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

WHO Health Emergencies Programme Information Session Briefing

28 June 2024

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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

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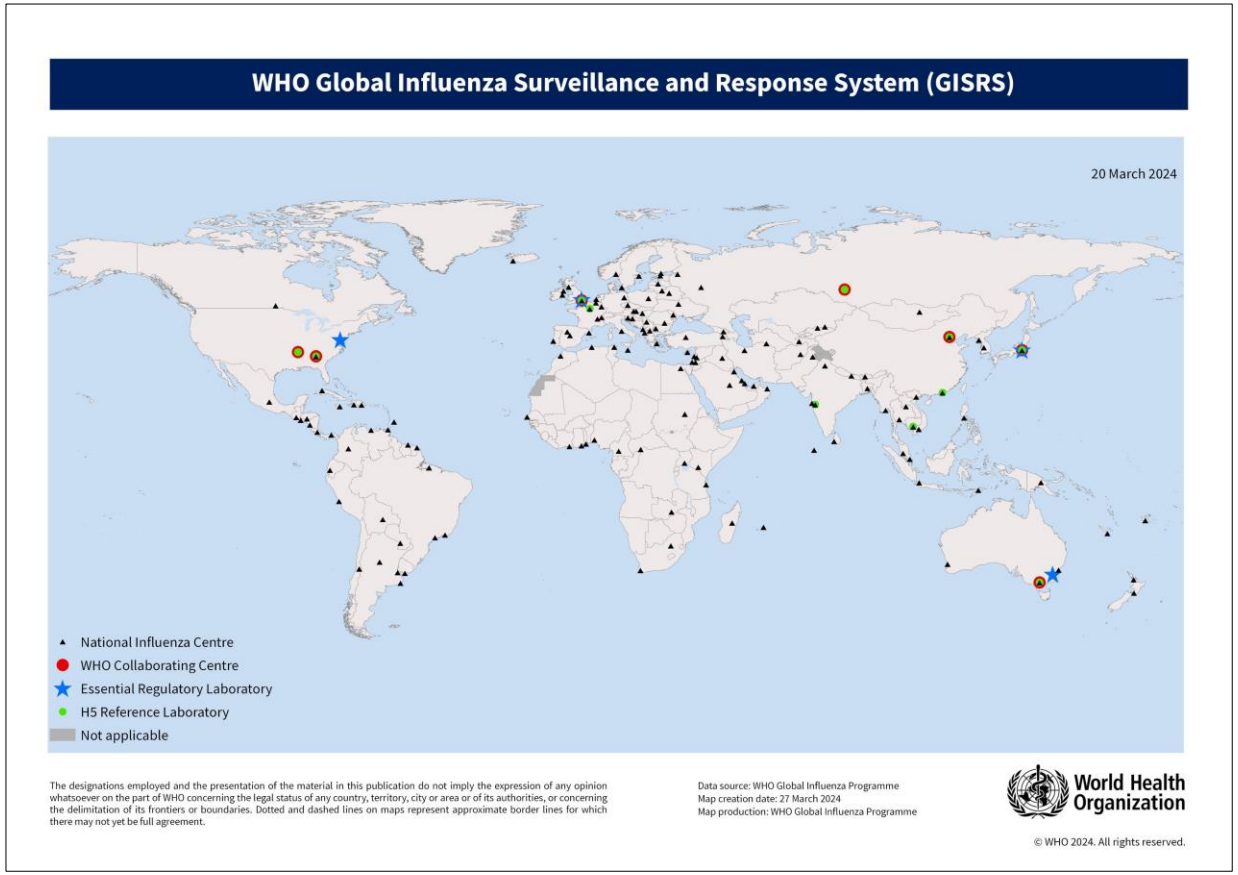
WHO approach to influenza since 1952 - GISRS

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



https://www.who.int/initiatives/global-influenza-surveillance-and-response-system

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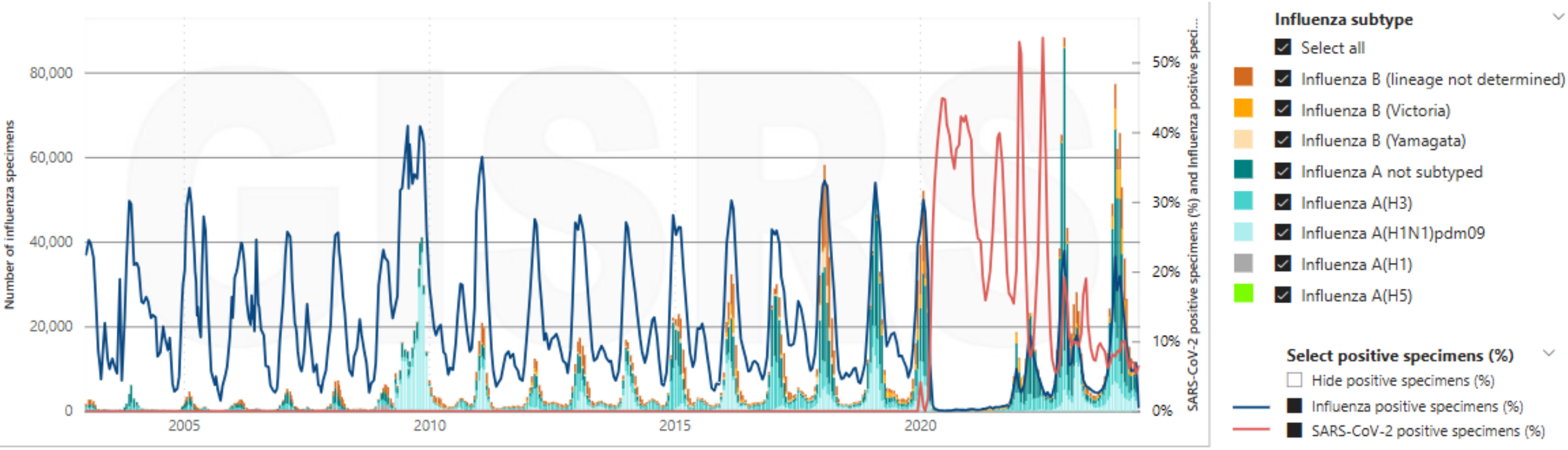
GISRS monitoring of seasonal influenza & other respiratory viruses

RespiMART FluNet



*Surveillance site type:

