Review of global activities and achievements for GAP since 2006

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OBJECTIVE 1. Increase in seasonal vaccine influenza use

OBJECTIVE 2. Increase in production capacity

OBJECTIVE 3. Further research and development
OBJECTIVE 1.

Increase in seasonal influenza vaccine use
INFLUENZA VIRUS SURVEILLANCE
WHO Global Influenza Surveillance and Response System
GISRS* - Activities

- Virus monitoring and laboratory response
- Laboratory diagnostics
- Vaccine support – vaccine strain selection and provision
- Capacity building
- Communication and networking

*formerly GISN
GISRS: surveillance of circulating viruses and vaccine composition recommendations

- 136 National Influenza Centres (NICs)
- 106 WHO Member States (MS)
- 6 Collaborating Centres (CCs)
- 4 Essential Regulatory Laboratories (ERLs)
- 12 H5 reference laboratories
Cumulative number of specimens processed by GISRS

Data source: FluNet, Global Influenza Surveillance Network (8 February 2011)
Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO (Cambodia, China, Egypt, Indonesia)
INFLUENZA VACCINE STRAIN SELECTION
Vaccine availability
Time is of the essence

Counting by WEEKS … by DAYS …

WHO Recom. ➔ NRA

HGR ➔ SRD serum ➔ SRD Ag ➔ Clinical trial

Vaccine production/formulation/QC ➔ Batch release

Public sector Vaccine manufacturers

Vacc. available
INFLUENZA DISEASE SURVEILLANCE
Impact of seasonal influenza in:

- **Temperate countries:**
  World-wide (annual estimates)$^3$
  - 250, - 500,000 deaths; extrapolation from industrialized world in 2002
  $^1$Molinari et al. 2007; $^2$Pitman et al. 2007; $^3$WHO 2005

- **East and SE Asia (Hong Kong SAR, China):**
  - Children and elderly most affected
  - Mortality rates similar to USA

- **Sub-Saharan Africa (1980-2009):**
  - 1-25% of outpatient ARI visits were due to influenza (n=11)
  - 0.6-15.6% of children hospitalized for ARI had influenza identified (n=15)
  - Influenza was highly seasonal in southern Africa
INFLUENZA VACCINE POLICY
Countries Providing Seasonal Influenza Vaccination in National Immunization Schedule

Data as of February 2011
Member States with Seasonal Influenza in National Immunization Schedule by region

*based on VENICE survey in 2008 and JRF survey in 2008 - 2009*
Distribution of Seasonal Influenza Vaccine Use 2004 - 2009 by WHO Region

Source: IFPMA – Options for the control of influenza (Hong Kong, 3-7 September 2010)
### % of countries by region recommending seasonal influenza vaccination for specific target groups, 2010

<table>
<thead>
<tr>
<th>Region</th>
<th>Children</th>
<th>Adults</th>
<th>Elderly &gt;65</th>
<th>At-risk groups</th>
<th>Essential Personnel including HCWs</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>AMR</td>
<td>79%</td>
<td>50%</td>
<td>90%</td>
<td>67%</td>
<td>87%</td>
</tr>
<tr>
<td>EMR</td>
<td>11%</td>
<td>22%</td>
<td>67%</td>
<td>100%</td>
<td>89%</td>
</tr>
<tr>
<td>EUR</td>
<td>22%</td>
<td>41%</td>
<td>100%</td>
<td>100%</td>
<td>85%</td>
</tr>
<tr>
<td>SEAR</td>
<td>100%</td>
<td>0%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>WPR</td>
<td>64%</td>
<td>54%</td>
<td>85%</td>
<td>92%</td>
<td>78%</td>
</tr>
</tbody>
</table>

*Source: WHO 2010 Global Survey for the mapping of seasonal influenza vaccine*
At risk groups recommended for annual seasonal influenza vaccination at global level (n=75)

- Chronic pulmonary
- Cardiovascular
- Renal
- Immune Disorders
- Haemat./metabolic disorders
- HIV/AIDS
- Hepatic diseases
- Pregnancy

Source: WHO 2010 Global Survey for the mapping of seasonal influenza vaccine
Challenges

- Low proportion of Member States with seasonal influenza vaccination as part of the national immunization programme (46% in 2010, 50% in 2012)

- Few countries are on target to meet WHA 56.19 (75% coverage in elderly),

- High vaccine costs, competing priority and public opinion on the vaccine may play a major role in the above.

