# Vaccines: The Week in Review 12 September 2011

# Center for Vaccine Ethics & Policy (CVEP)

http://centerforvaccineethicsandpolicy.wordpress.com/

A program of

- Center for Bioethics, University of Pennsylvania http://www.bioethics.upenn.edu/
- The Wistar Institute Vaccine Center http://www.wistar.org/vaccinecenter/default.html
- Children's Hospital of Philadelphia, Vaccine Education Center http://www.chop.edu/consumer/jsp/microsite/microsite.jsp

This weekly summary targets news and events in global vaccines ethics and policy gathered from key governmental, NGO and industry sources, key journals and other sources. This summary supports ongoing initiatives of the Center for Vaccine Ethics & Policy, and is not intended to be exhaustive in its coverage. Vaccines: The Week in Review is now also posted in pdf form and as a set of blog posts at <u>http://centerforvaccineethicsandpolicy.wordpress.com/</u>. This blog allows full-texting searching of some 2,000 content items. Comments and suggestions should be directed to David R. Curry, MS Editor and

Executive Director Center for Vaccine Ethics & Policy david.r.curry@centerforvaccineethicsandpolicy.org

**The International Vaccine Institute (IVI announced the appointment of Dr. Christian Loucq as the organization's next Director General**. Dr. Loucq will take up his new role in November. Ragnar Norrby, chairman of the IVI's board of trustees, commented, "Christian Loucq is well-versed in the management and leadership of private- and public-sector organizations in the vaccine arena, and he has extensive experience in working with public-private partnerships and private collaborations. His distinguished track record and background in global public health and business makes him an ideal leader to effectively set the course for the IVI's continued success and further growth and development as an institute." Most recently, Dr. Loucq was the Director of the Malaria Vaccine Initiative (MVI), a product development partnership based at PATH in the U.S.

Dr. Loucq commented, "I am honored and very enthusiastic to be joining the IVI team as Director General. From research and development to epidemiology, from local manufacturing to access, the IVI has been a pioneering organization in many aspects of vaccinology when applied to preventing infectious diseases among the worlds poorest children. I look forward to working with the IVI team, its board and advisors, the many generous donors, and the IVI's collaborators throughout the world to help the IVI have an even greater impact."

The International Vaccine Institute (IVI) describes itself as "the world's only international organization devoted exclusively to developing and introducing new and improved vaccines to protect the world's poorest people, especially children in developing countries. Established as an initiative of the United Nations Development Programme in 1997, the IVI operates as an independent international organization under a treaty signed by 40 countries and the World Health Organization. The Institute conducts research in 30 countries of Asia, Africa, and Latin America on vaccines against diarrheal infections, bacterial meningitis and pneumonia, as well as Japanese encephalitis and dengue fever, and develops new and improved vaccines, routes of delivery and adjuvants at its headquarters in Seoul, Korea."

The NIH announced results of a study that found that "two doses of the human papillomavirus (HPV) vaccine Cervarix were as effective as the current standard three-dose regimen after four years of follow-up." The results of the study, based on data from a community-based clinical trial of Cervarix in Costa Rica, appeared online Sept. 9, 2011, in the *Journal of the National Cancer Institute*. NIH said the NCI-sponsored Costa Rica Vaccine Trial was designed to assess the efficacy of Cervarix in a community-based setting. Women ages 18 to 25 years were randomly assigned to receive the HPV vaccine or a Hepatitis A vaccine as the control treatment. Although the investigators intended to administer all three doses of the assigned vaccine to all 7,466 women in the study, about 20 percent of the participants received only one or two doses of the HPV or control vaccine. A third of women did not complete the vaccine series because they became pregnant or were found to have possible cervical abnormalities, reasons that would not likely bias the findings.

