of various strategies. This work will be part of an initiative of another DVI partner, World Health Organization’s Initiative for Vaccine Research, to coordinate and promote an ongoing international group of modelers.

A series of talks described the national epidemiological situation and preparations for a dengue vaccine in Cambodia, Cook Islands, Indonesia, Malaysia, Philippines, Singapore, and Sri Lanka. The information presented illustrated the enormous heterogeneity of the countries concerned and the complexity of formulating policies. At one end of the spectrum, the reappearance of dengue in Singapore in the past decade surprised the authorities, who had been conducting good surveillance and what appeared to be thorough vector-control activities, and resulted in a rigorous reappraisal by the government of its approaches. This experience demonstrated again the great urgency of having a dengue vaccine.

At the other end of the spectrum, in the Pacific, the extraordinary logistical difficulties in getting vaccines to remote islands were illustrated by the Cook Islands, where it can take up to a month to get vaccines to all the islands (“team members must be good sailors” commented Dr Rangiau Fariu, the Director of Community Health Services). The country had nevertheless successfully introduced new vaccines and drawn lessons from its experiences. Thus challenges such as catch-up immunization, although formidable, can be overcome.
Several themes of issues deserving intensive examination to prepare for dengue vaccine introduction emerged during the meeting. These included national policies (e.g. access to health care), competing priorities, identified demand, costs and benefits, vaccine manufacturing capacity, financing, immunization schedules, monitoring and evaluation, training of health-care staff, and the value of high political commitment, which was evident in many of the countries concerned. Technical aspects included good surveillance data, vaccine safety and efficacy, WHO pre-qualification certification, logistics, improved case management, and better vector control with appropriate resources. Other factors include the length of time needed for preparation, the involvement of stakeholders (and definition of their roles and responsibilities), a multidisciplinary approach, partnerships, good educational materials, and the early gaining of consent and support from community leaders. Advocacy for dengue vaccines was also highlighted, through political leaders and other champions as well as from international entities. Country-specific investment cases would form a vital element in ensuring full political and financial commitments.

Finally, it was recognized that the work has only just started. Much more needs to be done, and many questions remain unanswered. Regional forums would facilitate exchanges of information and experience, and marking international days and other events would show commitment and solidarity. Input into the WHO’s Strategic Advisory Group of Experts on Immunization would contribute towards the formulation of recommendations for dengue vaccine delivery that many countries will rely on. Donors and governments must be persuaded of the value to individuals and families as well as to the state of the introduction of dengue vaccines.

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**Dengue Decision-Making Framework**

For success we need to:

- Seek win-win solution sets through analysis
- Use solution sets in discussions with key constituents
- Refine input assumptions as information shared
- Continually update analyses as information evolves

Dengue averted where willingness overlaps

*Source: Adapted from PneumoADIP/Applied Strategies SDF (2005)*
The mission of the Dengue Vaccine Initiative (DVI) is to encourage the development and use of vaccines to prevent the estimated 50 million dengue cases that occur annually. 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.