Report of the Third
WHO Consultation
on the Global Action Plan for
Influenza Vaccines

Geneva, Switzerland, 15–16 November 2016
CONTENTS

ABBREVIATIONS AND ACRONYMS ........................................................................................................ iv
EXECUTIVE SUMMARY .......................................................................................................................... 1
1. INTRODUCTION ................................................................................................................................ 3
   Background ............................................................................................................................................... 3
2. GAP FROM 2011 TO 2016: ACHIEVEMENTS AND REMAINING CHALLENGES .................. 4
   Progress towards the GAP target ........................................................................................................ 4
   Objective 1: Increase the use of seasonal influenza vaccine ............................................................. 5
   Objective 2: Increase influenza vaccine production and related regulatory capacities .................... 8
   Lessons learned from the response to pandemics .............................................................................. 11
   Objective 3: Research and development for influenza vaccines ....................................................... 12
3. BRINGING GAP TO A CLOSE: CONCLUSIONS AND NEXT STEPS ........................................ 16
4. ANNEX 1. LIST OF PARTICIPANTS .............................................................................................. 17
5. ANNEX 2. AGENDA ......................................................................................................................... 22
6. REFERENCES ................................................................................................................................... 24
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALRI</td>
<td>Acute Lower Respiratory Infections</td>
</tr>
<tr>
<td>BARDA</td>
<td>United States Biomedical Advanced Research Development Authority (of the USA)</td>
</tr>
<tr>
<td>CEPI</td>
<td>Coalition for Epidemic Preparedness Innovations</td>
</tr>
<tr>
<td>CVV</td>
<td>candidate virus vaccine</td>
</tr>
<tr>
<td>DCVMN</td>
<td>Developing Countries Vaccine Manufacturers’ Network</td>
</tr>
<tr>
<td>GAP</td>
<td>Global Action Plan for Influenza Vaccines</td>
</tr>
<tr>
<td>GMP</td>
<td>Good manufacturing practice</td>
</tr>
<tr>
<td>GAVI</td>
<td>the Vaccine Alliance</td>
</tr>
<tr>
<td>IFPMA</td>
<td>International Federation of Pharmaceutical Manufacturers and Associations</td>
</tr>
<tr>
<td>ILI</td>
<td>Influenza like Illness</td>
</tr>
<tr>
<td>LAIV</td>
<td>live attenuated influenza vaccine</td>
</tr>
<tr>
<td>LMICs</td>
<td>low- and middle-income countries</td>
</tr>
<tr>
<td>NRA</td>
<td>national regulatory authority</td>
</tr>
<tr>
<td>PIP</td>
<td>Pandemic Influenza Preparedness Framework</td>
</tr>
<tr>
<td>PPC</td>
<td>preferred product characteristic</td>
</tr>
<tr>
<td>SAGE</td>
<td>WHO Strategic Advisory Group of Experts on Immunization</td>
</tr>
<tr>
<td>SARI</td>
<td>Severe Acute Respiratory Infections</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
EXECUTIVE SUMMARY

The Global Action Plan for Influenza Vaccines (GAP), established in 2006, sought to increase the production capacity for influenza vaccines in order to reduce the anticipated shortfall in vaccine supply in the event of a pandemic. The ten-year strategy was brought to a close with a consultation in November 2016, bringing together over 120 participants from national governments, United Nations agencies, funders, regulatory authorities, WHO technology-transfer projects, manufacturers, nongovernmental organizations and the research community. The participation of industry representatives was coordinated by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) and the Developing Countries Vaccine Manufacturers’ Network (DCVMN).

While substantial progress has been made over the 10 years of the Plan, the world is still not ready to respond to an influenza pandemic. Approaches used over the past decade have resulted in an increase in seasonal influenza vaccine use; a quadrupling of the potential production capacity for pandemic influenza vaccine; the establishment of local production in low- and middle-income countries (LMICs) and improved production methods reducing the dependency on eggs and shortening timelines. However, these approaches appear unlikely to achieve the further progress required.

Ten billion doses of pandemic influenza vaccine would be needed to administer two vaccinations to 70% of the global population, which is expected to provide sufficient protection, through herd immunity. Current potential production capacity is 6.4 billion doses over a 12 month period, i.e. a shortfall of 3.6 billion doses. Making up that shortfall will require a new approach, as the strategy of expanding seasonal influenza vaccination rates and corresponding production capacity appears to have reached its limits. While global levels of influenza vaccination have increased overall, use has stagnated in recent years in most regions and there has even been a marked decrease in others.

Significant investment has gone into transferring vaccine production technology to developing countries. However, this production capacity is dependent on demand for seasonal vaccines and needs to be made sustainable through reliable procurement, including as part of national security strategies in these countries.

Increasing the use of seasonal influenza vaccine relies on evidence of burden of disease and vaccine effectiveness. However, available data are still weak or lacking in many parts of the world. In addition, hesitancy is affecting vaccine uptake, even in countries where data are available. The protection offered by current seasonal influenza vaccines is not optimal and the need to update the vaccine and revaccinate every year is time-consuming and costly. Better vaccines or improved vaccination strategies are needed and different approaches may be needed for different risk groups. More research is required in this area.

Research and development of new, more broadly effective, more long-lasting, and more cost-effective influenza vaccines will be vital to improving preparedness for a pandemic. This will require reliable, long-term funding. Meanwhile, improvements on current vaccines and vaccination strategies must be pursued, as the availability of next-generation influenza vaccines appears to be some years away.

These and other challenges do not detract from the significant progress made under GAP.

- Potential pandemic influenza vaccine production capacity has more than quadrupled, from an estimated 1.5 billion doses in 2006 to 6.4 billion in 2016, with developing country manufacturers contributing up to 1.1 billion doses in 2019.
• Production of influenza vaccine, which a decade ago was confined mostly to high-income countries, has expanded to include middle-income countries.
• 115 countries have national influenza immunization policies in place, from only 74 in 2006.
• There has been an overall increase in the distribution of seasonal vaccines in some regions, particularly in the Americas (although this has been offset by minimal progress and even decreases in some other regions).

There was consensus from participants that the current approach to ensure adequate supply of pandemic vaccine, based on expansion of seasonal vaccine production capacity, has reached its limits. Alternative strategies should be explored.

Noting that a future influenza pandemic is inevitable, participants strongly urged WHO and GAP partners to continue efforts towards achieving full readiness, in terms of vaccine supply, for influenza pandemics and that a global coordination mechanism for influenza vaccination be maintained at WHO to aid, encourage, and monitor progress.
1. INTRODUCTION

The Global Action Plan for Influenza Vaccines (GAP), established in 2006, sought to increase the production capacity for influenza vaccines in order to reduce the anticipated shortfall in vaccine supply in the event of a pandemic. The ten-year strategy came to an end with a consultation on 15–16 November 2016, bringing together over 120 participants from national governments, United Nations agencies, funders, regulatory authorities, WHO technology-transfer projects, manufacturers, nongovernmental organizations and the research community (a list of participants is provided in Annex 1). The participation of industry representatives was coordinated by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) and the Developing Countries Vaccine Manufacturers’ Network (DCVMN).

Background

In 2003, the Fifty-sixth World Health Assembly adopted resolution WHA 56.19 on prevention and control of influenza pandemics and annual epidemics, which urged Member States:

- where national influenza vaccination policies exist, to establish and implement strategies to increase vaccination coverage of all people at high risk; and
- where no national influenza vaccination policies exist, to assess the disease burden and economic impact of annual influenza epidemics as a basis for framing and implementing influenza prevention policies within the context of other national health priorities.

and requested the WHO Director-General to provide support to developing countries in assessing the disease burden and economic impact of influenza and in framing and implementing appropriate national policies for influenza prevention.