NIH said that the investigators found that, "after four years of follow up, two doses of the vaccine conferred the same strong protection against persistent infection with HPV 16 and 18 as did the full three-dose regimen. From just a single dose, they also observed a high level of protection, but they are cautious about the long-term efficacy of a single dose because other vaccines of this type usually require a booster dose. Additional studies are needed to evaluate the efficacy of a single dose, as well as the duration of protection for both one and two doses." Aimée R. Kreimer, Ph.D., lead author and investigator in NCI's Division of Cancer Epidemiology and Genetics, commented, "Our study provides evidence that an HPV vaccine program using two doses will work. It may be that vaccinating more women, with fewer doses for each, will reduce cervical cancer incidence more than a standard three-dose program that vaccinates fewer women. The main question will be whether the duration of protection from fewer doses is adequate."

http://www.nih.gov/news/health/sep2011/nci-09.htm

The **MMWR Weekly for September 9, 2011** / Vol. 60 / No. 35 includes: - <u>Maternal and Infant Outcomes Among Severely Ill Pregnant and Postpartum Women</u> with 2009 Pandemic Influenza A (H1N1) --- United States, April 2009--August 2010 - <u>Swine-Origin Influenza A (H3N2) Virus Infection in Two Children --- Indiana and</u> <u>Pennsylvania, July--August 2011</u> <u>http://www.cdc.gov/mmwr/pdf/wk/mm6035.pdf</u>

WHO released a new issue of GIN (Global Immunization News) dated 31 August 2011, available at: <a href="http://www.who.int/entity/immunization/GIN\_August\_2011.pdf">http://www.who.int/entity/immunization/GIN\_August\_2011.pdf</a>

The **Weekly Epidemiological Record (WER) for 9 September 2011**, vol. 86, 37 (pp 401–416) includes: Revised recommendations for yellow fever vaccination for international travelers; Performance of acute flaccid paralysis (AFP) surveillance and incidence of poliomyelitis, 2011

http://www.who.int/entity/wer/2011/wer8637.pdf

#### Twitter Watch

A selection of items of interest from a variety of twitter feeds associated with immunization, vaccines and global public health. This capture is highly selective and by no means intended to be exhaustive.

#### GAVIAlliance GAVI Alliance

Global rollout of pneumococcal <u>#vaccine</u> is underway across three continents.650,000 future deaths can be averted by 2015! <u>http://ht.ly/6qIwX</u>

#### PublicHealth APHA

Health impact assessments essential for solving nation's health problems, says National Research Council report: <u>goo.gl/WCsnI</u>

#### Eurovaccine ECDC Eurovaccine

RT <u>@hpscireland</u>: Over 86% of measles cases in current outbreak are in Dublin. Ensure kids are vaccinated w/ 2 MMR doses <u>bit.ly/rsFLOI</u>

#### NIAIDNews NIAID News

A new <u>#malaria</u> <u>#vaccine</u> strategy? Results of a NIAID clinical trial and follow-up animal studies, and what comes next: <u>go.usa.gov/09e</u>

#### mrcglobal MRC Global Health

Do u have an innovative idea to strengthen <u>#public</u> & <u>#political</u> support for <u>#vaccines</u> in LMICs? www.vaccinechallenge.org

<u>HIVEnterprise</u> HIVVaccineEnterprise by AIDSvaccine AIDS Vaccine 2011 (#AIDSVax11) opens 12 Sept. in Bangkok - will present the latest advances in vaccine development and testing

## <u>Journal Watch</u>

[Editor's Note]

*Vaccines: The Week in Review* continues its weekly scanning of key journals to identify and cite articles, commentary and editorials, books reviews and other content supporting our focus on vaccine ethics and policy. *Journal Watch* is not intended to be exhaustive, but indicative of themes and issues the Center is actively tracking. We selectively provide full text of some editorial and comment articles that are specifically relevant to our work. Successful access to some of the links provided may require subscription or other access arrangement unique to the publisher. If you would like to suggest other journal titles to include in this service, please contact David Curry at: david.r.curry@centerforvaccineethicsandpolicy.org

### **Annals of Internal Medicine**

September 6, 2011; 155 (5) http://www.annals.org/content/current [No relevant content]

