FORDYMACKI, Jacek, ŁAGOWSKI, Ryszard, KOSĘDA, Julia and FETNER, Barbara. Is Avian influenza virus still threatening humans? Preventative measures and treatment. Quality in Sport. 2025;37:57463. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.37.57463
https://apcz.umk.pl/QS/article/view/57463

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 31.12.2024. Revised: 03.01.2025. Accepted: 03.01.2025 Published: 14.01.2025.

Is Avian influenza virus still threatening humans? Preventative measures and treatment

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Introduction
Global shift in the ecology of highly pathogenic avian influenza strains like H5N1 and the spread of avian influenza to mammals are raising concerns and prompting action in the event of a pandemic. Due to the nature of viruses, a future influenza pandemic is inevitable and preparedness for it vital. The aim of this article is to present the developed strategies for preventing pandemic influenza as a measure of preparedness for the upcoming threat.
State of knowledge
For public health purposes, influenza is divided into: seasonal, zoonotic and pandemic [1]. Although pandemic influenza spread very rare, it is of great concern due to its global reach and high mortality rate [2]. Health experts are concerned that a future pandemic could be caused by the H5N1 strain of the virus, an infection that can spread from birds to humans [3]. WHO, in collaboration with other institutions, continuously monitors influenza viruses. Based on risk assessment, it issues guidelines, develops surveillance strategies, and establishes a pandemic response plan. As part of preparedness for the next pandemic, specific influenza vaccines are developed and available antiviral drugs are being tested for their effectiveness against strains with pandemic potential.
Summary
Having appropriate policy and planning in place facilitates early response in order to suppress an influenza outbreak quickly, thus reducing the potentially catastrophic future impacts of a pandemic. Currently available antiviral medicines are mostly effective against the highly pathogenic strains of influenza A virus of concern. The Zoonotic influenza vaccines contains a strain matching the currently circulating clade to ensure protection. Effective plans will not succeed without the will to implement and execute them.

Keywords: Zoonotic influenza, pandemic influenza, preparedness, vaccine

Introduction and purpose

Influenza is a highly contagious respiratory disease caused by influenza viruses types A, B and C belonging to the Orthomyxoviridae family, typically occurring seasonally in the form of local epidemics (seasonal influenza). However, periodically, when a new, highly infectious strain of the virus begins to circulate in a population with low immunity, pandemics can occur. Type A virus is responsible for pandemics, which can cause illness in both humans and animals of different species. Type A influenza viruses are divided into subtypes based on two surface proteins: hemagglutinin (HA) and neuraminidase (NA). So far, 18 types of HA and 11 types of NA have been identified, most of which infect birds [4]. Animal influenza viruses do not easily transmit between humans, because they are distinct from human seasonal influenza viruses (caused most often by subtypes A(H1N1) and A(H3N2)). However, animal influenza viruses that may occasionally infect humans through direct or indirect contact - can cause disease in humans ranging from a mild illness to death. Each case of zoonotic infection poses a serious public health problem because such viruses, as a result of their high variability, can cause pandemics. Preliminary findings have shown that animal subtypes A(H5Nx), A(H7N9), A(H9N2), A(H10Nx) are most likely to transmit to humans and have pandemic potential [5,6]. Avian virus, subtype A (H5N1) is attracting the most attention due to its widespread occurrence among wild birds, pathogenicity and direct transmission to humans.

