The worldwide campaign to eradicate poliomyelitis is nearing its 20th anniversary, and has encountered a number of unanticipated obstacles in the last seven years. For this reason, a unique, open symposium was convened to bring together virologists, epidemiologists, public health workers, policy-makers and representatives from the pharmaceutical industry, to review current progress and propose directions for the future. The meeting, “Polio Immunization: Moving Forward”, was organized by the National Institute of Allergy and Infectious Diseases and Fogarty International Center at NIH in Bethesda, MD, and included 135 participants from 18 countries. The conference was structured as a series of panel discussions to facilitate exchange and analysis of new data and ideas on how to best use the existing vaccines against polio, and to explore the role they will play in future vaccination programs. Many diverse perspectives and approaches were presented at the meeting; clear consensus emerged regarding several important issues, which are highlighted in the summary below. Details of each individual presentation can be viewed under the Presentations link at http://www3.niaid.nih.gov/news/events/meetings/polio.

The delay in completing the final stages of the initially highly successful polio eradication campaign led by the World Health Organization (WHO) has been attributed to the failure of oral polio vaccine (OPV) to interrupt circulation of wild virus in a few densely populated locations (e.g. Uttar Pradesh and Bihar states in India), as well as the failure to immunize because of political and military turmoil (e.g., northern Nigeria, and remote areas of Pakistan and Afghanistan). These two factors led to resurgence of the disease in more than a dozen other countries. The reasons for the low efficacy of OPV in northern India are unknown. Each dose of vaccine is estimated to result in <10% seroconversion, requiring more than 15 consecutive administrations of vaccine to bring the population immunity to a desirable level. In combination with a high birth rate, a significant proportion of very young children remains susceptible to polio and serves as a reservoir for poliovirus circulation. Recent introduction by WHO of supplementary doses of monovalent OPV into the immunization schedule may help reduce this reservoir, as monovalent vaccine improves seroconversion rates for the relevant serotype, compared with trivalent OPV.

A new proposal broadly supported at this meeting was to add inactivated polio vaccine (IPV) to the toolbox of the eradication program. Numerous studies have demonstrated that IPV can induce superior seroconversion in tropical countries. Therefore its use in combination with OPV to immunize very young children could help close the immunity gap in this critically important age cohort, and tip the balance to eliminate wild poliovirus circulation. The initial reasons for the choice of OPV as the tool for polio eradication was its low cost, ease of administration, and superior ability to induce herd immunity. Data available from developed countries suggest that IPV also has a herd effect, albeit less than OPV. Further studies of the ability of IPV to reduce transmission in tropical settings are urgently needed to assess the utility of IPV as an additional tool to stop wild poliovirus transmission, as well as to control outbreaks in the post-eradication era.
The consensus that emerged at the meeting is that use of OPV must eventually stop. Neurovirulent vaccine-derived polioviruses (VDPVs) generated by reversion in OPV recipients can sometimes circulate (cVDPV) in poorly immunized populations and cause outbreaks of the disease. Other VDPVs are isolated from persons with specific types of immunodeficiency (iVDPV), or from sources that do not allow them to be classified (ambiguous or aVDPV). All these VDPVs consistently emerge as a consequence of the inherent genetic instability of poliovirus. It has been argued previously that VDPVs are relatively unfit, “weak” cousins of wild poliovirus, and therefore would only survive to a limited extent in field environments. However, recent experimental results on the mechanisms underlying the evolution and genetic flexibility of these viruses led to a general consensus among meeting attendees that if allowed to circulate, VDPVs will evolve into strains indistinguishable in pathogenicity from wild viruses. Therefore the world can never be considered free from poliovirus while OPV is being used. Several groups described potential vaccine strains with increased genetic stability, but their trials would face insurmountable regulatory and epidemiological challenges, and there was little enthusiasm for their development.

Several scenarios on how best to stop OPV use were discussed. A current proposal is to synchronously stop OPV use simultaneously throughout the world once wild polioviruses are no longer detected, to avoid spread of VDPV from countries still using OPV to populations in countries that have stopped vaccination. This scenario involves creation of large non-immune populations, and it is acknowledged by all that outbreaks should be expected to occur after cessation of OPV immunization. Some participants hoped that such outbreaks would be readily contained with local OPV administration. Others felt that this scenario would, for the first time in human history, create large populations with no polio immunity and represented an experiment with serious risks that cannot be accurately assessed.

