Global influenza situation update and critical pandemic preparedness, readiness and response actions

WHO Health Emergencies Programme Information Session Briefing
28 June 2024
Seasonal, pandemic, zoonotic influenza

Animal influenza
- Influenza viruses that circulate in animals; includes avian and swine influenza viruses; H5 and H7 avian influenza viruses can be high or low pathogenicity in birds

Zoonotic influenza
- An animal influenza virus that crosses species to humans

Pandemic influenza
- An animal influenza virus that begins to spread among humans, who have no or little natural immunity

Seasonal influenza
- An influenza virus that has adapted to humans, causing seasonal epidemics.

Need for:
- Global approach to monitor, prevent, and control seasonal influenza, detect and respond to novel and pandemic influenza
- Monitoring the interface between humans and animals
WHO approach to influenza since 1952 - GISRS

For over 70 years, the Global Influenza Surveillance and Response System (GISRS) has been the foundation for influenza surveillance, preparedness and response.

Enormous commitment from Member States
Enormous support from international agencies & partners

GISRS monitoring of seasonal influenza & other respiratory viruses
Percentage of specimens testing positive for influenza and virus type and subtype

- In most temperate northern hemisphere countries, influenza activity remained low.
- Elevated influenza activity in countries in Central America and the Caribbean and in South Asia, primarily due to influenza A(H3N2) viruses.
- In the Southern hemisphere, influenza activity in countries in South America, South Africa, and Oceania continues to be elevated but activity may have peaked in some countries in South America and South Africa.
- In South America activity was primarily due to A(H3N2) viruses, in South Africa A(H1N1)pdm09 viruses predominated, and in Oceania A(H1N1)pdm09 and A(H3N2) viruses circulated.
GISRS monitoring of zoonotic influenza, 2003-2024
Avian influenza
Geographic spread and spillover (H5) to mammals

Global avian influenza events in animals

Since 2020, avian influenza viruses, notably, H5N1 2.3.4.4b viruses spread predominantly via migratory birds to many parts of Africa, Asia, Europe, North & South America and Antarctica.

More species, including wild birds and terrestrial and marine mammals have been infected with H5 viruses over the past few years.

Avian influenza viruses with zoonotic potential and human cases, Oct 2023-2024

Continuous monitoring and response for animal influenza viruses with zoonotic potential

For example:
- Various surveillance approaches
- Specimen sharing
- Genetic sequence data sharing
- Notifying WHO (IHR)

For example:
- Virus characterization
- Routine & ad hoc risk assessments including joint risk assessments and TIPRA

For example:
- Event investigation and response
- Candidate vaccine virus selection & development
- Advice, guidance and technical support
At the present time, based on available information, including sequencing analyses, transmission studies in animals, and ongoing monitoring of epidemiology in humans, WHO assesses the overall public health risk posed by A(H5N1) to the general population to be low, and for those with exposure to infected birds or animals or contaminated environments, the risk of infection is considered low-to-moderate.

This risk is reliant on strong surveillance, timely detection and sharing of information, sequences and viruses; currently being updated.
Candidate Vaccine Viruses – continuous update for pandemic preparedness purposes

Genetic and antigenic characteristics of zoonotic influenza A viruses and development of candidate vaccine viruses for pandemic preparedness, February 2024

Genetic and antigenic characteristics of clade 2.3.4.4b A(H5N1) viruses identified in dairy cattle in the United States of America

• Based on current genetic, antigenic and epidemiologic data, no new CVVs are proposed
• Current CVVs cover the H5 viruses in circulation

Table 2a. Hemagglutination inhibition assay of HPAI A(H5Nx) viruses

<table>
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<th>REFERENCE ANTIGENS</th>
<th>Subtype</th>
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</tr>
</tbody>
</table>

A(H5N1) - Northern hemisphere 2024-2025
TIPRA: WHO Tool for Influenza Pandemic Risk Assessment

1. Methodology

1) Questions to be evaluated

- What’s the likelihood of the virus acquiring the capacity for sustained human-to-human transmission?
- What’s the public health impact should the virus cause human-to-human transmission?

2) Ten risk elements for calculating overall likelihood and impact scores

2. Likelihood and impact of sustained human-to-human transmission of various influenza A viruses assessed as of June 2024 (results finalized)
WHO strategy on influenza, 2019-2030

Strategic objectives

- Promote research and innovation to address unmet public health needs
- Strengthen global influenza surveillance, monitoring and data utilization
- Expand seasonal influenza prevention and control policies and programmes to protect the vulnerable
- Strengthen pandemic preparedness and response for influenza to make the world safer

https://www.who.int/publications/i/item/9789241515320
The inequities witnessed during the COVID-19 response must not be repeated.

The PIP Framework is a Member State negotiated instrument that provides a holistic approach to pandemic influenza preparedness and response, with equity at its core.