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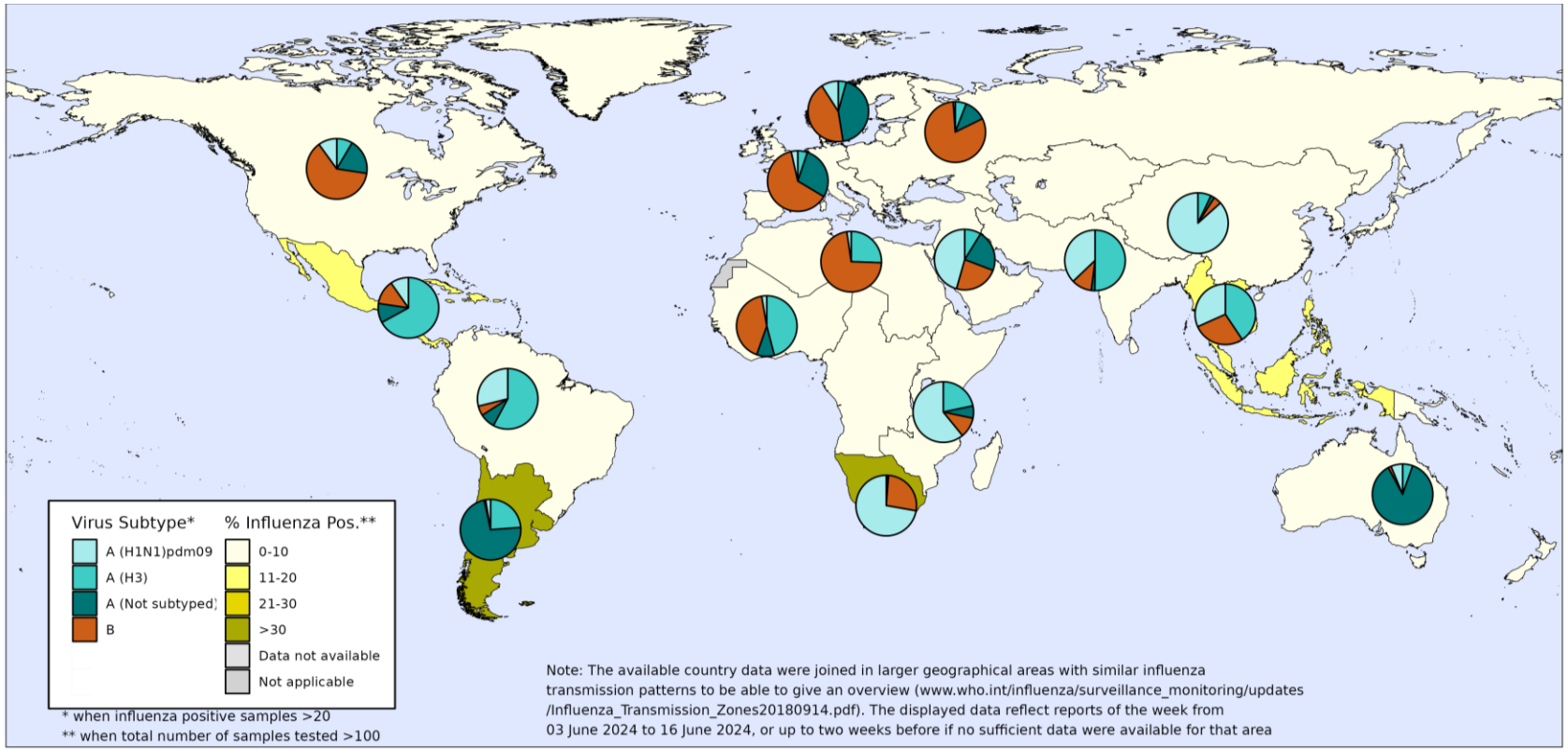
Seasonal influenza situation (3-16 June 2024)

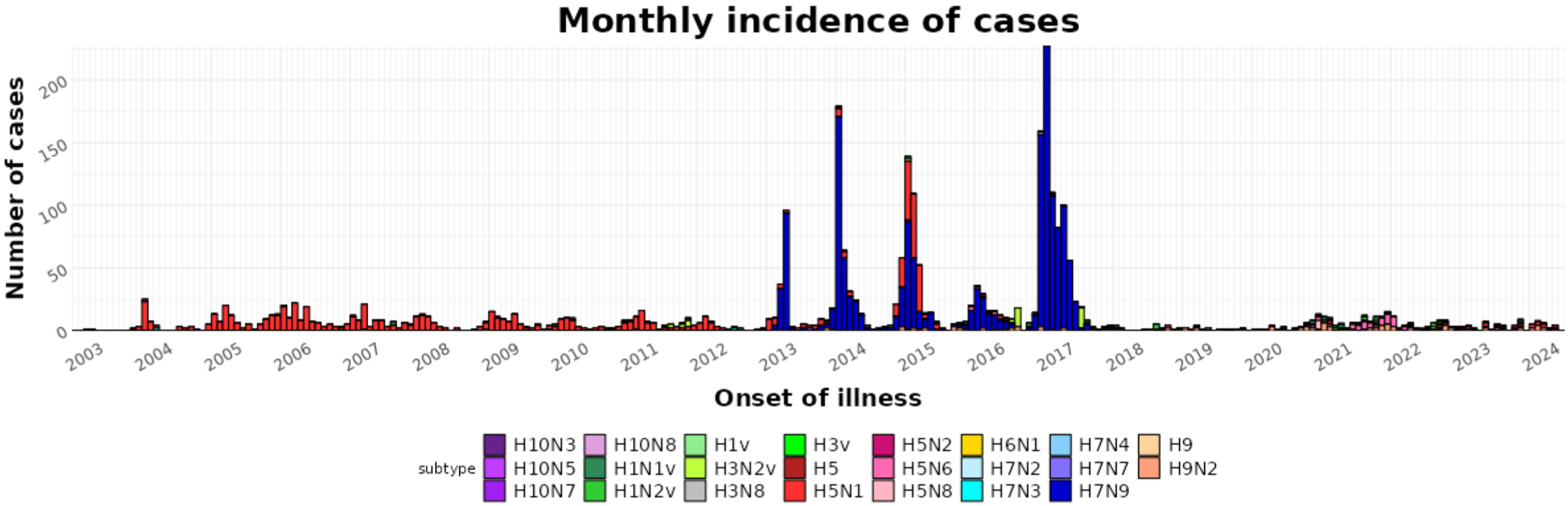
Percentage of specimens testing positive for influenza and virus type and subtype



Data source: Global Influenza Surveillance and Response System (GISRS), FluNet (www.who.int/flunet)

