The Global Action Plan for Influenza Vaccines

Report of the fifth meeting of the Advisory Group of the WHO Global Action Plan for Influenza Vaccines

Cancun, Mexico, 5 May 2011
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## Abbreviations and Acronyms

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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AFA</td>
<td>African Flu Alliance</td>
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<tr>
<td>AfriFlu</td>
<td>International Conference on Influenza Disease Burden in Africa</td>
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<td>AG</td>
<td>Advisory Group</td>
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<td>AMP</td>
<td>Agence de Médecine préventive</td>
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<td>GAP I</td>
<td>Global Action Plan to increase supply of pandemic influenza vaccines</td>
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<td>GAP II / GAP</td>
<td>Global Action Plan for Influenza Vaccines</td>
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<td>CDC</td>
<td>Centers for Disease Control and Prevention, Atlanta, USA</td>
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<td>DCVMN</td>
<td>Developing Countries Vaccine Manufacturers Network</td>
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<td>GACVS</td>
<td>Global Advisory Committee on Vaccine Safety</td>
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<td>IFPMA</td>
<td>International Federation of Pharmaceutical Manufacturers &amp; Associations</td>
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<td>LAIV</td>
<td>Live Attenuated Influenza Vaccines</td>
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<td>OEWG</td>
<td>Open-Ended Working Group</td>
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<td>PIP</td>
<td>Pandemic Influenza Preparedness Framework</td>
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<td>SAGE</td>
<td>Strategic Advisory Group of Experts on Immunization</td>
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<td>TAG</td>
<td>Technical Advisory Group</td>
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<td>WHO</td>
<td>World Health Organization</td>
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1. Objectives

In May 2006, a 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 industrialized/developing countries with/without manufacturing capacity.

The GAP AG held four annual meetings since 2006:

1st GAP AG meeting – 19 October, 2007, WHO headquarters, Geneva
2nd GAP AG meeting – 26 November 2008, Pune, Maharashtra, India.
3rd GAP AG meeting – 22 May, 2009, by teleconference
4th GAP AG meeting – 6 May 2010, Nha Trang, Viet Nam

The purpose of the 5th AG meeting was to provide updates to the AG on progress made since its 2010 meeting; to report on actions undertaken by the WHO secretariat following the previous year recommendations; to seek guidance on future priority activities, including preparation to the second GAP consultation (GAP II) on 12-14 July, 2011, and to propose advocacy strategy to support the implementation of GAP for the next five years.

The present document summarizes the discussions and recommendations at the 5th GAP AG meeting.

2. Agenda

The GAP AG meeting was held in closed session on 5 May 2011, immediately following the meeting organized by WHO with international partners on prospects for influenza vaccine technology transfer to developing countries (May 4-5, 2011) in Cancun, Mexico with the following agenda.

- Summary of progress on recommendations since the 4th meeting of the GAP AG in May 2010
- Discussion of planning and organization of the GAP-II meeting to be held in Geneva on 12-14 July 2011
- Update on the GAP-II draft agenda and speakers list
- Overview of proposed GAP-II advocacy and communication plan (web site, partnership and publication strategy)
- Discussion
- Drafting of 2011 GAP AG recommendations
3. Summary of main recommendations

The following provides a summary of the major recommendations of the Advisory Group in 2011:

1) WHO should change the name of GAP from "Global Action Plan to increase supply of pandemic influenza vaccines" (GAP-I) to "Global Action Plan for Influenza Vaccines" (GAP-II) given the expanding scope of the plan.

2) WHO should use work undertaken around the Decade of Vaccines as an advocacy platform to promote the objectives of GAP for influenza vaccines.

3) A careful analysis should be made on the desirable total number of new influenza vaccine manufacturers in low- and middle-income countries and on the number of countries and regional projects that WHO should cover with its technology transfer project. In particular, attention should be given to country and region-balanced approach for grantees' selection. Analyses should also be made on the long-term production capacity for pandemic vaccine in developing countries, based on manufacturers' business plans for provision of vaccine on both domestic and export markets.

4) WHO should investigate further the linkage between supply and demand of both seasonal and pandemic vaccines, in particular in developing countries.

5) Regular updates on acceptance and use of influenza vaccines should be produced by the WHO secretariat.