#### **British Medical Bulletin**

Volume 99 Issue 1 September 2011 http://bmb.oxfordjournals.org/content/current [No relevant content]

#### **British Medical Journal**

10 September 2011 Volume 343, Issue 7822 http://www.bmj.com/content/current

# Analysis

# Evidence of comparative efficacy should have a formal role in European drug approvals

Corinna Sorenson, Huseyin Naci, Jonathan Cylus, Elias Mossialos BMJ 2011;343:doi:10.1136/bmj.d4849 (Published 6 September 2011) *Extract* 

Despite methodological concerns, comparative efficacy evidence should be required at the time of drug approval, says Corinna Sorenson and colleagues, to allow patients, clinicians, and other healthcare decision makers to determine whether a new drug is superior, equivalent, or inferior to its existing alternatives

Manufacturers of new drugs need to demonstrate that their products are efficacious and safe for a defined group of patients to obtain market approval. However, demonstrating these outcomes relative to existing therapies is required by regulators only when use of placebo is deemed unethical. 1 2 Regulators, clinicians, patients, and payers therefore often lack the necessary information to distinguish between available medicines in terms of their comparative therapeutic value and safety.

Comparative efficacy evidence at the time of drug approval is important, and there are methodological tools available to generate such information. When one or more treatment alternatives are available, demonstrating lack of inferiority through comparative assessment should be a formal requirement, and there are ways to support this objective in European drug licensing.

#### Need for comparative efficacy evidence

When a drug comes to market, evidence on the comparative risks and benefits is needed to help regulatory authorities to safeguard public health from inferior and unsafe treatments, to ensure that health technology assessment agencies and payers make funding decisions based on the best available evidence of different treatments, and to aid clinicians' and patients' understanding of what therapies work best and their appropriate position in the treatment pathway. 3 However, comparative assessment (box 1) is often conducted or made available only once a therapy is already on the market. This is partly because pre-marketing comparative efficacy studies entail potential uncertainty and risk for manufacturers, as failure to demonstrate a therapeutic advantage over older, and less costly, alternatives may affect drug sales or result in a drug not being approved. 2 ...

# **Clinical Infectious Diseases**

Volume 53 Issue 7 October 1, 2011 http://www.journals.uchicago.edu/toc/cid/current [Reviewed last week]

#### Cost Effectiveness and Resource Allocation

(accessed 11 September 2011) http://www.resource-allocation.com/ [No new relevant content]

#### **Emerging Infectious Diseases**

Volume 17, Number 9–September 2011 http://www.cdc.gov/ncidod/EID/index.htm [Reviewed earlier; No relevant content]

#### **Health Affairs**

September 2011; Volume 30, Issue 9 *The New Urgency To Lower Costs* <u>http://content.healthaffairs.org/content/current</u> [No relevant content]

#### Health Economics, Policy and Law

Volume 6 - Issue 04 - 01 October 2011

# http://journals.cambridge.org/action/displayIssue?jid=HEP&tab=currentissue

# Articles

# Searchers vs surveyors in estimating the monetary value of a QALY: resolving a nasty dilemma for NICE

Rachel Baker, Sue Chilton, Cam Donaldson, Michael Jones-Lee, Emily Lancsar, Helen Mason, Hugh Metcalf, Mark Pennington and John Wildman *Abstract* 

Recently, for many health economics researchers, empirical estimation of the monetary valuation of a quality-adjusted life year (QALY) has become an important endeavour. Different philosophical and practical approaches to this have emerged. On the one hand, there is a view that, with health-care budgets set centrally, decision-making bodies within the system can iterate, from observation of a series of previous decisions, towards the value of a QALY, thus searching for such a value. Alternatively, and more consistent with the approach taken in other public sectors, individual members of the public are surveyed with the aim of directly eliciting a preference-based – also known as a willingness-to-pay-based (WTP-based) – value of a QALY. While the former is based on supply-side factors and the latter on demand, both in fact suffer from informational deficiencies. Sole reliance on either would necessitate an acceptance or accommodation of chronic inefficiencies in health-care resource allocation. On the basis of this observation, this paper makes the case that in order to approach optimal decision making in health-care provision, a framework incorporating and thus, to a degree, reconciling these two approaches is to be preferred.