In 2005, with growing recognition of the threat posed by pandemic influenza and the need significantly to strengthen global preparedness and response, the Fifty-eighth World Health Assembly adopted a follow-up resolution (WHA58.5), which urged Member States to consider developing domestic influenza-vaccine production capacity and requested the WHO Director-General to work with partners “to reduce the … global shortage of influenza vaccines … including vaccine strategies that economize on the use of antigens, and development and licensing of antigen-sparing vaccine formulations.”

In May 2006, WHO convened a consultation to identify the most promising approaches to increasing the availability of vaccines during an influenza pandemic and to develop a corresponding plan for achieving that goal. At that time, there were marked differences in capacities, priorities, and resources for establishing seasonal vaccination policies and national influenza vaccination programmes in countries. All the major influenza vaccine producers operated and supplied primarily in Australia, North America, and Europe, and to a limited extent in Asia. Most resource-constrained countries did not have access to seasonal influenza vaccines and were likely to face challenges in obtaining supplies during an influenza pandemic. It was important, therefore, to increase the supply of pandemic vaccine and thereby reduce the gap between the potential vaccine demand and supply anticipated during an influenza pandemic.

The target was set to achieve the capacity to produce enough pandemic vaccine to immunize the world’s population, and three mutually reinforcing strategies to achieve this were specified:

1. to increase the evidence-based use of seasonal influenza vaccine;
2. to increase influenza vaccine production capacity and related regulatory capacities; and
3. to promote influenza vaccine research and development.
The three strategies became the objectives of the Global Action Plan for Influenza Vaccines. It was clear that implementation of GAP would require substantial funding and that a range of actors – including governments, industry, international agencies, nongovernmental organizations, and the research community – would have important and complementary roles to play.

It was also recognized from the outset that the gap between vaccine demand and supply could not be closed in the short term; however, it was considered that immediate action could produce some progress within five years, and that longer-term goals could be achieved within a decade.  

A second GAP consultation held in July 2011, at the halfway point of the 10-year programme, reviewed the progress made. There had been some notable advances, with GAP serving as the catalyst for a significant expansion in vaccine manufacturing. Global production capacity had increased, although it still fell short of the GAP target. A feasible and implementable framework for increasing the number of countries with vaccine production capabilities had been established and, at that time, eleven manufacturers in developing countries had received seed funding and technology transfer support from WHO. Five had already brought licensed influenza vaccines onto the market. The second Consultation concluded that, taking into account the effects of herd immunity, it would be sufficient to immunize 70% of the world population. Considering that two doses might be required for sufficient protection, the target for production capacity was set at 10 billion doses.

2. GAP FROM 2011 TO 2016: ACHIEVEMENTS AND REMAINING CHALLENGES

Progress towards the GAP target

The third (and final) GAP Consultation recognized that progress towards the target set had been significant, but had fallen short; overcoming the shortfall would be especially challenging and a different approach may be needed.

Between 2006 and 2016, potential production capacity for pandemic vaccine increased from an estimated 1.5 billion doses to an estimated 6.4 billion doses, thus remaining below the target of 10 billion doses. In addition, it was noted that this estimate of 6.4 billion doses is over a 12 month period and represents a best-case scenario projection, based on a number of assumptions, as outlined below.

- **Assumption: the pandemic influenza strain will grow in eggs with the same yield as the seasonal strain.** While this was the case for the A(H1N1) virus, it was not so for A(H5N1). In reality the yield may be significantly lower than for seasonal vaccine, resulting in a lower than expected global capacity.
- **Assumption: the supply of eggs for vaccine development will not be affected by the pandemic strain.** As avian influenza is one of the most probable sources of a pandemic influenza strain, it is possible that egg production would be affected by the virus. In addition, depending on when the pandemic is declared in relation to seasonal vaccine production, it is possible that the egg supply may not be immediately available.
- **Assumption: 15 µg of antigen is sufficient for an effective vaccine dose without adjuvant.** While 15 µg is sufficient for an effective A(H1N1) influenza vaccine, some A(H5N1) vaccines require 90 µg to be effective.
- **Assumption: there will be a sufficient supply of vials, syringes, etc. and functioning transport networks to disperse and dispense the vaccine, and this will be equitable across populations.**
Objective 1: Increase the use of seasonal influenza vaccine

Efforts to increase the evidence-based use of seasonal influenza vaccine have seen a rise in the number of countries with influenza vaccination policies from 74 in 2006 to 115 in 2014. However, 83% of these countries are high-income or upper-middle-income countries; only 17% are lower-middle-income, and only one is a low-income country.7

In 2006, about 350 million doses of seasonal influenza vaccine were administered. By 2013, some 490 million doses were distributed globally by members of the IFPMA. However, there was no significant increase in vaccine use in the regions of South-East Asia, the Eastern Mediterranean, and Africa. There was even a decrease in use in Europe towards the end of the period.8 Hesitancy about vaccine use on the part of the public and health care workers continues to be a concern.

In 2012, based on a review of disease-burden studies and vaccine performance among high-risk groups, the WHO Strategic Advisory Group of Experts on Immunization (SAGE) issued recommendations for seasonal influenza vaccination. SAGE concluded that pregnant women were the most important group for influenza vaccination, and identified other risk groups as children aged <5 years, the elderly, individuals with chronic medical conditions, and health care workers.9

There are still significant gaps in understanding of disease burden, especially in developing countries. More data are needed to inform decision-makers in LMICs, who must make careful choices on how to use limited health care funding. Further studies are under way, but the resulting data will need to be interpreted with caution because of both differences in the methodologies used and limitations in study design.

The following tools have been published by WHO to assist countries in evaluating disease burden and economic impact:

- a manual for estimating the disease burden associated with seasonal influenza;10
- a manual for estimating the economic burden of seasonal influenza;11
- Evaluation of influenza vaccine effectiveness: a guide to the design and interpretation of observational studies.12
- guidance on maternal influenza immunization in low- and middle-income countries.13

A WHO project, supported through the Pandemic Influenza Preparedness Partnership Contribution, was under way with the objective of improving understanding of the burden of influenza disease. Sixty countries are using WHO methods of measuring disease burden to obtain national estimates, which will then be used to derive regionally representative and global estimates.

Systematic protection of vulnerable groups is hard to achieve without appropriate policies. In addition, vaccine-delivery platforms in low-income countries are not well suited for influenza vaccines, especially for delivering the vaccines to important risk groups, such as the elderly or adults with chronic illness. Other challenges for the delivery of influenza vaccine in low-income settings include: a lack of strong regulatory capacity to review new vaccine formulations annually or biannually, and to conduct lot release; insufficient personnel to administer the vaccine; and inadequate cold chain and waste disposal systems.

Because of these challenges, it has been difficult to make the case for investment in seasonal influenza vaccines in LMICs; new products as well as additional and better data for decision-making are needed.
The continuing lack of convincing evidence of the value of influenza vaccination in low-income countries was driven home by a representative of GAVI. GAVI had examined in 2013 the possibility of funding vaccination for pregnant women, but had finally decided not to proceed because there was a lack of demand from low-income countries for influenza vaccination, and the modelling of the impact on young children was based on relatively few studies and that the studies themselves were not sufficiently rigorous. GAVI will reconsider funding for maternal influenza vaccination in low-income countries in 2018.

A literature review of hesitancy issues related to influenza vaccination indicated that research to date has focused overwhelmingly on high-income countries. Causes of hesitancy in LMICs may well be different. This is an important issue that deserves to be studied, since coverage of influenza vaccination in such countries can only be increased if people accept vaccination. Research so far (as noted, largely in high-income countries) has shown that barriers include: worry about the safety of vaccines; low perceived risk of contracting influenza; low concern about the effects of the disease; and high perceived risks of side-effects of vaccination. There appears to be a continuum of hesitancy, from people who refuse all vaccines, to those who refuse some, to those who accept all vaccines and eagerly seek out vaccination. There is a lack of research on hesitancy among high-risk groups, and more psychological insight is needed into the factors involved. There is also a need for further investigation of what causes hesitancy among health care workers.