6) The evidence supporting the use of adjuvanted vaccines and their safety should be continuously monitored.

7) The PIP Advisory Committee will advise WHO on the amount of resources to be put aside for pandemic preparedness and response, including those for vaccine-related activities. GAP was clearly mentioned in the PIP framework as an important element of benefit sharing, and should therefore be able to benefit from funding under the PIP Framework.

8) WHO and other stakeholders should consider longer term mechanisms and strategies to ensure sustainability of the GAP initiative.

9) WHO should promote studies on surveillance and burden of disease in different target groups, in particular in developing countries.

10) SAGE review of priority target groups for immunization against influenza and of cost-effectiveness of influenza vaccines should be encouraged.
4. Proceedings

The chair (Dr Pathom Sawanpanyalert) welcomed and introduced the participants.

Dr Kieny presented the agenda and provided an update on the recommendations made at the previous AG's meeting in May, 2010 in Nha Trang, Viet Nam, and on their status of implementation. The Group reviewed the progress under previous year recommendations as follows:

4.1 Increase use of seasonal influenza vaccine - public health, economic and social impact of seasonal influenza:

**Advocacy for seasonal vaccination should be based on the best available evidence:** In response to this recommendation, WHO has established a SAGE working group on influenza vaccines and immunization chaired by Dr Elizabeth Miller, UK. This group will review, provide evidence on and propose to SAGE new WHO recommendations on target groups and coverage goals.

**WHO and other stakeholders should strengthen collaboration with media on the benefit of influenza vaccination:** Dr Kieny stressed the importance of this issue in the light of the recommendations released by the International Health Regulations Review Committee in March, 2011. WHO is currently working with a number of stakeholders to develop effective advocacy and communication strategies to support influenza vaccination in the Member States. Internally, WHO will be consolidating communication activities under one department that would help to ensure the consistency of outgoing messages.

**Gradual and demand-based increase in production capacities of influenza vaccines is warranted:** Dr Kieny reported that WHO is gathering data in developing countries on the burden of seasonal influenza, both in terms of disease and economic impact. These data will support evidence-based increase of demand for seasonal and pandemic influenza vaccines.

Vaccine probe studies on influenza vaccine efficacy have been initiated in several countries such as the CDC-supported studies on LAIV in Senegal and India. A number of related initiatives have emerged in the African region. Africa-focused influenza networks such as CDC Anise, AMP AfriFlu, WHO AFA have influenza vaccine issues on their agenda.

**Discussion**

The AG congratulated WHO on the considerable efforts that had been made in response to AG recommendations. The members of the group raised a number of issues for debate such as:

- **Linkage of GAP with the Decade of Vaccines:** Dr Tam explained that the Decade of Vaccines covers all kind of vaccines. At the same time, influenza vaccines are seen as one of the priority topics both inside and outside WHO.

**Recommendation**

The AG agreed on the following point:

- WHO should use work undertaken around the Decade of Vaccines as an advocacy platform to promote the objectives of GAP for influenza vaccines.
4.2 Increased production capacity in developing countries

Besides advocating for increasing use of seasonal vaccines, newer approaches should be considered for ensuring global access to pandemic vaccine: Dr Kieny noted that this question is reflected in the Pandemic Influenza Preparedness (PIP) Framework. This issue will be further discussed during the GAP-II consultation in July 2011.

WHO should continue to facilitate technology transfer for influenza vaccine production as a major benefit sharing tool: Dr Kieny emphasized that the WHO technology transfer initiative continues with its targeted objectives. Eleven vaccine manufactures from Brazil, Egypt, India, Indonesia, Iran, Mexico, Republic of Korea, Romania, Serbia, Thailand and Viet Nam are operating under this initiative in 2011. Selection of new projects is currently under way. WHO has received letters of intent from two Sub-Saharan African manufacturers (South Africa, Senegal), three in India, one from Kazakhstan and one from Argentina. The Technical Advisory Group (TAG) will provide guidance on selection on May 6, 2011, by which successful applicants will be invited to submit a full proposal.

Analyses should be made on the opportunity to establish multi-usage production facilities, which could be used to produce both influenza and other vaccines: Dr Kieny informed the AG group that this work is ongoing. The concept of multi-usage production facilities could be piloted by one of the new grantees. The current situation is that most human vaccines are produced by one facility for each product, while production by campaigns - the approach applied by some industrial vaccine manufactures - would help significantly to optimize production capacity.