- Vaccine coverage data is still very limited as the majority of the Member States are unable to calculate coverage by target group due to the reasons such as its registration system and denominators.
PANDEMIC PREPAREDNESS PLAN
WHO MS with publicly available Pandemic Preparedness Plans before the Pandemic (H1N1) 2009

Source: Comparative Analysis of national pandemic influenza preparedness plans, 2011
National Pandemic Preparedness Plans (PPP)

Cumulative number of countries with Pandemic Preparedness Plans published

Year of Publication | National PPP
--- | ---
2002 | 2
2003 | 1
2004 | 1
2005 | 40
2006 | 68
2007 | 12
2008 | 6
2009 | 14
No data | 11

TOTAL: 168 National PPP

Sources: SPC, World Bank, WHO
OBJECTIVE 2.

Increase in production capacity
Vaccine Production Targets 2015

Two targets have been pursued: Target 1 is the 2006 GAP target; Target 2 is based on evidence of herd immunity*.

- **Target 1**: Vaccinate 100% of the world with 2 doses of pandemic vaccine within 6 months of availability of pandemic strain

- **Target 2**: Vaccinate 70% of the world with 2 doses of pandemic vaccine within 6 months of availability of pandemic strain

* protecting one group against a disease by vaccinating another group
Global pandemic influenza vaccine production capacity is still insufficient

- Annual vaccine production: ~ 850 million doses
- Estimated annual vaccine production capacity (2015): 1.7 billion doses

Strategies to increase production capacity include:

- Shifting to higher yielding technologies including live attenuated vaccine and use of adjuvants
- Building (and maintaining) new capacity
### Seasonal trivalent vaccine production capacity (2009 survey)

<table>
<thead>
<tr>
<th>Manufacturers</th>
<th>Total annual capacity (10^6 doses)</th>
<th>2008 Northern hemisphere production (10^6 doses)</th>
<th>2009 Southern hemisphere production (10^6 doses)</th>
<th>2009 planned Northern hemisphere production (10^6 doses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Companies A</td>
<td>656.7</td>
<td>368.6</td>
<td>107.5</td>
<td>387.7</td>
</tr>
<tr>
<td>Companies B</td>
<td>195.3</td>
<td>92.5</td>
<td>5.0</td>
<td>96.0</td>
</tr>
<tr>
<td>All</td>
<td>852.0*</td>
<td>461.1</td>
<td>112.5</td>
<td>483.7</td>
</tr>
</tbody>
</table>

**Companies A:** capacity to produce at least \(2.10^6\) doses of novel H1N1 vaccine per week  
**Companies B:** capacity to produce less than \(2.10^6\) doses of novel H1N1 vaccine per week  
*Not including LAIV (MedImmune)*
Even with the projected expansion, multinational capacity will be insufficient to allow access of developing countries to pandemic vaccine in a timely manner.

Future production capacity (2008 – 2016)
Seasonal doses per year, assuming 10 months of operation

Source: Expert interviews; company statements; news articles; UBS Report: “Flu Vaccine Capacity Outstripping Demand” – Nov. 2006; Oliver Wyman analysis.
GAP Technology Transfer Project

- Help developing countries to develop influenza vaccine manufacturing capabilities and capacity for pandemic readiness

- Help achieve sustainable influenza vaccine production capacity
Major Accomplishments

- Financial and technical assistance was provided to 11 developing country manufacturers:
  - Brazil -- Indonesia -- Mexico -- Thailand
  - Egypt -- Iran -- Romania -- Vietnam
  - India -- South Korea -- Serbia

- 6 of the 11 have produced clinical lots of pandemic vaccine
- 4 have completed pandemic vaccine clinical trials
- 3 have licensed pandemic vaccine for human use
- A royalty-free licensed for LAIV technology was granted to 2 DC manufacturers. Others are being identified
Countries with influenza vaccine production capacity in 2006 following WHO Technology transfer initiative

- Countries with influenza vaccine production capacity in 2006
- Countries with new or planned influenza vaccine production capacity after 2006

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. ©WHO 2010. All rights reserved.
It is essential to:

- Sustain both technical and financial support for the new manufacturers until registration of a product

- Strengthen capacity of their respective National Regulatory Authorities;

- Initiate new projects in under-served regions, notably sub-Saharan Africa and Central Asia. Eight new proposals were reviewed in May 2011

- Expand the types of technologies currently available under the GAP
OBJECTIVE 3.