The virus is spread through bird faeces, saliva or contaminated food and water but also through ingestion of an infected animal [7]. People in close contact with birds, such as workers on poultry farms and veterinarians, are most at risk of infection. Zoonotic influenza can be mild or very severe and in many cases leads to death. The first recorded human death caused by a highly pathogenic avian virus occurred in Hong Kong in 1997. The H5N1 virus infected 18 people, and six people died as a result of severe illness [8]. Between 2003 and 2024 (until 29.02.2024), a total of 887 human cases of avian influenza A(H5N1) were reported to WHO with 462 deaths, a fatality rate of 52% [9]. Over the years H5N1 has undergone numerous antigenic and genetic changes and in recent years has caused large outbreaks of poultry disease in many Asian countries and then spread predominantly via migratory birds to many parts of Africa, Asia and Europe [10]. 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 [11] and, more recently in goats and dairy cattle in the United States of America [12]. Recently, outbreaks have been detected on a mink farm in Spain, where transmission of the virus from mink to mink has been observed [13]. As proven, highly pathogenic avian influenza (HPAI) A(H5N1) clade 2.3.4.4b viruses arose from previously circulating influenza A(H5Nx), which has now become dominant in the environment, is responsible for recent outbreaks among animals [14,15]. 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. Human cases of zoonotic influenza caused by other influenza virus subtypes are also being recorded. In February 2021, the IHR National Focal Point in the Russian Federation notified WHO of the detection of avian influenza A(H5N8) in seven human samples. This is the first reported detection of avian influenza A(H5N8) in humans [16]. The latest WHO monthly report on human zoonotic influenza cases covering the period from May 4 to June 7, 2024 reports four cases of human infection with influenza A(H5N1), one case of A(H5N2), two cases of A(H5N6) and three cases of A(H9N2) [17]. It is difficult to predict future influenza pandemics in terms of virus strain, time of occurrence or geographic origin [2]. It seems that the outbreak of another influenza pandemic is inevitable therefore maintaining systems in place to prevent and mitigate the effects of a new influenza pandemic is now a top global public health priority.

The article aims to present the strategies developed to prevent pandemic influenza and a review of available medicinal products as a measure of preparedness for the coming threat.

Description of the state of knowledge

Strategies to limit the spread of the virus and prevent an influenza pandemic can be considered under the categories of antiviral, vaccine and non-pharmaceutical measures. Among non-pharmaceutical measures, the most important are influenza virus monitoring systems and rapid data sharing which is essential to conduct a thorough risk assessment and develop or adjust targeted response measures. As these viruses are constantly evolving and spreading in animal populations, and with an increased risk of exposure for humans, there is a continuous need to re-assess the risks as the situation evolves and when more information becomes available.

Non-pharmaceutical strategies - Monitoring and surveillance systems

Influenza has been recognized by the WHO as a public health threat, and as a result, the Global Influenza Programme (GIP) was developed as early as 1947 to support the prevention and treatment of influenza [18]. This strategy includes virological surveillance of influenza conducted through the Global Influenza Surveillance and Response System (GIRS) [19]. Surveillance is designed to identify antigenic changes occurring in circulating viruses, as well as to quickly report the emergence of new types and subtypes. In 2004, when the threat of human infection with avian influenza A(H5N1) virus increased, a network of WHO reference laboratories was established as part of GIRS to collect and identify animal virus strains causing infection in humans [20]. These activities are helpful in determining the genetic and antigenic characteristics of circulating viruses and selecting candidates for influenza vaccines, including zoonotic ones [21]. Twice a year WHO consults with experts from WHO Collaborating Centers, regulatory laboratories and other partners to review data prepared by data collection systems, on influenza viruses with pandemic potential, and assesses the need for additional vaccine candidate viruses to prepare for a pandemic. Recommendations for the composition of zoonotic influenza vaccines for the season are published annually and candidate strains of antigens for vaccine production are identified [22].

As part of its strategy, the WHO, in cooperation with the World Organization for Animal Health (WOAH) and the Food and Agriculture Organization of the United Nations (FAO), conducts surveillance at the human-animal interface, assesses associated risks and coordinates responses to zoonotic influenza outbreaks and other public health threats. Periodically, depending on the changing epidemiological situation, it issues animal influenza virus risk assessment reports in cooperation with other organizations.