Member States adopted the PIP Framework in 2011, and mandated WHO to “coordinate influenza pandemic preparedness and response in accordance with applicable International Health Regulations (2005) provisions and this [PIP] Framework.” (PIPF Section 6.1)

Since then, WHO has used the foundational principles and mechanisms of the PIP Framework, to put in place a global system that will enable an equitable response to an influenza pandemic.
How PIP enables an equitable response

**Access**

Virus sharing:
- MS share influenza viruses with pandemic potential with GISRS, in a rapid, systematic and timely manner
- GISRS develops risk assessments, sequences the viruses, conducts analyses, and develops candidate vaccine viruses, reference reagents and other information and materials that are broadly shared with MS and manufacturers

**Benefit Sharing**

Benefit sharing includes:
- Annual monetary contributions from influenza product manufacturers to WHO (Partnership Contribution)
- Advance supply contracts with WHO for real-time access to pandemic influenza response products (Standard Material Transfer Agreements 2)
- Other provisions for further access by WHO to products such as inter-pandemic vaccines.
What PIP has secured to date for an equitable pandemic response

**Partnership Contribution**
- Over US$ 300M
- Preparedness capacity building - funds implemented* ~US$ 127M
- Response funds set aside US$ 90M

**Products**
- **Diagnostics:** 250,000 kits
- **Syringes:** 25M
- **Vaccines:** ~10% of real time production from 15 manufacturers
- **Antivirals:** up to 5 million treatment courses

* At global, regional and country levels, including in 100 priority countries, as of 31 Dec 2023
PIP Framework Governance: Promoting equity

PIP Framework 3-pillared governance structure ensures oversight and strengthens ownership by WHO’s 194 Member States

**World Health Assembly**
- Oversees implementation through biennial reporting

**Director-General**
- Promotes implementation of the Framework

**Advisory Group**
- Provides independent, evidence-based reporting, assessment and recommendations to strengthen the functioning of the Framework

The PIP Framework has the strength of its 194 WHO Member States and has been implemented since 2011 by the WHO Secretariat under the guidance of the PIP Advisory Group.
Interim mechanism to enhance collaboration for timely and equitable access to medical countermeasures (i-MCM-Net)

Multiple partners & stakeholders operate in a complex ecosystem...

...a “network of networks” mechanism to connect & strengthen coordination

- Global & Regional R&D
- Regulatory & policy guidance
- Global & regional procurement
- Market shaping & scaled manufacturing
- In-country delivery & systems
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i-MCM-net landscape report: How prepared are we?

1. What are the existing and potential MCMs and their state of development, gaps and challenges?

2. How to rapidly scale-up and scale-out production?

3. How to optimally organize a coordinated supply and demand for products that are available.

4. How to enable equitable, needs-based allotments of MCMs to risk groups?

5. How to prepare countries and communities for last mile distribution and integrated into national response delivery?
Fast-track research and development - state of play

H5 influenza vaccines and candidates

- 15 licensed H5 vaccines (currently 14 licensed H5N1 vaccines of which 1 is WHO P qed), 4 candidates in preclinical development, 8 in clinical development, of which 2 in Phase I, 3 in Phase I/II, and 3 in Phase II

- H5N1 candidate vaccine viruses (CVVs) available through GISRS
  - 2 CVVs – clade 2.3.4.4b of which one; recommended for the current circulating H5N1A/American wigeon/South Carolina/22-000345-001/2021-like. This CVV is available to manufacturers from US CDC and NIID Japan
  - One CVV clade 2.3.4.4b pending (A/chicken/Ghana/AVL-76321VIR7050-39/2021-like)

Influenza therapeutics

- A total of 10 licensed antivirals for seasonal influenza. A range of therapeutic candidates in preclinical development and clinical development – either for pre-, post-exposure prophylaxis or treatments.
- Monoclonal antibodies for influenza are in clinical development, none in phase 3

Diagnostics

- Viral culture and RT-PCR are gold standards for influenza diagnosis, with RT-PCR centralized in labs like GISRS.
- Ongoing development for point-of-care test - at present POCT do not differentiate between human and zoonotic influenza infections.

Other relevant health products

- Global Oxygen Alliance launched to boost access to life saving oxygen, but degree of operationalization unclear

Scalable manufacturing – How can existing platforms produce at scale?

**Pandemic influenza vaccines**

- **Pandemic production capacity** (annual) estimated at approximately 4 - 8 billion doses (estimate based on seasonal and potential pandemic production)
- Additional 6 - 8 billion doses **potentially available from mRNA platforms** (estimate based on COVID-19)
- **Seasonal influenza manufacturing:** globally, 30 manufacturers produce bulk seasonal influenza vaccine, with seven make up over 85% of the global supply
  - 19 manufactures supply both hemispheres, 10 exclusively for the northern hemisphere, and 1 exclusively for the southern hemisphere.
- **Pandemic influenza manufacturing:**
  - 14 influenza manufacturers have a pandemic vaccine licensed.
  - 3 manufacturers have the ability to rapidly produce H5N1 mRNA vaccines – best case scenario is ~3 months, but 6 months is more reasonable.
    - For most mRNA tech transfer partners, production of mRNA vaccines is likely to be 1+ years
- **Global Action Plan (GAP) for influenza vaccine technology transfer partners** - that are still in operation - mostly use egg-based platforms
- Inactivated pandemic influenza vaccines require adjuvants. To date only AS03 and MF59 approved for this and some companies have access agreements for these adjuvants.

