

Help wanted—to immunize the world

For the past two centuries, vaccines have triumphed over communicable diseases with remarkable efficacy. Yet numerous obstacles have stalled us in our march to eradicate major infections. Objections against vaccination in affluent societies are starting to threaten 'herd immunity', which is essential for protection from preventable diseases such as whooping cough and measles. In contrast, impoverished societies are unable to successfully obtain or deliver vaccines even when they become available. In addition, obliteration of scourges such as AIDS, malaria and tuberculosis is hindered by the lack of effective vaccines. These problems stem from a common cause: the lack of sufficient incentive for the development of new vaccines. In this issue of *Nature Immunology*, three eminent authors, Gustav Nossal, Myron Levine and Christine Grady, discuss the current climate for vaccine research and development (R&D) and its application to, and implications for, the general population.

The glaring lack of effective vaccines to prevent certain diseases and the emergence of new threats such as severe acute respiratory syndrome and bioterrorism have renewed the call for more vaccine R&D. Such R&D, not unlike that of other drugs, is hugely expensive. However, vaccines do not rank high on the list of priorities for pharmaceutical companies. They do not make good business sense: vaccination 'eliminates' the customer base. Many potential vaccines, such as for HIV, are required predominantly by people who cannot afford to pay, and vaccines production may expose pharmaceutical companies to litigation. Although pharmaceutical companies have not abandoned vaccine R&D, market forces are not conducive to their participation.

However, the world cannot afford to sit by and let a *laissez-faire* economy dictate its priorities. Research and development are essential for resolving current problems with vaccination programs. Vaccination is a unique medical intervention, calling for healthy members of the society to understand the idea of a 'greater good' served by putting individuals at a minimal 'acceptable' risk. Most people agree that the benefits far outweigh the risks, whereas the consequences of not vaccinating are intolerably severe. Nevertheless, in a modern society that values individual rights, educating the public can only achieve partial success. To alleviate fears and to encourage participation, even safer vaccines are needed, which requires R&D. In contrast, vaccination programs in impoverished societies face different hurdles. Apart from the issue of affordability, authorities face significant logistical difficulties in reaching the needy population. Although strategic planning and infrastructure improvements are important, many of the problems are inherent to the vaccines and may be eliminated with new designs, such as those that avoid restrictive storage conditions and require only a single, rather than multiple, administration. This improvement also relies on R&D. Most importantly, that trio of global killers, AIDS, malaria and tuberculosis, simply need viable vaccines—another essential arena for more R&D.

The world certainly has not been 'sitting by'. As Nossal discusses in his commentary, such an important and urgent endeavor requires the intervention of national governments, with significant help from generous individual and corporate philanthropists. Nonprofit organizations that coordinate various aspects of vaccine programs, such as the Global Alliance for Vaccines and Immunization (GAVI); the International AIDS Vaccine Initiative; the Wellcome Trust, Program for Appropriate Technology in Health; and the Global Fund to Fight AIDS, Tuberculosis and Malaria, have helped to address urgent issues in certain countries and have provided substantial funding to develop better vaccines.

The hope for better vaccines must start with an understanding of past failures. Levine and Szein highlight in their commentary the characteristics of an ideal vaccine, shaped by lessons from previous disappointments. The design of such vaccines is more feasible than ever because of constant scientific advances and recent progress in genomics and proteomics. The intersection between new design strategies and ideal vaccine characteristics will enhance the chances of candidate vaccines progressing to clinical trials and eventual mass application.

Clinical trials of vaccines present another unique set of challenges because of the effect of the trial on both healthy and sick individuals. Although the basic tenets of medical ethics apply to vaccine trials, the 'mindset' of such an intervention is different from that of other drugs. Healthy subjects need to understand the risks involved as well as appreciate their 'sacrifice' for the community. Developers of new vaccines must value the cultural sensitivities of the communities that they are targeting, such that appropriate ethical guidelines may be instituted without imposing inappropriate 'Western values'. This controversial subject is examined by Grady in her commentary.

Using estimates from the World Health Organization, GAVI shows that there were over two million deaths in 2002 from vaccine-preventable diseases and an additional two million deaths in 2001 from diseases for which vaccines will be available soon. Despite the best efforts of governments and certain private sectors to raise funds for more vaccine R&D, resources remain inadequate, especially during the final stages of clinical trials. With the world facing so urgent a problem, it is imperative that vaccine organizations and governments enlist help from the vast resources of pharmaceutical companies. Guaranteeing a market may not be sufficient, as bulk purchase by nonprofit agencies is a driving force for reduced profitability and, hence, a deterrent for vaccine R&D. Instead, creative strategies that provide lucrative economic incentives, such as specific tax breaks for vaccine sales or particular patent extensions, may encourage long-term R&D. Pharmaceutical companies could promote their vaccine R&D to burnish their images as socially responsible members of the business community. The problem at hand is multifaceted, but not insurmountable. Dedication from all sectors of the society is the only way to achieve the colossal goal of global immunization. 