The last joint FAO/WHO/WOAH risk assessment from 23rd April 2024 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. Although the current risk to humans posed by these viruses has been assessed as low, active case finding around reported human cases has been ongoing and should continue to determine if there is any human-to-human transmission. Individuals with activities that involve exposure to infected animals and/or contaminated environments are at higher risk and should take necessary precautions to prevent infection. Countries should maintain surveillance in birds, monitor and investigate cases in non-avian species including livestock, report cases of HPAI in all animal species to WOAH and other international organizations, prevent spread in animals through strict biosecurity measures and protect persons in contact with suspected/infected animals. It is recommended that national authorities fully assess the risk among occupationally exposed persons using active case finding and serologic methods, as well as work with national agencies to understand the exposure and risk from milk and milk products. Clinicians should also be alerted to potential zoonotic infection in patients with an exposure history to birds or animals in areas where avian influenza viruses are known to be circulating in animals. Epidemiologic and virologic surveillance and the follow-up of suspected and confirmed human cases should be conducted systematically. Procedures to reduce human exposure to birds and mammals potentially infected with avian and other animal influenza viruses should be implemented to minimize the risk of zoonotic infections.

Those who are exposed to potentially infected animals should wear personal protective equipment including eye protection. If they develop respiratory symptoms or conjunctivitis, they should be rapidly sampled, and precautionary infection control measures should be put in place to prevent potential further spread among humans and to animals [13].

Pharmaceutical strategies - antiviral drugs

Effective antiviral drugs can serve as first-line measures against emerging pandemic strains of influenza virus. As already established, proper treatment can reduce viral titers, limit viral transmission and help treat severe infections, thereby reducing morbidity and mortality until effective and antigen-matched vaccines become available [23]. At a later stage, they may also be the only means of protection for people who fail to develop immunity through vaccination or cannot receive vaccines due to a medical condition. Five influenza antiviral drugs are registered in EU/EEA countries. Considering the mechanism of action, these drugs belong to 3 classes: M protein inhibitors (amantadine, rimantadine), neuraminidase inhibitors (oseltamivir, zanamivir) and polymerase inhibitors (baloxavir).

M-protein inhibitors. Most avian influenza A(H7N9), A(H5N1) and A(H5N6) viruses are resistant to M-protein inhibitors. Therefore, amantadine and rimantadine are not recommended for the treatment of new influenza type A virus infections [24].

Neuraminidase inhibitors. Currently registered drugs belonging to the neuraminidase inhibitors are zanamivir and oseltamivir. Zanamivir in the form of powder for inhalation (Relenza) is indicated for the treatment of non-complicated acute influenza (both A and B) within 2 days of symptom onset (adults and children) [25]. Zanamivir infusion solution (Dectova) is indicated for the treatment of severe and potentially threatening infections [26]. It allows for the treatment of patients whose condition does not allow for the use of drugs suitable for oral or inhaled administration [27]. The indication for oral oseltamivir (Tamiflu, Ebifunin, Tmivil, Segosana, Oseltix) is the treatment of influenza in adults and children (aged 1 year or 6 years or older - depending on the manufacturer) and post-exposure prevention in children and adults. Zanamivir and oseltamivir are active against both influenza A and B viruses. So far, highly pathogenic avian influenza A(H5N1) viruses are sensitive to neuraminidase inhibitors, although several viruses of the Egyptian clade have shown resistance [28]. Viruses of another subtype A(H9N2) have also shown signs of resistance to this group of drugs [29].

Polymerase inhibitors. A representative of the new class of anti-influenza drugs is Baloxavir (Xofluza. This drug has been approved for the early treatment of paediatric and adult patients with non-complicated influenza based on phase II and III trials [30]. Baloxavir is the first anti-influenza drug to inhibit the viral polymerase activity of several influenza A virus subtypes [A(H1N2), A(H5N1), A(H5N2), A(H5N6), A(H7N9) and A(H9N2)] [31]. In an in vitro study, baloxavir was shown to have broad-spectrum activity and inhibit replication of type A, B, C and D viruses [32]. Detailed treatment guidelines for pandemic influenza can be found in a WHO document issued in January 2022 [33].

These recommendations are common to the treatment of seasonal influenza, pandemic influenza and zoonotic influenza, and apply to people with suspected or confirmed influenza virus infection or at risk of severe illness. Clinical management of patients consists of providing optimal intensive care for severe clinical syndromes and administering effective influenza-specific antiviral drugs as soon as possible. The WHO recommends administering oseltamivir as soon as possible, but does not recommend inhaled zanamivir and intravenous infusion of peramivir due to insufficient clinical evidence of use in this patient group.