Discussion of hesitancy over the use of influenza vaccine led to consideration of the need for effective communication to convince governments, especially in developing countries, as well as physicians, other health care workers, and the public of the importance of seasonal and pandemic influenza vaccination. Experience to date indicates that satisfactory coverage can only be achieved if there is a government mandate or a successful effort to convince people of the value of vaccination. Communication programmes need to be well conceived and executed, and carefully designed to appeal both emotionally and practically to their target audiences; communication aimed at physicians, for example, should differ from that aimed at the public. Modern communication should rely also on social media platforms to inform risk groups, which would also be beneficial during a pandemic given its real time effects. Communication programmes should seek to establish trust as well as to convey information, and should foster collaboration, cooperation, and dialogue; simply creating and disseminating a message was termed “not a strategy, but wishful thinking.” GAP carried out several communication workshops and found that restoring confidence and trust required a reconsideration of communication systems “from manufacture to the jab”, that it was vital to build communication skills among health care workers, and that communication strategies should be continually monitored, evaluated, and modified as necessary.
Panel discussion

What evidence is needed to increase the evidence-based and rational use of seasonal influenza vaccines?

Panellists reiterated that evidence on the influenza disease burden is often lacking in individual countries. Low-income countries frequently make decisions about vaccines based on evidence that vaccination prevents serious illness and death; if such evidence is not available, they are likely to be disinclined to undertake the expense of a vaccination programme. Including an extra vaccine in an immunization programme is a major decision for countries that have limited health resources. In contrast, in high-income and some middle-income countries, the case for influenza vaccination has been made fairly effectively by looking also at the economic impact and the total cost to society. Such data are often not available in low-income countries and decisions may be based on recommendations from WHO or national immunization technical advisory groups. More data are needed on the vaccine-preventable burden of severe influenza in low-income countries.

There is also a shortage of information, especially in low-income countries, on influenza-associated events such as ILI, SARI or ALRI and influenza-triggered events such as an acute myocardial event triggered by influenza infection. This makes it difficult to estimate the true burden of influenza illness. Solid evidence from low-income countries is needed to allow governments to compare alternative strategies; for example, whether it is better to target pregnant women or the elderly. There is also a lack of evidence on the relative efficacy and effectiveness of influenza vaccination compared with other disease interventions. There is a growing body of evidence that people with influenza are more prone to develop viral or bacterial pneumonia; large-scale studies on this association could be valuable in supporting the case for increasing influenza vaccination.

Information on seasonal vaccination and pandemic influenza preparedness should be combined to provide a broader view of the benefits of introducing seasonal vaccine and to make a stronger case for investment by countries. The potential impact on antimicrobial resistance should also be considered, if influenza vaccination is shown to reduce bacterial pneumonia.

Reducing hesitancy was considered to be not so much about vaccination per se but about trust. Further information is required on existing levels of trust and on how to strengthen it. Three groups were cited as important: government decision-makers, health care workers, and people at high risk. Work is needed to determine how best to communicate with each group, from both a scientific and an emotional standpoint. Communication needs may differ between countries or regions, and this needs to be further explored.

Countries that decide to introduce influenza vaccines need to consider where they will procure the vaccine and what the cost will be. Countries in tropical or subtropical areas will also need data on circulating strains, to allow them to decide whether they should acquire the vaccine specified for the northern or southern hemisphere.
Objective 2: Increase influenza vaccine production and related regulatory capacities

Projects jointly sponsored by WHO and the Biomedical Advanced Research Development Authority (BARDA) of the United States of America have produced positive results. Since the inception of GAP, 14 vaccine manufacturers in developing countries have received seed funding and technical support to establish local influenza vaccine production. As a result of the programme, eight pandemic vaccines have been approved, of which two have been prequalified by WHO; three seasonal vaccines have also been approved, of which two have been prequalified. Several other vaccines are in late-stage clinical development, and a number are expected to be licensed in the near future. A concern, however, is ensuring that production is sustainable under current market conditions.

An update on production capacity for seasonal and pandemic influenza vaccines from 2006 to 2016 noted that, from 2013 to 2015, seasonal vaccine production capacity fell slightly as a result of the closure of some European manufacturers. Some Asian and Latin American manufacturers had begun production during that period, but this was not sufficient to compensate for the loss of production elsewhere. A mitigating factor, however, was that many producers shifted from trivalent to quadrivalent vaccine, so that although seasonal capacity fell, the potential for production of pandemic vaccine actually rose. Furthermore, the number of manufacturers with access to adjuvants increased, allowing dose-sparing for pandemic vaccines.

Production capacity in developing countries is expected to continue to increase over the next two years. Some manufacturers have obtained approval of live attenuated influenza vaccines. However, there is still no influenza vaccine production capacity in the African region. A major question is whether the current approaches to expanding pandemic capacity will continue to work, given the recent reduction in seasonal capacity and uptake of seasonal vaccines. Sustaining current production levels is a significant challenge; the building of more production facilities will depend to some extent on whether they are likely to be economically viable.

Some lessons learned in relation to vaccine production in developing countries and in the transfer of technology are listed below.

- More attention and resources need to be given to egg supplies, as they may be inadequate in the event of a pandemic. The number of local suppliers may be limited and the eggs may not be of sufficient quality, which means that eggs will need to be imported.
- Hiring, training, and retaining competent employees are major concerns; frequent training is needed. There is a high turnover of qualified staff.
- Equipment often has to be imported, and delivery times may be long. Overall, the need to import equipment raises both initial costs and maintenance costs.
- Obtaining candidate vaccine viruses (CVVs) and reagents requires effective communication between manufacturers, suppliers, and government to ensure that importation procedures run smoothly.
- The transfer of all appropriate technology needs to be accompanied by continued exchange of information and visits between manufacturers and the organizations overseeing the transfer, even in the post-transfer period.

Technical know-how was deemed more important than equipment in technology transfer of vaccine manufacturing. Such capacities are needed for manufacturing operations, quality assurance and validation, regulatory functions, research and development, and commercial issues, such as marketing. As one participant noted, the complexity of the entire process “cannot be underestimated – although it often
is”. Problems and setbacks are to be expected, and ample resources must be available as well as high-level support for the long term.

A provider of technical support to vaccine manufacturers in developing countries explained that challenges included the development of analytical capacity and the establishment of effective quality management systems. Other issues include implementing clinical trials of vaccine candidates in LMICs, including setting up appropriate regulatory frameworks, ethical review processes, pharmacovigilance, and effective engagement with communities.

The policy coherence needed to sustain production for pandemic preparedness centres on manufacturers and governments, but includes numerous other entities. Aspects to consider include broad industrial policies, procurement policies and practices, national and international trade arrangements, educational and talent-development systems, management and coordination of animal health and human–animal interactions, especially in agriculture.

Increasing vaccine production capacity also requires strengthening of national regulatory capacities to license influenza vaccines, whether imported or manufactured locally. The response to the H1N1 pandemic in 2009 highlighted the importance of WHO prequalification. Six vaccines were prequalified by the end of 2009, and five more were prequalified in the first half of 2010; the review of dossiers and reports took between one and 20 days. The process proved extremely important to vaccine deployment around the world: 75% of countries required prequalification for the registration of a vaccine, while the remaining 25% accepted prequalification as the sole requirement for deployment of a vaccine. Although prequalification sped up the approval process, regulatory requirements created hurdles to timely deployment of vaccines.

A review of lessons learned during the 2009 pandemic made the following recommendations:  

- promote acceptance of WHO prequalified vaccines by national regulatory authorities (NRAs) in order to reduce delays related to country-specific registration and other regulatory issues;  
- clarify the roles and responsibilities of NRAs in countries using donated vaccines in emergency contexts;  
- encourage manufacturers to prequalify more seasonal vaccines; and  
- investigate whether provisional licences/mock dossiers in the countries of manufacture might have an impact on the overall regulatory process, for later conversion to full licences for the production of actual pandemic vaccines.

