EXECUTIVE SUMMARY

Sustainable Influenza Vaccine Production Capacity Stakeholders' Workshop

January 11-13, 2010 - Washington, D.C.

Introduction

Influenza pandemics have occurred for centuries and reoccur when a new easily transmissible strain of influenza arises for which the human population has no immunity. Influenza pandemics can infect and kill millions and can overwhelm healthcare systems. In the modern era, pandemic-strain-specific influenza vaccine is an important defense to reduce morbidity and mortality and potentially to decrease economic and social disruption and instability.

Current influenza vaccine manufacturing capacity has been concentrated in North America, Europe, Australia, Japan, Russia, and China. In recent years, global production capacity has expanded somewhat, largely in response to the 2003 re-emergence of H5N1 influenza viruses, which are not yet easily transmissible but which are highly lethal in humans. In 2006, the World Health Organization (WHO) initiated a Global Pandemic Influenza Action Plan to Increase Vaccine Supply. The Biomedical Advanced Research and Development Authority (BARDA) of the U.S. Department of Health and Human Services (HHS) has partnered with Japan, Canada, and the Asian Development Bank to provide financial support for this initiative. WHO is now working with vaccine manufacturers in 11 developing countries to increase production capacity. Commercial-scale production has been reached or is imminent in some cases. Despite these efforts, however, major gaps remain in influenza vaccine production capacity, particularly in sub-Saharan Africa, Eastern Europe and Central Asia.

The (H1N1) 2009 pandemic revealed enduring weaknesses in the world's ability to protect itself using influenza vaccines. Whereas, the H1N1 virus was rapidly isolated and characterized, and safe effective vaccines were developed, licensed and produced in record time, early access to pandemic vaccine was limited to developed countries. Large quantities of vaccine were not available until late in the epidemic course in the global population. Many poor countries have yet to receive any H1N1 pandemic vaccine for priority risk groups. The world remains poorly prepared to meet the vaccine needs for another influenza pandemic, especially one that could be more deadly than H1N1 turned out to be.

The Stakeholders' Workshop on Sustainable Influenza Vaccine Production Capacity, organized by HHS and WHO, convened in Washington D.C. January 11-13, 2010. Its primary purpose was to generate ideas for a comprehensive framework and strategic plan describing the present state, challenges, future vision, and steps necessary to reach the shared goal of creating regionally-based, independent, sustainable vaccine production capacity in developing and emerging-economy countries. Workshop participants represented a wide range of stakeholders, including

non-governmental and philanthropic organizations, academia, vaccine manufacturers, and developing and emerging-economy countries.

This Executive Summary briefly describes the major themes and outcomes of the Workshop discussions as well as proposed next steps to further develop sustainable influenza vaccine manufacturing capacity in developing countries.

Challenges in Vaccine Readiness

Current approaches to “vaccine readiness” (the ability to meet the vaccine needs for another influenza pandemic) are insufficient and unsustainable. Over the course of the meeting, participants identified a complex array of technological, political, financial, and logistical issues that affect sustainability in developing and emerging-economy countries. These issues are summarized below.

Development of Sustainable Influenza Vaccine Production Capacity

Surge capacity: Expanding global influenza vaccine production capacity will increase the available surge capacity for responding to a pandemic.

Old vs. New Influenza Vaccine Technology: Growth of virus in chicken eggs remains the dominant method for producing influenza vaccines. Drawbacks include the time needed to produce vaccine once a virus strain has been identified (about 22 weeks), and the need to procure large quantities of fertilized eggs quickly in order to surge production in response to a pandemic. This is a mature technology with large-scale vaccine production capacity. Some influenza vaccine is on the market that has been produced by growing virus in a variety of cells, but depending on the virus strains, this method may be no quicker than egg-culture for producing pandemic vaccine. Recombinant vaccine production methods, which do not require culture of influenza virus, are likely to be faster and more easily surged, but are so far only at the stage of pilot projects.

Workshop participants concluded that, for now, egg-based technology is likely to be the most reliable way to introduce vaccine production into developing countries. Other methods may have advantages in the longer term, but the introduction of new technology brings additional intellectual property and licensing issues into play. Some Workshop participants argued that a push to develop recombinant vaccines would be a valuable medium- to long-term strategy.

Technology Transfer: Building up vaccine production capacity in developing countries requires skilled personnel and administrative infrastructure as well as the technology itself. The "technology hub" developed by WHO at the Netherlands Vaccine Institute, which packages a training program with a complete egg-based pilot plant, as well as support activities of the Program for Appropriate Technology in Health (PATH) have been successful in assisting development of influenza vaccine production in Vietnam and other countries. However, variations in the nature of the technology being transferred, the needs and capabilities of the recipient countries, and the terms on which international partners and vaccine manufacturers are involved have meant that partnerships need to be negotiated on a case-by-case basis.

