BETTER GLOBAL TOOLS
FOR INFLUENZA

Technical consultation on product research & innovation for influenza prevention, control & treatment
11–12 June 2019 | Geneva, Switzerland

BETTER GLOBAL TOOLS FOR INFLUENZA

Technical consultation on product research & innovation for influenza prevention, control & treatment
## CONTENTS

<table>
<thead>
<tr>
<th>Part</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>PART I</td>
<td>Setting the scene</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Introduction</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>WHO framework</td>
<td>6</td>
</tr>
<tr>
<td>PART II</td>
<td>The role of innovation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Innovating for influenza</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Understanding virus characteristics and host factors</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Building on lessons learnt</td>
<td>10</td>
</tr>
<tr>
<td>PART III</td>
<td>Towards better tools</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Landscape overview</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Diagnostics</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Vaccines</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Therapeutics</td>
<td>17</td>
</tr>
<tr>
<td>PART IV</td>
<td>Action planning</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Scenario planning</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Recommendations for action</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Next steps</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Annex I: Meeting agenda</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Annex II: List of participants</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Annex III: Individual suggestions</td>
<td>32</td>
</tr>
</tbody>
</table>
This report aims to capture key messages that emerged from the presentations and discussions rather than trying to provide a strictly chronological account of the meeting. The priorities for innovation and recommendations for action include suggestions made by all meeting participants (across all sessions), and do not necessarily imply consensus. Some priorities for innovation are repeated to reflect their emphasis by participants in different sessions and contexts.

The presentations and background reading for the meeting are available at: https://www.who.int/influenza/global_influenza_strategy_2019_2030/en/.
# ACRONYMS AND ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMR</td>
<td>antimicrobial resistance</td>
</tr>
<tr>
<td>BARDA</td>
<td>Biomedical Advanced Research and Development Authority</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control</td>
</tr>
<tr>
<td>CVV</td>
<td>candidate vaccine virus</td>
</tr>
<tr>
<td>DIA</td>
<td>digital immunoassay</td>
</tr>
<tr>
<td>FAO</td>
<td>Food and Agriculture Organization of the United Nations</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>GAP</td>
<td>Global Action Plan for Influenza Vaccines</td>
</tr>
<tr>
<td>GISRS</td>
<td>Global Influenza Surveillance and Response System</td>
</tr>
<tr>
<td>HA</td>
<td>hemagglutinin</td>
</tr>
<tr>
<td>HICs</td>
<td>high-income countries</td>
</tr>
<tr>
<td>IHR</td>
<td>International Health Regulations (2005)</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>mAbs</td>
<td>monoclonal antibodies</td>
</tr>
<tr>
<td>NAAT</td>
<td>nucleic acid amplification test</td>
</tr>
<tr>
<td>NAI</td>
<td>neuraminidase inhibitor</td>
</tr>
<tr>
<td>NPI</td>
<td>nonpharmaceutical intervention</td>
</tr>
<tr>
<td>PAI</td>
<td>polymerase inhibitor</td>
</tr>
<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
</tr>
<tr>
<td>PIP</td>
<td>Pandemic Influenza Preparedness</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>research and development</td>
</tr>
<tr>
<td>RIDT</td>
<td>rapid influenza diagnostic test</td>
</tr>
<tr>
<td>RCT</td>
<td>randomized control trial</td>
</tr>
<tr>
<td>SDG</td>
<td>Sustainable Development Goal</td>
</tr>
<tr>
<td>WHE</td>
<td>WHO Health Emergencies Programme</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
EXECUTIVE SUMMARY

The 2019–2030 Global Influenza Strategy aims to protect all people and communities from the threat of influenza by delivering better global tools and stronger country capacities for tackling the virus and disease.

As a first step towards implementing the strategy, WHO convened a meeting of experts in June 2019 to explore the challenges and opportunities in research and innovation for developing new and improved products to prevent, treat, and potentially control influenza.

Meeting participants reviewed the latest trends and current product pipelines in diagnostics, vaccines, and therapeutics. For each type of product, they identified knowledge gaps and barriers to development and utilization and put forward a selection of priorities for innovation. These ranged from broad goals, for example to improve the way we collect and share data, to very specific suggestions such as conducting fixed and focused studies to better understand influenza transmission patterns in hospitals.

Key recommendations are highlighted throughout this report and summarized in Table 1. A common theme across product types was the need to focus on making tools as relevant and effective as possible. This is not necessarily about only creating new tools or technologies, although participants agreed that developing a universal vaccine would be a significant leap forward. Rather, it is also about improving and increasing the utilization of the currently available products and technologies through incremental innovations.

Several speakers suggested that small technological innovations could make a big difference to efficiency and effectiveness, for example by expanding breadth of protection for seasonal influenza vaccines. Incorporating public health outcomes in clinical trials or redesigning clinical trials to focus on public health outcomes would help make influenza products more relevant to health ministers and key decision makers. And tailoring existing diagnostics, vaccines, and therapeutics to resource-limited contexts would make them more appealing, relevant, and accessible to the low- and middle-income countries (LMICs) that are often most heavily impacted by epidemic and pandemic influenza viruses, in addition to zoonotic events.

Following the June 2019 meeting, the WHO Secretariat will review all suggestions made and prioritize activities to implement the Global Influenza Strategy and accelerate the development of new and improved vaccines, antivirals and treatments.

Table 1. Summary recommendations for delivering better global tools to tackle influenza

<table>
<thead>
<tr>
<th>Area</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boost public understanding, confidence &amp; uptake</td>
<td>• Find new ways to engage &amp; inform the public&lt;br&gt;• Target messaging to key groups</td>
</tr>
<tr>
<td>Build political will</td>
<td>• Turn global strategy into call for action&lt;br&gt;• Make an effective case for investment&lt;br&gt;• Leverage burden of disease studies</td>
</tr>
<tr>
<td>Secure funds and direct investors</td>
<td>• Fundraise beyond the private sector&lt;br&gt;• Coordinate donors&lt;br&gt;• Direct investors towards high impact action</td>
</tr>
<tr>
<td>Work together to align efforts</td>
<td>• Build partnerships across research &amp; clinical practice&lt;br&gt;• Improve infrastructure for alignment &amp; collaboration&lt;br&gt;• Harness new applications &amp; methods for data sharing&lt;br&gt;• Adopt a holistic view of production</td>
</tr>
<tr>
<td>Strengthen the evidence base</td>
<td>• Improve understanding of the virus&lt;br&gt;• Leverage existing or establish new clinical networks&lt;br&gt;• Harness existing evidence&lt;br&gt;• Harmonize clinical trial methods</td>
</tr>
<tr>
<td>Support early detection &amp; rapid data sharing</td>
<td>• Develop deployable diagnostics&lt;br&gt;• Strengthen global surveillance</td>
</tr>
<tr>
<td>Improve vaccine production efficiencies</td>
<td>• Speed up vaccine production&lt;br&gt;• Streamline manufacturing processes</td>
</tr>
<tr>
<td>Establish clear regulatory pathways</td>
<td>• Develop pandemic plans&lt;br&gt;• Build partnerships with manufacturers&lt;br&gt;• Gather more data on safety &amp; efficacy&lt;br&gt;• Clarify approval pathways for emerging products</td>
</tr>
<tr>
<td>Make influenza products sustainable</td>
<td>• Ensure guidance accompanies new products&lt;br&gt;• Secure demand for new products&lt;br&gt;• Drive improvements of existing products</td>
</tr>
<tr>
<td>Focus on LMIC needs</td>
<td>• Promote tools for resource-limited settings&lt;br&gt;• Tailor studies to LMIC contexts&lt;br&gt;• Build capacity for seasonal influenza&lt;br&gt;• Strengthen LMIC manufacturing base&lt;br&gt;• Secure supply chains</td>
</tr>
</tbody>
</table>
PART I.
SETTING THE SCENE

Introduction

Influenza affects all countries, communities, and individuals. Seasonal influenza viruses will continue to circulate, and influenza viruses with pandemic potential will continue to emerge. In March 2019, building on its 70 years of global health leadership and experience in the field, WHO launched the Global Influenza Strategy for 2019–2030, aimed at protecting people in all countries from the threat of influenza.

The strategy provides a common framework for WHO, countries, and partners to jointly enhance global and national pandemic preparedness, combat the ongoing threat of zoonotic influenza, and improve seasonal influenza prevention and control. With strong links to major existing global health strategies and programmes (including the Thirteenth WHO General Programme of Work, the International Health Regulations (2005) and the Public Health Research Agenda for Influenza), the new strategy is designed around two high-level outcomes (see Figure 1):

1. Better global tools. A focused, consensus-driven plan leads to greater research, innovation, and availability of improved tools to prevent, detect, control, and treat influenza.

2. Stronger country capacities. Every country has a prioritized influenza programme that is evidence-based; optimized to fit their needs; and contributes to national and global preparedness, response and health security.

In June 2019, WHO convened a meeting of experts to shape action towards the first of these high-level outcomes by exploring the opportunities and challenges in research and innovation for new and improved products to treat, control, and prevent influenza. This ‘better global tools meeting’, which had more than 85 participants, had three key objectives:

- Identify synergies among existing global initiatives and funders.
- Discuss actions for WHO and partners to accelerate research and innovation for better global tools.

