

# **The Global Action Plan to increase supply of pandemic influenza vaccines**

Report of the fourth meeting of the WHO  
Global Action Plan of the Advisory Group

Nha Trang, Viet Nam, 6 May 2010

**Immunization, Vaccines and Biologicals**



World Health  
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# Abbreviations and Acronyms

AFA	African Flu Alliance
AG	Advisory Group
AMP	Agence de Médecine préventive
CDC	Centers for Disease Control and Prevention
DC	Developing Countries
GAP	Global Action Plan
GPO	Governmental Pharmaceutical Organization (Thailand)
IVR	Initiative for Vaccine Research
LAIV	Live Attenuated Influenza Vaccines
SAGE	Strategic Advisory Group of Experts on Immunization
SII	Serum Institute of India
WHO	World Health Organization

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# 1. Objectives

In May 2006, Global Action Plan (GAP) was developed by WHO for increasing supply of influenza pandemic vaccines in order to reduce the anticipated gap between potential vaccine demand and supply during an influenza pandemic. To oversee the implementation of GAP, an Advisory Group (AG) was established, composed of representatives from countries-industrialized/developing countries with/without manufacturing capacity. The GAP Advisory Group held its first meeting in October 2007 at WHO headquarters, Geneva. The second meeting of AG was held in November 2008 in Pune, Maharashtra, India. Following the outbreak of a new influenza A (H1N1) virus, the third meeting AG was held as teleconference in Geneva on 22 May 2009.

The purpose of this fourth meeting was to update the AG on progress made since the 2007 meeting, to report on the action taken by the WHO secretariat following the previous year recommendations, and to seek guidance on future priority activities. The present document summarizes the discussions at the fourth meeting of the GAP Advisory Group.

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## 2. Agenda

The GAP-AG meeting was held in closed session on 6 May 2010, immediately following the meeting organized by WHO with **international partners on prospects for influenza vaccine technology transfer to developing countries** (May 5-6, 2010), in Nha Trang, Viet Nam, with the following agenda.

- Summary of progress on recommendations since the second meeting and teleconference of the GAP-AG meeting held in November 2008 and May 2009, respectively
- Discussion of the 2010 estimate of global influenza vaccine production capacity. How much more capacity is needed for pandemic preparedness?
- Plans to update the WHA56.19 resolution
- Discussion
- Drafting of 2010 GAP-AG recommendations

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# 3. Summary of main recommendations

The following provides a summary of the major recommendations of the Advisory Group.

- 1) Advocacy for seasonal vaccination should be based on the best available evidence.
- 2) WHO and other stakeholders should strengthen collaboration with media on the benefit of influenza vaccination.
- 3) Better diagnostics should be developed for influenza disease surveillance, in order to facilitate understanding of disease burden in developing countries.
- 4) Coordination between Member Countries should be streamlined on surveillance and virus sharing on fair, equitable and transparent basis.
- 5) Accessibility and affordability of influenza vaccines should be promoted.
- 6) Besides advocating for increased use of seasonal vaccines, newer approaches should be considered for ensuring global access to pandemic vaccine.
- 7) Gradual and demand-based increase in production capacities is warranted.
- 8) Analyses should be made of the opportunity to establish multi-usage production facilities, which could be used to produce both influenza and other vaccines.
- 9) Particular focus should be given to “mature” new technologies such as adjuvants and LAIV. Of particular interest are also those recombinant influenza vaccine technologies which might be approved for human use in the near future.
- 10) Research towards the development of broad-spectrum and long-lasting influenza vaccines should be encouraged and enhanced.
- 11) WHO should investigate approaches to reduce regulatory hurdles for new technologies.
- 12) WHO should continue to facilitate influenza vaccine production technology transfer as a major benefit sharing tool.

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## 4. Proceedings

The chair (Dr Pathom Sawanpanyalert) welcomed and introduced the participants. He then requested Dr Kieny to present the agenda and progress in implementing strategies of the GAP.

The Group reviewed the progress under previous year recommendations as follow:

### 4.1 Increase use of seasonal influenza vaccine

**Public health, economic and social impact of seasonal influenza:** Dr Kieny presented an overview of current global efforts to assess impact of seasonal influenza. Several vaccine probe studies have been initiated by United States CDC, notably in India and in Senegal. Numerous Africa-based influenza networks have emerged recently such as the CDC Anise, AMP Afriflu or WHO AFA. The WHO will launch a survey in June 2010 to assess current usage of seasonal vaccine globally. All these activities will be helpful for the formulation of evidence-based policies on seasonal vaccine usage.

