

Statement from WHO Global Advisory Committee on Vaccine Safety about the safety profile of pandemic influenza A (H1N1) 2009 vaccines

Since its emergence in March 2009, influenza A (H1N1) 2009 virus has caused significant morbidity and mortality. For example, the U.S. Centers for Disease Control and Prevention (CDC) estimates that in the U.S. there have been about 100,000 hospitalizations and nearly 4,000 deaths due to pandemic (H1N1) 2009 virus during the period April to October 17, 2009. In response to the pandemic, more than 30 pandemic (H1N1) 2009 vaccines have been developed and licensed. Since September 2009, more than 50 countries have implemented immunization programs targeting various populations. These populations include health-care workers, children, pregnant women, and persons with certain underlying medical conditions, including chronic lung disease, diabetes, and heart disease, as well as persons whose immune systems are compromised.^{1,2}

From 21 September through 2 December, tens of million of doses of the pandemic (H1N1) 2009 vaccine have been administered, thereby providing the basis for this first safety review by the World Health Organization (WHO) Global Advisory Committee on Vaccine Safety (GACVS). The review is mainly based on passive surveillance data.³ Under the coordination of WHO, there is an unprecedented, ongoing exchange of safety information among regulatory and public health authorities from many countries around the world.

Pandemic influenza vaccines include live attenuated vaccines, inactivated unadjuvanted vaccines (split, sub-unit virion, or whole virion), and inactivated adjuvanted vaccines (split or sub-unit virion). At the time of the GACVS review, it was estimated that nearly 150 million vaccine doses had been distributed in many countries around the world. Approximately 30% of those 150 million doses are adjuvanted vaccines. No unexpected safety concerns have been identified for any of the pandemic (H1N1) 2009 vaccines. Product labelling for each vaccine contains a summary of expected side effects.⁴

¹ World Health Organization (WHO), 2009. Strategic Advisory Group of Experts on Immunization -- report of the extraordinary meeting on the influenza A (H1N1) 2009 pandemic, 7 July 2009. *Weekly Epidemiological Report*, 2009, Vol. 84(30):301-308. Available at <http://www.who.int/wer/2009/wer8430.pdf>. Accessed on December 16, 2009.

² WHO, 2009. Pandemic influenza A (H1N1) 2009 virus vaccine -- conclusions and recommendations from the October 2009 meeting of the immunization Strategic Advisory Group of Experts. *Weekly Epidemiological Report*, 2009, Vol. 84(49):505-516. Available at <http://www.who.int/wer/2009/wer8449.pdf>. Accessed on December 16, 2009.

³ Passive surveillance refers to a system designed to collect adverse events that follow vaccination. This type of surveillance typically relies on health professionals noting and reporting to the appropriate authority adverse events that occur in individuals after vaccination. This system relies on spontaneous reporting by health-care staff. By contrast, active surveillance is a mechanism through which specific health conditions are monitored through a systematic and continuous review of medical records.

⁴ The Committee noted the recent warning from the European Medicines Agency (EMA), after review of data from an ongoing clinical trial submitted by the manufacturer, that a higher

In the ongoing immunization campaigns, deaths in temporal association with vaccination have been reported in many countries. Given the large number of persons who have been vaccinated, it is expected that deaths that were unrelated to vaccination would occur in temporal association with vaccination.⁵ Investigation of deaths that have been reported after immunization have identified that the cause of death has been unrelated to vaccination in all but a few instances. There have been a few individual reports of deaths associated with anaphylactic reactions to vaccination.

Immediate hypersensitivity reactions have been reported after the use of all types of pandemic (H1N1) 2009 vaccines. These events include urticaria, angioedema, and anaphylaxis, with reactions ranging from mild to serious. The overall reporting rates for anaphylaxis range from 0.1 to 1.0 per 100,000 doses distributed. Anaphylaxis is a known, potentially life-threatening adverse effect of all vaccines and is a very rare event. Nonetheless, immunization providers must be prepared to recognize and appropriately treat such reactions.⁶

Although some cases of Guillain-Barré syndrome (GBS) have been reported after receipt of pandemic (H1N1) 2009 vaccines, the evidence to date is reassuring, with no increase in reporting rates above what is expected, based on background rates. Active surveillance for GBS has been instituted in several countries and should provide additional information by the first quarter of 2010.

Concerns have been raised about the use of adjuvanted pandemic vaccines in patients with immune disorders, such as immunodeficiency, autoimmune disorders, and solid organ transplants. To date, post-marketing surveillance has not found evidence for causality of any safety issues in such patients. Viral infections, such as influenza, can lead to severe complications in immunocompromised patients. Thus, the benefit of pandemic (H1N1) 2009 vaccines, adjuvanted or unadjuvanted, far outweighs the potential risks in these patients.

Programmatic errors have also been reported, including erroneously administering other drugs instead of vaccine, or errors in mixing adjuvant and antigen components as required for some of the vaccines. Immunization programmes should take appropriate measures to prevent such errors.

proportion of young children may experience fever after their second dose of an adjuvanted pandemic influenza vaccine, Pandemrix, than after their first dose. The EMA recommended that prescribers and parents should monitor the temperature of the vaccinated child and, if necessary, take measures to lower the fever. Additional information can be found here: <http://www.emea.europa.eu/pdfs/general/direct/pr/78440409en.pdf>. Accessed on December 16, 2009.

⁵ Black S, Eskola J, Siegrist CA et al. Importance of background rates of disease in assessment of vaccine safety during mass immunisation with pandemic H1N1 influenza vaccines. *Lancet*, 2009 doi:10.1016/S0140-6736(09)61877-8.

⁶ Public Health Authority of Canada identified a higher-than-normal rate of anaphylaxis (4.1/100,000 doses distributed) linked to one particular lot of the adjuvanted pandemic (H1N1) 2009 vaccine. Pending further investigation of adverse event reports linked to the lot, unused vaccines from this lot were withdrawn from use on 24 November 2009.

Conclusion

1. Ten weeks into the worldwide immunization campaign against pandemic (H1N1) 2009 influenza, the GACVS reviewed the safety of pandemic (H1N1) 2009 vaccines currently in use. To date, the safety data are reassuring.
2. Most of the adverse events that have been reported after immunization have not been serious. To date, no unexpected safety concerns have been identified.
3. Reporting mechanisms have been enhanced. Ongoing vaccine safety monitoring (pharmacovigilance) is critical, including regular information sharing with WHO by national regulatory and health authorities. Most of the safety information to date is from passive surveillance. Data from active surveillance will be assessed as they become available.³