Figure 1. Global Influenza Strategy 2019–2030

OBJECTIVES

<table>
<thead>
<tr>
<th>Research &amp; innovation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance, monitoring &amp; data utilization</td>
</tr>
<tr>
<td>Seasonal prevention &amp; control policies &amp; programmes</td>
</tr>
<tr>
<td>Pandemic preparedness &amp; response</td>
</tr>
</tbody>
</table>

OUTCOMES

Better global tools
- Improved, novel and universal vaccines
- More effective treatments
- Better understanding of virus & host response
- Better detection methods
- Optimized use of current tools

Stronger country capacities
- Integrated capacity building
- Seasonal influenza prevention programmes
- Early detection capacity
- Up-to-date preparedness plans

GOALS

- Reduced burden of seasonal influenza
- Minimal risk of zoonotic influenza
- Mitigated impact of pandemic influenza
The WHO Framework

The new Global Influenza Strategy builds on WHO’s existing influenza initiatives and the significant achievements and advancements these have made since the last global strategy was published in 2002. These include, for example, enhanced surveillance built through the Global Influenza Surveillance and Response System (GISRS), broader virus and benefit sharing achieved through the Pandemic Influenza Preparedness (PIP) Framework, and expanded access to vaccines through the Global Action Plan for Influenza Vaccines (GAP).

The focus of the better global tools meeting was the strategy’s first objective to promote research and innovation, which includes three specific priorities:

a. promote research and innovation for improved and novel diagnostics, vaccines and treatments;

b. promote operational research for influenza prevention, control and programme delivery; and

c. promote research to better understand the virus characteristics and host factors that drive impact.

In considering how to achieve each of these, participants at the meeting were asked to adhere to the five guiding principles of the new strategy: enable country ownership, strengthen existing influenza programmes and initiatives, secure continued implementation of the PIP Framework, expand multisectoral partnerships, and ensure value for money.

Public health research agenda for influenza

Any suggestions for promoting research and innovation under the Global Influenza Strategy should build on and focus those already outlined in the WHO Public Health Research Agenda for Influenza, which serves to guide research so that knowledge gained improves public health decision-making in the prevention, control, and preparedness for influenza.

Last updated in 2017, the Public Health Research Agenda for Influenza promotes research in priority areas across five streams of work: reducing risk, limiting spread, minimizing impact, optimizing treatment, and promoting tools. Participants at the better global tools meeting received a summary of the latest recommendations on two of these: minimizing impact and optimizing treatment (see Table 2).

### Table 2. Relevant research recommendations (in brief) to emerge from the Public Health Research Agenda for Influenza

<table>
<thead>
<tr>
<th>WORK STREAM</th>
<th>RESEARCH RECOMMENDATIONS</th>
</tr>
</thead>
</table>
| Minimizing impact | • Improve vaccine strain selection  
• Enhance clinical applications of existing vaccines  
• Improve vaccine production processes  
• Optimize and standardize animal models  
• Develop new vaccines, platforms, and formulations  
• Identify correlates of protection for different vaccines  
• Develop innovative clinical trial methods |
| Optimizing treatment | • Develop rapid, sensitive and affordable point-of-care diagnostic tests  
• Develop improved point-of-care tools for prognosis and clinical management  
• Optimize use of current antivirals  
• Optimize the effectiveness of current and novel antivirals  
• Develop new and effective treatment strategies  
• Optimize management of patients with severe influenza disease |

“**When the next pandemic virus hits, will we have predicted the strain at hand? Will we have treatments that work? Will we be able to quickly get vaccines to those who need them most?”**

---

PART II. THE ROLE OF INNOVATION

Innovating for influenza

In discussing the role of innovation in influenza prevention, control, and treatment, Dr Robert Johnson from the US Biomedical Advanced Research and Development Authority (BARDA) highlighted four critical ingredients for success:

1. A continuum of innovation. Innovation is rarely defined by a single action but by a range of activities.

2. An open mindset. This is a cornerstone of innovation, however you define it.

3. A long-term outlook. Innovation requires thinking about the long-term sustainment of the overall effort, including for example, finding ways to sustain capabilities after successful development, while also maintaining resources to continue research and development (R&D).

4. Incremental improvements. Small, well-timed steps also advance public health. For example, every step in the vaccine production process offers an opportunity for innovation, and small gains can make a big difference to potentially improving the timely availability, effectiveness, and better use of the current influenza vaccines.

Priorities for innovation

Improve point-of-care testing so that it is readily accessible and easy to use. Early identification of infection enables earlier intervention that can save lives and reduce transmission risk. In particular, developing and incorporating home-based diagnostics that can detect influenza early and ensure the patient never needs to leave the house can change the dynamic of care for influenza patients. This empowers the patient to seek early treatment and reduce transmission.

Improve production efficiencies. It could take up to six to nine months to get a pandemic vaccine to the people that need it. Research and innovation are required at every step to speed up the process, including securing the supply chain of raw materials. It is also critical to have an implementation plan to introduce improvements into established production processes. At the same time, research into longer-lasting formulations may enable more cost-effective stockpiling, where applicable.

“Each step in the vaccine production chain offers an opportunity for innovation.”

Increase effectiveness of vaccines. In part, this is about moving towards a universal vaccine, even though in practice such a vaccine may still be many years away. It is also about improving the vaccines that are currently available; studies of seasonal influenza vaccine effectiveness conducted by the US Centers for Disease Control and Prevention (CDC) show that vaccines have generally not achieved more than 60% effectiveness (which refers to the prevention of medically-attended influenza in outpatients but not of that in hospitalized patients) for more than a decade (see Figure 2). Note that the methods for assessing vaccine effectiveness have changed within the last decade so the decrease may be an artifact of methodology. Innovation in current vaccine formulation, dosing and composition may all contribute to improvements in our existing influenza vaccines. Additionally, there are benefits to reducing the risk of severe influenza that results in hospitalization and we collectively need to do a better job of communicating/messaging this to the public, particularly to persons who are at high-risk for influenza complications.

Figure 2. Seasonal influenza vaccine effectiveness as calculated by US CDC

---

2 Data published by US CDC (https://www.cdc.gov/flu/vaccines-work/past-seasons-estimates.html) and shared at the better tools meeting by speakers from the Johns Hopkins Center for Health Security.
Make vaccine delivery more accessible. Reliance on specialised healthcare to deliver and administer influenza vaccines puts them out of reach for many of the people that need them most, especially in resource-limited settings in LMICs and during mass vaccination campaigns. Innovation in the formulation and presentation of vaccines, for example by using patches for self-administration, could significantly improve the reach of influenza vaccines during a pandemic.

Adapt existing tools for influenza. There are opportunities to harness innovation to improve how we detect and treat influenza, for example in the chain of events leading to a patient accessing an antiviral drug. In many cases, this may not be about coming up with new tools, but about finding ways to adapt existing tools to the challenges of influenza.

Understanding virus characteristics and host factors

Bearing in mind the need to promote research to better understand the virus and host factors that drive impact, a panel of scientific experts shared their perspectives on how best to improve the basic knowledge underlining the development of influenza interventions.

The constant diversification of viruses, limited surveillance at the animal-human interface, and poor understanding of some animal reservoirs (such as pigs) are major challenges that make it particularly difficult to identify new strains as they emerge and to predict which of these poses a real public health risk. It is important to acknowledge that even if we had full knowledge of what is circulating we would still not be able to say what the next pandemic would be, so we have to be modest about what we can predict.

Other challenges cited by the panel include limited progress in understanding host factors that reduce influenza propagation, poor understanding of transmission, and significant knowledge gaps in immunology. We still do not fully understand how and why people get infected with the virus and why it causes such severe problems in some patients but not others.

Together, the panel identified six research priorities that would impact influenza product development and innovation:

- Improve early detection.
- Better understand and predict virus evolution.
- Improve understanding of immunology and transmission.
- Target host factors to block replication.
- Improve seasonal influenza vaccines.
- Strengthen data sharing and analyses across sectors.

Redesign phase III clinical trials to be more consistent, efficient, relevant, and less expensive. Clinical studies of hospitalized patients with influenza pose a particular challenge because they are expensive and inefficient. It often takes several years to enroll the numbers of required patients. In addition, these trials are conducted globally and different hospitals around the world have different standards and protocols for clinical care of influenza patients; there are no generally agreed upon or validated clinical endpoints. Pooling data from patients through clinical networks worldwide might help to address this, but this would require the collection of standardized data variables and standardization of supportive clinical management across clinical networks worldwide.

Reimagine respiratory protection. The primary respiratory protective device used today is the disposable N95 respirator. It remains almost identical to the one used 100 years ago during the 1918 influenza pandemic. Such respirators are generally only designed for adults, must be fit-tested to work properly, and are uncomfortable to wear. Moreover, if a pandemic were to emerge tomorrow, demand for respiratory protective devices would far exceed supply. A Quickfire Challenge to Reimagine Respiratory Protection was launched by BARDA and Johnson and Johnson Innovation, JLABS to catalyse innovation to modernize and improve respiratory protection. Innovators with the best ideas will be announced in 2019. One participant suggested that a similar effort is required for eye protection.

Building on lessons learnt

Participants at the better global tools meeting agreed that any effort to strengthen global preparedness and response to pandemic influenza should build on knowledge gained from past pandemics.

Dr Michael Worobey from the University of Arizona highlighted two key lessons learnt from his evolutionary studies of the 1918 pandemic of influenza A (H1N1) that highlight the critical role of childhood and secondary infections in determining the severity of influenza virus infection, as summarized below.

“Initial childhood infection starts a time-bomb ticking; then bacterial pneumonia completes the explosion.”
1. Initial childhood infection

Dr Worobey summarized the data on hemagglutinin (HA) imprinting, which suggests that children imprint to whichever HA subtype causes their first infection and that may contribute to lifelong protection against all subtypes in the same phylogenetic group.

Armed with the knowledge of which viruses were circulating through the 20th century, Dr Worobey and colleagues used studies of incidence and mortality for H7N9 and H5N1 virus infections according to birth year to show that differences in exposure history match differences in immunity (see Figure 4). Indeed, their results show that people have 75-80% protection against infection by a zoonotic subtype from the HA group matching their first childhood influenza virus infection (and 80–85% protection against death).

