National Vaccine Advisory Committee

February 2nd, 2016

Challenges for Global Vaccines Development

Adel Mahmoud, M.D., Ph.D.
Princeton University

Vaccine Discovery & Development

Exciting turn of the Century

- Pneumo and Mening Conjugate
- Rotavirus
- HPV and HPV 9
- Cell-based flu
- Mening B
- Combination vaccines
- New Adjuvants

Lessons learned from Ebola

- If *just one* candidate Ebola vaccine had been tested for safety and immunogenicity in humans before the 2013 outbreak in West Africa, thousands of lives and billions of dollars could have been saved

- At least *seven* Ebola candidate vaccines got stuck in animal studies and did not move forward to human clinical trials for lack of money

- Failure to develop an Ebola vaccine represents a *collective failure* that cannot be repeated

- If vaccine manufacturers are not going to invest in the development of vaccines with small market potential, others will have to step in

The New York Times

THE WALL STREET JOURNAL.

REUTERS

BUSINESS INSIDER

CIDRAP News

FierceVaccines

The Opinion Pages | EDITORIAL

The Ebola Vaccine We Needed

By THE EDITORIAL BOARD AUG. 14, 2015

About 27,000 people in West Africa have been infected with the Ebola virus and more than 11,000 of them have died since the outbreak began last year. Many could have been saved if an effective vaccine had been available. But the world relies on drug companies to create new vaccines and medications, and they have no financial incentive to do so for diseases that mostly affect poor countries. Clearly, the world needs a better mechanism for vaccine development.

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

JULY 23, 2015

Establishing a Global Vaccine-Development Fund

Stanley A. Plotkin, M.D., Adel A.F. Mahmoud, M.D., Ph.D., and Jeremy Farrar, M.D., Ph.D.

As the Ebola epidemic in West Africa continues, albeit at a much lower level than it reached in the spring, we still lack a vaccine that has been shown to be safe and effective. There has been no shortage of basic research: by 2009, at least seven Ebola vaccines had been tested in monkeys, with encouraging results.[1] But before the West African epidemic, only one of these vaccine candidates was tested in healthy humans, in phase 1 trials to evaluate its safety, and it was subsequently abandoned.[2] No vaccine had reached the later processes that would lead to licensure, and none was available in sufficient supply to be deployed in an emergency. Unfortunately, the same applies to many other infections: vaccines against them are not available because collectively we have not been willing or able to invest in the costly and complex development process that would be required to establish safety and immunogenicity, at a minimum.

Vaccine development is facing a crisis for three reasons: the complexity of the most challenging targets, which necessitates substantial investment of capital and human expertise; the diminishing numbers of vaccine manufacturers able to devote the necessary resources to research, development, and production; and the prevailing business model, which prioritizes the development of vaccines with a large market potential. We consider an international vaccine-development fund to be urgently needed to provide the resources and the momentum to carry vaccines from their conception in academic and government laboratories and small biotechnology firms to development and licensure by industry. Such a fund would enable basic scientists to move candidate vaccines from the laboratory through the so-called valley of death — the critical steps after good preclinical data have been obtained, comprising manufacture to Food and Drug Administration standards, a phase 1 clinical trial, and proof of concept in terms of protective immune responses. This support would permit efficacy assessment to begin — and thereby avert a repetition of the Ebola crisis.

Much attention has appropriately been directed at major disease targets such as human immunodeficiency virus (HIV), tuberculosis, and malaria, for which organizations such as the National Institutes of Health, the Bill and Melinda Gates Foundation, and the Wellcome Trust are providing considerable financial sup-

Challenges for vaccine development

- Reduced investments in vaccine R&D by industry
- Lack of *meaningful* market incentives to develop vaccines with small market potential
- Consolidation in industry shifts vaccine discovery to organizations less able to finance early-stage research
- Biotechs face a daunting challenge raising the capital to get candidate vaccines through the *Valley of Death*
- Funding chasm impedes candidate vaccines from being tested for safety and immunogenicity in humans

Global health and security

- Disease outbreaks are threats to global health, regional stability and security
- For every major disease and infection for which we have a vaccine, there are *at least two others* for which we don’t
- The science and technology are there, the resources are not
- An investment of $2 billion a year could lead to the development of several new vaccines that could cut global health risks and reduce disease burden worldwide

Why do we need a new fund?