Unknown factors include the prevalence of chronic excretors, the length of time that wild or vaccine-derived poliovirus can circulate without causing detectable disease, the force of spread of virus and the severity of disease in immunologically naïve communities. Many participants felt that leaving significant unprotected populations in poor countries would create the possibility for pathogenic viruses to spread and reignite new epidemics, and would be unacceptable for a number of ethical and political reasons. The risk could be reduced by gradually replacing OPV with IPV, on a country-by-country basis, for at least an interim period until the risk factors can be better defined.

A gradual shift from OPV to universal use of IPV might help to resolve a number of otherwise daunting tasks that would arise during the transition to a post-eradication strategy. Maintaining high population immunity throughout the world would minimize the risk for runaway outbreaks caused by potential re-introduction of poliovirus, and would make the proposed poliovirus facility containment measures less critical. This could help save resources spent on this activity, and also minimize the potential threat from chemically synthesized poliovirus, which has been demonstrated to be technically feasible. Economic and logistical aspects of creation and maintenance of a vaccine stockpile for response to outbreaks would be simplified, and the tactic of having to use OPV for emergency response in an environment where a significant part of the population has no immunity to poliovirus (“fighting fire with fire”) would be eliminated. Synchronous OPV cessation, which is a formidable political and logistical task, would not be required under this scenario. Industry in developed and developing countries would have time to
develop and expand its manufacturing capacities to supply the world with IPV, and to accumulate experience and information about the safety of the transition.

High production cost has always been one of the leading obstacles to wide use of IPV in low-income countries. Representatives of major IPV manufacturers suggested at the meeting that significant expansion of production could lead to price reduction. Trials to reduce vaccine dosage and introduce intradermal delivery of IPV (which could additionally eliminate the need for highly trained medical personnel to perform conventional intramuscular injections) are already being sponsored by WHO. Intradermal injection of IPV was shown in laboratory animals to produce higher immunity at reduced doses of vaccine. Adjuvants have been shown to increase immunogenicity of IPV, providing another possible route to dose reduction. Preliminary studies of novel adjuvants in animals showed promise of not only boosting immunogenicity, but also increasing the ability of IPV to induce local (mucosal) immunity. Combination vaccines containing IPV along with other antigens and alum adjuvant were shown to possess superior immunogenicity. The use of IPV-containing combination vaccines could significantly increase cost-efficiency of the product, because it would simultaneously control a number of other vaccine-preventable diseases. This would also have an added benefit of re-vitalizing enthusiasm of local health workers and combat program fatigue. Making IPV a part of routine world-wide immunization programs was enthusiastically supported among meeting participants.

Strengthening the expanded program on immunization (EPI) must become the next long-term goal of the international public health and infectious diseases community.

The establishment of production facilities in developing countries was proposed as a major cost savings measure, but concerns exist about containment of virus in new, less experienced facilities located in regions with potentially sub-optimal immunization coverage. Several participants discussed pilot projects to develop IPV from attenuated (e.g. Sabin) strains, which could also link to creation and maintenance of OPV stockpiles. Sabin products differ from the conventional IPV in their immunogenicity in laboratory animals and humans, as well as other immunochemical properties, but increasing the amount of type 2 and type 3 antigens and decreasing type 1 antigen was shown to produce IPV with immunogenicity comparable to the conventional vaccines, but may result in increased cost.

In the interest of having multiple tools with which to undertake and safely complete the eradication and post-eradication effort, a number of potential drugs targeting different viral proteins are currently under investigation. Such drugs could be used to treat chronically infected individuals, as well as for emergency prophylactic and post-exposure treatment in outbreaks. A new class of drugs targeting cellular chaperone pathways critical for viral replication was proposed that suppress viral replication but do not allow the emergence of resistant mutations.

In conclusion, the meeting found broad support for 1) achieving the global goal of polio eradication, 2) using IPV in conjunction with OPV to interrupt poliovirus transmission in high risk areas, 3) stopping OPV worldwide when IPV coverage makes it safe to do so, and 4) unifying IPV goals with universal coverage of all essential childhood vaccines. For the near future, continued global vigilance, surveillance, and vaccine response capacity will be needed to respond to the risks of variable immunization coverage and susceptible subpopulations in some countries. Basic and field research efforts to better understand poliovirus genetics and biology, investigate the role of antiviral drugs, and improve vaccines are crucial components of the evolving strategy to eliminate polio as a threat to all future generations.