Of course, this poses a challenge in protecting against the threat of influenza in that each individual is only naturally protected against the known influenza subtypes belonging to the phylogenetic group to which they were originally exposed. But it also presents a key opportunity in that if we can give young children a live attenuated influenza vaccine (LAIV) that includes epitopes from both HA groups before their first natural infection then we may be able to effectively educate their immune systems to tackle viruses from both groups and lay down a strong long-term immunity to influenza. In theory, this would protect
dividuals from severe outcomes later in life; but it would also build up a generation (and eventually an entire population) of people shielded against severe disease by establishing protection against both influenza A HA groups. This would require substantial pre-clinical validation.

2. Secondary infections

The second lesson learnt from the 1918 influenza pandemic is the importance of securing access to antibiotics and pneumonia-agent vaccines. Medical and scientific experts broadly agree that many of the deaths in 1918–1919 were not caused by the influenza virus alone but also by the bacterial pneumonia that followed influenza. Without adequate stocks of antibiotics, secondary bacterial infections could still be a major killer in an influenza outbreak and there would be the added risk of increasing antimicrobial resistance. Secondary bacterial infections should not be treated as an afterthought in planning for the next pandemic.

Figure 4. Hemagglutinin (HA) imprinting provides lifelong protection against all subtypes in the same group.
PART III.
TOWARDS BETTER PRODUCTS

A large part of the agenda at the better global tools meeting was given to reviewing the product landscape and pipeline for influenza detection, prevention, and control; and to exploring ideas for strengthening these. The details of individual products available on the market and in development were given in the presentations.

A summary of the key messages to emerge on challenges, opportunities, and priorities for innovation is presented below.

Landscape overview

Mr Matthew Watson and Ms Sanjana Ravi from the John Hopkins Center for Health Security shared the results of their broad survey of available vaccines, therapeutics, and diagnostics to try and quantify the product pipeline and describe the global distribution of innovation for the next generation of medical countermeasures. They collected data from national and regional clinical trial databases, and supported it with information published in academic research, press releases, and organisational websites.

Key messages

Vaccine development receives the bulk of investment. Both the global R&D landscape and the manufacturing capacity for therapeutics and diagnostics are far more limited compared with vaccines. For example, the review found approximately 200 vaccines in various stages of pre-clinical and clinical development, compared with less than 50 antiviral or other therapeutic products (see Figure 5). A quick analysis of the vaccines in development shows that while there is a robust influx of candidates into Phase I studies, there is a steep drop off after that, with only 27 products around the world that are approved for use. There are 14 universal vaccine candidates in various stages of development from pre-clinical to Phase III trials.

The pipeline for treatments and diagnostics is unclear. The diagnostics and therapeutics pipelines are significantly less transparent that that of vaccines. The diagnostics landscape is especially difficult to access, so the review presented at the meeting was limited to only listing licensed diagnostics, with a particular focus on polymerase chain reaction (PCR) assays.

More effort is needed to catalyse the emergence of new products. In particular, speakers recommended supporting additional research partnerships, networks, and investment.

New products need support tools. Even after a new vaccine, therapeutic, or diagnostic is developed, a suite of ancillary and support tools, such as technical guidance, must be created to ensure they are used effectively and appropriately.

Figure 5. An overview of the medical countermeasures in pre-clinical and clinical development.
Diagnostics

A look at the diagnostics landscape, presented by Dr Daniel Jernigan from the Influenza Division at the US CDC, showed that it is populated by devices using different technologies and varying in complexity, duration, and place of testing. Dr Jernigan highlighted some of the key trends in diagnostics for influenza and showed that, in general, these are becoming smaller, cheaper, and more connected (see Table 3).

Priorities for innovation

Support R&D for novel, low-resource diagnostics. This includes supporting new methods like CRISPR diagnostics, which already show promise for low-cost, high-sensitivity influenza tests.

Develop a connectivity strategy for accessing and using the cloud data of next-generation medicine. The Internet of Medical Things is transforming healthcare, potentially opening the door to much faster diagnosis and treatment. The challenge remains of finding ways to aggregate distributed results for better public health surveillance. This requires developing a standard and effective interface for cloud services that can allow users to access and share information quickly, safely, and easily.

Develop a next-generation sequencing strategy. This should focus on deployable sequencing to support influenza surveillance, including predicting virus susceptibility to antivirals; and should foster the development of field-based technologies to support that. There are already efforts underway towards field-based diagnostics, for example portable PCR, environmental testing in bird markets, mobile virus recovery, and improvements in specimen preparation and assay performance.

"As the cost and footprint of sequencing continues to decrease, next-generation efforts should focus on technologies that can be used in the field."

Support R&D for new technologies and wearables. The growing interest in smartphone-enabled testing and next-generation medicine means that there are already several wearable products available to monitor things like temperature, blood pressure, and oxygen levels. Recent efforts for influenza include looking at the potential of wearables for pre-symptom detection and outcome prediction.

"One encouraging trend is the emergence of universal vaccines."

Table 3. Summary of key trends in influenza diagnostics

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>KEY TRENDS</th>
</tr>
</thead>
</table>
| Size and cost    | • Diagnostics vary in cost, and many still require specialized equipment.  
                  | • Novel digital immunoassays (DIAs) and rapid nucleic acid amplification tests (NAATs) are coming down in cost, can be run by batteries, and should be promoted.  
                  | • Sequencing is becoming faster and cheaper, but it remains a challenge for sustained use in traditional virologic surveillance. |
| Sensitivity      | • Novel DIAs and NAATs have markedly higher sensitivities for influenza A and B in both children and adults than traditional rapid influenza diagnostic tests (RIDTs), with equally high specificities.  
                  | • Other new technologies, such as CRISPR diagnostics have high sensitivities that could be used to detect clades of influenza and antiviral resistance. |
| Complexity       | • Of the US FDA-cleared rapid DIAs and NAATs, a small number can be done outside a laboratory.  
                  | • There is a definite trend in NAATs towards lower-complexity, point of care tests.  
                  | • New CRISPR diagnostics, which do not require cold chain storage and are quick and easy to use, are further reducing complexity of available influenza diagnostics. |
| Connectivity     | • The "Internet of Medical Things" allows medical devices to be connected to the cloud and to applications; and there are already several cloud-connected devices available that report results and share data anonymously. |
Vaccines

Dr Bruce Innis from PATH’s Center for Vaccine Innovation and Access provided an overview of the vaccine R&D landscape—those available now and what lies on the horizon. He emphasized that while the current set of approved vaccines against seasonal influenza does significantly reduce the risk of severe disease, it remains inadequate to equitably prevent and control influenza (including for a pandemic response). In large part that is because of low programmatic suitability: the need for annual administration and cold-chain management significantly limits global use of seasonal influenza vaccines. In many LMICs, use is further limited by an underestimate of the public health benefit of influenza vaccination (especially given the limited effectiveness of current vaccines), which drives down demand. Where there is demand in LMICs, access to the vaccines is often significantly constrained by manufacturing capacity and cost.

“There is simply not enough vaccine and the high-income countries get the bulk of it.”

The diversity and complexity of influenza viruses continue to pose a major challenge to developing effective vaccines. And the ongoing huge investment in facilities for egg-based production is a similarly significant barrier to innovation. Nevertheless, there are several initiatives working to advance vaccine R&D (see Box ‘Vaccine R&D initiatives’) and many technologies under development to improve the efficacy, programmatic suitability, and access to influenza vaccines. Dr Innis highlighted eight broad types of these: virus-vectored vaccines, novel adjuvants, nano-particle vaccines, nucleic acid vaccines, cell-based vaccines, alternate delivery models, anti-HA stalk vaccines, and T-cell vaccines.

According to Dr Innis, across these new technologies, there are several promising technical innovations that may increase the breadth of protection within the timescale of the new Global Influenza Strategy: 11 products are already in late development (Phase III trials) and any product that enters Phase II by 2020 could potentially be pre-qualified for global use by 2030. But several participants warned that more investment—especially from beyond the private sector—will be required to drive that innovation forward. And across all technologies, more collaboration to address the needs of LMICs should be encouraged to accelerate development.

Vaccine R&D initiatives

The WHO Secretariat summarized some of the global and regional R&D initiatives for influenza vaccines, many of which focus on developing a universal influenza vaccine.

Initiatives mentioned by speakers and participants include:

- Global Funders Consortium for Universal Influenza Vaccine Development
- Universal Influenza Vaccine Development Grand Challenge
- The Influenzer Initiative
- Influenza Vaccines Roadmap
- K.G. Jebsen Centre for Influenza Vaccine Research
- Universal Influenza Vaccine Initiative
- EU-India Collaboration for Next Generation Influenza Vaccines
- WHO Technology Transfer Initiative
- US National Institutes of Health Universal Influenza Vaccine Research

Several industry associations were also mentioned for their role in promoting high standards of quality and fostering innovation. These include: the Biotechnology Innovation Organization, the Developing Countries Vaccine Manufacturers Network, and the International Federations of Pharmaceutical Manufacturers & Associations.

The need to coordinate efforts across funders and innovators was underscored by several participants. The Global Funders Consortium already provides a coordinating mechanism of sorts, but one participant suggested that WHO could offer further coordination support beyond just universal influenza vaccines.
Priorities for innovation

Two panel discussions at the better global tools meeting provided the industry and public health perspectives on challenges, opportunities and priorities for innovation in influenza vaccines.

“No funding or policy means no predictable demand, which means no incentive to build capacity or invest in innovation.”

Industry speakers highlighted high capital and development and production costs as significant challenges, particularly when coupled with regulatory barriers and poor demand for influenza vaccines in many countries. One speaker argued that the reason there is no high-volume, low-cost manufacturing base for influenza vaccines is because most countries have no clear funding or policy for influenza immunization and little-to-no governmental demand for vaccines.

Industrializing the process for vaccine manufacturing so that vaccines can be supplied reliably, efficiently, and at the scale required for a global response was another commonly cited challenge by the industry panel of experts.

From the public health perspective, the lack of government commitment and public confidence in influenza vaccines was also seen as a major barrier to their use and to the investment needed to improve them. This in turn reflects challenges in the efficacy and cost-effectiveness of existing vaccines. Some speakers highlighted the need to focus on safe vaccines for the very young by supporting clinical trials of LAIVs among infants or by developing criteria for recommending adjuvanted vaccines for children.