**Political awareness of influenza and influenza vaccines:** WHO noted that media coverage of H1N1 pandemic influenza has had a significant and global impact on political awareness of influenza vaccination.

**Updating 2003 WHA recommendations on seasonal influenza vaccination:** Dr Kieny updated GAP-AG members on WHO activities in this regard. WHO is setting up a Working Group of the Strategic Advisory Group of Experts (SAGE) which will be tasked to assist SAGE in the review of the best evidence to formulate new recommendations on influenza vaccination target groups and coverage goals.

### *Discussion*

The AG noted that significant progress has been made and agreed on following points:

- 1) Advocacy for seasonal vaccination should be based on best practices and available evidence on disease burden, health priorities, economic impact and global responsibilities.
- 2) Print and electronic media were recognized to have significant impact on public perceptions of immunization. Therefore, special efforts should be made by WHO and other stakeholders to strengthen collaboration with media communicating to the public on the safety and effectiveness of influenza vaccination.

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- 3) Better and affordable diagnostics should be developed for enhancing disease surveillance, in order to facilitate understanding of disease burden in developing countries.
  - 4) Coordination between member countries on surveillance and virus sharing should be streamlined on fair, equitable and transparent basis.

#### **4.2 Increased production capacity in developing countries (DC)**

Major progress in development of new production capacity has been achieved through WHO support to 11 DC manufacturers since 2007. Two grantees (Green Cross and Cantacuzino) licensed pandemic vaccines in 2009. Three grantees (SII, GPO, BioFarma) produced clinical lots and two of them initiated clinical trials in December 2009 or January 2010. This second GAP approach also met broad interest from international agencies, and PATH joined WHO efforts in strengthening DC manufacturer's capacities. Additionally, WHO efforts in organizing regulatory authority networking across the world during the pandemic were summarized.

##### **Medium term investment planning for current WHO Grantees.**

Analysis of responses to the April 2010 survey targeting WHO grantees gave the following results:

- Seasonal influenza vaccination programme: - 55% of new manufacturers reported that seasonal influenza vaccination is already part of their national immunization programme, and by 2015 - 73%.
- Forecasted production capacity is very encouraging: By end 2012, most manufacturers will be able to sell or distribute influenza vaccine in their country.
- By 2015, 91% of manufacturers in 11 countries will be able to produce and meet at least part of the demand for influenza vaccine in their country.

##### **Pandemic A (H1N1) 2009 Vaccine Global Production Capacity.**

Dr Kieny briefed the AG on results of two surveys conducted by WHO to assess the global influenza vaccine production capacity since the inception of GAP. WHO conducted these survey in May 2009 and January 2010 respectively, and compared the results from a similar survey conducted in 2006-07. The findings are summarized below:

- The global influenza vaccine production capacity has increased sharply to over 800 million doses trivalent seasonal vaccine from 350 million in 2006, thanks to considerable investments by established manufacturers.
- In spite of global efforts on early deployment of vaccine, pandemic vaccine available for use in vaccination programs was below the WHO GAP's target. The pandemic A (H1N1) vaccine produced over a 12 month period reached only 26% of what was expected in June 2009 due to following issues:
  - lower than expected virus yields
  - inability of manufacturers to use their dose sparing formulations, due to a reluctance of certain regulatory authorities to register low dose adjuvanted vaccine

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- use of capacity to produce seasonal influenza vaccine
  - sudden collapse in demand in 2010.
  - New manufacturers have been established in developing countries, which brings hopes to more adequate production capacity and equitable access in case of a future pandemic.
  - Adequate production capacity is still lacking in some regions of the world, in particular in sub-Saharan Africa and Eastern Europe.

### *Discussion*

The AG applauded WHO efforts and achievements in strengthening DC production capacity and enhancing research. There were wide ranging discussions on approaches for sustaining pandemic influenza production capacities and the following issues were debated.

- Interdependency of seasonal vaccine demand and sustainability of pandemic vaccine production capacities. Complexities further increase for countries that do not have policy and/or market demand of seasonal vaccine.
- Low uptake of pandemic influenza vaccine during 2009-2010 because of several issues including public concerns about safety and efficacy of pandemic vaccines.
- Need for strengthening local national regulatory authorities and removal of unnecessary regulatory barriers for newer vaccine formulations.
- Political and economical implications of seasonal vaccine advocacy in developing countries as they have additional health priorities.
- Technologies such as LAIV, oil-in-water emulsion adjuvants should be promoted and prioritized as they increase time effective production capacities.
- Need for strengthening quality control, quality assurance and post marketing surveillance activities especially on newer adjuvanted vaccine formulations.
- Concrete actions to be implemented targeting regions of the world where influenza vaccine production capacity is least adequate.

