A.1. Introduction

The Global Action Plan for Influenza Vaccines (GAP) was launched in 2006 as a ten year initiative to address the anticipated shortfall in vaccine supply in the event of an influenza pandemic. GAP aims to reduce the global shortage of influenza vaccines for seasonal epidemics and pandemics through three key objectives/areas of work:

- Objective 1: Increase in the evidence-based use of vaccines to protect against seasonal influenza
- Objective 2: Increase in vaccine production and regulatory capacity
- Objective 3: Research and development in influenza vaccines

GAP works alongside other existing influenza programmes and represents only one aspect of the World Health Organisation’s (WHO’s) efforts towards pandemic influenza preparedness.

A consultation in November 2016 will mark the end of the ten years of GAP. Over these years, much progress has been made in each of the three GAP objectives outlined above, however key gaps also remain. WHO is issuing this questionnaire to solicit feedback on the progress made to date and remaining gaps, which will feed into the development of the agenda for the final GAP consultation.

The questionnaire comprises a total of 22 questions, of which 14 require responses and 8 are optional or dependent on previous answers. The questionnaire should take approximately 20 minutes to complete. The majority of the questions included in the survey are general influenza-related questions and can be answered even if you are not familiar with GAP. The survey will close on 29 February 2016. All responses will be treated in confidence and aggregated in anonymised formats.

If you have any questions on the survey please contact sparrowe@who.int.

For more information on GAP, please visit: www.who.int/influenza_vaccines_plan/en/ and the 2006-2013 Progress report: apps.who.int/iris/bitstream/10665/112307/1/9789241507011_eng.pdf?ua=1

Additional information on WHO’s influenza-related programmes can be accessed here:

Global Influenza Programme (GIP): www.who.int/influenza/en/
Influenza Research Agenda: www.who.int/influenza/resources/research/about/en/
WHO programme for strengthening national regulatory systems: www.who.int/immunization_standards/national_regulatoryAuthorities/strengthening

WHO appreciates you taking the time to complete this survey.

A.2. Background information on respondent

1. Field of work/study (please check all that apply):
   - Vaccine/pharmaceutical manufacturing
   - Vaccine research
   - Biotechnology
   - Medical doctor
   - Healthcare worker
   - National Influenza Centre
   - Country Expanded Programme on Immunization
   - National influenza programme
   - National regulatory authority
   - National policy/planning department
   - Surveillance/disease control centre
   - Health promotion centre
   - WHO Collaborating Centre
   - Donor/foundation
   - Multilateral organisation
   - Non-governmental organisation/Civil Society Organisation
   - Other (please specify)

2. Name of organization (optional):

3. Country:

4. How familiar are you with the Global Action Plan for Influenza Vaccines?
   - Very familiar
   - Somewhat familiar
   - Not familiar

A.3. Overall goal of the GAP

The GAP II consultation, held in 2011, agreed that in order to bring pandemic virus transmission under control, 70% of the global population should be immunized with two
doses of vaccine within six months of the pandemic candidate vaccine virus being available, given the effects of herd immunity.

5. Is this goal still relevant?
   - Yes
   - No
   - No opinion

6. If your answer to the above question is "no":
   - Please explain why you do not think that this goal is relevant (limit 500 characters)
   - Please suggest a revised goal/target (limit 500 characters)

A.4. Objective 1 – Increase in the evidence-based use of vaccines to protect against seasonal influenza

To ensure pandemic influenza preparedness through the availability of pandemic vaccines, countries are encouraged to increase the evidence-based use of seasonal influenza vaccines. Increased use of seasonal vaccines will reduce the disease burden of seasonal influenza infections; provide a distribution system that works routinely and can be scaled up in the event of a pandemic; contribute towards country preparedness to respond to an eventual pandemic; and motivate industry to develop increased capacity for manufacturing vaccines.

There has been an increase in the global use of seasonal influenza vaccination over the years, with 46 countries reporting to having a seasonal influenza vaccination policy to vaccinate at least one “at-risk” population group in 2006, increasing to 72 countries in 2012 and 102 countries in 2014.¹ There has also been an increase in the total number of doses of seasonal influenza vaccine distributed between 2004 and 2013 by 87% (from approximately 262–490 million doses).² However, seasonal vaccine uptake remains low or absent in many countries, especially in low and middle income countries (LMICs); and in some regions there has been a decrease in seasonal vaccine use.