- 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



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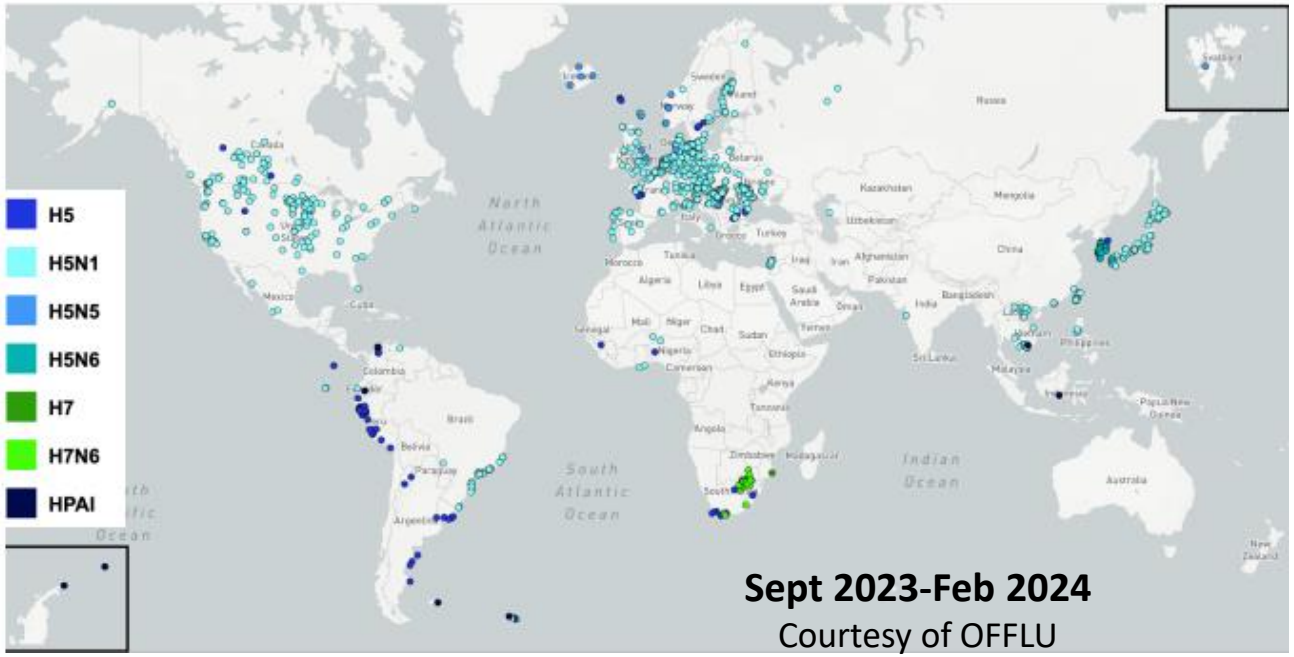
Avian influenza

Geographic spread and spillover (H5) to mammals

Global avian influenza events in animals



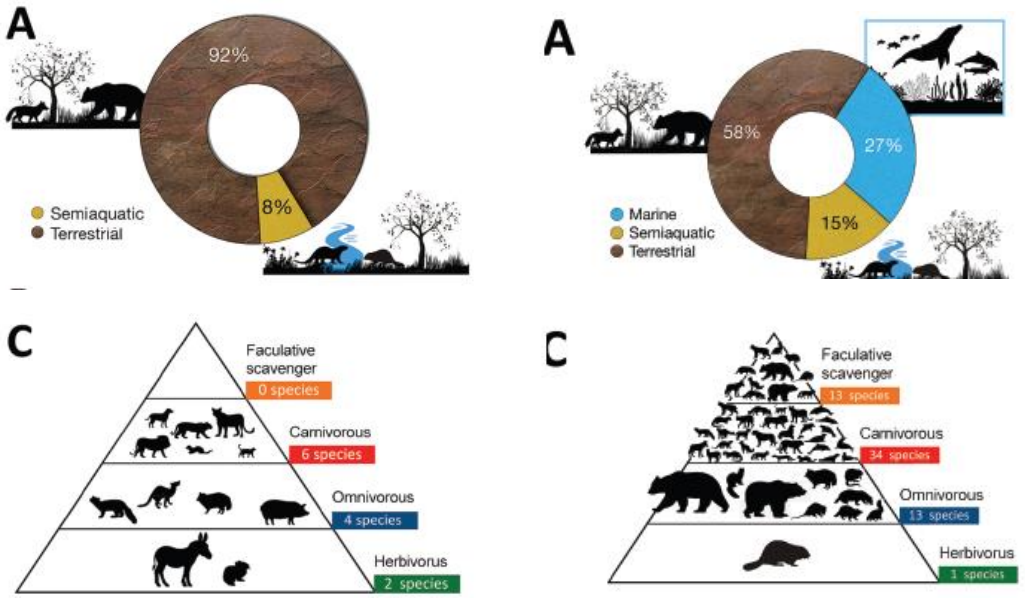
Sept 2023-Feb 2024

Courtesy of OFFLU

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.

2003-2019 → **2020-2023**



Emerg Infect Dis. 2024;30(3):444-452.

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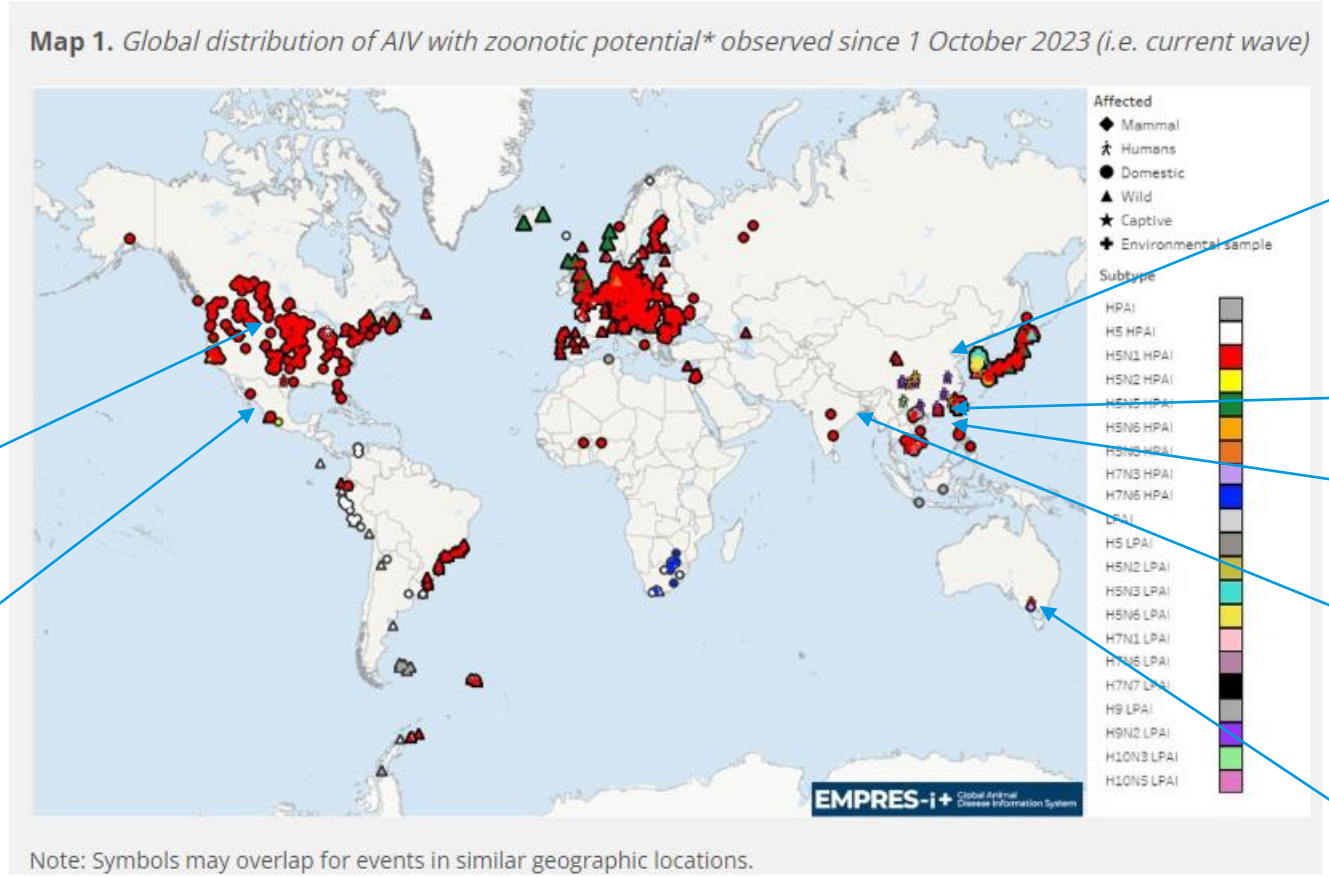
Avian influenza viruses with zoonotic potential and human cases, Oct 2023-2024