Speakers from both panels made specific suggestions for action, which are included in Part IV below. They also pointed to their own priorities for innovation, identifying specific areas of research where greater attention and investment are required (see Figure 6). In many cases these were not about developing a universal vaccine, which most participants agreed was still years away, but about making incremental innovations to improve the current suite of vaccines available. This includes, for example, increasing the breadth of protection of current vaccines by using adjuvants or by making a two-dose vaccine that is less strain-specific.

One speaker from the United Kingdom highlighted the value of using different approaches for different target groups, based on what has been shown to be most effective. For example, using a live quadrivalent influenza vaccine for children and young people and an adjuvanted trivalent vaccine for the elderly. Introducing differentiated products into a government immunization programme can be good for innovation because it can stimulate studies of effectiveness and create R&D around the policy change.

“We need to focus on improving what we’ve got... including both the technology itself and how we use it.”
Therapeutics

There are three broad types of therapeutics that can potentially be used to treat influenza: antivirals, immunotherapies, and host-directed therapies that modulate the innate immune response. Antivirals are the only type with market-approved drugs, although there are a range of products across all three types that are currently under clinical investigation (see Table 4).

Table 4. Potential strategies for treating influenza, with products in various stages of clinical development

<table>
<thead>
<tr>
<th>STRATEGY</th>
<th>EXAMPLES UNDER CLINICAL INVESTIGATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct-acting antivirals</td>
<td>• Pimodivir, baloxavir, favipravir, arbidol (umifenovir)</td>
</tr>
<tr>
<td>Immunotherapies</td>
<td>• Immune plasma, hyperimmune globulin, monoclonal antibodies</td>
</tr>
<tr>
<td>Host-directed therapies</td>
<td>• DAS181, nitazoxanide, diltiazem (some of these compounds have been shown to possess both antiviral and immunomodulatory effects in experimental models)</td>
</tr>
<tr>
<td></td>
<td>• Potential strategies: macrolides, cyclooxygenase inhibitors, sirolimus, statins</td>
</tr>
</tbody>
</table>

Plus numerous combinations of the above

Antivirals

Professor Frederick Hayden from the University of Virginia provided a state of the art of influenza antivirals. Antivirals provide the mainstay of influenza treatment, with seven licensed drugs currently available in different countries across the world and one listed in WHO’s Model List of Essential Medicines. These include neuraminidase inhibitors (NAIs) such as oseltamivir and peramivir, as well as M2 inhibitors (adamantanes) such as rimantadine and amantadine. In 2018, the polymerase inhibitor (PAI) baloxavir became the first antiviral of a different class of drugs for the treatment of influenza to be approved.

In Europe, intravenous zanamivir is the latest antiviral (an NAI) to be approved for treating influenza A and B and is expected to prove particularly useful in cases where oseltamivir resistance is known or suspected to be a problem.

Several antivirals are in various stages of pre-clinical and clinical development, although arguably not as many as there should be. In most cases, antivirals tend to move from one stage of development to another very slowly.

“The reality of whether you are going to present to hospital within three days of symptom onset is patchy and in most health systems highly unlikely.”

Speakers and participants cited numerous challenges to using and developing effective antivirals, including:

- **Variable use.** Patients in different countries use antivirals in different ways. In Japan, for example, most people with influenza seek medical care promptly after illness onset, and those who test positive for influenza are prescribed antivirals. The result is early initiation of antiviral treatment for most people with influenza. Whereas in most other countries, individuals with influenza typically do not seek medical care early in their illness or not at all. Standardizing use and educating the prescribing population and the public on appropriate use remains a top priority.

- **Resistance.** The emergence of resistant influenza virus strains remains a problem across all available classes of antivirals, which makes careful monitoring of susceptibility patterns and diversification of antiviral stockpiles a clear priority for use.

- **Timeliness of treatment.** In all cases, rapid access and distribution of antivirals are essential because the earlier the treatment, the better the outcome. This important time-to-treatment initiation of antivirals is challenging for testing experimental therapies in hospitalized patients because most patients with severe disease are admitted after the period of time when antiviral treatment has been shown to be beneficial studies among outpatients.

- **Randomized control trials (RCTs) as gold standard.** The emphasis on RCTs, which have focused on illness duration and symptom reduction as primary endpoints, may be detrimental as they ignore the huge amount of observational data that are also important and potentially more accessible for studying clinical endpoints, including antibiotic use, hospitalizations, length of hospital stay, and mortality.

---

4 Oseltamivir is listed in the current edition of the WHO Model List of Essential Medicines. See https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf?ua=1
For direct-acting antivirals, the benefits are marginal. However, the potential to increase potency while reducing risk of resistance is not ideal and, in a pandemic situation, unrealistic for most LMICs. The need for intravenous administration of small molecule antivirals, which means that most products may not be affordable or cost-effective. The need for intravenous administration of small molecule antivirals, which means that most products may not be affordable or cost-effective. Production cost is a major barrier and combined with the fact that when used as a treatment (in products tested so far in clinical trials), there appears to be marginal therapeutic benefit compared with direct-acting antivirals. At the better global level, the product pipeline shows that while there are many candidates for alternative endpoints in Phase III clinical trials was emphasized by speakers and participants. These should focus on outcomes that drive public health utility and that serve the reality of clinical practice. However, such trials will require much larger sample sizes than those utilizing illness alleviation in uncomplicated influenza. Observational studies remain a priority.

Find ways to improve targets. For direct-acting antivirals, the number of potential targets is limited, and emergence of resistance can be a problem. A look at the current development pipeline suggests that we have nearly reached a limit in testing viral targets, which underscores the need to focus R&D efforts on optimizing agents for current targets. In this regard, novel inhibitors targeting neuraminidase, polymerase, and the HA stem have been recently described.

Redesign RCTs to focus on public health outcomes. The need for alternative endpoints in Phase III clinical trials was emphasized by speakers and participants. These should focus on outcomes that drive public health utility and that serve the reality of clinical practice. However, such trials will require much larger sample sizes than those utilizing illness alleviation in uncomplicated influenza. Observational studies remain a priority.

Explore new platforms for drug development. This includes further exploring the use of monoclonal antibodies as well as the use of other platforms, such as self-amplifying RNA arrays.

Monoclonal antibodies

Immunotherapy using broadly neutralizing antibodies that bind to multiple, structurally diverse strains of influenza are, in theory, an attractive alternative to direct-acting antivirals. At the better global tools meeting, participants heard about the range of these monoclonal antibodies (mAbs) that are currently in clinical development as a means for treating or preventing severe influenza. All the mAbs presented were specific to influenza A and all target epitopes on the HA stalk.

In short, the product pipeline shows that while there are many candidates in preclinical trials, only a handful make it to clinical development and many drop out before reaching Phase III. The challenges are multi-fold. Production cost is a major barrier and combined with the fact that when used as a treatment (in products tested so far in clinical trials), there appears to be marginal therapeutic benefit compared with small molecule antivirals, which means that most products may not be affordable or cost-effective. The need for intravenous administration is not ideal and, in a pandemic situation, unrealistic for most LMICs.

Focus on antiviral combination therapies. Several antiviral combinations in development (for example, combining NAs and PAs) have the potential to increase potency while reducing risk of resistance. In all cases, speakers agreed that combination therapies are the most likely way forward for improving influenza treatment. Some have suggested there is a need for studies of combination antiviral treatment (i.e. two antiviral drugs with different mechanisms of action) combined with immunomodulatory therapy.

Priorities for innovation in antivirals as cited by speakers include:

- **Demonstrate efficacy.** To be cost effective in treating severe seasonal influenza, mAbs need to show a much higher clinical benefit than antivirals. In particular, a range of in vitro and animal and human challenge studies are needed to demonstrate efficacy against non-circulating strains of influenza. Studies are also needed to prove the efficacy of mAbs as prophylaxes for potential use during a pandemic.

- **Improve production.** More research is needed to drive down the cost of mAbs through production improvements focused on, for example, strengthening binding affinities, extending the half-life or making the manufacturing process more efficient.

"There is a definite use for mAbs as prophylaxis during a pandemic, but it needs demonstrating... If stability could be proven over time, mAbs would be worth stockpiling as source of immediate protection while people wait for vaccines."

Priorities for innovation identified by speakers include:

- **Explore new platforms for drug development.** This includes further exploring the use of monoclonal antibodies as well as the use of other platforms, such as self-amplifying RNA arrays.

- **Redesign RCTs to focus on public health outcomes.** The need for alternative endpoints in Phase III clinical trials was emphasized by speakers and participants. These should focus on outcomes that drive public health utility and that serve the reality of clinical practice. However, such trials will require much larger sample sizes than those utilizing illness alleviation in uncomplicated influenza. Observational studies remain a priority.

- **Find ways to improve targets.** For direct-acting antivirals, the number of potential targets is limited, and emergence of resistance can be a problem. A look at the current development pipeline suggests that we have nearly reached a limit in testing viral targets, which underscores the need to focus R&D efforts on optimizing agents for current targets. In this regard, novel inhibitors targeting neuraminidase, polymerase, and the HA stem have been recently described.

- **Demonstrate efficacy.** To be cost effective in treating severe seasonal influenza, mAbs need to show a much higher clinical benefit than antivirals. In particular, a range of in vitro and animal and human challenge studies are needed to demonstrate efficacy against non-circulating strains of influenza. Studies are also needed to prove the efficacy of mAbs as prophylaxes for potential use during a pandemic.

- **Improve production.** More research is needed to drive down the cost of mAbs through production improvements focused on, for example, strengthening binding affinities, extending the half-life or making the manufacturing process more efficient.