- Fundamental challenges face the development of new vaccines. These are growing in significance and can no longer be ignored
- The lack of resources at critical stages of the early development process is the key rate-limiting factor
- A relatively modest, strategic investment upfront could save thousands of lives and billions of dollars down the line
- The VSV-Ebola vaccine trial provides proof of concept that we can accelerate the development of new vaccines
- The fund will enable a multitude of future vaccines to be verified as safe and effective in humans, accelerating the public health response to future outbreaks

Global Vaccine Development Fund
Overview

- Establish a $2 billion vaccine development fund to accelerate the development of new and improved vaccines

- Provide the resources to move candidate vaccines from the laboratory through the *Valley of Death*
  - The critical period after obtaining good preclinical data
  - Clinical lot manufacture to international regulatory standards
  - Phase 1 clinical trial
  - Proof of concept in phase 2 studies
  - Production of a small stockpile that could be rapidly expanded in case of an outbreak, allowing a *limited* phase 3 evaluation

- Fund will not finance discovery research, nor large phase 3 trials needed for licensure and sale

Global Vaccine Development Fund
Overview

- Source of funds: Donor governments, multilateral banks, pharmaceutical industry, foundations, non-traditional sources
- Eligibility: Organizations engaged in vaccine development, *including governmental laboratories and biotechs*
- Rigorous scientific review of proposals by an independent panel of experts
- Performance-based model will emphasize results, transparency, and accountability; independent auditors will monitor and assess grant performance
- Streamlined governance structure, medium-sized board, majority of voting members representing donors

Positioning and comparative advantage

- The proposed fund will be an independent, global,stand-alone **public-private partnership** with the sole mandate of accelerating vaccine development globally for new and emerging infectious diseases, *as well as diseases and infections endemic in developing countries for which there is low market potential*

- The fund fills a strategic financial gap in the international architecture to fight infectious diseases

- There are multibillion dollar funds for:
  - Discovery research (NIH, philanthropy)
  - Domestic development funds
  - Prevention, treatment, care and support for specific infectious diseases (Global Fund, UNITAID)
  - Purchase and delivery of childhood vaccines (GAVI)

- There is no global fund to finance vaccine development

Positioning and comparative advantage

- The fund fits within the framework of
  - The Global Health Security Agenda (GHSA)
  - The Policy Recommendations to the G7 of the Independent Expert Group convened post-Ebola
  - The WHO blueprint for R&D preparedness and rapid research response

- Fund is additive to NIH and BARDA efforts to develop new vaccines, and complementary to GAVI
  - NIH funds basic and discovery research and vaccine R&D through the Vaccine Research Center (VRC)
  - BARDA manages the procurement and advanced development of domestic medical countermeasures for chemical, biological, radiological and nuclear agents
  - GAVI procures and delivers childhood vaccines but does not conduct vaccine R&D

Next steps

- Consult with international partners and other stakeholders
- Develop a prospectus and action plan
- Set up a working group with a secretariat
- World Economic Forum Summit at Davos 2016
- G7 summit in Japan 2016

Who List

Initial list of disease priorities needing urgent R&D attention comprises

1. Crimean Congo haemorrhagic fever
2. Ebola virus disease
3. Marburg
4. Lassa fever
5. MERS and SARS coronavirus diseases
6. Nipah and
7. Rift Valley fever

Designated serious:

1. Chikungunya
2. SFTS
3. Zika

GVDF Updated List

Ebola, Lassa, Marburg

SARS, MERS

Crimean-Congo hemorrhagic fever

Chikingunya , Zika, Nipah

Hepatitis E virus

EV71, EV68 and CA16

Paratyphoid A

West Nile virus

Rift Valley fever

Plague (Yersinia pestis)