# Social preferences for the inclusion of indirect benefits in the evaluation of publicly funded health services: results from an Australian survey John McKiea and Jeff Richardsona

# Abstract

The inclusion of both monetary and non-monetary indirect benefits in economic evaluations of public health programmes and services can have significant distributive effects between patient groups. As a result, some patients may be advantaged and others disadvantaged for reasons not directly related to health outcomes or (direct) treatment costs. In pluralistic democracies, there is a case for consulting the community on the fairness of policies that have such distributive implications. This paper reports the results of two pilot studies aimed at uncovering the preferences of the Australian public for the inclusion of indirect benefits in the evaluation of services for its national health scheme, Medicare. The initial survey found some support for taking account of nonmonetary indirect benefits - for example, the social contribution made by parents of young children and carers of elderly relatives. By contrast, there was little support for giving high taxpayers priority access to general Medicare services, to life-saving organ transplants, or to very costly drugs, despite the indirect social benefits of doing so. However, such support increased significantly in the follow-up study when the outcomes were characterised as certain, identifiable and health related, and the opportunity costs of failing to take account of indirect benefits were made very clear. The follow-up survey provided evidence of public scepticism about the willingness or ability of government to use additional tax receipts for socially beneficial purposes, and/or a preference for programmes and services that focus on health rather than welfare more generally.

# **Human Vaccines**

Volume 7, Issue 9 September 2011 http://www.landesbioscience.com/journals/vaccines/toc/volume/7/issue/8/ [Reviewed last week]

# **International Journal of Infectious Diseases**

Volume 15, Issue 9 pp. e583-e654 (September 2011) http://www.sciencedirect.com/science/journal/12019712 [Reviewed last week]

# JAMA

September 7, 2011, Vol 306, No. 9, pp 907-1044 http://jama.ama-assn.org/current.dtl [No relevant content]

# **Journal of Infectious Diseases**

Volume 204 Issue 7 October 1, 2011 http://www.journals.uchicago.edu/toc/jid/current [Reviewed last week]

# The Lancet

Sep 10, 2011 Volume 378 Number 9795 p961 - 1048 http://www.thelancet.com/journals/lancet/issue/current *Editorial* 

# Time for action in New York on non-communicable diseases

The Lancet

Preview

A major opportunity to advance global health is in danger of being lost. On Sept 19–20, heads of states and governments will gather in New York, NY, USA, at the UN High-Level Meeting on Non-communicable Diseases (NCDs) to approve a political statement on responding to the global NCD crisis. These diseases, principally cardiovascular diseases, cancer, diabetes, and chronic respiratory diseases, are responsible for two-thirds of the 57 million deaths worldwide each year, with four of five NCD deaths occurring in low-income and middle-income countries; at least half these deaths are readily preventable.

# The Lancet Infectious Disease

Sep 2011 Volume 11 Number 9 p651 - 720 http://www.thelancet.com/journals/laninf/issue/current [Reviewed earlier]

# Medical Decision Making (MDM)

July/August 2011; 31 (4)

http://mdm.sagepub.com/content/current [Reviewed earlier]

#### Nature

Volume 477 Number 7363 pp131-244 8 September 2011 http://www.nature.com/nature/current\_issue.html [No relevant content]

#### **Nature Medicine**

September 2011, Volume 17 No 9 http://www.nature.com/nm/index.html *Editorial* 

# Get it together

Nature Medicine 17, 1021 (2011) doi:10.1038/nm0911-1021 Published online 07 September 2011 Global health programs have made great strides in the last ten years, mobilizing billions

of dollars to provide life-saving drugs and immunizations to people in resource-poor settings. But these myriad initiatives need to get in step to improve integration of healthcare delivery.