The WHO Strategic Advisory Group of Experts on Immunization (SAGE) recommends that countries with an influenza vaccine programme should consider immunizing the at-risk groups shown in the table below against seasonal influenza (with pregnant women being the highest priority).³

¹ WHO-UNICEF Joint Reporting Form (JRF)
³ www.who.int/wer/2012/wer8747.pdf?ua=1
7. In your opinion, do we have adequate data on disease burden and vaccine effectiveness to understand the following at-risk groups identified in the SAGE recommendations for influenza vaccination? (Yes, No, Don’t know)

- Pregnant women
- Children aged 6 to 59 months
- Elderly
- Health care workers
- Those with “high risk” conditions

8. If you have selected “no” for any of the at-risk groups above, please explain the main areas where improved data is required.

9. Please score the items below as “very important”, “somewhat important” or “not important” in terms of their role in facilitating the introduction and uptake of seasonal influenza vaccines:

- Availability of better vaccines
- Availability of cheaper vaccines
- Better understanding of vaccine-attributable reduction of severe influenza disease
- Better understanding of disease burden associated with influenza, particularly severe influenza disease
- Better understanding of economic burden associated with influenza
- Better understanding of influenza vaccine performance in additional sub-populations and risk groups
- Better understanding of cost-effectiveness of influenza vaccines
- Additional investment in activities to reduce vaccination hesitancy
- Addressing of strain mismatch
- Greater efforts towards advocacy and educational programmes
- Lack of financing for countries
- Poor infrastructure and supply chain in countries
- Competitive health priorities in countries
- Other (please specify)

10. How would you rate the global progress made under objective 1 of GAP?

- Very good
- Good
- Poor
- Very poor
- No opinion

Please explain your response
A.5. **Objective 2 – Increase in vaccine production capacity**

The second GAP objective is to increase pandemic vaccine production capacity towards the target of producing enough doses of vaccine to vaccinate at least 70% of the world’s population in the event of a pandemic. A further objective is to spread production across the world to facilitate rapid and equitable access, and to align national production capacity with a corresponding functional national regulatory agency (NRA) according to WHO’s indicators for functional NRAs.4

In 2006, annual global production capacity of trivalent seasonal influenza vaccines was estimated to be 500 million doses. In 2013 this capacity was estimated to have grown to 1.5 billion doses of seasonal influenza vaccine (or the potential to generate as many as 6.2 billion doses of monovalent influenza vaccine in the event of a pandemic). This is enough to vaccinate 45% of the population with two doses. Preliminary results from a survey conducted in 2015 suggest this figure has further increased, however will still fall short of the GAP goal to immunize 70% of the world population with two doses of pandemic vaccine. Production capacity has also increased in terms of the number of countries producing influenza vaccines with 16 low- and middle-income countries (LMICs) working to establish production capacity, however global production continues to be inequitably distributed, with some regions such as Africa without production capacity and others where only minimal production is taking place.

There has been much progress in the strengthening of national regulatory systems, both in vaccine producing and non-producing countries, empowering them to approve locally produced and imported influenza vaccines. During the past five years, at least half a dozen seasonal influenza vaccines received WHO prequalification status, both from developed and developing country vaccine manufacturers; and there are additional influenza vaccines which have been submitted or expected to be submitted for prequalification in the near future.

11. **Is there a need to further expand the number of influenza vaccine manufacturers in LMICs?**
   - Yes
   - No
   - No opinion

Please provide comments if any (limit 1000 characters)

12. **In 10 years’ time, do you expect the production capacity for influenza vaccines will have:**
   - Increased
   - Decreased

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• Remained the same
• No opinion

If you have selected "decreased" or "remained the same", please explain your response and suggest possible solutions

13. Please score the items below as “very important”, “somewhat important” or “not important” in terms of their role in ensuring that additional production capacity remains sustainable:

• Demonstrated value proposition for influenza vaccine programme investment in LMICs
• Availability of a more efficacious vaccine
• Predictable demand in terms of a seasonal influenza vaccine market
• Favourable procurement policies for locally produced vaccines
• Effective communications about the benefits of influenza vaccination
• Functioning national regulatory agencies
• Competitively priced vaccine
• Increased political will to support influenza programmes
• Existence of a national seasonal influenza vaccination policy that is implemented in practice
• Potential for export to other countries
• Pooled procurement options for “small” countries (i.e. countries with a small demand)
• Sound business planning by vaccine manufacturers
• WHO vaccine prequalification to allow UN agency procurement
• Other (please specify)