China: H5N1 (1), H10N3 (1), H10N5 (1), H5N6 (4), H9N2 (9)

Cambodia: H5N1 (9)

Viet Nam: H5N1 (1)

India: H9N2 (1)

Australia: H5N1 (1)

USA: H5N1 (3)

Mexico: H5N2 (1)

https://www.fao.org/animal-health/situation-updates/global-aiv-with-zoonotic-potential

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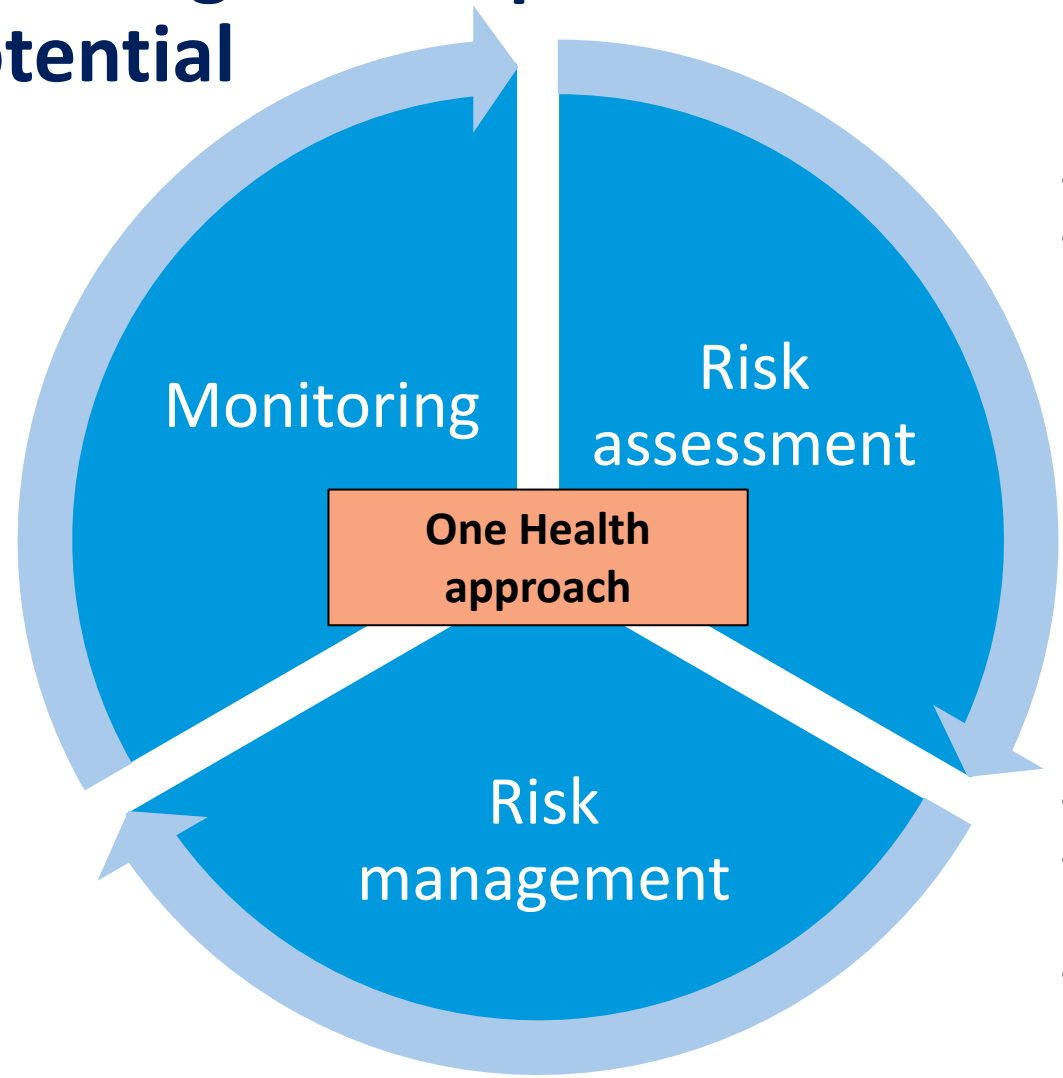
Continuous monitoring and response for animal influenza viruses with zoonotic potential

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

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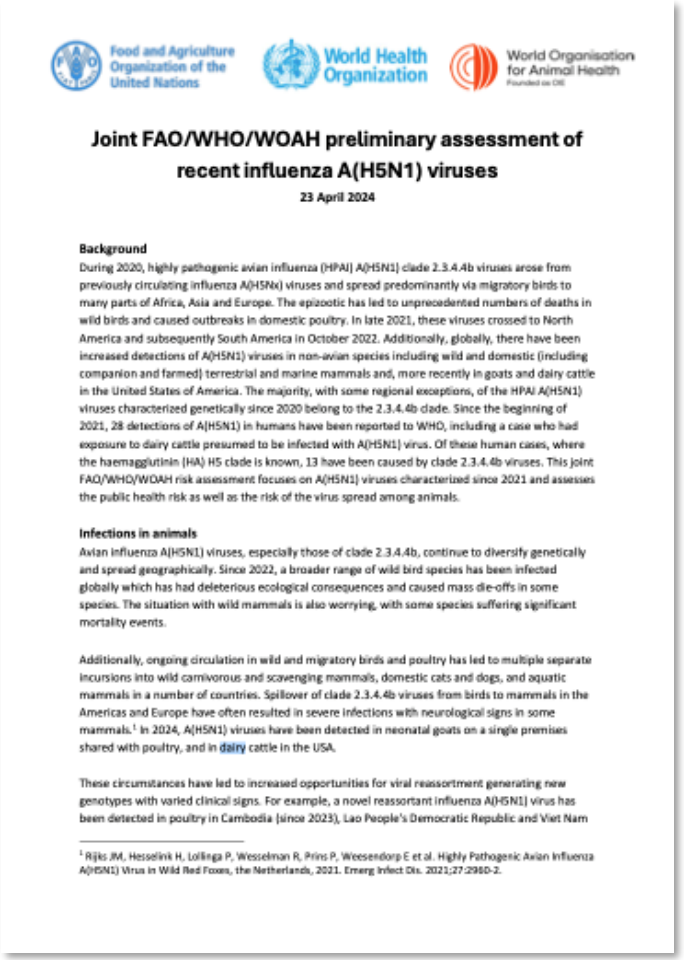
Ongoing WHO-FAO-OIE avian influenza risk assessments

- 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*



Food and Agriculture Organization of the United Nations | World Health Organization | World Organisation for Animal Health