One complication in establishing vaccine production and carrying out effective regulatory approval in developing countries is the seasonality of influenza in the tropics and subtropics, where many developing countries are located. Some tropical and subtropical areas have near-continuous influenza “seasons”; others have one or two peaks. Some countries get best results with vaccines designed for the northern hemisphere, even though they are located in the southern hemisphere; some are in the opposite situation. Several countries are large enough to have more than one seasonality and to need northern-hemisphere formulations in some parts of the country and southern-hemisphere formulations in others. Collaborative analyses have been carried out, but more information is needed. The unanswered questions include which vaccines are appropriate and when they should be used. In countries with inadequate data, decisions are currently often made by extrapolating from neighbouring countries. Distinct seasonality patterns, though complex, should be ascertainable for most countries through appropriate studies. Meanwhile, from an antigenic perspective, there is no evidence that a third WHO consultation to recommend vaccine viruses is needed to develop a vaccine composition for the tropics and subtropics. Governments in these countries
should decide which vaccines to use, even though information is still not comprehensive for all the
countries concerned. Countries in these regions could use the most recent recommendation, independent
of which hemisphere they are in.

Panel discussion

What is needed to maintain or increase sustainable influenza vaccine production?

Before trying to further increase production, it is important to address the sustainability of current
production. Influenza vaccine supply can only be sustainable if demand is sustainable and predictable,
and this is only possible if there is public confidence and trust in the vaccine. This depends on the
existence of good quality data from reliable studies that can be compared. It was suggested that vaccine
effectiveness studies should be looked at over five-year periods, rather than on a year-by-year basis.

The retention of trained and knowledgeable staff is also a key requirement. The development of new
methods and technologies is important for improving and streamlining the production of influenza
vaccines.

Another pandemic is considered inevitable, and influenza presents a biosecurity threat. From a
governmental perspective, investing in domestic influenza vaccine production is a security issue.

Without an increase in uptake of vaccines, production will not be sustained. Funding and policies for
appropriate stockpiling of vaccines and reagents can help by supporting markets and ensuring better
pandemic preparedness. Governments should look at how they can help with purchasing, thus increasing
demand. Better information is needed on the level of purchases needed to sustain vaccine production
capacity. When continued production is threatened, governments or funding agencies could perhaps agree
to purchase the production that is surplus to market demand.

It was also stressed that governments need to finalize their pandemic preparedness plans, including
projections of vaccine purchasing and deployment.

Increasing the supply of pandemic influenza vaccine requires not only expanded production capacity but
also the development of a range of novel influenza vaccines. Manufacturers will only do this if they are
sure that there will be sufficient income to support production. Bringing novel influenza vaccines onto the
market is difficult; consideration should be given to how to make the process simpler and faster.

National immunization policies are important, and need to be implemented through robust vaccination
programmes. Consideration could be given to increasing and diversifying the groups of health workers
who are authorized to administer vaccines to include, for example, pharmacists; this will help ensure that
patient demand is met by increasing access.

A major concern is the recent decision of the Advisory Committee on Immunization Practices in the USA
to not recommend the use of live attenuated influenza vaccines (LAIVs) in children because of concerns
over vaccine effectiveness. These concerns need to be addressed, otherwise LAIV production capacity
may decline.
Lessons learned from the response to pandemics

There are numerous bottlenecks that could affect the timely production of vaccines in the event of a pandemic, beginning with the complexities of deciding to switch production from seasonal to pandemic vaccine and the timing of the switch. It may not be possible or desirable to switch production immediately when a pandemic is declared: manufacturers have contract obligations to consider, there may be a continuing need for seasonal vaccines, and candidate virus vaccines (CVVs) need to be available. A conservative estimate is that a pandemic vaccine could be available 24 weeks after a pandemic is declared; however, if any major component of the process is delayed, the entire timeline could shift.

A WHO meeting in 2016 reviewed the bottlenecks, together with potential solutions. Delays may be related to: risk assessments on whether or not to switch to production of pandemic vaccine; lack of suitable biosecurity level 3 laboratories for early small-scale work; insufficient laboratories producing CVVs, especially from highly pathogenic viruses; uncertainty about manufacturers’ obligations to share synthetic seed viruses; shipping; availability of clinical trial vaccine lots; review of clinical trial protocols; serology assays; reagent supply; and the use of prefilled syringes, which are slow to fill and use more antigen. A small-scale facility for R&D and production of GMP lots of vaccines could help address some of the bottlenecks.\(^{18}\)

Bottlenecks frequently occur in the delivery and use of vaccines during a pandemic. On the global level, a major challenge is to close the gap between being “ready” with the vaccine and actually delivering it. Shipping too early can be a risk, as demand in different locations can change quickly and drastically, and once material has been shipped it can be hard to arrange its return so that it can be used elsewhere. In principle, stock should be held at the top of the distribution chain, where there is most flexibility, and delivered efficiently as needed. Operational planning for the transport of large volumes of vaccine, often devised during disaster-scenario “brainstorming” sessions, can help to reduce confusion and delays. Experience has shown that it is critical for public health authorities to oversee distribution, without getting directly involved in the minutiae of the massive transport of air freight containers; that should be contracted to professional air-transport firms. During the 2009–10 influenza A(H1N1) pandemic, some 2000 large air-freight containers were shipped, using carriers and airports accustomed to handling large one-off freight shipments. Conformity with the distribution plan was monitored by health officials using global tracking systems.

One lesson learned during the 2009 pandemic was that, when vaccine supplies are scarce, they should be shipped only when the receiving country is ready. Many countries faced problems in preparing for large-scale vaccination: fast-track emergency procedures were not established or were inadequate, and considerable expert support was needed to prepare for receipt of vaccine. Technical assistance needs to be ready at the international level to help countries that are struggling with practical arrangements during a pandemic. In addition, in many countries, while the market for medicines has increased sharply in recent years as development advances and populations grow, improvements to supply systems have not kept pace. Some countries do not have national vaccine deployment plans, and the large number of countries without a seasonal influenza vaccinations plan resulted in significant barriers to the deployment of vaccine during the 2009 pandemic.\(^{19}\)

Equitable access to vaccine is a further issue. The influenza A(H1N1) Pandemic Donation Campaign aimed to ensure equitable access to pandemic vaccine in countries lacking purchasing power or manufacturing capacity, or that had other unmet needs.
Fairness and equity were also the basis of the Pandemic Influenza Preparedness Framework (PIP), established in 2011 after four years of negotiations on ensuring developing country access to vaccines during crises. The Framework aims to improve global preparedness and response, notably through increased, equitable, timely access by WHO to pandemic vaccine for use in developing countries. Under the agreement, WHO coordinates timely sharing and access to influenza viruses with human pandemic potential, and negotiates contracts to secure predictable, equitable, and timely access to pandemic vaccines for use by countries in need. One focus of PIP is establishing contracts with companies, including those in developing countries. The aim is to increase the number of vaccine producers receiving prequalification, so that they can contribute vaccines to WHO when needed. PIP is now being reviewed, and the next steps for the programme are expected to be outlined in the coming months. Issues being considered include whether or not it makes sense to expand PIP to cover seasonal influenza, and the way in which genetic sequencing data will be used for the development of pandemic vaccines. Meanwhile, in the event of a pandemic, WHO, through PIP, would currently have access to over 350 million doses of pandemic vaccine, a threefold increase over the amount available to the Organization in 2009–10.