**Host-directed therapies**

The idea of a host-targeted approach to treating influenza is appealing because we know that many of the disease manifestations in severe influenza are due to the host responses rather than just the virus itself. It could also prove an effective way of reducing the risk of resistance emergence.

Professor Nelson Lee from the University of Alberta provided an overview of the R&D landscape for drugs that can control virus-induced host immune responses. He showed that there are many potential immunomodulatory agents under clinical investigation, including corticosteroids, macrolides, nonsteroidal anti-inflammatory drugs, statins, and mTOR inhibitors among others. Many of these have shown through experimental models that they can control one or more components of the host response; some also have direct or indirect antiviral properties. But very few have human data to support their results and most of those that do, show negative results. For example, there is a broad consensus that the risks of using high-dose corticosteroids to treat influenza outweigh the benefits so they should not be used. And RCTs of several other agents, including nitazoxanide and over-the-counter medicines like paracetamol, show little clinical benefit compared with direct-acting antivirals.
In the search for new agents that might be useful in treating influenza, the idea of drug repurposing is rapidly gaining traction. In 2019, a research team published the results of their work to study global transcriptomic signatures of infection in influenza patients and shortlist drug candidates with host-targeted inhibitory properties. They identified 31 candidates and have selected three of these for further research, including Diltiazem which is being evaluated for the treatment of acute influenza infection in the context of a phase IIb clinical trial. Many other drugs are also being investigated for potential repurposing. These range from interferons to herbal medicine; most remain in early stages of development.

In considering the priorities for innovation in host-directed responses to influenza, participants and speakers suggested four areas of focus.

**Explore adjunctive therapy.** Future research on adjunctive therapy should include investigating its potential use to: downregulate proinflammatory, innate responses; preserve host-adaptive immunity for effective viral clearance; and provide additive or synergistic effects to antivirals.

**Develop a better animal model.** Several participants highlighted the need for a better animal model to study influenza treatments because the current mouse models do not correlate well with human immunity and disease.

**Explore the potential for tailored therapy.** This includes investigating the potential for tailoring therapies according to age group and underlying conditions (which are two of the most significant factors influencing host response).

**Gather more data on repurposing.** Drug repurposing is an attractive option, but it requires the development of well-designed trials to assess for clinical efficacy, virological changes, and immunological responses.

“First we need to understand the pathogenesis of severe influenza and identify critical pathways… then we must search for molecules using a more scientific approach… and then we have to come up with a more accurate animal model to study effects.”

Top three priorities for influenza therapeutics

Across all three types of influenza therapeutics—antivirals, mAbs, and host-directed therapies—participants at the better global tools meeting identified three common priorities for research and innovation. These include developing a supportive clinical trial structure; establishing new development pathways; and further exploring the potential for drug repurposing (see Figure 7).
Figure 7. Research priorities to support development of new and improved influenza therapeutics

**SUPPORTIVE CLINICAL TRIAL STRUCTURE**
- Ensure coordination and collaboration among existing clinical networks
- Ensure standard management protocols
- Include ability to enroll patients with zoonotic influenza
- Achieve better enrolment per site

**NEW DEVELOPMENT PATHWAYS**
- Establish different clinical and virological end points
- Use alternative models in pre-clinical evaluation (i.e. in vitro and animal models that better correlate with human influenza disease)
- Do trials initiating therapy immediately upon admission
- Monitor for safety and emergence of resistance

**DRUG REPURPOSING**
- Develop systematic approach to retest potential candidates for repurposing
- Expand testing to include “shelved” compounds
- Utilize well-designed clinical trials to investigate clinical efficacy, impact on viral clearance, dosing and toxicity
- Promote clinical testing of combinations of antivirals and host-directed therapies
PART IV.
ACTION PLANNING

Scenario planning

To focus participants’ minds on the key gaps in existing products and tools for influenza, a panel of experts were asked to consider a scenario in which a fictional novel strain of influenza A virus has emerged and has already killed 1,500 people across two countries. Assuming that every nonpharmaceutical intervention (NPI) available is already in play, what action can and should be taken to mobilize pharmaceutical interventions to limit the impact of the new virus as soon as possible? The panel was asked to provide its suggestions for action.

Almost all of the recommendations focused on speeding up our collective processes to detect, prevent and treat influenza (see Table 5).

The scenario planning exercise also highlighted several areas where strong preparation by countries, manufacturers, WHO, and partners now could help ensure a more effective pandemic response in the future. These include:

- Work with Member States to develop or revise their influenza pandemic preparedness plans.
- Focus on LMIC needs and priorities for equitable access, including agreeing upon conditions of provision.
- Strengthen infrastructure for seasonal influenza.
- Work on fit-for-purpose technologies that will work in resource-limited settings.
- Establish data-sharing agreements to enable swift severity assessments.
- Carry out citizen juries to identify and address public concerns.
- Support demonstration projects to show value of potential prophylaxes (such as mAbs).
- Encourage manufacturers to get their products prequalified, if applicable.
- Evaluate stockpiles (antivirals, antibiotics, masks, ventilators, etc.) to see what is available and where.

<table>
<thead>
<tr>
<th>SUGGESTION</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Make sure we know what we’re dealing with</td>
<td>• Collect as much epidemiological data as possible to enable a quick and accurate severity assessment and ensure a proper understanding of susceptibility (to target our efforts at highest risk groups).</td>
</tr>
</tbody>
</table>
| Detect and track the pandemic as far as we are able | • Ramp up all available surveillance in affected and neighbouring countries.  
• Deploy appropriate diagnostics to the field as quickly as possible to ‘follow the virus’ and conduct antiviral susceptibility testing.  
• Use smart technology as much as possible. |
| Communicate widely and effectively             | • Inform stakeholders of the situation to prevent panic.  
• Provide advice on what action people can and should take to protect themselves and others (in affected and nonaffected countries).  
• Give health workers and the general public guidance on clinical management, including the benefits of early initiation of antiviral treatment.  
• Prepare people for a potential outbreak (in nonaffected countries). |
| Line up all the products we can                | • Kickstart vaccine development and production as fast as possible, including getting the candidate vaccine virus (CVV) and potency reagents.  
• Look for ways to speed up vaccine production, for example by fast-tracking approval or using alternatives like LAIVs.  
• If possible, use pneumococcal and Haemophilus influenzae vaccines to prevent secondary infections (noting that this may not be an option for LMICs). |
| Trigger our pandemic plans                     | • Get countries and organizations to ‘turn on’ their pandemic plans wherever these exist (including national pandemic preparedness plans, regulatory plans, PIP Framework manufacturer agreements, WHO distribution plans). |
Recommendations for action

In addition to identifying the product-specific innovations that are required to deliver better global tools (detailed as ‘priorities for innovation’ in Parts II and III above), much of the discussion at the meeting focused on exploring ways in which WHO and other stakeholders can promote influenza research and innovation more broadly.

A wide range of suggestions emerged from their deliberations across both days of the meeting. These are listed below, grouped by broad category but presented in no particular order. The final session of the meeting included a group exercise to distil these into priorities for action to accelerate the development of new and improved vaccines, antivirals, and other treatments (see Figure 8).6 Participants highlighted the roles that stakeholders have in promoting research and innovation to implement the Global Influenza Strategy, including WHO, Member States, academia, industry, regulatory agencies, and funders. In a break-out session, participants articulated some of the roles and responsibilities of these stakeholders (see Annex III); as part of its next steps to this meeting, the WHO Secretariat will review all suggestions and identify those to take forward.

Figure 8. Priority actions to accelerate the development of vaccines, antivirals and treatments

1. Boost public understanding, confidence, and uptake.

Find new ways to engage and inform the public. It is not enough to simply communicate the need for, and benefits of, influenza diagnostics, vaccines, and therapeutics, because this has been done for years with marginal success. We need to find new ways to engage and inform the public to improve understanding, uptake, and use of influenza products. This may include using citizen juries or focus groups to identify key concerns or evaluate patient preferences for technologies.

Target messaging to key groups. A key priority is to target messaging to key stakeholders, including high-risk groups and clinicians. Improved messaging is also very much needed. This messaging must emphasize and educate high-risk patients and clinicians, including the benefits of influenza vaccines, antivirals, and other treatments.

VACCINES
- Communicate benefits of influenza vaccines
- Strengthen political will using burden of disease studies
- Secure funding
- Ensure regulatory approval
- Coordinate research
- Explore alternative delivery methods

ANTIVIRALS
- Raise awareness among governments and public
- Increase demand & use for seasonal influenza
- Improve clinical guidelines for diagnosis and early antiviral treatment, especially in high-risk patients.
- Understand and tackle barriers to stockpiling
- Ensure coordination and collaboration among existing clinical networks

OTHER TREATMENTS
- Prioritize products to take into clinical trials
- Support clinical networks that can do studies on hospitalized patients
- Use large datasets more effectively to correlate outcomes with treatments
- Harmonize methods for doing trials (including using standard trial outcomes)

6 All the individual suggestions made by participants on post-it notes were collected by the WHO Secretariat and will be collated and reviewed in parallel to the drafting of this report.
2. Build political will

**Turn the global strategy into a global call for action.** In many countries, convincing governments that influenza poses a real threat remains the first step to enabling action. The priority for WHO and partners should be to build the political will needed to secure demand and investment for influenza products.

**Make an effective case for investment.** This is about developing a strong narrative that can present the risks of influenza more coherently and show finance ministers that influenza poses an unacceptable threat to productivity and that investing in detection, prevention, and control makes financial sense. The World Economic Forum could have a natural role in developing the case for investment.

**Leverage burden of disease studies.** Experiences in Thailand and other countries suggest that burden of disease studies can be effective vehicles in raising awareness of the health and economic impacts of influenza and in garnering the political commitment needed to strengthen surveillance systems and invest in seasonal influenza prevention and control programmes and pandemic preparedness.

3. Secure funds and direct investors

**Fundraise beyond the private sector.** Sustaining innovation in influenza tools requires investment beyond the private sector.

