# on Vaccine Research

## Abstracts of Invited Presentations

### S1 Promoting Vaccine Discovery: A Vision for the Future

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Substantial challenges must be overcome to achieve the full potential that advances in biomedical technology offer. Priorities for vaccine development and evaluation should consider global health impact; thus, political will must be generated to facilitate development of new or improved vaccines to prevent diseases that currently predominate in the developing world like malaria, dengue, and tuberculosis, as well as diseases that continue to cause illness, sequelae, and death globally like influenza, *Streptococcus pneumoniae*, hepatitis C, respiratory syncytial virus, parainfluenza, and group A streptococcus. Prevention of cancer through immunization has already been demonstrated by hepatitis B vaccine programs and the potential for prevention of a wide array of other cancers and possibly other degenerative diseases has a solid basis for optimism. Key issues facing us include ensuring our ability to optimize the safety of vaccines and to document and communicate the benefits and risks of vaccines; as more vaccines become available, public confidence in immunization programs will be crucial. Balancing the need for society to appropriately value vaccines, we need to find ways to make them more affordable, particularly where needed most within developing countries. As the capacity to prevent more diseases increases, it is already becoming critical to limit the number of injections. While combining antigens for safe and effective parenteral delivery is the acute answer, for many vaccines the more logical approach will be through mucosal delivery. Ultimately, priority-driven (based on public health impact) and expedited vaccine development will depend on a dynamic and effective collaboration between government, the vaccine industry, academia, and global and community organizations and foundations.

### S2 Experimental Challenge Models to Test the Efficacy of Enteric, Respiratory, and Other Vaccines in Volunteers—Rationale, Advantages, and Limitations

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Experimental challenge models in healthy volunteers have been developed for several infectious diseases, including those caused by bacteria, viruses, and parasites. These models have been applied to test the efficacy of vaccine candidates and other biologics, to verify pathogenicity, and to delineate mechanisms of pathogenesis. Several criteria must be met to justify a human challenge model; these include characteristics of the disease, the study design, and the volunteer. The disease must be one for which the natural history and spectrum of illness are known; effective treatment is available; the means of transmission and containment are known; the incubation period is short; and for which there are no long-term sequelae. The study design must be rigorous in that endpoints must be defined meticulously, timing of treatment must be precise, and statistical power must be adequate to show meaningful differences. Examples of diseases for which a challenge model has contributed to vaccine evaluation include the following: cholera, typhoid fever, influenza, gonorrhea, and malaria. Challenge models have in some cases expedited the development of potentially effective vaccines and, in others, led to the rapid rejection of ineffective vaccines. Challenge models are limited if the model fails to reproduce natural infections because of differences in the characteristics of participants compared to those at risk of natural infection or if the experimental challenge overwhelms protective immunity.

### S3 Evaluating the Performance of New Vaccines: Efficacy vs. Effectiveness

*John Clemens, MD,* NICHD, NIH*

Despite the profusion of promising new vaccines against illnesses prevalent in developing countries, uncertainties about the balance between costs and benefits of new vaccines have retarded their use in public health practice. Conventional prelicensure trials of vaccine protection can exacerbate these uncertainties by focusing on measurement of vaccine efficacy, or the performance of a vaccine under idealized conditions. Vaccine effectiveness trials provide a more pragmatic perspective by addressing the performance of vaccine under the ordinary conditions of a public health program, by capturing direct as well as indirect effects of vaccination, and by comprehensively addressing outcomes of public health concern. The use of effectiveness trials should enable more rational triaging of new vaccines for developing countries, and may accelerate the introduction of new vaccines into public health practice.

### S4 Challenges in HIV Vaccine Development: Institutional Roles and Response

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The development of safe and effective HIV vaccines requires a complex combination and appropriate balance of activities, including research, product development, and public policy. The requisite expertise, experience, and capability resides within several federal government agencies, and among partners including industry, academia, and intergovernmental and non-governmental organizations. Currently, vaccine development is hampered by fragmented, incomplete, and overlapping mandates and roles of key players. Therefore, a strategic approach to HIV vaccine development is needed, based upon a coherent, milestone-driven process for all stages of development, taking into account the comparative advantages of key partners.