Objective 3: Research and development for influenza vaccines

Since 2006, some progress has been made in promoting influenza vaccine research and development. A recombinant influenza vaccine has been approved, as well as additional LAIVs and quadrivalent vaccines containing an additional influenza B strain. High-dose seasonal vaccines and seasonal vaccines containing an adjuvant have also come onto the market. Monovalent vaccines, such as that for H5N1, have also been approved. However, all these vaccines are affected by antigenic drift and need to be updated regularly. The complexity, expense, and financing challenges involved in research and development for influenza vaccines make it difficult for new entities to enter the market, and also make it difficult to undertake projects aimed at developing potentially game-changing new vaccines, e.g. vaccines based on non-traditional ways of stimulating immunity, or that could be effective for 5–10 years, rather than just one season, or a universal vaccine that would provide long term protection against all strains of the virus.

A universal vaccine is generally considered to be years, even decades, in the future. However, significant short-term progress may be achievable through incremental improvements in current vaccines or vaccination strategies and schedules.

WHO has issued draft preferred product characteristics (PPCs) for the next generation of influenza vaccines. The target is to produce safe and well-tolerated vaccines that prevent severe influenza illness, provide protection beyond a single year, and are suitable for use in low- and middle-income countries. The finalized PPCs will be posted on the WHO website in 2017.

BARDA is also pursuing the development of influenza vaccine candidates with the potential to stimulate broader, more durable and more effective immunity than currently licensed products and that could act as a primer for a pandemic virus.

An overview of potentially more effective influenza vaccine candidates was presented, showing the various targets on the influenza virus and the immune responses being explored, including humoral, cell-mediated and mucosal responses. Different vaccination strategies – such as priming and boosting to improve the immune response – were also discussed in detail. Cooperation among researchers, to bring together disparate approaches for stimulating both humoral and cell-mediated immunity was deemed highly important. Consortia to bring together candidate vaccines could help, and could stimulate new ideas and strategies through shared research pathways.
Progress in creating broad-spectrum vaccines depends in part on better study designs; it is important to have standardized study designs and clinical trials with appropriate endpoints. Consensus is needed on the conduct of clinical effectiveness studies. Broad-spectrum vaccines would have obvious advantages in many low-resource countries, especially in the tropics, which need year-round availability of effective vaccines. A vaccine that works against different virus strains would cut costs, yield greater benefits, and reduce the economic and social damage caused by severe illness. A cost-benefit analysis of new vaccines will be needed, especially if the costs are much higher than those of current vaccines.

The WHO public health research agenda for influenza currently has five streams: (1) reducing influenza risk, including by focusing on zoonotic influenza; (2) limiting spread of the disease, through public health measures; (3) minimizing impact by expanding vaccine availability and vaccination; (4) optimizing treatment through effective clinical management; and (5) developing tools to improve early detection, modelling, and communication.22

Minimizing impact through vaccination (stream 3) is a major point of emphasis. Progress is needed in determining disease burden and the resulting social costs. The goals for public health research include improving the immunogenicity, availability and delivery of influenza vaccines.

One objective for the next 5–10 years is to prioritize areas in influenza research that can yield strong global public health benefits. The process will include identifying indicators for monitoring and evaluating the public health impacts of the application of research results.

Panel discussion

Do we need better vaccines, and how can that goal be realized?

The “genetic plasticity” of the influenza virus, which mutates from season to season, means that new vaccines need to be developed each year. There is thus an urgent need for a vaccine that would remain effective despite changes in the virus; this would overcome numerous obstacles, greatly reduce costs, and allow protection against the disease to be greatly expanded in low-income countries, by making it more cost-effective. “Better” in the case of influenza vaccines also means more rapid production, since a major issue in combating and preventing pandemics is response time. Faster vaccine production, combined with better surveillance, monitoring, and quick vaccination responses in affected communities, could help prevent potential pandemics.

The challenges are significant. They include the high cost and complexity of vaccine development and production, which makes it difficult for new manufacturers with fresh ideas to enter the field. In addition, many scientists with expertise in influenza virology are approaching retirement age; steps should be taken to allow them to pass on their knowledge and accumulated experience to younger workers in the field. Common platforms need to be established for determining vaccine effectiveness, how much better a new vaccine may be, and whether there is a good value proposition, in terms of the cost-benefit for developing and introducing better delivery systems such as microarray patches. Current assessment methods and the inherent complexity of the vaccine development process make it hard to predict which novel approaches and technologies are going to work. It takes considerable time to collect data on potential success or failure, which means that costly dead ends are inevitable. New techniques may turn out not to be workable for both seasonal and pandemic influenza, causing problems when there is a need to switch
from seasonal to pandemic vaccine production. It will be important to make research data and preliminary results available, e.g. through a data-sharing hub.

One potential avenue for further research is the finding that some people have immune systems that are resistant to virtually all types of influenza. If it can be discovered how this immunity operates, it may be possible to produce the same effect through vaccines. Different perspectives on and approaches to epitopes may also lead to significant new vaccine strategies.

Panellists emphasized that the next generation of vaccines will not come easily or quickly; persistence and long-term funding are vital. Meanwhile, a two-pronged approach is needed: a persistent, long-term commitment to developing the next generation of vaccines; and a practical, effective system for coping with influenza challenges and threats making better use of what is available today.

In dealing with a pandemic, it will be essential to determine the role of vaccines within the overall response to the emergency. Mass vaccination will only be effective if it is preceded by enhanced surveillance, diagnostics, risk assessment, and the preparation of CVVs and reagents. The switch from seasonal to pandemic vaccine production also requires a number of carefully timed and considered decisions. The delivery and administration of vaccines pose challenges, especially in low-income settings: logistic issues have to be solved and agreements on transfer and use must be reached. A recently raised hurdle – one that could potentially stop a pandemic response in its tracks – involves liability: insurance arrangements need to be developed or some other solution found for the matter of who will bear the costs if the pandemic vaccine has adverse effects in individuals. Vaccine manufacturers will be disincentivized to produce vaccines if they are potentially liable for negative outcomes.

In the longer term, weak health systems in many developing countries will need to be strengthened to allow better preparation and response to pandemics, as well as successful deployment and administration of vaccine during pandemics. It is also essential to ensure that sufficient doses of vaccine will be available. The target for production capacity of 10 billion doses has yet to be reached; persuading governments to invest in a pandemic response is difficult when they know that the vaccine required will not be available.

A review of alternative financing models for research and development of influenza vaccines began with the observation that such models should provide additional investment rather than replacing current modes of financing. More financing is needed from a wider variety of sources, as private venture capital has not proved to be sufficient. Advance purchase commitments and plans for stockpiling of vaccines may help to ensure predictable, long-term funding for research and development. Alternative models appear necessary because of a number of recent market failures, especially involving research into pandemic vaccines, problems in the transition to new seasonal vaccines, and efforts to develop a universal vaccine. In some cases, there has been insufficient demand to justify the costs of research and development. The mobilization of new resources may also help to complement the limited reward mechanisms that incentivize research and development in the field of influenza vaccines. Approaches could include novel methods of fund-raising, e.g. further private-sector financing, funding by governments and philanthropists, and investments based on indirect rewards, such as knowledge gained and access to new markets.

The Consultative Expert Working Group on Research and Development: Financing and Coordination\textsuperscript{73} has recommended balancing innovation and access through a series of criteria, including: delinkage of the price of the final product from the cost of research and development; using collaborative approaches,
especially open-knowledge innovation; using licensing approaches that secure access to final products; and mobilizing new sources of financing. An illustration of what such a mechanism might look like is the Coalition for Epidemic Preparedness Innovations (CEPI), an ambitious, recently established public–private partnership involving governments, industry, philanthropists, academia, civil society, and other entities active in global health issues. In response to several high-profile calls for efforts to close research and development gaps related to pandemic preparedness and global health security, CEPI seeks to aid development of new vaccines for priority emerging infectious diseases with the aim of stopping future outbreaks before they become public health emergencies.