**Coordinate donors.** Coordination is important to develop a consensus-driven plan for research and innovation. In some cases, achieving it requires building on existing mechanisms, such as the Global Funders Consortium for Universal Influenza Vaccine Development. In other cases, WHO may need to take a larger role in engaging and convening funding and research partners to align efforts.

**Direct investors towards high impact action.** This includes developing a concise list of priorities, preferred product characteristics, and activities that funders can use to inform and focus their investments.

“**The world needs to wake up politically to the threat of influenza.”**

4. Work together to align efforts

**Build partnerships across research and clinical practice.** In particular, partnerships between virologists, immunologists, and clinicians are needed to identify and address research and clinical management needs; to share data (both clinical and preclinical); and to integrate analyses of clinical, virologic, and immunologic data.

**Improve infrastructure for alignment and collaboration.** This includes providing standardized clinical protocols and data collection instruments to support alignment across countries and regions. It also includes supporting collaboration across sectors, for example by increasing the use of initiatives like Genbank or streamlining data sharing through initiatives like OFFLU.

**Harness new applications and methods for data sharing.** With the right planning and development, next generation medical devices, smart technologies, and rapidly expanding connectivity could all open the door to quicker, broader data sharing for detecting, tracking, and assessing circulating strains of influenza.

**Adopt a holistic view of production.** All stakeholders want to enable the quick and sustainable supply of, and access to, influenza vaccines and other products; all stakeholders should therefore share the responsibility of improving production processes as a whole, from start to finish.

5. Strengthen the evidence base

**Improve understanding of the virus.** Robust evidence is needed to better understand and predict the evolution, immunology, and transmission of influenza viruses.

**Leverage existing or establish new clinical networks.** Getting the evidence needed to deliver better tools for influenza will rely on global networks of hospitals and investigators that can carry out the right kind of clinical trials, with the right kind of clinical endpoints quickly and effectively. Important studies can be conducted during seasonal and zoonotic influenza outbreaks. These provide the foundation for rapid response in the event of a pandemic.
Harness existing evidence. This includes reviewing past outbreaks to learn from successes and failures. It also includes using large datasets more effectively to match treatments with outcomes and synthesizing findings from observational studies to inform standards of care.

Redesign and harmonize clinical trial methods. Beyond making trials cheaper and easier to run, this includes harmonizing methods for carrying out trials as well as using standard and more relevant trial outcomes.

6. Support early detection and rapid data sharing

**Develop deployable diagnostics.** To track outbreaks fully and in real time, diagnostics need to be field-deployable for use at point of care, on farms, and in markets to get quick results.

**Strengthen global surveillance.** This applies in both animal and human populations and, most particularly, at the animal-human interface.

"The faster a pandemic strain is spotted and a vaccine is developed and distributed, the easier it is to contain and control."

7. Improve vaccine production efficiencies

**Speed up vaccine production.** This includes a broad range of activities, from exploring the use of synthetic seeds to reduce the time required to get a CVV to fast-tracking approval during a pandemic.

**Streamline and strengthen manufacturing processes.** This includes looking for opportunities to improve the availability and reliability of products, including reagents, and to increase yields for manufacturers (for example, by broadening the immune response of products, extending their shelf-life, etc.).

8. Establish fast and clear regulatory pathways

Develop pandemic plans. Regulatory approval can be fast-tracked with a good pandemic preparedness plan. But planning can only get you so far: even with a plan in place in Europe during the last pandemic, pre-approval of the vaccine still took months to clear. Involvement of regulators in pandemic planning is critical to future responses.

Build partnerships with manufacturers. Preparedness plans can be supported with partnerships between authorities and manufacturers and with standing agreements to work together to assess options for speeding up production and distribution during a pandemic.

Gather more robust data on safety and efficacy. Any new vaccine must demonstrate it is both safe to use and effective in protecting against influenza. The more data that can be gathered in advance of a pandemic, the faster regulatory approval can be secured.

Clarify regulatory pathways for emerging products. This particularly applies to products such as mAbs that may be effective as a prophylaxis during early stages of a pandemic while countries wait for a vaccine.

9. Make influenza products sustainable

**Ensure guidance accompanies new products.** The development of new and innovative products should also include the development of accompanying support documents, such as technical guidance and recommendations on programmatic considerations (i.e. when and how to use them).

**Secure demand for new products.** Companies will not invest in developing new products if there is no market for them. Improving sustainability requires more effort to secure demand, particularly through government decision makers and supportive policies and programmes.

**Drive improvements of existing products.** Incremental innovations could improve the effectiveness and usability of existing tools as well as current manufacturing processes and technologies.
10. Focus on LMIC needs

Promote products for use in resource-limited settings. Such products need to be robust, sensitive, and specific; easy to use; and relatively cheap. In particular, they should not require specialised equipment to be distributed or administered.

Tailor studies to LMIC contexts. This includes both enabling human challenge studies in LMICs and matching clinical trial outcomes to local public health concerns; both are important to ensure products are relevant and effective in the countries where outbreaks can be most damaging.

Build capacity for seasonal influenza. Establishing seasonal influenza programmes and infrastructure sustains pandemic preparedness.

Strengthen LMIC manufacturing base. For example, by building on initiatives such as the Technology Transfer Initiative that has enabled the expansion of influenza vaccine production capacity in several LMICs.

Secure supply chains. This applies not only to the main influenza pharmaceutical products (vaccines, diagnostics and antivirals) but also to the broad range of NPIs (such as face masks), ancillary products (such as vials and syringes), and raw materials (such as eggs, reagents etc).

Next steps

Before the close of the meeting, WHO articulated its next steps. This includes a meeting of the newly-established WHO Working Group on Influenza Preparedness and Response on 13 June 2019, where members will review the outcomes of this meeting and discuss how to implement the Global Influenza Strategy.

Following that meeting, the WHO Secretariat will:

- share all presentations from the meeting with participants, subject to approval by individual presenters;
- finalize and share a meeting report; and
- meet with WHO colleagues in HQ and regions to review and prioritize suggestions for action.

“Unless we come up with tools that are available to the masses in LMICs, we won’t turn the problem around.”
# APPENDIX 1.
## MEETING AGENDA

### DAY 1

<table>
<thead>
<tr>
<th>11 June</th>
<th>Session</th>
<th>Facilitators / Presenters</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:15 – 9:00</td>
<td>Registration</td>
<td></td>
</tr>
<tr>
<td>9:00 – 9:10</td>
<td>Welcome</td>
<td>Mike Ryan</td>
</tr>
<tr>
<td>9:10 – 9:20</td>
<td>Chair’s remarks</td>
<td>Kanta Subbarao</td>
</tr>
<tr>
<td>9:20 – 9:50</td>
<td>Setting the scene:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Global Influenza Strategy 2019-2030</td>
<td>Ann Moen</td>
</tr>
<tr>
<td></td>
<td>• Public Health Research Agenda for Influenza</td>
<td>Wenqing Zhang</td>
</tr>
<tr>
<td></td>
<td>• Where do we need to go?</td>
<td>Martin Friede</td>
</tr>
<tr>
<td>9:50 – 10:10</td>
<td>What we’ve learned from previous pandemics</td>
<td>Michael Worobey</td>
</tr>
<tr>
<td>10:10 – 10:30</td>
<td>Role of innovation in influenza prevention, control and treatment</td>
<td>Robert Johnson</td>
</tr>
<tr>
<td>10:30 – 11:00</td>
<td>Coffee break</td>
<td></td>
</tr>
<tr>
<td>11:00 – 11:20</td>
<td>Influenza product landscape and pipeline</td>
<td>Matt Watson &amp; Sanjana Ravi</td>
</tr>
<tr>
<td>11:20 – 12:00</td>
<td>Panel discussion:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Current understanding of the virus, transmission, host factors, pathology,</td>
<td>Moderator: Arnold Monto, Bruno Lina</td>
</tr>
<tr>
<td></td>
<td>and immune response</td>
<td>Sophie Von Dobschuetz, Thorsten Wolff, Michael Worobey</td>
</tr>
<tr>
<td>12:00 – 13:30</td>
<td>Lunch</td>
<td></td>
</tr>
<tr>
<td>13:30 – 14:00</td>
<td>State of the art of influenza diagnostics and contributions to surveillance and research and development needs</td>
<td>Daniel Jernigan</td>
</tr>
<tr>
<td>14:00 – 15:00</td>
<td>State of the art of influenza vaccines:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Current technologies; universal and next generation vaccines</td>
<td>Bruce Innis</td>
</tr>
<tr>
<td></td>
<td>• Global and regional initiatives to advance research and development</td>
<td>Chris Chadwick</td>
</tr>
<tr>
<td>15:00 – 15:30</td>
<td>Panel discussion:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Industry capacity and seasonal and pandemic response</td>
<td>Moderator: Bruce Gellin, Samir Desai, Beverly Taylor, Mike Watson</td>
</tr>
<tr>
<td>15:30 – 16:00</td>
<td>Coffee break</td>
<td></td>
</tr>
<tr>
<td>16:00 – 17:00</td>
<td>Panel discussion:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Opportunities and challenges to advance influenza vaccine R&amp;D and to encourage better use of current vaccines</td>
<td>Moderator: Rebecca Cox, Supanit Chunsuttiwat, Josie Golding, Larisa Rudenko, Kanta Subbarao</td>
</tr>
<tr>
<td>17:00 – 17:15</td>
<td>Day 1 summary</td>
<td>Chair</td>
</tr>
</tbody>
</table>
# Technical consultation on product research and innovation for influenza prevention, control and treatment