Further research and development
GOAL:

Support the development of evidences needed to strengthen public health guidance and actions essential for limiting the impact of influenza on individuals and populations

Stream 1. Reducing risk of emergence of pandemic influenza

Stream 2. Limiting spread of pandemic, zoonotic and seasonal influenza

Stream 3. Minimizing impact of pandemic, zoonotic and seasonal influenza

Stream 4. Optimizing treatment of patients

Stream 5. Promoting development and application of modern public health tools in influenza control
Stream 3. Minimizing the impact of influenza

Research Recommendations:

• Determining disease burden and social impact

• Improve immunogenicity, availability and delivery of influenza vaccines

• Public health policies to reduce the impact of disease
Currently licensed Influenza Vaccine Production technologies

- Egg-derived inactivated split
- Egg-derived inactivated whole virion
- Tissue-culture derived inactivated virus (split or whole)
- Egg-derived Live Attenuated Influenza Vaccine (LAIV)
Characteristics of current influenza vaccines

- Safe and efficacious
- Formulated and standardized based on HA content to induce neutralizing antibodies
- Vulnerable to drift/shift of HA and NA
- Long established production processes primarily in eggs
- Require constant reformulation (northern and southern hemispheres)
- Suffer from unpredictable yields and growth properties
- Poorly responsive to surge capacity for a pandemic outbreak
Need for new high performance Platform Technologies

Goal: Development of technology that will address unmet needs

- Live attenuated influenza viruses (LAIV)
- Recombinant virus-like particles (VLPs)
- Plant-based production of vaccines
- “Universal” influenza vaccine

Safety
Capacity
Low Cost
Rapid Response
Simple Manufacture
An additional GAP strategy (since 2008)

- Ensure access to pandemic vaccine in low and middle income countries through establishment of a stockpile of H5N1 vaccine
- 150 million doses pledged by manufacturers
- Logistics and strategy under review by the WHO Strategic Advisory Group of Experts in Immunization (SAGE) in the light of lessons learnt during the pandemic
Advisory structures in WHO for GAP

- SAGE H5N1 Working Group (Chaired by Dr Supamit)
- SAGE H1N1 Working Group (Chaired by Dr Salisbury)
- SAGE influenza Working Group (Chaired by Dr Miller)
- TAG for the Technology transfer initiative
- GAP Advisory Group (Chaired by Dr Pathom)

Our most sincere gratitude for their critical strategic and technical advice
Current context of the GAP
Current Context
IHR recommendations


Recommendation 8. Develop and apply measures to assess severity.

Recommendation 11. Set up advance agreements for vaccine distribution and delivery.

Recommendation 14. Reach agreement on sharing of viruses and access to vaccines.

Recommendation 15. Pursue a comprehensive influenza research programme.
**PIP Framework**

- **Pandemic influenza preparedness system for sharing of H5N1 and other influenza viruses with human pandemic potential**

- **Pandemic influenza preparedness benefit sharing system**
  - Pandemic risk assessment and risk response
  - Provision of PIP Candidate Vaccine Viruses
  - Provision of diagnostic reagents and test kits
  - Provision of reference reagents for potency determination of vaccines
  - Laboratory and influenza surveillance capacity building
  - Regulatory capacity building
  - Antivirals stockpiles
  - Pandemic influenza preparedness vaccine stockpile
  - Access to vaccines in the inter-pandemic period for developing countries
  - Access to pandemic influenza vaccines
  - Tiered pricing
  - Technology transfer
  - Sustainable and innovative financing mechanisms
Conclusion

My personal assessment:

- Impressive progress over five years
- Clear need to pursue and amplify the effort in all GAP strategies

Next steps:

- Seek your collective input and advice
- Revise the GAP strategies >>> GAP - II