Throughout the consultation, participants were invited to provide specific inputs, which have been integrated in the report.
3. BRINGING GAP TO A CLOSE: CONCLUSIONS AND NEXT STEPS

Participants agreed on several broad conclusions:

- The current model to ensure availability of pandemic influenza vaccines relies on the expansion of seasonal influenza vaccine production through increased demand – and hence supply. This approach has now reached its limits. This dogma needs to be challenged; new strategies are needed to close the gap and achieve the capacity to produce 10 billion doses of pandemic vaccine to immunize 70% of the global population.

- The data gap between high-income and low-income countries on disease burden and cost-benefit of vaccination is vast. New concerted approaches are needed to close it. Significantly more evidence-based information is needed to support influenza vaccination in developing countries, where health funding is limited.

- More evidence is also needed to inform seasonal vaccination strategies, especially for high-risk groups, such as children and pregnant women, with a specific focus on low- and middle-income countries.

- The reasons behind hesitancy to use influenza vaccine have not been determined with sufficient clarity. This is important, because communication efforts to overcome hesitancy need to be tailored to the underlying causes; research is needed on effective communication.

- Action is needed to ensure that the influenza vaccine manufacturing capability in developing countries remains sustainable. Pandemic influenza is a national security threat and governments should view support of this capacity as part of funding preparedness.

- It is also of concern to developing countries that global pandemic vaccine production capacity is still not sufficient to protect everyone. Despite efforts to ensure equity and fairness in the distribution of vaccines, access in many countries will be delayed and limited.

- Research and development of new, more broadly effective, longer-lasting, and even universal game-changing influenza vaccines is an important aspect of the search for more effective measures for use in low-income countries. R&D must be continued and expanded.

- The next generation of influenza vaccines may not be available for a decade or longer – it is important to maintain the resources, readiness, and commitment to cope with a potential pandemic using the tools currently available.

- Work begun under GAP should be continued in part by the GAP partners and by specific WHO programmes. It would be useful to continue to maintain a global coordination mechanism, in particular to conduct the global monitoring that GAP provided.
4. ANNEX 1. LIST OF PARTICIPANTS

PARTICIPANTS/OBSERVERS

Dr Atika Abelin, Director, Public Affairs (IFPMA IVS policy member), Sanofi Pasteur, Lyon, France
Dr Jon S. Abramson, Professor, Department of Pediatrics, Wake Forest Baptist Health, Winston-Salem, United States of America
Dr Suleiman Abusrewil, Professor of Child Health, University of Tripoli, Tripoli, Libya
Dr William Kwabena Ampofo, Senior Research Fellow & Head - Virology, Noguchi Memorial Institute for Medical Research, Legon Accra, Ghana
Dr Fatma Nur Baran Aksakal, Department of Public Health, Gazi University, Ankara, Turkey
Ms Paula Barbosa, Manager, Vaccines Policy, International Federation of Pharmaceutical Manufacturers & Associations, Geneva, Switzerland
Dr Francesco Berlinda Scorza, Project Director, Influenza vaccines, PATH, Seattle, United States of America
Dr Peter Bogner, President, GISAiD, Washington, United States of America
Dr Joseph S. Bresee, Chief, Epidemiology and Prevention Branch, Influenza Division, Centers for Disease Control and Prevention, Atlanta, United States of America
Dr Rick Bright, Director, Biomedical Advanced Research & Development Authority (BARDA), US Department of Health and Human Services (HHS), Washington DC, United States of America
Dr Juliet Bryant, Consultant, Hanoi, Viet Nam
Dr Janet Byaruhanga, Health Officer, Social Affairs Department, Health, Nutrition & Population Division, African Union Commission, Addis Ababa, Ethiopia
Professor Daniel Camus, Lille Pasteur Institute, Lille, France
Mr Christopher Chadwick, International Health Analyst, Office of Pandemics and Emerging Threats, US Department of Health and Human Services (HHS), Washington, United States of America
Ms Gina Charos, Director, Immunization Programs and Pandemic Preparedness Division, Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada, Ottawa, Canada
Dr Ze Chen, Professor, Shanghai Institute of Biological Products, Shanghai, People’s Republic of China
Dr Nicolas Collin, Head, Vaccine Formulation Laboratory, University of Lausanne, Epalinges sur Lausanne, Switzerland
Dr Manon Cox, President and Chief Executive Officer, Protein Sciences Corporation, Meriden, United States of America
Dr Nancy J. Cox, Consultant, Atlanta, United States of America
Dr William Cracknell, Director-Technical Specialist, Influenza Operations, Seqirus, Parkville, Australia
Dr Dr Ricardo das Neves Oliveira, Butantan Institute, São Paulo, Brazil
Dr Do Tuan Dat, Director, The Company for Vaccines and Biological Production No. 1 (VABIOTECH), Ha Noi, Viet Nam
Dr Martine Denis, Consultant, Mandelieu la Napoule, France
Dr Favzi Derrar, Head of National Influenza Centre, Viral Respiratory Laboratory, Pasteur Institute, Algiers, Algeria
Dr Armen Donabedian, Senior Programme Manager, Vaccine Advance Development, Biomedical Advanced Research and Development Authority (BARDA), Washington DC, United States of America
Dr Matthew Downham, Associate Director, Flu Manufacturing Sciences & Technology, Medimmune, Liverpool, United Kingdom of Great Britain & Northern Ireland
Dr Robert Duncan, Senior Technical Adviser, Imperial Health Sciences, Hampshire, United Kingdom of Great Britain & Northern Ireland
Dr Thai Huu Duong, Vice Director, Production, Institute of Vaccine and Medical Biologicals, Nha Trang, Viet Nam
Dr Othmar Engelhardt, Principal Scientist, National Institute for Biological Standards and Control, Health Protection Agency, Potters Bar, United Kingdom of Great Britain and Northern Ireland
Mr Ralf Fehrenbach, Managing Director, Fehrenbach Consult SPRL, Meux, Belgium
Dr Svetlana Filipovic-Vignjevic, Assistant Director, Institute of Virology, Vaccines and Sera Torlak, Belgrade, Serbia
Dr Chris Fox, Senior Scientist/Principal Investigator, Infectious Disease Research Institute, Seattle, United States of America
Dr Donald P. Francis, Executive Director, Global Solutions for Infectious Diseases, South San Francisco, United States of America
Dr Juliman Fuad, Production Director, PT Biofarma (Persero), Bandung, Indonesia
Dr Bruce Gellin, Director, National Vaccine Programme, Department of Health and Human Services, Washington, United States of America
Dr Masoud Ghasemi, Cardiology, Tehran university of Medical Science, Tehran, Iran (Islamic Republic of)
Mr Jan T. Hendriks, Institute for Translational Vaccinology, Bilthoven, Netherlands
Dr Siddhivinayak Hirve, Consultant, Mont-sur-Rolle, Switzerland
Dr Le Kim Hoa, Vice Director, Quality Control and Quality Assurance, Institute of Vaccine and Medical Biologicals, Nha Trang, Viet Nam
Dr Olav Hungnes, Senior Scientist, National Influenza Centre, Department of Influenza, Norwegian Institute of Public Health, Oslo, Norway
Mr Chuong Huynh, Interdisciplinary Scientist /Project Officer (COR-III), Division of Influenza, Biomedical Advanced Research and Development Authority (BARDA), Washington, United States of America
Dr Luis Guillermo Francisco Ibarra Ponce de Leon, General Director, Laboratorios de Biologicos y Reactivos de Mexico, Mexico DF, Mexico
Dr Suresh S. Jadhav, Executive Director, Quality Assurance & Regulatory Affairs, Serum Institute of India Limited (SIIL), Pune, India
Dr David C. Kaslow, Vice President, Product Development, PATH, Seattle, United States of America
Dr Markhabat Kassenov, Head of Laboratory, Research Institute for Biological Safety Problems (RIBSP), Gvardeiskiy, Kazakhstan
Dr Larry Kerr, Director, Office of Pandemics and Emerging Threats, US Department of Health and Human Services (HHS), Washington, United States of America
Dr Berik Khairullin, Deputy Director, Research Institute for Biological Safety Problems, Gvardeiskiy, Kazakhstan
Dr Igor Krasilnikov, Deputy Director, Saint-Petersburg Institute of Vaccines and Sera, Saint-Petersburg, Russian Federation
Dr Rosanna Lagos, Coordinator, Centre for Developing Vaccines - Chile, Children Hospital Roberto del Rio, Santiago, Chile
Dr Fernando Lobos, Director, Business Development, Sinergium Biotech, Garin, Argentina
Dr Kutub Mahmood, Scientific Director, Vaccine Development Global Program, PATH, Seattle, United States of America
Dr Morena Makhoana, Chief Executive Officer, Biovac Institute, Pinelands, South Africa
Dr Monica McGill, Global Industrial Leader, Flu Franchise, Vaccine Industrial Affairs, Sanofi Pasteur, Swiftwater, United States of America
Mr Kenneth McLean, Consultant, University of Edinburgh, Edinburgh, United Kingdom of Great Britain & Northern Ireland
Dr Raul Yanko Montano Chavez, Director, National Institute of Virology, Laboratorios de Biologicos y Reactivos de Mexico (BIRMEX), Cuautitlán Izcalli, Mexico
Dr Elisabeth Neumeier, Director, Manufacturing Sciences & PLCM, GlaxoSmithKline Biologicals SA, Dresden, Germany
Dr Kathleen Neuzil, Director, Centre for Vaccine Development, University of Maryland, Baltimore, United States of America
Third WHO Consultation on Global Action Plan for Influenza Vaccines (GAPIII)