## **New England Journal of Medicine**

September 8, 2011 Vol. 365 No. 10 http://content.nejm.org/current.shtml

# Perspective

# HIV Vaccine Development — Improving on Natural Immunity

Margaret I. Johnston, Ph.D., and Anthony S. Fauci, M.D. N Engl J Med 2011; 365:873-875<u>September 8, 2011</u> [Free full text]

Although a number of methods of preventing infection with the human immunodeficiency virus (HIV) have proven effective to varying degrees, it is generally agreed that a safe and effective vaccine against HIV infection would be a critical component of a highly effective prevention toolkit for controlling and ultimately ending the global AIDS pandemic. For nearly all important pathogens for which effective vaccines have been developed, such as smallpox, measles, and poliovirus, there exists a natural model of protection: the immune response to the pathogen ultimately clears the microbe from the body and confers durable protection against reinfection. Under these circumstances, the human immune system has already provided us with proof of the concept that it can generate a protective response. This fact has led to a fundamental tenet of vaccinology: the best way to develop an effective vaccine is to design a candidate that mimics infection and induces responses akin to natural immunity.

Unfortunately, this lesson does not apply to HIV infection. We have known since the mid-1980s that the body's natural immune response to HIV infection is completely inadequate. A "natural" immune response that might adequately control HIV infection

does not occur at all, occurs too rarely, is too weak, or is too slow to begin. Thus, a key goal for an effective HIV vaccine is to induce in the recipient a response that differs qualitatively, quantitatively, or both from that induced by natural infection — a response that has been referred to as "unnatural immunity."1

Although an HIV-vaccine candidate was recently shown to be modestly protective, it induced neither broadly neutralizing antiserum nor broadly reactive cytotoxic T-cell responses against HIV. This finding raises the possibility that a modest degree of protection against HIV acquisition could be mediated by non-neutralizing mechanisms for example, antibody-dependent cell-mediated cytotoxicity, antibody-dependent cellmediated viral inhibition, or other responses not classically associated with vaccine efficacy.2 Nonetheless, with most viral infections, the appearance of antibodies, particularly neutralizing antibodies, correlates closely with clearance of the virus and subsequent protection from reinfection. Thus, induction of neutralizing antibodies has served as the gold standard for vaccine-induced protection against infection — and is an appropriate goal for HIV infection as well, given that passive infusion of several broadly neutralizing antibodies completely prevented virus acquisition in nonhuman primate models of AIDS.<sup>3</sup> Although non-neutralizing antibody functions appeared to contribute somewhat to protection in this model, and although conserved regions of internal proteins could serve as important vaccine targets, an HIV vaccine that results in the production of broadly neutralizing antibodies before or very soon after exposure to HIV is likely to be highly effective. Since HIV infection does not naturally induce broadly neutralizing antibodies, a key challenge is inducing such antibodies.

Neutralizing antibodies generated during HIV infection are mostly directed toward exposed, highly variable portions of the HIV envelope protein on the viral particle. Antibodies found early in the course of HIV infection are directed at the infecting viral strain, which rapidly evolves to escape recognition. In contrast, antibodies that neutralize a broad array of HIV strains — broadly neutralizing antibodies — are directed against highly conserved regions of the envelope that are essential for viral entry into the host cell. Unfortunately, these conserved sites are recessed, hidden by glycans, partially embedded in the viral membrane, or otherwise relatively inaccessible to recognition by the immune system. For these reasons, broadly neutralizing antibodies are rarely found in the serum of acutely infected persons. When they do appear, they are detected at least 1 to 2 years after initial infection and do not seem to be clinically relevant.<u>4</u>