The committee in general agreed that sustaining pandemic influenza production capacities needs a prolonged and multifaceted approach based on the following characteristics:

- Accessibility and affordability of influenza vaccines should be promoted as human populations cannot be left vulnerable to future pandemics.
- Besides advocating for increased usage of seasonal vaccines, newer approaches should be considered for ensuring global access to pandemic vaccine.
- Gradual and demand-based increase in production capacities is warranted
- Analyses should be made of the opportunity to establish multi-usage production facilities , which could be used to produce both influenza and other vaccines. (e.g. cell-culture based influenza vaccine and rotavirus vaccine, or egg-derived influenza and yellow fever vaccines)
- Focus on “mature” new technologies such as adjuvants and LAIV to increase global production capacity.

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The AG recognized that progress will require political commitment, scientific innovation, significant funding, and close international cooperation.

### **4.3 Research and development of new technologies**

The AG noted the success of oil in water emulsion adjuvant technologies in development of antigen sparing formulations. There were discussions on development of broad-spectrum (multi-valent or multi-specific) seasonal vaccines. The group also considered potential developments in newer technologies such as baculovirus - or virus like particles technology-based platforms. The group discussed the potential of these technology platforms with respect to yield and cost. The AG made the following recommendations:

- More research should be pursued on development of broad spectrum influenza vaccines.
- Work should be undertaken with regulatory authorities to reduce regulatory hurdles for these technologies
- The committee applauded WHO achievements in facilitating access to the Russian LAIV technology to three developing country vaccine manufacturers. The AG recommended that WHO should continue facilitating technology transfers and benefit sharing approaches to promote access to new technologies.

### **4.4 H5N1 Vaccine Stockpile**

An overview of the WHO H1N1 pandemic vaccine deployment initiative was presented. The AG was appreciative of international effort to provide pandemic vaccine to low and middle-income countries, but regretted that no vaccine was available in these countries more than 6 months into the pandemic. In view of this reality, and considering the high case fatality rate of H5N1 influenza, there was consensus among the AG that WHO should accelerate its efforts to establish a physical stockpile of H5N1 vaccine. The size and extent of stockpiling may be subject to further studies and recommendations by SAGE.

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# 5. List of Participants

## Members

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The World Health Organization has provided technical support to its Member States in the field of vaccine-preventable diseases since 1975. The office carrying out this function at WHO headquarters is the Department of Immunization, Vaccines and Biologicals (IVB).

IVB's mission is the achievement of a world in which all people at risk are protected against vaccine-preventable diseases. The Department covers a range of activities including research and development, standard-setting, vaccine regulation and quality, vaccine supply and immunization financing, and immunization system strengthening.

These activities are carried out by three technical units: the Initiative for Vaccine Research; the Quality, Safety and Standards team; and the Expanded Programme on Immunization.

The Initiative for Vaccine Research guides, facilitates and provides a vision for worldwide vaccine and immunization technology research and development efforts. It focuses on current and emerging diseases of global public health importance, including pandemic influenza. Its main activities cover: i) research and development of key candidate vaccines; ii) implementation research to promote evidence-based decision-making on the early introduction of new vaccines; and iii) promotion of the development, evaluation and future availability of HIV, tuberculosis and malaria vaccines.

The Quality, Safety and Standards team focuses on supporting the use of vaccines, other biological products and immunization-related equipment that meet current international norms and standards of quality and safety. Activities cover: i) setting norms and standards and establishing reference preparation materials; ii) ensuring the use of quality vaccines and immunization equipment through prequalification activities and strengthening national regulatory authorities; and iii) monitoring, assessing and responding to immunization safety issues of global concern.

The Expanded Programme on Immunization focuses on maximizing access to high quality immunization services, accelerating disease control and linking to other health interventions that can be delivered during immunization contacts. Activities cover: i) immunization systems strengthening, including expansion of immunization services beyond the infant age group; ii) accelerated control of measles and maternal and neonatal tetanus; iii) introduction of new and underutilized vaccines; iv) vaccine supply and immunization financing; and v) disease surveillance and immunization coverage monitoring for tracking global progress.

The Director's Office directs the work of these units through oversight of immunization programme policy, planning, coordination and management. It also mobilizes resources and carries out communication, advocacy and media-related work.

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