Dr Ida Nurnaeni, Head of Department, Influenza Vaccines Department, PT Biofarma (Persero), Bandung, Indonesia
Mr Adrian Onu, Scientific Director, Cantacuzino Institute, Bucharest, Romania
Dr Hicham Oumzil, Head, Virology Department, National Institute of Hygiene, Rabat, Morocco
Dr Sonia Pagliusi, Executive Secretary, Developing Countries Vaccine Manufacturers Network (DCVMN), Nyon, Switzerland
Dr Bram Palache, Influenza scientist, CEO, Influenza Vaccines, FluPal Consultancy B.V., Amstelveen, Netherlands
Dr Laszlo Palkonyay, Consultant, Geneva, Switzerland
Dr John Parrish-Sprowl, Director, Global Health Communication Center, Indiana University Purdue, Indianapolis, United States of America
Ms Deepali Patel, Senior Programme Officer, Policy & Performance, GAVI, the Vaccine Alliance, Geneva, Switzerland
Mr Kittisak Poopipatpol, Influenza Vaccine Plant Manager, The Government Pharmaceutical Organization, Bangkok, Thailand
Professor Gustaaf Rimmelzwaan, Virosceince, Erasmus Medical Center, Rotterdam, Netherlands
Dr James S. Robertson, Independent Consultant, St Albans, United Kingdom of Great Britain and Northern Ireland
Dr Robin A. Robinson, Scientific Consultant, Dickerson, United States of America
Dr John-Arne Röttingen, Director, Division of Infectious Disease Control, Norwegian Institute of Public Health, Oslo, Norway
Professor Larisa Georgievna Rudenko, Head, Department of Virology, Institute of Experimental Medicine, Saint-Petersburg, Russian Federation
Mr Kim Sampson, Executive Director, Asia-Pacific Alliance for the Control of Influenza Ltd, Melbourne, Australia
Dr Carla Magda Santos Domingues, EPI Manager, Secretaria de Vigilância em Saúde, Ministério da Saúde, Brasília, Brazil
Dr Kellen Santos Rezende, Consultant, Brasilia, Brazil
Ms Julie Schafer, Chief of Staff, Biomedical Advanced Research & Development Authority, Department of Health and Human Services, Washington, United States of America
Dr Philipp Schmid, Department of Psychology, University of Erfurt, Erfurt, Germany
Dr Jane Seward, Partnership for Influenza Vaccine Introduction (PIVI), The Task Force for Global Health, Decatur, United States of America
Dr Amine Slim, Head, Microbiology Department, Reference Laboratory for Influenza, Charles Nicolle Hospital, Tunis, Tunisia
Ms Muriel Socquet, Programme Manager - VAC, PATH, Grand Saconnex, Switzerland
Dr Jaspal Sokhey, Consultant, New Delhi, India
Dr Vera Stoiljkovic, Managing Director, Institute of Virology, Vaccines and Sera Torlak, Belgrade, Serbia
Dr John Siu Lun Tam, Professor, Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, People’s Republic of China
Professor Hisham Tarraf, Professor of Medicine and Allergy, Faculty of Medicine, Cairo, Egypt
Dr Beverly Taylor, IFPMA - IVS SPR Coordinator, Head of Manufacturing Science & Technology, Novartis Vaccines & Diagnostics Ltd, Liverpool, United Kingdom of Great Britain & Northern Ireland
Mr Sit Thirapakpoomanunt, Director, Viral Division, The Government Pharmaceutical Organization, Bangkok, Thailand
Mr Patrick Tippoo, R&D Manager, Biovac Institute, Pinelands, South Africa
Professor Han van den Bosch, ATHENA Institute, Free University, Amsterdam, Netherlands
Professor Sylvie van der Werf, Head, Unité de Génétique moléculaire des Virus respiratoires, Institut Pasteur, Paris, France
Mrs Elly van Riet, Institute for Translational Vaccinology, Bilthoven, Netherlands
Dr Roland Ventura, Vaccine Formulation Laboratory, University of Lausanne, Epalinges, Switzerland
Dr Rahnuma Wahid, Senior Program Officer, Vaccine Development, PATH, Seattle, United States of America
Dr Niteen Wairagkar, Senior Programme Officer, Infectious Diseases, Global Health Program, The Bill and Melinda Gates Foundation, Seattle, United States of America
Dr Yajun Wang, Director, LAIV Department, Changchun BCHT Biotechnology Co., Changchun, People’s Republic of China
Professor John Martin Watson, Deputy Chief Medical Officer, Department of Health, London, United Kingdom of Great Britain and Northern Ireland
Dr Jerry Weir, Director, Division of Viral Products - Center for Biologics Evaluation and Research, Food and Drug Administration, Silver Spring, United States of America
Dr Ponthip Wirachwong, Director of Biological Research Group, Research and Development Institute, Government Pharmaceutical Organization, Bangkok, Thailand
Dr Jinchang Wu, Director R&D, International Affairs, Changchun BCHT Biotechnology Co., Changchun, Jilin, People’s Republic of China
Ms Margarita Xydia-Charmanta, Manager, Vaccines Policy, International Federation of Pharmaceutical Manufacturers & Associations, Geneva, Switzerland
Professor Maria Zambon, Director, Reference Microbiology, Microbiology Services, Public Health England, London, United Kingdom of Great Britain & Northern Ireland

WHO SECRETARIAT

Dr Marie-Paule Kieny, Assistant Director-General, Health Systems and Innovation

Technology Transfer initiative, Essential Medicines and Health Products
  Ms Florence Barthelemy, Team Assistant
  Dr Gary Grohmann, Technical Officer
  Ms Myriam Grubo, Technical Officer
  Ms Erin Sparrow, Project Officer
  Mr Guido Torelli, Programme Manager
  Mr Alan Sternberg, Rapporteur

Essential Medicines and Health Products
  Ms Lisa Hedman, Technical Officer, Policy, Access and Use
  Ms Claudia Nannei, Technical Officer, Public Health, Innovation and Intellectual Property
  Ms Asiya Odugleh-Kolev, Technical Officer, Service Delivery and Safety