14. It is estimated that following the declaration of an influenza pandemic by WHO and the WHO recommendation for the vaccine virus strain, it will take about 5-6 months before the first doses of vaccine will be available to the general population. This is taking into account timelines to complete the following steps (note that some steps can be completed in parallel):
### Activities at WHO Collaborating Centres:

<table>
<thead>
<tr>
<th>Activities</th>
<th>Time required (approx.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generation of the candidate vaccine viruses (CVVs)</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Testing of the CVVs growth and safety</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Shipment of CVVs to manufacturers</td>
<td>dependent on import/customs permits</td>
</tr>
<tr>
<td>Generation of reagents for potency testing of CVVs</td>
<td>3 months</td>
</tr>
<tr>
<td>Shipment of reagents to manufacturers</td>
<td>dependent on import/customs permits</td>
</tr>
</tbody>
</table>

### Activities at vaccine manufacturers:

<table>
<thead>
<tr>
<th>Activities</th>
<th>Time required (approx.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimization of virus growth conditions to produce working seeds</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Vaccine batch production</td>
<td>2 weeks per lot - volume will depend on the facility capacity and yield per egg (if egg based production)</td>
</tr>
<tr>
<td>Quality control of bulk vaccine</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Vaccine filling and release of vaccine (testing for sterility, potency and safety in animals)</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Clinical trials (if required)</td>
<td>at least 4 weeks</td>
</tr>
</tbody>
</table>

### Activities at regulatory agency:

<table>
<thead>
<tr>
<th>Activities</th>
<th>Time required (approx.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review and approval by regulatory agency</td>
<td>dependent on regulatory agency</td>
</tr>
</tbody>
</table>

### Could any of these steps be shortened?

- Yes
- No
- No opinion

If yes, how?

15. How would you rate the global progress made under objective 2 of GAP?

- Very good
- Good
- Poor
- Very poor
- No opinion

Please explain your response
A.6. **Objective 3 – Research and development in influenza vaccines**

The scientific community is engaged in the development of better influenza vaccines that are quicker to produce, broader in protection and/or provide longer duration of protection when compared with traditional egg-based inactivated influenza vaccines. These novel vaccines may overcome challenges associated with current vaccines and could be better suited to the needs of developing countries faced with budget constraints, competing priorities and weak delivery infrastructures. Such vaccines would make a substantial contribution to the control of influenza seasonal epidemics and potential pandemics.

While there has been an increase in the past few years in the total number of novel vaccines in early and late stage clinical development, the number coming to market is still relatively low. Novel vaccines licensed since 2006 all still require seasonal strain updates (Live Attenuated, Quadrivalent, Cell based and Recombinant).

16. In order to develop better vaccines that elicit a broader, longer lasting immune response, what do you see as the major challenges to R&D in terms of: (limit 1000 characters per line)

- Regulatory science
- Scientific knowledge
- Financial availability
- Intellectual Property rights
- Other factors

17. The highly desirable characteristics of a “universal” influenza vaccine profile would be to eliminate the need for annual vaccination while maintaining protection. In this regard:

- What other characteristics should a universal influenza vaccine comprise?
- What do you see as the major barriers in developing such a vaccine?

18. How would you rate the global progress made under objective 3 of GAP?

- Very good
- Good
- Poor
- Very poor
- No opinion

Please explain your response
A.7. Cross-cutting questions

19. Please score the items below as “very important”, “somewhat important” or “not important” in terms of whether they should be prioritized to ensure timely availability of sufficient pandemic influenza vaccine in the event of a pandemic.

- Strengthening influenza surveillance
- A decision making mechanism in place on switch from seasonal vaccine production to pandemic vaccine production
- Generating more studies on burden of severe disease and vaccine effectiveness
- Generating studies on vaccine impact on reduction of severe influenza disease
- Addressing vaccine hesitancy to increase uptake of seasonal influenza vaccines
- Increasing further the capacity of current vaccine production using current technologies
- Continued strengthening of NRAs
- Promoting R&D of better vaccines
- Promoting R&D of universal influenza vaccines
- Premarket commitments for poor countries
- Other (please specify)

20. How would you rate the global progress made under the objectives of GAP?

- Very good
- Good
- Poor
- Very poor
- No opinion

21. What do you see as the main successes of the GAP?

22. What do you see as the main shortcomings of the GAP?