Joint FAO/WHO/WOAH preliminary assessment of recent influenza A(H5N1) viruses

23 April 2024

Background

During 2020, highly pathogenic avian influenza (HPAI) A(H5N1) clade 2.3.4.4b viruses arose from previously circulating influenza A(H5Nx) viruses and spread predominantly via migratory birds to many parts of Africa, Asia and Europe. The epizootic has led to unprecedented numbers of deaths in wild birds and caused outbreaks in domestic poultry. In late 2021, these viruses crossed to North America and subsequently South America in October 2022. Additionally, globally, there have been increased detections of A(H5N1) viruses in non-avian species including wild and domestic (including companion and farmed) terrestrial and marine mammals and, more recently in goats and dairy cattle in the United States of America. The majority, with some regional exceptions, of the HPAI A(H5N1) viruses characterized genetically since 2020 belong to the 2.3.4.4b clade. Since the beginning of 2021, 28 detections of A(H5N1) in humans have been reported to WHO, including a case who had exposure to dairy cattle presumed to be infected with A(H5N1) virus. Of these human cases, where the haemagglutinin (HA) H5 clade is known, 13 have been caused by clade 2.3.4.4b viruses. This joint FAO/WHO/WOAH risk assessment focuses on A(H5N1) viruses characterized since 2021 and assesses the public health risk as well as the risk of the virus spread among animals.

Infections in animals

Avian influenza A(H5N1) viruses, especially those of clade 2.3.4.4b, continue to diversify genetically and spread geographically. Since 2022, a broader range of wild bird species has been infected globally which has had deleterious ecological consequences and caused mass die-offs in some species. The situation with wild mammals is also worrying, with some species suffering significant mortality events.

Additionally, ongoing circulation in wild and migratory birds and poultry has led to multiple separate incursions into wild carnivorous and scavenging mammals, domestic cats and dogs, and aquatic mammals in a number of countries. Spillover of clade 2.3.4.4b viruses from birds to mammals in the Americas and Europe have often resulted in severe infections with neurological signs in some mammals.[1] In 2024, A(H5N1) viruses have been detected in neonatal goats on a single premises shared with poultry, and in dairy cattle in the USA.

These circumstances have led to increased opportunities for viral reassortment generating new genotypes with varied clinical signs. For example, a novel reassortant influenza A(H5N1) virus has been detected in poultry in Cambodia (since 2023), Lao People's Democratic Republic and Viet Nam

[1] Rijks JM, Hesselink H, Lollinga P, Wesselman R, Prins P, Weesendorp E et al. Highly Pathogenic Avian Influenza A(H5N1) Virus in Wild Red Foxes, the Netherlands, 2021. Emerg Infect Dis. 2021;27:2960-2.

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Joint FAO/WHO/WOAH preliminary assessment of recent influenza A(H5N1) viruses

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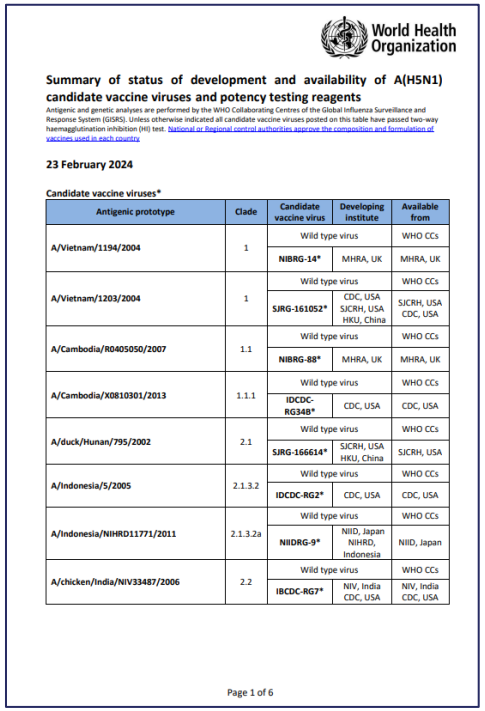
Candidate Vaccine Viruses – continuous update for pandemic preparedness purposes

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



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Summary of status of development and availability of A(H5N1) candidate vaccine viruses and potency testing reagents

Antigenic and genetic analyses are performed by the WHO Collaborating Centres of the Global Influenza Surveillance and Response System (GISRS). Unless otherwise indicated all candidate vaccine viruses posted on this table have passed two-way haemagglutination inhibition (HI) test. National or Regional control authorities approve the composition and formulation of vaccines used in each country.

23 February 2024

Candidate vaccine viruses*

Antigenic prototype	Clade	Candidate vaccine virus	Developing institute	Available from
A/Vietnam/1194/2004	1	Wild type virus		WHO CCs
		NIBRG-14*	MHRA, UK	MHRA, UK
A/Vietnam/1203/2004	1	Wild type virus		WHO CCs
		SJRG-161052*	CDC, USA SJCRH, USA HKU, China	SJCRH, USA CDC, USA
A/Cambodia/R0405050/2007	1.1	Wild type virus		WHO CCs
		NIBRG-88*	MHRA, UK	MHRA, UK
A/Cambodia/X0810301/2013	1.1.1	Wild type virus		WHO CCs
		IDCDC-RG34B*	CDC, USA	CDC, USA
A/duck/Hunan/795/2002	2.1	Wild type virus		WHO CCs
		SJRG-166614*	SJCRH, USA HKU, China	SJCRH, USA
A/Indonesia/5/2005	2.1.3.2	Wild type virus		WHO CCs
		IDCDC-RG2*	CDC, USA	CDC, USA
A/Indonesia/NIHRD11771/2011	2.1.3.2a	Wild type virus		WHO CCs
		NIIDRG-9*	NIID, Japan NIHRD, Indonesia	NIID, Japan
A/chicken/India/NIV33487/2006	2.2	Wild type virus		WHO CCs
		IBCDC-RG7*	NIV, India CDC, USA	NIV, India CDC, USA

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A(H5N1) - Northern hemisphere 2024-2025

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

REFERENCE ANTIGENS[7,8]	Subtype	Clade	IDCDC-RG71A	IDCDC-RG78A	IDCDC-RG80A
IDCDC-RG71A (A/Astrakhan/3212/2020-like)	H5N8	2.3.4.4b	**160**	80	160
IDCDC-RG78A (A/American Wigeon/South Carolina/22-000345-001/2021-like)	H5N1	2.3.4.4b	80	**160**	320
IDCDC-RG80A (A/chicken/Ghana/AVL-763_21VIR7050-39/2021-like)	H5N1	2.3.4.4b	40	40	**320**
TEST ANTIGENS					
A/Texas/37/2024, conjunctival swab isolate	H5N1	2.3.4.4b	80	160	320
A/Texas/37/2024, nasopharyngeal swab isolate	H5N1	2.3.4.4b	40	160	320

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TIPRA: WHO Tool for Influenza Pandemic Risk Assessment