## BETTER GLOBAL TOOLS FOR INFLUENZA

### Technical consultation on product research and innovation for influenza prevention, control and treatment

### BETTER GLOBAL TOOLS FOR INFLUENZA

#### 12 June

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Facilitators / Presenters</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 – 9:15</td>
<td>Recap of day 1 and plan for day 2</td>
<td>Ann Moen</td>
</tr>
<tr>
<td>9:15 – 9:45</td>
<td>State of the art of antivirals and current challenges and opportunities</td>
<td>Frederick Hayden</td>
</tr>
<tr>
<td>9:45-10:00</td>
<td>Monoclonal antibody overview</td>
<td>Erin Sparrow</td>
</tr>
<tr>
<td>10:00-10:30</td>
<td>Panel discussion: Opportunities and challenges to advance influenza antiviral R&amp;D and to encourage better use of current antivirals</td>
<td><strong>Moderator: Frederick Hayden, Yolly Gomez, Jonathan Van Tam Andrey Vasin, Hassan Zaraket</strong></td>
</tr>
<tr>
<td>10:30-11:00</td>
<td>Coffee break</td>
<td></td>
</tr>
<tr>
<td>11:00-11:20</td>
<td>Host-directed responses and repurposing of existing therapies</td>
<td>Nelson Lee</td>
</tr>
<tr>
<td>11:20-12:00</td>
<td>Panel discussion: Testing of therapies and treatments and what is needed to promote understanding and policy on improved influenza treatments</td>
<td><strong>Moderator: Nelson Lee, Olivier Terrie, Tim Uyeki</strong></td>
</tr>
<tr>
<td>12:00-13:30</td>
<td>Lunch</td>
<td></td>
</tr>
<tr>
<td>13:30-14:30</td>
<td>Scenario-based panel discussion: Bringing it all together</td>
<td><strong>Moderator: Larry Kerr, Marco Cavaleri, Ab Osterhaus, Bryna Warshawsky, Maria Zambon</strong></td>
</tr>
</tbody>
</table>
| 14:30-15:30| Action planning through 2030 Groups spend 15 minutes at each table to discuss (1) what needs to be put in place to accelerate development of improved vaccines, antivirals, and treatments and (2) what are the roles of the relevant stakeholders? | Table 1: Vaccines  
Table 2: Antivirals  
Table 3: Treatments  
Table 4: Roles and responsibilities |
| 15:30-16:00| Coffee break                                                             |                           |
| 16:00-16:30| Group discussion                                                         | Chair to facilitate       |
| 16:30-16:50| Summary                                                                  | Kanta Subbarao            |
| 16:50-17:00| Next steps and closing remarks                                           | Martin Friede             |
APPENDIX 2.
LIST OF PARTICIPANTS

Dr Atika Abelin  
Global Head, Public Affairs for Vaccines – Influenza and RSV  
Sanofi Pasteur, France

Ms Phyllis Arthur  
Vice President, Infectious Diseases & Diagnostics Policy, Biotechnology Innovation Organization  
Washington, DC, United States of America

Dr Paula Barbosa  
Manager, Vaccines Policy, International Federation for Pharmaceutical Manufacturers and Associations  
Geneva, Switzerland

Dr Francesco Berlanda Scorza  
Project Director, Influenza Vaccines, PATH  
Washington, DC, United States of America

Dr Joseph Bresee  
Director, Partnership for Influenza Vaccine Introduction, Taskforce for Global Health  
Atlanta, United States of America

Dr Kate Broderick  
Vice President, Inovio Pharmaceuticals  
San Diego, United States of America

Dr Marco Cavaleri  
Head of Office, Anti-Infectives and Vaccines, European Medicines Agency  
London, United Kingdom of Great Britain and Northern Ireland

Dr Andrew Clements  
Senior Scientific Advisor, Emerging Threats Division, Office of Infectious Diseases, Bureau for Global Health, US Agency for International Development  
Geneva, Switzerland

Dr Rebecca Cox  
Professor, Department of Clinical Science, University of Bergen  
Bergen, Norway

Mr Samir Desai  
President, Zydus Cadila  
Ahmedabad, India

Dr Lee Dunster  
Head, Global Access Policy Team, Roche  
Basel, Switzerland

Dr Luzhao Feng  
Chinese Center for Disease Control and Prevention  
Beijing, People’s Republic of China

Ms Tina Flores  
Lead, Global Health Security Agenda Private Sector Roundtable  
New York, United States of America

Dr Josie Golding  
Programme Officer, Epidemic Preparedness, Wellcome Trust  
London, United Kingdom of Great Britain and Northern Ireland

Mr Suraj Goyle  
Program Analyst, Department of Health and Human Services  
Washington, DC, United States of America

Ms Yolly Gomez  
Global Access Policy Leader, Roche  
Basel, Switzerland

Mr Suraj Goyle  
Program Analyst, Department of Health and Human Services  
Washington, DC, United States of America

Dr Peter Hart  
Project Officer, Wellcome Trust  
London, United Kingdom of Great Britain and Northern Ireland

Prof Frederick Hayden  
Professor Emeritus  
University of Virginia, Charlottesville, United States of America

Dr Rosalind Hollingsworth  
Global Medical Affairs Lead, Influenza Vaccines, Sanofi Pasteur  
Philadelphia, United States of America

Dr Bruce Innis  
Global Head, Respiratory Infections and Maternal Immunizations, Center for Vaccine Innovation and Access, PATH  
Washington, DC, United States of America

Dr Suresh Jadhav  
Executive Director, Quality Assurance & Regulatory Affairs, Serum Institute of India Pvt. Ltd.  
Pune, India

Dr Robert Johnson  
Director, Influenza and Emerging Infectious Diseases Division, Biomedical Advanced Research and Development Authority, Department of Health and Human Services  
Washington, DC, United States of America
WHO Working Group on Influenza Preparedness and Response

Dr Ximena Aguilera
Director, Centre of Epidemiology and Public Health Policies, Universidad del Desarrollo
Santiago, Chile

Dr Supamit Chunsuttiwat
Senior Medical Officer, Ministry of Public Health
Bangkok, Thailand

Dr Bruce Gellin
President, Global Immunization, Sabin Vaccine Institute
Washington, DC, United States of America

Dr Daniel Jernigan
Director, Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention
Atlanta, United States of America

Dr Talat Mokhtari-Azad
Director, Virology Department, School of Public Health, Tehran University of Medical Sciences
Tehran, Iran

Prof Jonathan Van Tam
Deputy Chief Medical Officer, Department of Health and Social Care
United Kingdom of Great Britain and Northern Ireland

Dr Ly Sovann
Director, Communicable Disease Control Department, Ministry of Health, Phnom Penh, Cambodia

Dr Kanta Subbarao
Director, Victorian Infectious Diseases Reference Laboratory, The Peter Doherty Institute for Infection and Immunity
Melbourne, Australia

Dr Andrey Vasin
Director, Smorodintsey Research Institute of Influenza; Head, Department of Molecular Biology of Viruses
St Petersburg, Russian Federation
WHO Secretariat

Dr Michael Ryan  
Executive Director  
Health Emergencies Programme

Dr Soumya Swaminathan  
Chief Scientist

Dr Sylvie Briand  
Director  
Infectious Hazard Management

Dr Claudia Alfonso  
Scientist  
Global Influenza Programme

Dr Lubna Al Ariqi  
Consultant  
Infectious Hazard Management - Cairo, Egypt

Ms Florence Barthelemy  
Assistant  
Technology Transfer Initiative

Dr Isabel Bergeri  
Technical Officer  
Global Influenza Programme

Dr Caroline Brown  
Programme Area Manager  
Infectious Hazard Management - Copenhagen, Denmark

Mr Christopher Chadwick  
Technical Officer  
Influenza Preparedness and Response

Dr Julia Fitzner  
Medical Officer  
Global Influenza Programme

Dr Martin Friede  
Coordinator  
Initiative for Vaccine Research

Ms Iona Ghiga  
Technical Officer  
Support for Response

Ms Shoshanna Goldin  
Technical Officer  
Influenza Preparedness and Response

Dr Aspen Hammond  
Technical Officer  
Global Influenza Programme

Ms Anne Huvos  
Manager  
Pandemic Influenza Preparedness Framework Secretariat

Mr Henry Laurenson-Schafer  
Consultant  
Global Influenza Programme

Ms Ann Moen  
Chief  
Influenza Preparedness and Response

Mr Tim Nguyen  
Team Leader  
Stockpile Governance

Dr Magdi Samaan  
Technical Officer  
Global Influenza Programme

Dr Nahoko Shindo  
Manager  
Expert Networks and Interventions

Dr Siddhivinayak Hirve  
Technical Officer  
Global Influenza Programme

Ms Erin Sparrow  
Technical Officer  
Technology Transfer Initiative

Mr Guido Torelli  
Programme Manager  
Technology Transfer Initiative

Dr Katelijn Vandemaele  
Medical Officer  
Global Influenza Programme

Dr Andrea Vicari  
Advisor  
Epidemic-prone Diseases, Health Emergencies Department, Washington DC, United States of America

Dr Wenqing Zhang  
Manager  
Global Influenza Programme

Dr Weigong Zhou  
Medical Officer  
Global Influenza Programme
## APPENDIX 3.
### INDIVIDUAL PARTICIPANT SUGGESTIONS FOR ACTION

Table 6. Participant suggestions for supporting development of new and improved vaccines

