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Published by the Alliance for Case Studies for Global Health

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Evolution of a Product Development Partnership: Advancing the Dengue Vaccine -- UPDATE

[NOTE: This is an UPDATE to a case study initially published in 2009. Read the original case study for appropriate context.]

The World Health Organization has called dengue “the most important mosquito-borne viral disease in the world,” citing the fourfold increase since 1970 in the number of countries that have seen cases of dengue hemorrhagic fever, a serious, often deadly form of the disease. Without highly effective vector control, antiviral drugs and a reliable diagnostic test for the early days of infection, the strongest hope for fighting dengue is a vaccine. While a dengue vaccine has been sought since the 1940s, there are now several advanced candidates at a number of developers, and a preeminent international partnership is helping to pave the way.

The Dengue Vaccine Initiative (DVI) evolved in 2009 and 2010 out of the Pediatric Dengue Vaccine Initiative (PDVI). PDVI had successfully begun to mobilize and connect key players worldwide in the quest for a dengue vaccine—planning and conducting international research, convening meetings for consensus-building and creating other channels for collaboration and knowledge-sharing.

The initiative’s evolution grew out of a commitment to find “a different way of doing things, if not a different set of activities,” according to Richard Mahoney, Ph.D., coordinator for policy and access for the Dengue Vaccine Initiative at the International Vaccine Institute (IVI). “We saw that we needed additional capabilities and resources.”

To meet this need, IVI engaged three new partners to help scale-up the skill base devoted to dengue research and vaccine development and introduction: the World Health Organization (WHO), Sabin Vaccine Institute, and International Vaccine Access Center (IVAC) at the Johns Hopkins Bloomberg School of Public Health. Together, the four bring together unique talents into a formidable product development partnership (PDP).

South Korea-based IVI has extensive experience in dengue and leads the DVI consortium. IVI has the chief responsibility for field studies and for making the case for global investment and focal country vaccine introductions. Sabin, one of the world’s leading forces in advocacy for vaccines, leads DVI’s advocacy, coalition development and communications, working to raise awareness of the need for a dengue vaccine and the growing burden of the disease. Hopkins’ IVAC brings to the partnership deep expertise in regulatory affairs and in examining economic factors. IVAC leads the consortium’s vaccine financing activities, such as budget impact analysis and strategic demand forecasting, and supports WHO’s activities in regulatory affairs. WHO’s primary role in the partnership is regulatory training and development of guidance documents, tapping its knowledge of quality control and manufacturing processes for vaccines.

Mahoney sees this initiative’s evolution as indicative of the PDP model maturing over the decade or so that it has existed.

Ciro de Quadros, MD, MPH, executive vice president at Sabin, notes, “No organization in global health can accomplish its goals alone. Public-private partnerships are very important to advance the public health agenda. The four organizations behind the Dengue Vaccine Initiative together bring incredible strength.”

Dagna O. Constenla, MPH, PhD, director of economics and financing for Hopkins’ IVAC, says, “DVI capitalizes on the new environment of accelerated vaccine development and licensure, with unmatched technical knowledge and expertise. DVI leverages a wide range of effective partnerships with the private sector, government—Brazil is a good example—international organizations, academia and others to help assure that dengue vaccines are developed, licensed, recommended and funded.”

Funding the Search for a Dengue Vaccine

A dengue vaccine has not always been a priority in the global health community or among donor agencies. “The approach that DVI is using to successfully build evidence-based demand for dengue vaccines—supporting policy development and providing actionable investment cases for these vaccines to key stakeholders—can help advance dengue vaccines over the next four years,” says Constenla.

Indeed, DVI is now seeing diversification in its funding sources. The Bill & Melinda Gates Foundation continues to support DVI’s work through 2015, as part of its increased commitment overall to developing-nation vaccine initiatives. In early 2011, DVI received unrestricted educational grants from vaccine developers to facilitate discussions among top decision makers about creating the right conditions to make a vaccine widely accessible to countries where dengue is endemic.

A Vaccine, at What Cost?

Because someone previously infected with one of the four dengue virus strains is at greater risk for the more virulent forms of the illness if infected subsequently with a different strain, a successful vaccine must be tetravalent—four vaccines combined. This has raised concerns about the cost of a vaccine in the developing countries where the disease is present. A few vaccine candidates in the later stages of development have shown promise.

To lay the groundwork for quick progress once a vaccine is approved and licensed, DVI and Instituto Butantan in Brazil conducted a cost-of-goods study. The authors conclude that “the vaccine can be made available at a price that most ministries of health in
developing countries could afford.”

Mahoney said, “This study has three points of resonance: first, how manufacturers and a PDP can work together to address pricing questions; second, the role of developing countries in bringing vaccines to the marketplace; and third, how a PDP can act in a professional, rigorous way to bring a vaccine to market.”

**A New Model: Laying the Pathway Prior to Vaccine Approval**

In the long term, the Dengue Vaccine Initiative partners anticipate that the model they are creating will help policy makers develop plans to introduce a vaccine not just for dengue but other diseases as well.

“This is one of the first instances of advocacy for a vaccine that doesn’t exist. As such, it provides an important model for other diseases,” says de Quadros. “For instance, we are learning how we can start motivating a population before a vaccine is introduced.”

Sabin is using all forms of print and electronic media to reach key audiences, from individuals at risk in developing countries to global health policy decision makers. Sabin also has initiated consultations with stakeholders in Asia and Latin America to help lay this groundwork, organizing a regional consultation and other stakeholder meetings.

Despite the explosion in the number of dengue cases—in 2011, Pakistan and the Bahamas experienced their worst recorded outbreaks—there is a lack of published, peer-reviewed studies about the epidemiology of dengue. To lay a foundation for such studies, IVI has worked with WHO to agree on the best methodology and has launched a major study with partners in Colombia and Thailand.

IVI also continues to work, particularly through WHO and IVAC, with Brazil and other countries to prepare the regulatory path for a dengue vaccine’s review and approval.

Says Constenla, “In the long term, we hope to build and communicate the evidence needed for rational global and national dengue vaccine introduction plans, to facilitate the harmonized regulatory procedures for evaluating applications for dengue vaccine clinical trials, licensure and manufacture and to enhance awareness about dengue and the value of dengue vaccines among global and national policy makers, opinion leaders and donors.”

WHO has published new guidelines on developing dengue vaccines, and DVI has held workshops and training sessions to prepare for the expected 2012 results of the lead vaccine candidate, which is being tested by Sanofi Pasteur in a trial in Thailand.

The result of this groundwork will help shape policy issues and strategies for dengue vaccine advocacy in the coming years and will help smooth the introduction, perhaps soon, of a long-sought solution to one of the world’s most rapidly growing infectious disease threats.

*By Heather Jameson*