Discussion

- **Total number of grantees that WHO is willing to take on board and funding procedure:** Dr Kieny clarified that WHO regards the technology transfer initiative as an important mechanism that could stimulate the dynamics of regional preparedness, in particular in the African region that does not have local producers at the moment. The aim of the programme is not to establish vaccine manufacturing capacities in every country, but rather to make sure that the supply of vaccines will be sufficient to cover the local and regional population needs. The annual funding coming to WHO for grant distribution has decreased over the past 2 years. At present, USD 5 million are available for this purpose, and the plan is to support up to 3-4 new grantees.

- **Selection of grantees:** GAP AG discussed the criteria that should be used to select new projects. While some countries are planning to produce significant amounts of vaccines, others remain rather uncertain about their plans. Therefore, there should be some indicators that could help grantees to assess their objectives when selected for this project. Dr Kieny explained that the selection algorithm is based on a set of indispensable criteria such as a letter of support from the Government, demonstrated capacity to produce vaccines or biologicals, or credible plans to register and manufacture such products within a 3-4 years horizon.

- **Building capacity and business plan for long-term pandemic vaccine production in developing countries:** GAP AG noted that there is a high probability that vaccine manufacturers from some large developing countries such as China or India may start exporting their products which will inevitably affect the overall supply of influenza vaccine
in the world. Assessment of intentions of multinational producers as well as manufactures from the developing world regarding both external and domestic markets is needed.

- **Country/Regional balance:** GAP AG noted that it is important to build capacity equitably in all regions. For example, it is reassuring that for the first time, two applications were received from Sub-Saharan Africa. It was also considered as acceptable to support more than one Indian manufacturer given the size of the country.

### Recommendations

The AG agreed on the following points:

- A careful analysis should be made on the desirable total number of new influenza vaccine manufacturers in low- and middle-income countries and on the number of countries and regional projects that WHO should cover with its technology transfer project. In particular, attention should be given to country and region-balanced approach for grantees' selection. Analyses should be made on the long-term production capacity for pandemic vaccine in developing countries, based on manufacturers' business plans for provision of vaccine on both domestic and export markets.

- WHO should investigate further the linkage between supply and demand of both seasonal and pandemic vaccines, in particular in developing countries.

#### 4.3 Research and development of new technologies

**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:** WHO was granted a royalty-free non-exclusive licence on the Russian LAIV technology to developing country vaccine manufacturers in India and Thailand in 2009. Several other companies are currently negotiating with WHO on such a license. A "technology transfer hub" at the University of Lausanne has made considerable progress in transferring technology for adjuvants.

**Research towards the development of broad-spectrum and long-lasting influenza vaccines should be encouraged and enhanced:** Dr Kieny informed the AG that these topics are still qualified as pressing research issues. The research in this field has promising potentials thanks to the significant funding available. WHO holds regular conferences to gather information on novel influenza vaccines that induce broad-spectrum and long lasting immunity. One such meeting is being organized in November this year in Geneva.

**WHO should investigate approaches to reduce regulatory hurdles for new technologies:** WHO keeps on working on these approaches. Particular attention is being paid to adjuvanted products.
Discussion

- **The impact of the US position regarding not using adjuvanted pandemic vaccine on GAP implementation strategy**: Dr Kieny pointed out that concerns associated with squalene-adjuvanted vaccines were raised mainly at the initial stage of their deployment. The only significant issue for the time being is the link between adjuvanted vaccines and development of narcolepsy in Nordic countries. This is being monitored closely by the Global Advisory Committee on Vaccine Safety (GACVS).

- **OEWG, PIP framework on virus and benefit sharing and other issues that will affect vaccine supply**: Dr Kieny informed the GAP AG that a Fund will be established for partnership contributions to which vaccine manufacturers would make financial contributions in exchange for materials or viruses. Total annual contributions are estimated at USD 28 million for both preparedness and response purposes. These contributions are expected to help generating financial revenues to be used in response operations. An Advisory Committee will advise on the amount of resources to be invested into various activities. GAP is recognized in the PIP Framework as a main vehicle for benefit sharing. This fact is regarded as a positive sign for the GAP to be able to have some funding under the PIP Framework.