**Diagnostics**

- **Influenza diagnostics production capacity landscape** remains highly concentrated in a few countries and regions (Europe, Asia and North America).
**End-to-end health emergency supply chains**

**What is the global access situation for current and future pandemic products?**

**Pandemic influenza vaccines**
- Through the PIP Framework contracting mechanism, WHO has access to ~10% of future of global pandemic influenza vaccine production from 15 manufacturers, in real time and regardless of the technology used.
- Advanced purchase agreements to be expected by countries and regional economic entities.

**Influenza therapeutics**
- Stockpiles of antivirals - outdated information publicly available for 10 countries; volumes ranging from 3,000 to 50,000,000 treatment courses. One country listed a stockpile containing favipiravir, oseltamivir, zanamivir, and baloxavir marboxil (approximately 47.7 million treatment courses). One country has a stockpile containing oseltamivir and zanamivir (2.1 million treatment courses).
- Through the PIP Framework contracting mechanism, WHO will have access to antivirals in real time.

**Other Pandemic Products**
- Global Oxygen Alliance launched to boost access to life saving oxygen, but degree of operationalization unclear
- Through the PIP Framework contracting mechanism, WHO has real-time access to other pandemic products, such as diagnostic kits and syringes.
Updating the public health research agenda for seasonal and zoonotic influenza

• **Objectives**
  - To review progress made since 2017 in the landscape of Influenza
  - Update the public health research agenda for influenza

• **Main areasstreams of research agenda**
  1. Reducing the risk of emergence of pandemic influenza
  2. Limiting the spread of pandemic, zoonotic and seasonal epidemic influenza
  3. Minimizing the impact of pandemic, zoonotic and seasonal epidemic influenza
  4. Optimizing the treatment of patients

  5A. New Technologies in Public Health, and Mathematical Modelling
  5B. Social Media Tools and Risk Communication

• **Setting research priorities for Low- and Middle-Income Countries**

Published in 2017, ongoing update process in 2024
Developing research priorities for H5N1

Preparing for the next pandemic threat
Key asks for Member States

• Seasonal influenza

  • Strengthen routine surveillance, maintain virus and data sharing for global monitoring, and include planned scale up of routine surveillance as part of pandemic preparedness.

  • Ensure systems for vaccination, & vaccination dissemination policies, plans, and cold chains are ready to serve as platforms for dissemination of future vaccines.
Key asks for Member States

• **Avian influenza**
  - Sequence data, clinical specimens and/or viruses from all novel influenza viruses should be rapidly shared for timely and ongoing risk assessment. All appropriate animal influenza virus detections should be reported to WOAH and human detections notified via IHR mechanisms.
  - Ensure timely detection of animal outbreaks through event-based surveillance and testing of animals as appropriate.
  - Strengthen routine cross-communication of information is in place between human and animal sectors at national and subnational levels.
  - Appropriate biosecurity measures and control mechanisms should be implemented for animal outbreaks following global WOAH guidance.
  - National and subnational RRT should ready and trained and to investigate outbreaks with effective human and animal authority coordination. These RRT should collect all essential clinical/epidemiologic data and appropriate specimens according to existing standards.
  - Enhance surveillance among occupationally exposed persons while emphasizing appropriate PPE. Any cases in occupationally exposed should be fully assessed using appropriate case finding, data collection, specimen collection, and serologic methods.
  - Clinician networks should be sensitized to report all unusual events including unexplained severe respiratory illness, or illness in potentially exposed individuals. They should understand what number to call with any reports so that their report can be verified and investigated.
  - Clinicians should also be provided with latest clinical guidance on management of severe acute respiratory illnesses.
Summary of the current situation

• We are in a concerning, evolving situation

• **Addressing urgent needs** of ramping up surveillance and sustaining lab capacities, addressing implementation of prevention interventions, advancing research and development and evaluation of PHSM, diagnostics, therapeutics and vaccines
  - Sharing of sequences and viruses from humans and animals is critical to rapidly assess risk

• **Partnerships and coordination are operational and are key**

• Regular engagement with WHO Member States and partners, including private sector
  - Regular risk assessments with FAO and WOAH
  - Strengthening surveillance in animals
  - Utilizing GISRS and PIP Framework
  - Operationalizing iMCM Net
  - Leveraging expanding partners

• **Prioritizing actions to optimize readiness**
  - Urgent actions across 5C’s to support Member State and Partner readiness
  - Updating the research agenda, addressing research gaps across the public health and R&D landscape
Thank you