<table>
<thead>
<tr>
<th>THEME</th>
<th>INDIVIDUAL SUGGESTIONS (SUBMITTED ON POST-IT NOTES): VACCINES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Awareness &amp; engagement</strong></td>
<td>• Address vaccine acceptance and demand</td>
</tr>
<tr>
<td></td>
<td>• Garner commitment from political leadership to get vaccinated</td>
</tr>
<tr>
<td></td>
<td>• Increase use of vaccine in LMICs</td>
</tr>
<tr>
<td></td>
<td>• Improve public awareness of the benefits of influenza vaccination to reduce the risk of severe disease, including hospitalization, intensive care admission, and death.</td>
</tr>
<tr>
<td></td>
<td>• Build sense of urgency around influenza prevention using available data</td>
</tr>
<tr>
<td></td>
<td>• Improve communication on benefits of influenza vaccines</td>
</tr>
<tr>
<td></td>
<td>• Talk to public about age group priority for vaccine</td>
</tr>
<tr>
<td></td>
<td>• Tell public about vaccine side effects</td>
</tr>
<tr>
<td><strong>Funding</strong></td>
<td>• Promote the funding of fit-for-purpose technologies</td>
</tr>
<tr>
<td></td>
<td>• Increased investment to develop new technologies of better vaccines</td>
</tr>
<tr>
<td><strong>Manufacturing &amp; regulation</strong></td>
<td>• Establish public-private partnerships for manufacturing facilities and industrialization of new platforms</td>
</tr>
<tr>
<td></td>
<td>• Establish mechanism to share and deliver technologies to manufacturers</td>
</tr>
<tr>
<td></td>
<td>• Streamline regulatory policies</td>
</tr>
<tr>
<td></td>
<td>• Ensure influenza virus sharing is not impeded by access and benefit-sharing systems</td>
</tr>
<tr>
<td><strong>Research topics</strong></td>
<td>• Increase fundamental understanding of immunology</td>
</tr>
<tr>
<td></td>
<td>• Consider/evaluate LAIV use in children younger than two</td>
</tr>
<tr>
<td></td>
<td>• Compare effectiveness of high-dose vs standard IIV in elderly and high-risk populations for seasonal influenza</td>
</tr>
<tr>
<td></td>
<td>• Better understand issue of repeat vaccination</td>
</tr>
<tr>
<td></td>
<td>• Identify alternative vaccine delivery options</td>
</tr>
<tr>
<td></td>
<td>• Promote group-specific vaccine interventions</td>
</tr>
<tr>
<td></td>
<td>• Promote research on the clinical efficacy and effectiveness of adding neuraminidase antigens to influenza vaccines</td>
</tr>
</tbody>
</table>
Table 7. Participant suggestions for supporting development of new and improved antivirals

<table>
<thead>
<tr>
<th>THEME</th>
<th>INDIVIDUAL SUGGESTIONS (SUBMITTED ON POST-IT NOTES): ANTIVIRALS</th>
</tr>
</thead>
</table>
| **Awareness & engagement**   | • Educate clinicians and the general public on the effectiveness of current antivirals  
• Improve use in seasonal influenza management, including early initiation of antiviral treatment in outpatients, especially high-risk outpatients, and all hospitalized patients with influenza  
• Increase awareness of need for antivirals in seasonal flu  
• Change the conversation about benefits-risks of antivirals  
• Promote benefit of antiviral treatment to reduce complications, especially in persons considered to be at high-risk for complications from influenza  
• Increase demand  
• Share Japan’s experience with wide-scale early initiation of antiviral treatment |
| **Funding**                  | • Effort to reduce antiviral cost to patients to promote use  
• Sustained investment and significant upfront funding  
• Increase advocacy for funding  
• Identify industry-independent funding for studies |
| **Stockpiling & access**     | • Need to optimize shelf-life of stockpiled antivirals  
• Create a global stockpile of critical antivirals for future epidemics and pandemics  
• Improve worldwide stockpiling and distribution capacity  
• Need detailed information on current antiviral stockpiles (i.e. composition, amounts, etc.)  
• Ensure all countries have equitable access to antivirals  
• Ensure sufficient supplies of antibiotics are available at hospitals and other relevant locations  
• Ensure sufficient supplies of ventilators, ancillary supplies, and trained respiratory therapists and clinicians |
| **Production**               | • Facilitate regulatory licensure of new antivirals  
• Help countries produce affordable antivirals (i.e. tech transfer)  
• Promote the development of novel antivirals |
| **Resistance & appropriate use** | • Rapidly determine resistance profile of the pandemic virus strain  
• Promote benefit of reducing inappropriate antibiotic use  
• Ensure stewardship lessons are applied to antivirals to minimise AMR  
• Advise on over-the-counter use and post-exposure prophylaxis |
| **Clinical networks & trials** | • Leverage existing and foster formation of new clinical research networks across countries and regions  
• Improve research collaboration and coordination  
• Fund clinical trial networks for testing antivirals in hospital settings  
• Strengthen coordination between academia and industry  
• Identify public-private partnerships to conduct trials on endpoints of public health significance |
| **Clinical guidelines**      | • Promote the development of national guidelines for antiviral use  
• Promote the updated WHO clinical guidelines, when available  
• Issue guidance for clinical end points that address public health value of intervention |
| **Research topics**          | • Promote the use of biologically-relevant models for pre-clinical evaluations  
• Evaluate dosing/age of currently available antivirals  
• Promote studies on the combination antiviral treatment plus immunomodulatory therapy in hospitalized influenza patients  
• Use observational data to help make better clinical management recommendations  
• Conduct RCTs on antiviral candidates during seasonal influenza epidemics  
• Promote research to better understand disease pathogenesis in severe influenza and the potential role of novel therapies |
<table>
<thead>
<tr>
<th>THEME</th>
<th>INDIVIDUAL SUGGESTIONS (SUBMITTED ON POST-IT NOTES): TREATMENTS</th>
</tr>
</thead>
</table>
| Awareness & engagement     | • Raise awareness among clinicians and the general public  
• Evaluate patients’ preferences for treatments                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Clinical networks & trials | • Invest in global clinical networks and trials  
• Prioritise protocols and R&D  
• Standardize trial protocols and endpoints  
• Utilize clinical networks for observational studies to inform standards of care  
• Use localized outbreaks to evaluate new treatments                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Clinical guidelines & management | • Need guidance on clinical management and supportive care  
• Develop crisis standards of care for pandemic and/or resource-limited settings  
• Organize hospital pandemic preparedness measures (i.e. standards of care)  
• Prioritize high-risk persons for early initiation of treatment  
• Need to optimize supportive clinical management (fluids, antibiotics, advanced organ support) of influenza patients with severe disease                                                                                                                                                                                                                                                                                                                                                                   |
| Production capacity        | • Develop strategies for warm-base manufacturing incentives  
• Prioritize compounds for evaluating in RCTs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Data mining & sharing      | • Promote sharing of data (preclinical/clinical)  
• Ensure databases are linked to correlate outcome with range of treatments                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Health system strengthening | • Understand health systems capacity to undertake new treatments  
• Encourage treatments that are appropriate for the majority of the world’s health systems                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Traditional medicines & repurposing | • Conduct RCTs of Chinese herbal formulas & investigate active ingredients in herbal medicines  
• Increase awareness of ‘traditional medicine’ therapies  
• Identify list of repurposed drugs and other treatments to be tested and drugs to be prioritized                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
## Table 9. Participant suggestions for roles and responsibilities of different stakeholders

<table>
<thead>
<tr>
<th>THEME</th>
<th>INDIVIDUAL SUGGESTIONS (SUBMITTED ON POST-IT NOTES): ROLES &amp; RESPONSIBILITIES</th>
</tr>
</thead>
</table>
| **WHO**                | • Support countries to develop and update pandemic plans  
• Monitor technological developments and their distribution to LMICs  
• Provide declaration of a pandemic  
• Provide continuous education on severity of influenza to stimulate greater research  
• Stress importance of regulatory harmonization of approval of novel vaccines and treatments  
• Formulate prioritized pandemic research agenda during interpandemic influenza seasons  
• Provide updated information about burden of disease  
• Enable the sharing sequence data, specimens, and viruses for product development  
• Issue recommendations to prioritize available vaccine doses to highest risk groups  
• Improve communications on benefits of influenza vaccines, antivirals and other treatments, including to groups at high risk for influenza complications, healthworkers, religious leaders, etc.  
• Establish standards for establishing/sustaining surveillance at the human-animal interface  
• Establish a coalition of partners to address priority problems  
• Seek collaborative investments among other funders  
• Identify funding priorities based on threats  
• Support R&D that helps pandemic planning efforts  
• Monitor activities that are funded and identify gaps  
• Diversify governmental funding  
• Sustain funding streams  
• Streamline funding application processes  |
| **Funders**            | • Establish administrative and logistic preparedness for diagnostics, vaccines, and therapeutics  
• Develop, update, and exercise pandemic influenza preparedness plans  
• Formulate national guidance for influenza vaccines, antivirals, and treatment  
• Promote utilization of current influenza vaccines and therapeutics  
• Develop and implement supportive national policies  
• Create technology integration hubs  
• Advocate for greater seasonal influenza prevention and control  
• Improve influenza surveillance infrastructure  
• Set clear priorities for product profiles (vaccines, antivirals, treatments) and target populations  
• Ensure national policies are aligned to WHO guidance  
• Coordinate seasonal epidemic and pandemic responses at the national and local levels  
• Conduct outreach to communities, including faith-based, schools, businesses, professional societies, etc.  |
| **Member States**      | • Support research capacity building in countries  
• Support the use of vaccines and antivirals for seasonal influenza  
• Continue PIP Framework obligations  
• Continue to innovate and to improve products  
• Help other countries to produce vaccines or therapeutics (i.e. through technology transfer)  
• Ensure vaccines are WHO prequalified, where applicable  
• Investigate new mechanisms of action for antivirals  
• Help communicate to diverse groups on importance of community participation  
• Share adjuvants  |
| **Private sector**     | • Consider new pathways for regulatory approval  
• Start WHO prequalification in parallel to global regulatory process for new products  
• Work with ministries of health to participate in pandemic planning efforts  |
| **Regulators**         | • Use existing clinical trial networks to conduct RCTs in seasonal influenza  
• Utilize clinical networks for testing influenza vaccines, antivirals, and other treatments  |
| **Clinical networks**  | • Use existing clinical trial networks to conduct RCTs in seasonal influenza  
• Utilize clinical networks for testing influenza vaccines, antivirals, and other treatments  |
For more information

Influenza Preparedness and Response
World Health Organization
20 Avenue Appia
CH 1211, Geneva 27
Switzerland

influenza@who.int

www.who.int/influenza/en/