Recommendations

The AG group agreed on the following points:

- Regular updates on acceptance and use of influenza vaccines should be produced by the WHO secretariat.

- The evidence supporting the use of adjuvanted vaccines and their safety should be continuously monitored.

- The PIP Advisory Committee will advise WHO on the amount of resources to be put aside for pandemic preparedness and response, including those for vaccine-related activities. GAP was clearly mentioned in the PIP framework as an important element of benefit sharing, and should therefore be able to benefit from funding under the PIP Framework.

4.4 General

**Better diagnostics should be developed for influenza disease surveillance, in order to facilitate understanding of disease burden in developing countries**: HHS/BARDA launched in 2010 a programme to support development of rapid diagnostics tools. Developing countries are expected to benefit from this initiative in the future.

**Accessibility and affordability of influenza vaccines should be promoted**: an analysis of the current trends shows that competition by developing country manufacturers is likely to result in a decrease in price.

**Coordination between Member Countries should be streamlined on surveillance and virus sharing on fair, equitable and transparent basis**: the OEWG concluded its work in April 2011 with agreement on a framework for sharing of benefits (including support to surveillance) and viruses. The PIP Framework is expected to be endorsed by the World Health Assembly in May 2011.
**Discussion**

- **Relationship between TAG and GAP AG:** Dr. Kieny explained that GAP AG is composed of public health experts. Its function is to advise WHO on policy and adaptation of GAP to new initiatives. TAG, on the other hand, is a group of predominantly technical experts in vaccine production with some participation of regulatory specialists. They assess the technical advancement of the new manufacturers (the "grantees"), make recommendations on the selection of technical proposals and review technical reports received from grantees on a three-monthly basis.

- **Sustainability of the project:** Sustainability of the project is closely tied to business plans of the various manufacturers. Some countries such as Viet Nam, Iran and Egypt target small populations for influenza immunization. Their production plans are supported by the willingness of their Governments to protect their populations and to ensure health security in their country in case of a pandemic.

- **Target groups for influenza vaccination:** GAP AG noted that increased attention should be paid to the quality of surveillance in different target groups. Dr. Tam informed the AG that SAGE will issue vaccine recommendations for targeted risk groups. As the WHO focal point for the SAGE working group on influenza vaccines and immunization, Dr. Tam is currently working on the materials that will support SAGE recommendations in November 2011 regarding disease burden and vaccine effectiveness for different risk groups, including infants under six months, children under two and five years of age, pregnant women and health care workers. One of the major problems at the present is that while a lot of data on surveillance in different countries have been collected by WHO Global Influenza Programme, very scarce data are available on disease burden and vaccine cost-effectiveness in low income countries particular in south-east Asian and African regions. WHO will address these issues by commissioning a number of studies on the related topics. GAP AG stressed the importance of promoting vaccination policy development and assessment of cost-effectiveness in different income-class countries.

**Recommendations**

The AG agreed on the following points:

- WHO and other stakeholders should consider longer term mechanisms and strategies to ensure sustainability of the GAP initiative.

- WHO should promote studies on surveillance and burden of disease in different target groups, in particular in developing countries.

- SAGE review of priority target groups for immunization against influenza and of cost-effectiveness of influenza vaccines should be encouraged.
5. Preparation for the second GAP consultation (GAP-II)

5.1 GAP-II meeting: preparation, logistics, agenda, future strategy

Dr John Tam briefed the AG on the preparation for the second GAP consultation, including objective setting, logistic arrangements, agenda, list of participants and future directions for the next five years.

There was general agreement that the full name title of GAP should be changed from its current name adopted in 2006 - "Global Action Plan to increase supply of pandemic influenza vaccines" (GAP-I) - to "Global Action Plan for Influenza Vaccines" (GAP-II).

The need for this modification is the current broadened scope of GAP that deals with both pandemic and seasonal vaccines. Also, GAP has significantly extended its community of stakeholders with active engagement by the WHO Regional offices as well as an increasing input from UN agencies, NGOs, industry, public health professionals, funders and other interested partners.

The scope of GAP-II will be aligned with the three approaches set under GAP-I, namely:
(A) increase in seasonal vaccine use
(B) increase in production capacity
(C) further research and development

The second GAP consultation will focus on assessing the progress and identifying challenges in achieving the 2006 strategic goals.