An important challenge for HIV vaccinologists is to design vaccines that induce these unnatural immune responses. The application of new research tools to the study of broadly neutralizing antibodies is helping to guide the design of vaccines that might induce such antibodies. Until recently, the body was thought to be incapable of producing these antibodies; only a few monoclonal antibodies that were broadly neutralizing had been found, and rarely were they derived from the B cells of HIV-infected patients. However, with the utilization of extremely-high-throughput screening of B-cell clones derived from HIV-infected persons, the rapid cloning of their immunoglobulin genes, and characterization of the resulting monoclonal antibodies. In this regard, the ability to screen tens of millions of B-cell clones for HIV-envelope specificity has allowed researchers to isolate additional broadly neutralizing monoclonal antibodies.

and precisely identify their target epitopes on the HIV envelope (see <u>figure</u>HIV-1 Epitopes Targeted by Broadly Neutralizing Human Monoclonal Antibodies.).

A recent research focus has been on "structure-based vaccine design" — that is, applying knowledge of the crystallographic structure and conformation of the HIV-envelope epitope in the context of the binding site of a broadly neutralizing monoclonal antibody to design a vaccine that effectively presents that epitope in its relevant conformation to the immune system. Crystallographic studies have revealed that broadly neutralizing and non-neutralizing antibodies can bind to the same conserved region of the envelope in similar but subtly different ways. <u>5</u> Thus, determining how to replicate the precise three-dimensional conformation of the HIV-envelope epitope as it resides in the antibody binding site will prove challenging. One approach being actively pursued is scaffolding the desired epitope onto an exposed portion of a soluble or membrane-associated protein.

However, producing an antibody with high avidity to the highly conserved regions of the HIV envelope may prove to be more complex than simply presenting the desired envelope epitope to the immune system. All potent broadly neutralizing antibodies that have been described to date have one or more unusual structural features that may result only from years of chronic viral infection and exposure to viral antigen. These structural features appear to arise through a complex evolutionary process, referred to as "somatic hypermutation," which over time generates B cells that produce antibodies of increasingly higher avidity. Whether a B cell must undergo a long evolutionary process to produce a broadly neutralizing antibody against HIV remains uncertain. If such a process were required, that would pose a sobering challenge to HIV vaccinologists. Researchers are now dissecting the steps in this evolutionary process to understand how B cells evolve for the production of broadly neutralizing HIV antibodies and to design novel vaccines that might accelerate that process.

Thus, we have learned that the body is indeed capable of producing potent, broadly neutralizing antibodies; however, it does not do so readily or efficiently. We are optimistic that the tools of modern science will enable us to develop HIV vaccines that induce effective immune responses that do better than natural immunity and prevent HIV infection.

**Global Noncommunicable Diseases — Lessons from the HIV–AIDS Experience** K.M. Venkat Narayan, M.D., Mohammed K. Ali, M.B., Ch.B., Carlos del Rio, M.D., Jeffrey P. Koplan, M.D., and James Curran, M.D.

N Engl J Med 2011; 365:876-878 <u>September 8, 2011</u> [Free full text: <u>http://www.nejm.org/doi/full/10.1056/NEJMp1107189</u> ]

#### **The Pediatric Infectious Disease Journal**

September 2011 - Volume 30 - Issue 9 pp: A7,731-820,e155-e178 http://journals.lww.com/pidj/pages/currenttoc.aspx [No relevant content]

#### Pediatrics

September 2011, VOLUME 128 / ISSUE 3 http://pediatrics.aappublications.org/current.shtml [Reviewed last week]

# Pharmacoeconomics

September 1, 2011 - Volume 29 - Issue 9 pp: 731-821 http://adisonline.com/pharmacoeconomics/pages/currenttoc.aspx [Reviewed earlier]

## PLoS One

[Accessed 11 September 2011] http://www.plosone.org/article/browse.action;jsessionid=577FD8B9E1F322DAA533C413 369CD6F3.ambra01?field=date [No new relevant content]

# **PLoS Medicine**

(Accessed 11 September 2011) http://www.plosmedicine.org/article/browse.action?field=date Informing the 2011 UN Session on Noncommunicable Diseases: Applying

Lessons from the AIDS Response

Peter Lamptey, Michael Merson, Peter Piot, K. Srinath Reddy, Rebecca Dirks Policy Forum, published 06 Sep 2011

doi:10.1371/journal.pmed.1001086

Summary Points

- The September 2011 UN High-Level Meeting on Noncommunicable Diseases provides an opportunity for the international community and national stakeholders to raise awareness and launch an effective global response to noncommunicable diseases (NCDs).