Vaccines as most important part of strategy to fight pandemia

Vaccines are one of the most effective means for preventing people from becoming ill and for controlling the spread of infection. Even a vaccine of limited efficacy, such a pre-pandemic vaccine, is expected to be able to mitigate a pandemic [34]. Immunization with surface antigens, especially HA, reduces the likelihood of infection and the severity of illness and is currently the most important method to reduce the effects of influenza. Influenza vaccination is associated with reduced rates of respiratory illness and influenza-related medical visits at all ages, hospitalizations and deaths among adults [35]. Seasonal influenza vaccines designed to provide protection against seasonal flu are not used during a flu pandemic as they contain different antigens and are unlikely to provide protection against pandemic flu. To prevent human influenza caused by infection with animal viruses, special products have been prepared, intended for use at a specific stage of the pandemic or in the inter-pandemic period (vaccines against zoonotic and pandemic influenza).

Zoonotic influenza vaccines

Zoonotic influenza vaccines were developed to protect against a potential influenza pandemic viral strain via early vaccination at the start of a pandemic or during pre-pandemic stages (e.g. to reduce mortality against a pandemic strain in those countries where infections are occurring). It may also help reducing the chance of the emergence of a reassortant pandemic strain by vaccinating those (e.g., veterinarians, poultry workers, operators involved in the manufacturing of vaccines with pandemic-like strains, laboratory workers) at high risk of infection from both avian and human viruses. [36]. The composition of vaccines against zoonotic influenza, similarly to seasonal influenza vaccines, is updated annually depending on the epidemic threat caused by currently circulating viruses, in accordance with the WHO recommendation [22]. Health experts are concerned that a future flu pandemic could be caused by the virus strain H5 of the virus, an infection that can spread from birds to humans. Currently, there are 3 vaccines registered against zoonotic influenza in EU countries (Table 1). The zoonotic flu vaccines currently available contain the virus strain A/H5N1 (bird flu) because health experts believe that this strain could cause a future flu pandemic and is responsible for recurrent outbreaks [3].

Table 1. Zoonotic influenza vaccines

Trade name	Active substance(s)	Pharmaceutical form	Marketing Authorisation Holder	Date of first authorisation/last update
Aflunov **Zoonotic influenza vaccine (H5N1)**[*]	Influenza virus surface antigens (haemagglutinin and neuraminidase)* of strain A/turkey/Turkey/1/2005 (H5N1) – like strain (NIBRG-23) (clade 2.2.1)	suspension for injection in pre-filled syringe	Seqirus S.r.l Italy	29 November 2010/ 21 October 2024
Zoonotic Influenza Vaccine Seqirus **Zoonotic influenza vaccine (H5N8)** [**]	Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain: A/Astrakhan/3212/2020 (H5N8) – like strain (CBER-RG8A) (clade 2.3.4.4b)	suspension for injection in pre-filled syringe	Seqirus S.r.l. Italy	9 October 2023/9 April 2024
Celldemic Zoonotic influenza vaccine (H5N1) [***]	Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain: A/turkey/Turkey/1/2005 (H5N1) - like strain (NIBRG-23) (clade 2.2.1)	suspension for injection in pre-filled syringe	Seqirus Netherlands B.V.	19 April 2024

[*]https://ec.europa.eu/health/documents/community-register/html/h658.htm
[**]https://ec.europa.eu/health/documents/community-register/html/h1761.htm
[***]https://ec.europa.eu/health/documents/community-register/html/h1806.htm

Many studies have been performed to obtain efficacious and safe H5N1 vaccines. One of these is Aflunov. **Aflunov** is a zoonotic monovalent A/H5N1 influenza vaccine adjuvanted with MF59 which is designed to increase and broaden the antigen-specific immune response and to extend the duration of the immune response. The vaccine contains parts of influenza viruses that have been inactivated. In nonclinical studies conducted in rabbits, Aflunov proved to be well-tolerated, did not cause maternal or embryofoetal toxicity, was not teratogenic, and had no effects on postnatal development.