Given the technical challenges of producing influenza vaccine, workshop participants suggested that development of any domestically registered vaccine for human use would be an important criterion to participate in enhancement of manufacturing capacity for influenza vaccine, while recognizing that this is only the beginning of an effort aimed at ensuring sustainable production capacity.

Financing and Partnership Models: International partnerships involving governmental and non-governmental bodies, with academic and industry collaboration, have demonstrated that influenza vaccination production can be developed in emerging-economy countries. National and local government support is essential. Successful partnerships require clear delineation of responsibilities and commitments. Going forward, further expansion of influenza vaccine production capacity will require novel and sustainable ways to raise funds. A variety of innovative programs have been suggested, but political acceptance and financial viability have yet to be demonstrated. Regionalization of vaccine production, allowing several countries to pool their resources, may offer economies of scale and other advantages, but has not yet been pursued in earnest.

Regulatory Infrastructure: For developing countries, building and maintaining an adequate regulatory system to guarantee influenza vaccine safety and efficacy may well be a harder task than making the vaccine itself. Development of regulatory expertise is particularly difficult because personnel typically acquire skills and experience through working in established regulatory authorities, alongside highly trained workers. It would not be practical for numerous developing countries to each develop its own regulatory system for influenza vaccine; instead, regionalization of vaccine regulatory efforts may be more productive. Preliminary demonstrations of successful regulatory cooperation can be found in collaborative efforts among member states of the European Union and among 19 countries belonging to the Africa vaccine regulatory forum. A country or region that establishes a trustworthy regulatory system also gives its pharmaceutical manufacturers a competitive advantage in world markets.

Systems and Infrastructure Development: International support to the establishment or strengthening of vaccine production capacity in developing countries must also include appropriate efforts to train and retain a skilled local workforce. Strong national and local commitment to partnerships can help to capitalize on the skills of workers who have received specialized training, who may otherwise be tempted to seek better paid opportunities elsewhere.

Commercial production of influenza vaccine demands long-term maintenance of quality control practices, which require a local, trained workforce and adequate infrastructure, even if regulatory matters are regionalized. Standardized operating procedures and good manufacturing practices, consistent reporting and documentation standards, and full access by developing countries to safety and efficacy information are areas that strongly contribute to quality maintenance, but which may not have received sufficient attention thus far.

Some countries may already have programs to vaccinate children against a variety of diseases, but seasonal influenza vaccination of adults as well as children raises logistical problems that many countries lack the infrastructure to tackle. International partnerships must include

strategies to build and maintain the necessary public health infrastructure, a task that also requires trained local personnel and strong local support.

In countries where general mortality rates are high, so that coincidental illness and death after vaccination can spur vaccine safety fears, reliable reporting of adverse events is essential to the maintenance of public trust. WHO has made adverse-event reporting a necessary element in its vaccination programs in developing countries, and this practice only becomes more important as vaccination reaches larger population segments.

Demand for Seasonal Influenza Vaccine: In developing countries, the burden of seasonal influenza is largely unknown, and other vaccine-preventable diseases receive higher priority. Improved and increased surveillance programs are needed to establish burden of disease as well as the economic and health costs of seasonal influenza as a first step in making a case for vaccination programs. Based on burden of disease studies and economic analyses, some nations, such as Thailand have embraced influenza vaccination programs and development of pharmaceutical manufacturing capacity as part of a strategy to decrease health care costs and to increase their economic and health security.

Overcoming public skepticism and fears about vaccine safety requires a constant and patient effort to provide reliable information and rebut misinformation. Engagement of trusted local figures and media goes a long way toward providing a strong foundation for such efforts.

General Conclusions

The Sustainable Influenza Vaccine Production Capacity Stakeholders' Workshop presented a unique opportunity to bring together a wide variety of partners (public health, academia, foreign affairs, industry, non-governmental organizations) to share their perspectives on solutions to increase vaccine manufacturing capacity in developing and emerging economy countries. The workshop proved to be a successful model for promoting inter-sectoral communication, collaboration, and joint problem-solving (”breaking down silos”) and led to many rich and productive discussions.

In terms of considerations for next steps, workshop participants stressed the need for follow-up discussions focusing on specific thematic areas, on possible revision and enhancement of WHO’s Global Action Plan to Increase Vaccine Supply, as well as development of a more detailed “blueprint” or “roadmap” for implementation.

A sustained proactive and collaborative approach among international partners is essential as the global community continues preparations for the next pandemic.