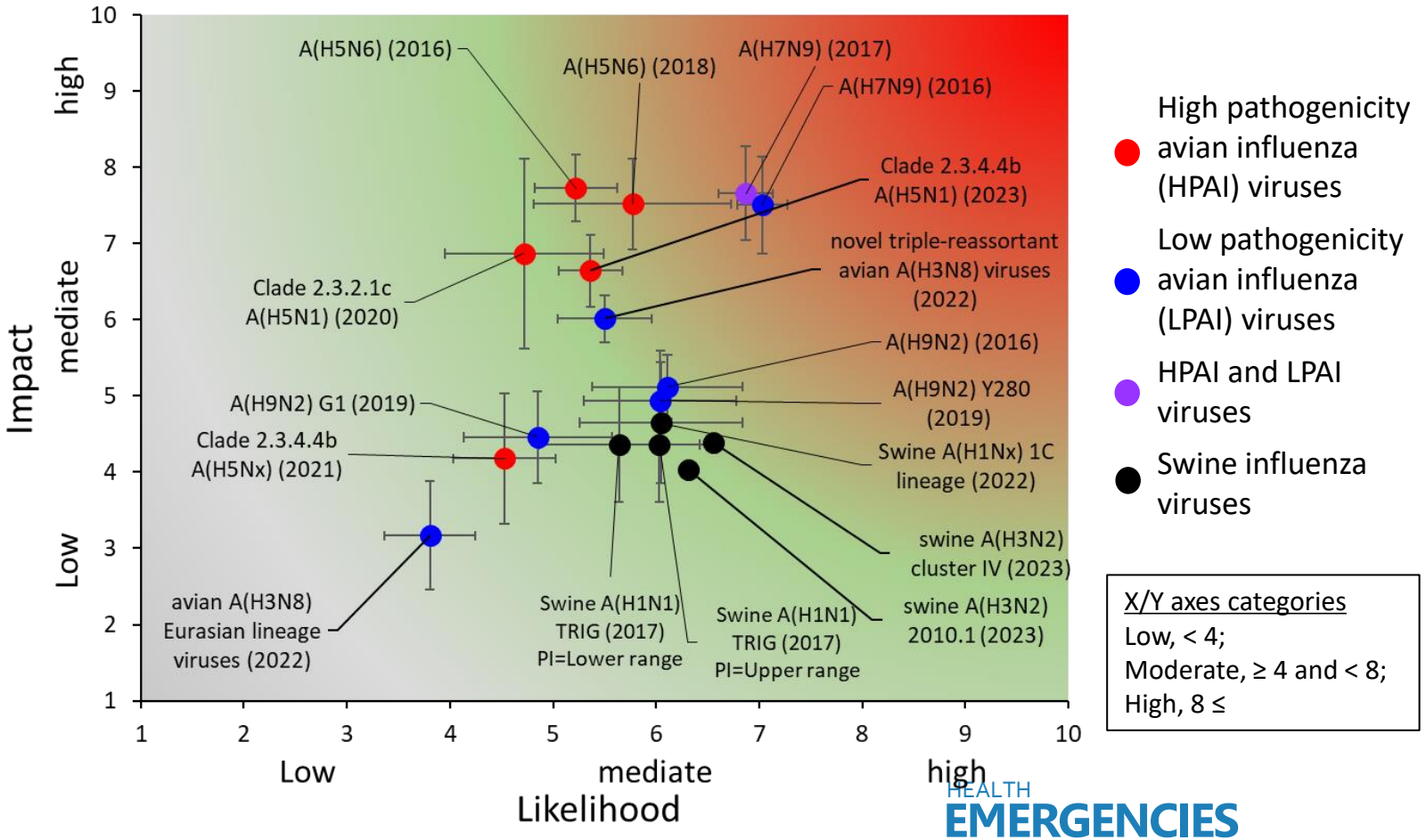
1. Methodology

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)



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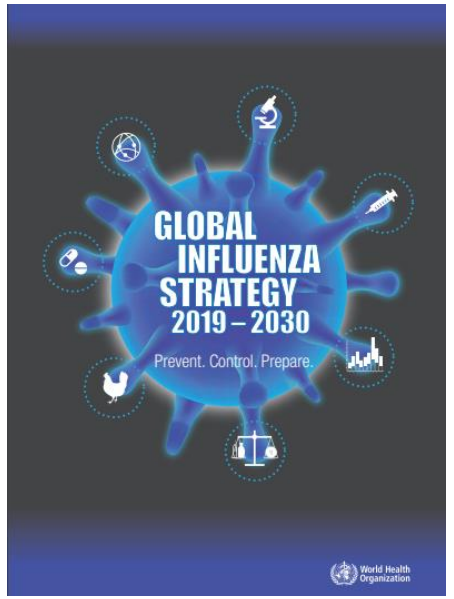
WHO strategy on influenza, 2019-2030

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

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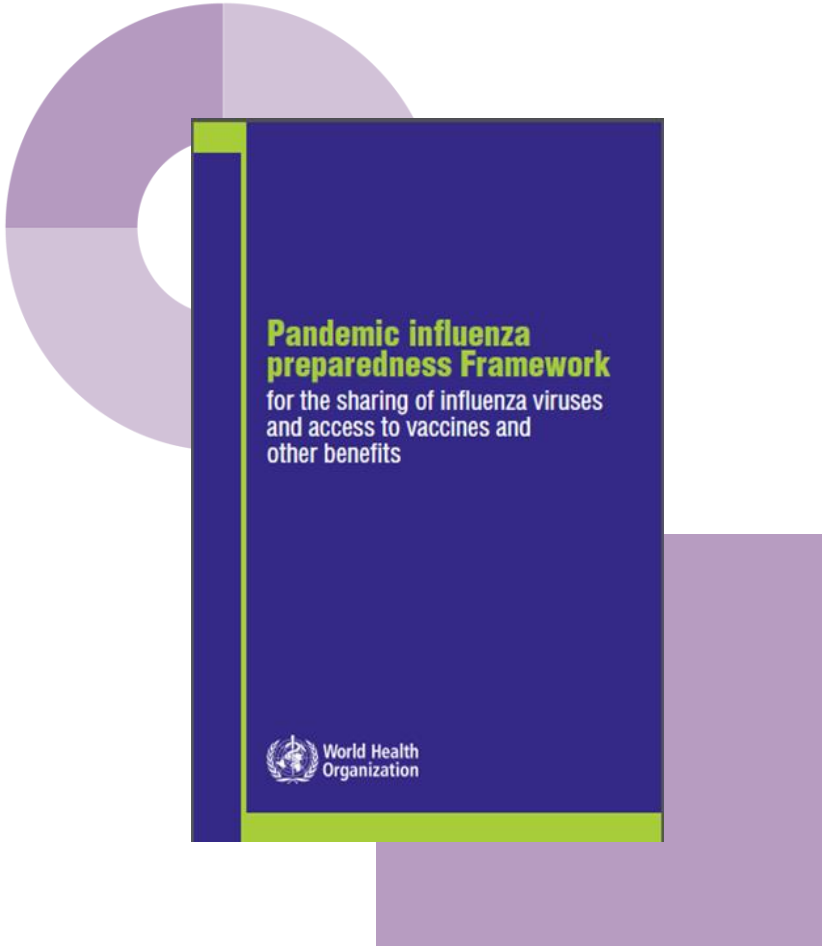
Ensuring an equitable response: PIP Framework



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.

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How PIP enables an equitable response

PIP is an access and benefit sharing system

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.