At the time of the initial marketing authorisation, two main studies using a strain called A/Vietnam/1194/2004 (H5N1)-like strain (NIBRG-14) provided data on vaccination with Aflunov in healthy adults aged below and above 60 years. In one study involving 3,372 people, subjects were given either a seasonal flu vaccine followed by two doses of Aflunov three weeks apart, or placebo followed by two doses of an adjuvanted seasonal vaccine three weeks apart. In the first study, 21 days after the second injection, around 90% of people aged below 60 years and around 80% of those aged above 60 years had levels of antibodies that would protect them against H5N1. In the second study involving 240 people, subjects were given Aflunov using different vaccination schedules. The studies looked at the ability of the vaccine to trigger the production of antibodies against the flu virus. This study established that Aflunov should be given as two doses at least three weeks apart. A third study, using a vaccine with strain A/turkey/Turkey/1/2005 (H5N1)-like strain (NIBRG-23), was carried out in 343 adults aged below and above 60 years. The study showed that 21 days after the second injection, around 70% of adults below 60 years and around 64% of adults above 60 years produced an acceptable antibody response. Extension of indication to include treatment of children 6 months of age and older for AFLUNOV is based on final results from study in 471 children from 6 months to 17 years of age. [37]. The pre-pandemic vaccine Aflunov has been approved for the active immunisation against H5N1 subtype of Influenza A virus in individuals 6 months of age and above, for prophylaxis before the pandemic is declared. Patients should receive two doses od vaccine. One dose of 0.5 ml at an elected date. A second dose of 0.5 ml should be given after an interval of at least 3 weeks. In the event of an officially declared influenza pandemic due to A/H5N1 virus, persons previously vaccinated with one or two doses of Aflunov that contained haemagglutinin (HA) antigen derived from a different clade of the same influenza subtype as the influenza pandemic strain may receive a single dose of Aflunov instead of two doses that are required in previously unvaccinated individuals . Some heterologous immune response against A/turkey/Turkey/1/2005 (NIBRG23; clade 2.2.1) and A/ Indonesia/5/2005 (clade 2.1) was detectable both after the second and third vaccinations, indicating cross-reactivity of the clade 1 vaccine against clade 2 strains. This means that the vaccine may be effective against subtypes of the virus other than the one present in the vaccine [38]. This vaccine could be very useful in the event of adaptation of the H5N1 virus to humans, which could cause a new pandemic.

The Zoonotic Influenza Vaccine Seqirus is a monovalent influenza avian vaccine (egg-based, surface antigen, inactivated, MF59C.1 adjuvanted). Initially, this vaccine was registered as a duplicate of the Aflunov vaccine with the same composition of active substances. Given the evolution of reassortant highly pathogenic avian influenza (HPAI) viruses (H5N1) and since an increasing number of avian influenza spillover into mammals with a limited number human cases have been registered recently, a strain update for the “Zoonotic Influenza Vaccine Seqirus” has been considered appropriate to more adequately target the currently circulating clade of the HPAI H5 virus and, thus, to strengthen the pandemic preparedness capabilities [39]. Recent infections of Russian poultry workers and grey seals [40] indicate a broader host range for A(H5N8) viruses, underlining their pandemic potential.

Currently, A(H5N8) clade 2.3.4.4 viruses have evolved into at least 8 distinct lineages, suggesting that A(H5N8) variants are emerging at an unprecedented rate and pose a public health threat [41]. Zoonotic Influenza Vaccine Seqirus H5N8 is indicated for active immunisation against H5 subtype influenza A viruses in adults 18 years of age and above. The vaccine is administered intramuscularly as a course of 2 doses of 0.5 ml each. The second dose should be administered at 3 weeks after the first dose. There are no clinical cross reactivity data with the Zoonotic Influenza Vaccine Seqirus H5N8. The degree of immune response that may be elicited to influenza A(H5) viruses of subtypes or clades different to that of the vaccine strain Zoonotic Influenza Vaccine Seqirus H5N8, is unknown [42]. The Zoonotic influenza vaccine Seqirus contains a strain matching the currently circulating clade 2.3.4.4b to ensure protection.