Outbreak and Health Emergency
  Dr Julia Fitzner, Medical Officer, Global Influenza Programme and PIP Framework
  Ms Anne Huvos, Legal Officer, PIP Framework Secretariat
  Dr Wenging Zhang, Scientist, Global Influenza Programme and PIP Framework
  Dr Weigong Zhou, Medical Officer, Global Influenza Programme and PIP Framework

Immunization, Vaccines and Biologicals, Family, Women's and Children's Health
  Dr Martin Friede, Coordinator, Initiative for Vaccine Research
  Dr Joachim Hombach, Senior Adviser, Initiative for Vaccine Research
  Dr Justin Ortiz, Medical Officer, Initiative for Vaccine Research
  Dr Ole Wichmann, Technical Officer
WHO/REGIONAL AND COUNTRY OFFICES SECRETARIAT

Professor Bartholomew Akanmori, Immunization and Vaccine Development Programme, WHO African Region, Brazzaville, Republic of Congo
Dr Maria Luz Pombo, Regional Adviser on Vaccines and Biotechnological Products, WHO Region of the Americas, Washington, DC, United States of America
Ms Pernille Jorgensen, Technical Officer, Influenza & other Respiratory Pathogens (IRP), Division of Communicable Diseases and Health Security, WHO European Region, Copenhagen, Denmark
Dr Erica Dueger, Medical Officer, Influenza Surveillance, WHO Western Pacific Region, Manila, Philippines
Dr James Heffelfinger, Technical Officer for New Vaccines, WHO Western Pacific Region, Manila, Philippines
Dr Felipe Dias Carvalho, Consultant for Health Technologies Innovation and Development, WHO Country Office, Brasilia, Brazil
Dr Emilia Cain Harari, Expanded Programme on Immunization, WHO Country Office, Mexico, Mexico

Mr Daniel Normandeau, Facilitator, Consultants ConversArt Consulting, Ottawa, Canada
5. ANNEX 2. AGENDA

Chair: Bruce Gellin

DAY 1 – Tuesday 15 November 2016

9:00 – 9:15 Opening and Introduction to Gap and Outbreak Preparedness (Dr Marie-Paule Kieny)

9:15 – 9:35 GAP: 2006 to 2016 – Progress (Dr Bruce Gellin)

SESSION 1 - PROGRESS UNDER OBJECTIVE 1: INCREASED EVIDENCE-BASED USE OF SEASONAL INFLUENZA VACCINE – Chair: Dr Bruce Gellin

9:35 – 9:50 Review of Disease Burden Studies and Vaccine Performance in SAGE Risk Groups (Dr Julia Fitzner)

9:50 – 10:05 Vaccination Policies and Vaccine Programmatic Considerations in Risk Groups (Dr Justin Ortiz)

10:05 – 10:20 Value Proposition for Influenza Vaccination: GAVI Vaccine Investment Strategy (Ms Deepali Patel)

10:50 – 11:05 Hesitancy Issues for Influenza Vaccination: A Literature Review (Dr Philipp Schmid)

11:05 – 11:20 Communication System Building Under GAP (Dr John Parrish-Sprowl)

11:20 – 12:05 Panel Discussion: What Evidence is Needed to Increase the Evidence-Based and Rational Use of Seasonal Influenza Vaccines? (Panellists: Dr Justin Ortiz, Dr William Ampofo, Ms Deepali Patel)

SESSION 2 - PROGRESS UNDER OBJECTIVE 2: INCREASE IN VACCINE PRODUCTION & REGULATORY CAPACITY – Chair: Dr James Roberston

13:15 – 13:25 Update on Production Capacity for Seasonal and Pandemic Influenza 2006-2016 (Dr Martin Friede)

13:25 – 13:55 Lessons Learnt from Manufacturers and Technology Transfer Facilitators on Establishing and Maintaining Production Capacity
  › DCVMN Butantan (Dr Ricardo das Neves Oliveira)
  › IFPMA Seqirus (Dr William Cracknell)
  › PATH (Dr Rahnuma Wahid)

13:55 – 14:10 Policy Coherence to Sustain Production for Pandemic Preparedness (Mr Christopher Chadwick)

14:10 – 14:25 Progress in Strengthening National Regulatory Authority Capacity to Approve and Import Influenza Vaccines (Dr Jaspal Sokhey)

14:25 – 14:35 Review of influenza seasonality in the Tropics and Subtropics (Dr Siddhivinayak Hirve)

14:35 – 15:20 Panel Discussion: What is Needed to Increase Sustainable Influenza Vaccine Production? (Panellists: Dr Suresh Jadhav, Dr Rick Bright, Dr Ricardo das Neves de Oliveira, Dr Monica McGill, Dr Bram Palache, Dr Matthew Downham)
SESSION 3 - LESSONS LEARNT FROM RESPONSE TO PANDEMICS – Chair: Dr William Ampofo

15:50 – 16:05 Bottlenecks to Timely Production of Vaccines in the Event of a Pandemic (Dr Gary Grohmann)

16:05 – 16:20 Bottlenecks to Delivery and Use of Vaccines in a Pandemic:
  ▶ Global level (Dr Robert Duncan)
  ▶ National level (Ms Lisa Hedman)

16:20 – 16:35 The Contribution of the PIP Framework to Pandemic Vaccine Response (Dr John Watson)

16:35 – 17:00 Wrap Up of Day 1

DAY 2 – Wednesday 16 November 2016

9:00 – 9:10 Opening of Day 2 (Chair)

SESSION 4 - PROGRESS UNDER OBJECTIVE 3: R&D FOR INFLUENZA VACCINES – Chair: Dr Kathleen Neuzil

9:10 – 9:30 Progress in R&D for Better Influenza Vaccines (Dr Armen Donabedian)

9:30 – 9:45 New Broad Spectrum Influenza Vaccines (Dr Kathleen Neuzil)

9:45 – 9:55 Updating WHO Public Health Research Agenda for Influenza (Dr Weigong Zhou)

9:55 – 10:15 Towards the Future: Preferred Product Characteristics’ Needs and Gaps (Dr Justin Ortiz)

10:45 – 11:30 Panel Discussion: Do We Need Better Vaccines and How Will We Bring Them to Reality? (Panellists: Dr Matthew Downham, Dr David Kaslow, Dr Robin Robinson, Dr Jerry Weir, Dr Gustaaf Rimmelzwaan)

11:30 – 11:50 Influenza Pandemic Response: (Dr William Ampofo)
  ▶ Where do vaccines fit within the overall response to an emergency?
  ▶ How does our increased vaccine response fit into the overall emergency response?

11:50 – 12:10 Alternative Financing Models for R&D of Influenza Vaccines (Dr John-Arne Röttingen)

SESSION 5 - BRINGING THE GAP TO A CLOSE – Chair: Dr Bruce Gellin

13:30 – 13:40 Setting the stage (Dr Bruce Gellin and Dr Marie-Paule Kieny)

13:40 – 15:30 Plenary Discussion: The Way Forward and Next Steps (Mr Daniel Normandeau, Facilitator)
  ▶ Shaping a Common Forward Agenda, together

15:30 – 16:00 Meeting close (Dr Bruce Gellin and Dr Marie-Paule Kieny)
6. REFERENCES

1 The Global Action Plan for Influenza Vaccines (http://www.who.int/influenza_vaccines_plan/en/).


19 See 15.

20 Pandemic Influenza Preparedness Framework (http://www.who.int/influenza/pip/en/)

21 WHO Preferred Product Characteristics for Next-Generation Influenza Vaccines (http://apps.who.int/iris/bitstream/10665/1058767/1/9789241512466-eng.pdf?ua=1)

22 The WHO public health research agenda for influenza (http://www.who.int/influenza/resources/research/en/)

23 Research and development to meet health needs in developing countries: strengthening global financing and coordination: report of the consultative expert working group on research and development: financing and coordination., WHO 2012. Available at: http://www.who.int/phi/CEWG_Report_5_April_2012.pdf