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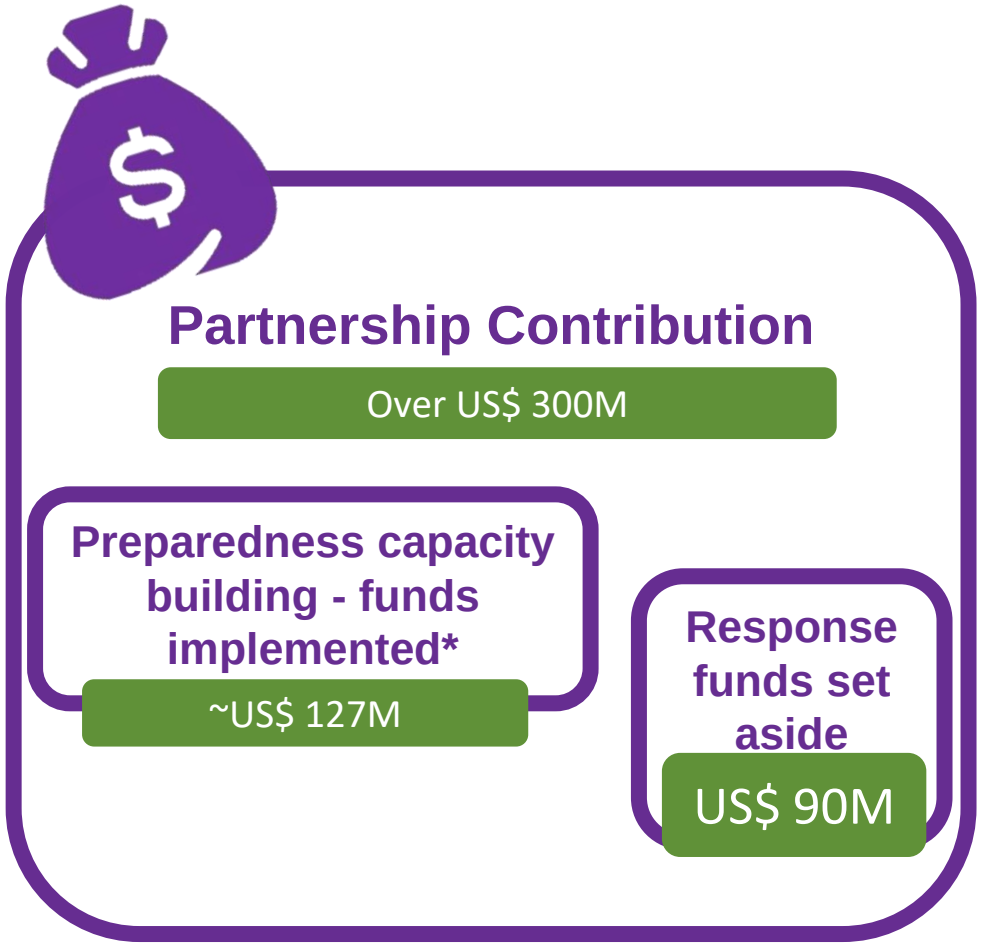
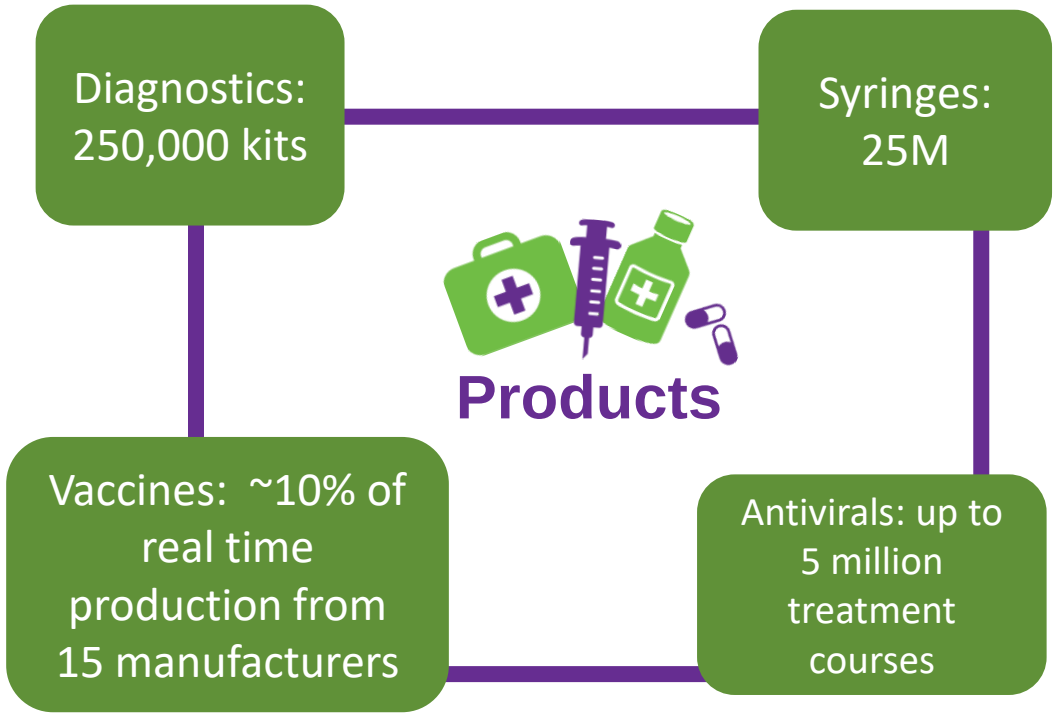
What PIP has secured to date for an equitable pandemic response





* At global, regional and country levels, including in 100 priority countries , as of **31 Dec 2023**

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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

World Health Organization
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.