Celldemic – new pandemic influenza vaccine contains the same antigens as Aflunov but is more advanced in terms of manufacturing method. Celldemic contains haemagglutinin (HA) and neuraminidase surface antigens derived from A/turkey/Turkey/1/2005 NIBRG-23, a reverse-genetic strain produced via a recombination of A/turkey/Turkey/1/2005 (H5N1) and influenza A PR8 strain. It is propagated in Madin Darby canine kidney cells, after which the antigens are purified and solubilised. The vaccine can be administered to patients who are allergic to egg proteins, as this ingredient is not present in the product formulation. Safety and efficacy of the vaccine have been evaluated based on 5 clinical studies in subjects aged 6 months and older. In addition, safety data are presented from three doseranging studies with MF59 adjuvanted cell culture-derived influenza vaccines of other subtypes. A main study involved around 3,200 adults who received 2 doses of Celldemic or placebo 3 weeks apart. Based on these results, the vaccine is expected to offer protection against influenza disease caused by the H5N1 strain included in the vaccine [43]. Celldemic is indicated for active immunisation against H5N1 subtype of Influenza A virus in adults and infants from 6 months of age and above. The vaccine is administered intramuscularly as a course of 2 doses of 0.5 ml each. It is recommended to administer the second dose 3 weeks after the first dose. The need for a booster dose(s) following the primary vaccination schedule has not been established.
Some cross-reactivity was observed towards five other H5N1 strains tested, however, this was only tested in those that had received the adjuvanted full dose. Immune responses were markedly lower compared to homologous strains and showed variation in immune responses according to strain and age group being consistently lower in the elderly. Since responses to heterologous strains was less robust, the potential protection and the duration of protection to heterologous strains is therefore uncertain. Potential cross-reactivity and response to clade 2.3.4.4b A(H5N1) have not been studied. It is therefore unknown whether the vaccine would be effective against strains currently prevalent in the environment [44]. Celldemic vaccine contains A/H5N1 strains belonging to older clades no longer circulating, so they are not expected to protect but if required they can be modified rapidly to match circulating viruses.

Pandemic influenza vaccines (pandemic preparedness vaccine) need to be specifically developed against the strain of virus causing the pandemic. Because the strain of flu virus causing a pandemic is not known before a pandemic is imminent, pandemic influenza vaccines can only be prepared once a pandemic has started and the exact strain of flu virus responsible can be identified.

There are a specific type of marketing authorisation to allow a vaccine to be developed and authorised before an influenza pandemic. The vaccines are tested to determine whether they will protect people against the virus strain that they contain. Often more than one virus strain is tested, in order to obtain as much information as possible on how the vaccine works, allowing for better preparedness. Pandemic preparedness vaccines can be authorised but not marketed before an influenza pandemic. The authorisation of the final pandemic vaccine can be very fast as relevant authorities have already assessed the vaccine safety and efficacy with other potential pandemic strains. In the event of a pandemic, once the virus strain causing the pandemic is identified, the manufacturer can include this strain in the authorised pandemic preparedness vaccine and apply for the vaccine to be authorised as a 'final' pandemic vaccine [36]. Four pandemic preparedness vaccines are currently authorised in the EU, which can be modified into pandemic influenza vaccines in a future pandemic (Table 2.)