- Valuable policy lessons have been learned in the control of AIDS that can help inform the global dialogue when designing a NCD response in developing countries.

- The AIDS response demonstrates successes in advocacy and resource mobilization, priority setting, coalition building, strong national and community leadership,

strengthening of community health infrastructures, and health systems strengthening.

- Weaknesses of the AIDS response to avoid when building a NCD response include creation of stove-pipe vertical programs, ineffectiveness of prevention efforts, and inefficient and uncoordinated use of resources.

- The lessons learned in the global response to AIDS are relevant to the likely outcomes of the UN High-Level Meeting on NCDs: (1) improvement in advocacy and recognition of the NCD burden, (2) greater attention in national planning and resource allocation, (3) a longer-term investment of donors, and (4) greater emphasis on strengthening health systems.

# Proceedings of the National Academy of Sciences of the United States of America

(Accessed 11 September 2011) http://www.pnas.org/content/early/recent [No new relevant content]

# Science

9 September 2011 vol 333, issue 6048, pages 1345-1536 http://www.sciencemag.org/current.dtl [No relevant content]

# **Science Translational Medicine**

7 September 2011 vol 3, issue 99 http://stm.sciencemag.org/content/current [No relevant content]

# **Tropical Medicine & International Health**

September 2011 Volume 16, Issue 9 Pages 1043–1189 http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1365-3156/currentissue [Reviewed earlier]

# Vaccine

http://www.sciencedirect.com/science/journal/0264410X

# Volume 29, Issue 42 pp. 7219-7284 (23 September 2011) The Development of Dengue Vaccines

Edited by Beth-Ann Coller, Alan D.T. Barrett and Stephen J. Thomas Introduction Pages 7219-7220 Beth-Ann Coller, Alan D.T. Barrett, Stephen J. Thomas The pathogenesis of dengue Pages 7221-7228 Jamie Whitehorn, Cameron P. Simmons From research to phase III: Preclinical, industrial and clinical development of the Sanofi Pasteur tetravalent dengue vaccine Pages 7229-7241 Bruno Guy, Beatrice Barrere, Claire Malinowski, Melanie Saville, Remy Teyssou, Jean Lang Development and clinical evaluation of multiple investigational monovalent DENV vaccines to identify components for inclusion in a live attenuated tetravalent DENV vaccine Pages 7242-7250 Anna P. Durbin, Beth D. Kirkpatrick, Kristen K. Pierce, Alexander C. Schmidt, Stephen S. Whitehead Development of DENVax: A chimeric dengue-2 PDK-53-based tetravalent vaccine for protection against dengue fever Pages 7251-7260

Jorge E. Osorio, Claire Y.-H. Huang, Richard M. Kinney, Dan T. Stinchcomb

Development of dengue DNA vaccines Pages 7261-7266 Janine R. Danko, Charmagne G. Beckett, Kevin R. Porter The development of recombinant subunit envelope-based vaccines to protect against dengue virus induced disease Pages 7267-7275 Beth-Ann G. Coller, David E. Clements, Andrew J. Bett, Sangeetha L. Sagar, Jan H. Ter Meulen Next generation dengue vaccines: A review of candidates in preclinical development Pages 7276-7284 Julia Schmitz, John Roehrig, Alan Barrett, Joachim Hombach

# Volume 29, Issue 41 pp. 7115-7218 (22 September 2011) Vaccine Technology III: Advances in Vaccine Technology

Value in Health July 2011, Vol. 14, No. 5 <u>http://www.valueinhealthjournal.com/home</u> [No relevant content]