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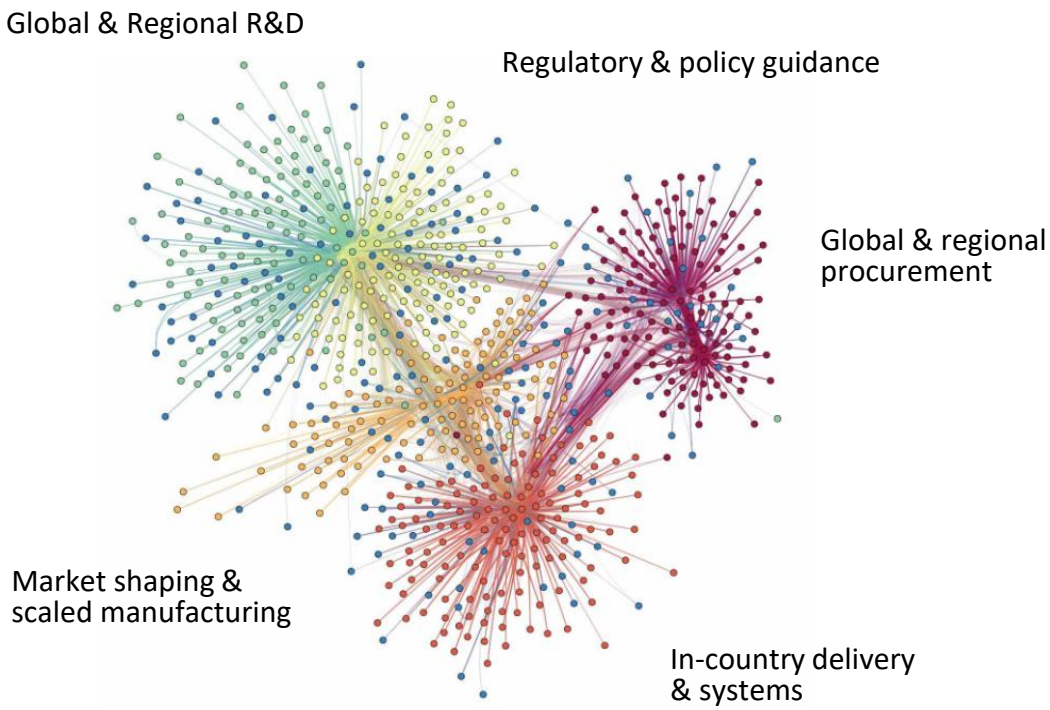
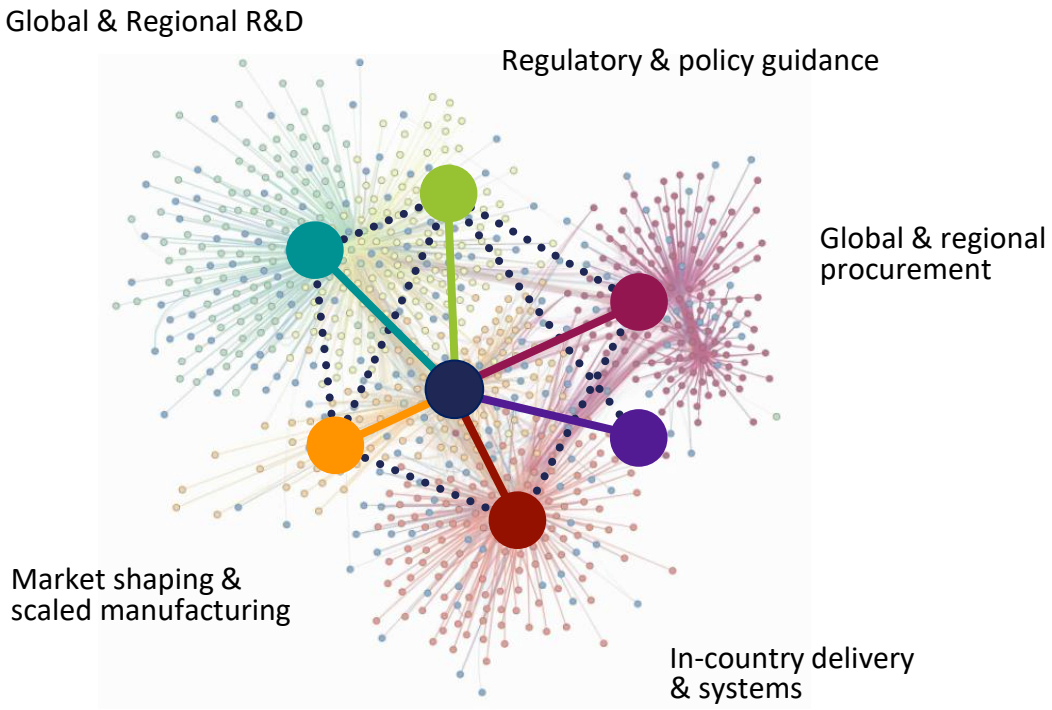
Interim mechanism to enhance collaboration for timely and equitable access to medical countermeasures (i-MCM-Net)

Multiple partners & stakeholders operate in a complex ecosystem…



…a "network of networks" mechanism to **connect & strengthen coordination**



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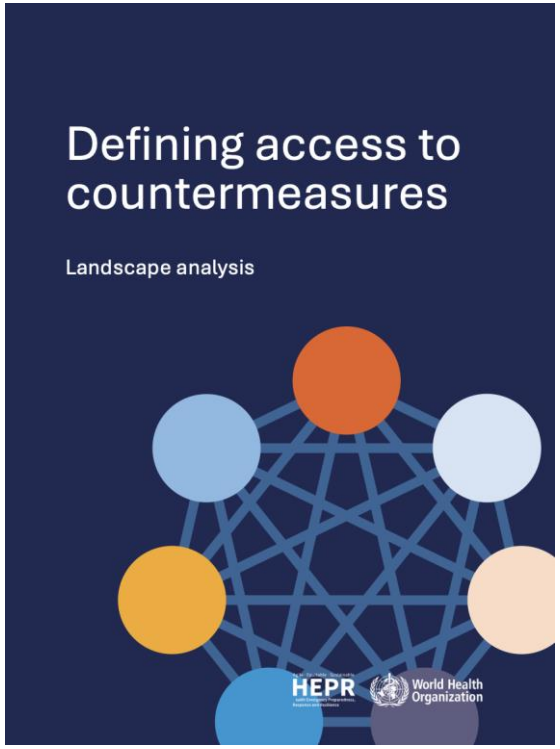
i-MCM-net landscape report: How prepared are we?



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 Pqed),** 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.

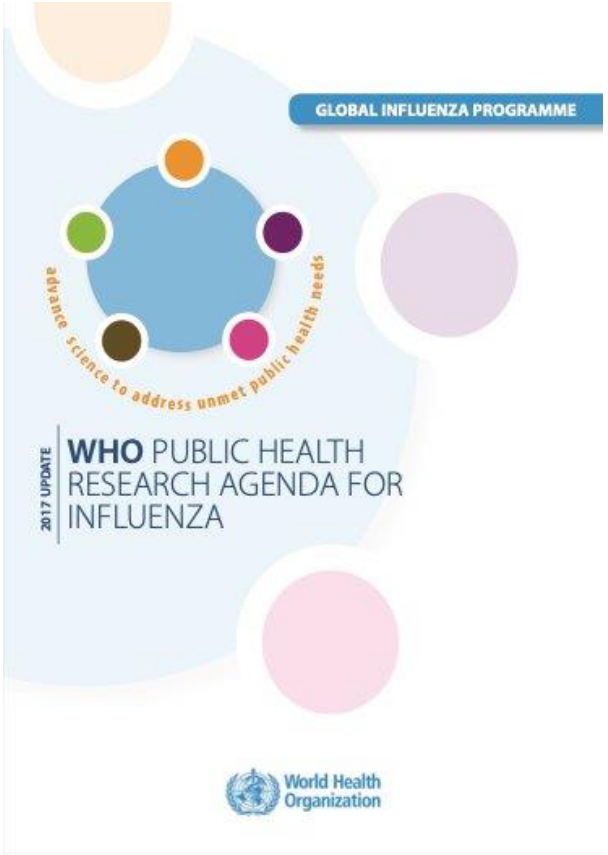
Influenza therapeutics

- 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 areas/streams 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

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Developing research priorities for H5N1

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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 subnationall 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 accordingt o existing standards.
  - Enhance surveilannce 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 potentiallly 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 implemention of prevention interventions, advancing research and development and evaluation of PHSM, dignostics, 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
  - Leverging expanding partners
- **Priortizing 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

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