Table 2. Pandemic preparedness vaccine

Trade name	Active substance (s)	Pharmaceutical form	Marketing Authorisation Holder	Date of first authorisation)/last update
Adjupanrix[*]	Split influenza virus, inactivated, containing antigen equivalent to: A/VietNam/1194/2004 (H5N1)	suspension and emulsion for emulsion for injection	GlaxoSmithKline Biologicals s.a., Belgium	19 October 2009/24 May 2024
Foclivia[**]	Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain: A/Vietnam/1194/2004 (H5N1) 7	suspension for injection in pre-filled syringe	Seqirus S.r.l. Italy	19 October 2009/16 August 2023
Pandemic influenza vaccine H5N1 AstraZeneca[***]	Reassortant influenza virus (live attenuated) of the following strain: A/Vietnam/1203/2004 (H5N1)	Nasal spray, suspension	AstraZeneca AB Sweden	20 May 2016/19 April 2024
Incellipan[****]	Influenza virus surface antigens (haemagglutinin and neuraminidase) of strain:	suspension for injection in pre-filled syringe	Seqirus Netherlands B.V. Netherlands	19 April 2024

	A/turkey/Turkey/1/2005 (H5N1)

[*] https://ec.europa.eu/health/documents/community-register/html/h578.htm
[**] https://ec.europa.eu/health/documents/community-register/html/h577.htm
[***] https://ec.europa.eu/health/documents/community-register/html/h1089.htm
[****] https://ec.europa.eu/health/documents/community-register/html/h1807.htm

In addition, special procedures have been developed for the marketing authorisation of medicinal products in the event of a pandemic, such as emergency procedure or modification procedure. The emergency procedure allows for fast-track approval of a new vaccine developed once an influenza pandemic is declared. Authorisation of these pandemic vaccines is faster than a normal vaccine, because competent authority assesses the information submitted by the manufacturer in an accelerated timeframe. Modification of seasonal flu vaccine procedure allows vaccines authorised for use against seasonal flu to be modified for use against pandemic flu, by swapping the seasonal virus strains with the pandemic strain [36].

Summary

Pandemic influenza viruses with novel antigenicity and the potential to exert significant impact on public health and socioeconomic impacts have emerged periodically throughout history. Future influenza pandemics are difficult to predict in terms of virus strain, timing of occurrence, or geographic origin [2]. Because these viruses continually evolve and spread in animal populations, and their risk of human exposure increases, there is a continuing need to reassess the risk as the situation evolves. Having appropriate policy and planning in place facilitates early response in order to suppress an influenza outbreak quickly, thus reducing the potentially catastrophic future impacts of an influenza pandemic. The efficient monitoring systems supervised by WHO, such as GIRS allow for early detection of threats and provide the ability to prepare for a future pandemic. Currently available antiviral medicines are mostly effective against the highly pathogenic strains of influenza A virus of concern, of which oseltamivir is the most important. These drugs can serve as first-line agents against emerging pandemic strains of influenza but can only be used for a short time due to emerging resistance [45]. The greatest weapon in the fight against the pandemic are vaccines closely matched to the circulating viral strains. The Zoonotic influenza vaccine Seqirus contains a A/H5N1 strain matching the currently circulating clade 2.3.4.4b to ensure protection. Other pandemic preparedness vaccines contain A/H5N1 strains belonging to older clades no longer circulating, so they are not expected to protect but if required they can be modified rapidly to match circulating viruses.

Pandemic preparedness and response is a complex phenomenon that combines science, societal beliefs, practical operational considerations, and political will. Effective plans will not succeed without the will to implement and execute them. There has been a recent wave of “pandemic fatigue” and a general doubt to take preventive measures. This could undermine efforts to prevent an influenza pandemic.

Disclosure

Authors' contribution

Conceptualisation: Jacek Fordymacki; methodology: Ryszard Łagowski; software: Ryszard Łagowski; check: Barbara Fetner; formal analysis: Jacek Fordymacki; investigation: Julia Kosęda; resources: Jacek Fordymacki; data curation: Barbara Fetner; writing – rough preparation: Ryszard Łagowski; writing – review and editing: Jacek Fordymacki; visualisation: Barbara Fetner; supervision: Julia Kosęda; project administration: Jacek Fordymacki; received funding – no specific funding; In preparing this work authors have not used any AI-assisted technologies.

All authors have read and agreed with the published version of the manuscript.

Financing statement

The study received no specific funding

Informed Consent Statement

Not applicable – Not Required

Data Availability Statement

The data presented in this study is available upon request from the corresponding author

Conflict of Interest

The authors deny any conflict of interest

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