The objectives of the meeting were set as follows:
- Review progress in the implementation of GAP (2006) action plan
- Identify further actions needed towards a sustainable approach on pandemic preparedness
- Document challenges, successes and lessons learnt from H1N1 pandemic vaccine development and usage
- Prioritize the most promising actions, with timelines, responsibilities and cost
- Evaluate the contribution of GAP in the context of public health
- Celebrate successes and learn about challenges from developing countries on pandemic preparedness and vaccine production

The GAP-II consultation will be held on 12-14 July 2011 at the WHO Headquarters. The meeting is expected to host over 100 participants from the public health sector, national governments, research communities, WHO technology transfer "grantees", regulatory authorities, UN agencies, funders and NGOs. Participation of industry representatives will be coordinated via the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) and the Developing Countries Vaccine Manufacturers Network (DCVMN).

The second GAP meeting will have a number of specific deliverables such as a WHO report summarizing discussions and recommendations for GAP-II and subsequent publications in peer reviewed journals highlighting the main conclusions of the consultation. The consultation is also
expected to put forward recommendations for the implementation of the GAP-II and mechanisms to enhance its sustainability for the upcoming five years.

**Recommenation**

The AG agreed on the following point:
- WHO should change the name of GAP from "Global Action Plan to increase supply of pandemic influenza vaccines" (GAP-I) to "Global Action Plan for Influenza Vaccines" (GAP-II) given the expanding scope of the plan.

5.2 GAP advocacy strategy

Dr Natasha Shapovalova updated the AG on the development and implementation of the GAP advocacy strategy. It was noted that GAP future implementation will require comprehensive and efficient advocacy strategies that will enable WHO to communicate important developments in this initiative to global partners.

The key components of the current advocacy plan aimed to support the introduction of GAP-II include:
- Launch of GAP web site
- Development and production of advocacy material
- Implementation of the publication strategy
- Expansion of GAP partnerships

The GAP web site ([http://www.who.int/influenza_vaccines_plan/en/](http://www.who.int/influenza_vaccines_plan/en/)) is envisaged as one of the key pillars of the advocacy strategy and is designed to become an important WHO information hub for influenza vaccines.

A specific visual identity concept was developed for GAP-II. The concept inherits some elements from the previous design experience with GAP-I to showcase the structure and technical substance of the GAP: three pillars that are associated with the three main objectives of GAP. This concept will be assumed as a basis for layout design of other GAP advocacy products: flyer, questions and answers, collaterals for the GAP-II meeting (banners, posters, leaflets, etc.) and GAP advocacy video.

The video will highlight the importance of the GAP initiative at global, regional and national levels. It will combine materials that are already available from different GAP stakeholders, in particular grantees, filmed interviews with selected GAP partners and video materials from the July GAP-II consultation.

To showcase countries' success stories in implementing the GAP objectives, the GAP Secretariat is currently working with the WHO grantees to collect facts, figures, information on particular achievements and relevant activities associated with GAP-I objectives conducted between 2006-2010.

WHO envisages a GAP-II publication strategy that includes web publication, publications in peer-reviewed journals as well as communication through broad mass media channels. Technical input of the AG in the planned publications is considered pivotal for the success of the strategy.
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<td>The AG noted the progress that has been made on the new GAP advocacy strategy and made additional remarks and suggestions:</td>
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<tr>
<td>- The GAP web site should contain information tailored to different target groups such as public health decision makers, funders, media. It should also provide a set of evidence-based messages supporting vaccine usage targeting general public.</td>
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<td>- The GAP advocacy strategy should address strategic communication issues.</td>
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<td>- GAP-II might consider social media options (blogs, etc.).</td>
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<td>- AG members suggested adding information on the GAP web site such as links to the Decade of Vaccines initiative, Report of the Review Meeting on Measures against Pandemic Influenza (A/H1N1) (Japan), etc.</td>
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6. List of Participants

Members

Dr Daniel Camus, Délégation interministérielle à la lutte contre la grippe aviaire, Paris, France

Dr Bruce Gellin, Director, National Vaccine Programme, Department of Health and Human Services, Washington, DC, United States of America

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