Pan American Health Organization
Regional Office of the World Health Organization

Comprehensive Family Immunization
Family and Community Health Area

FINAL RECOMMENDATIONS ON PANDEMIC INFLUENZA

TECHNICAL ADVISORY GROUP ON VACCINE-PREVENTABLE DISEASES

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Epidemiological Situation

Beginning in mid-March 2009, surveillance systems in Mexico began to report a sharp increase in cases of acute respiratory disease, characterized by cases of influenza, accompanied by severe pneumonia. This increase began when cases of seasonal influenza typically started to wane. The number of cases continued to increase during the first weeks of April when a new influenza A strain (H1N1) was identified. During the same time period, the United States and Canada also began to report confirmed cases of influenza A(H1N1).

Given the emergence of the new influenza strain and its subsequent global spread, WHO moved through the pandemic phases, declaring pandemic phase six on 11 June 2009. As of 6 August 2009, a total of 174,913 cases of influenza A(H1N1) had been recorded, including 1,411 deaths, in 166 countries and territories, the West Bank, and Gaza Strip. Previously healthy young adults have been a particularly affected population group. The majority of influenza A(H1N1) cases have presented with mild symptoms, including cough, fever, sore throat, malaise, and headache; gastrointestinal symptoms have also been observed. Severe illness has been characterized by pneumonia and respiratory insufficiency, whereas bacterial co-infection has been infrequent. Risk factors for severe illness are emerging and appear to include pregnancy, heart disease, diabetes, asthma, pulmonary emphysema, immunodeficiency, and obesity.

Status of Vaccine

Current WHO estimates calculate the optimal global production capacity of a novel monovalent influenza A(H1N1) vaccine at 94 million doses per week, assuming vaccine yield is equal to seasonal influenza and that dose-sparing techniques are employed. Using this baseline, WHO estimates that 2.4 billion doses of influenza A(H1N1) vaccine could be available in 6 months and 4.9 billion doses available after 1 year of production. However, due to multiple pre-existing advanced purchase agreements, large quantities of these vaccines have already been committed, severely limiting supply to the majority of countries in the Americas.

A number of uncertainties exist, including the number of vaccine doses that will be necessary to achieve a sufficient immune response, whether simultaneous administration of the influenza A(H1N1) vaccine and the seasonal influenza vaccine will be possible, and whether or not adjuvant technology will be employed. Adjuvants represent a key dose-sparing strategy but experience is limited in the Americas. Manufacturers' decisions regarding the final presentation and packaging of the vaccine are also not yet known. Many of the uncertainties will be resolved with the results of vaccine safety testing and clinical trials. PAHO's Revolving Fund will be a key procurement mechanism during this process to promote equity and access to available doses.

Using traditional egg-based production technology, manufacturers are producing the following pandemic influenza A(H1N1) vaccine formulations: inactivated non-adjuvanted vaccines, inactivated adjuvanted vaccines, and live attenuated vaccines. Concerns exist about the safety and the immunogenicity of these formulations, especially with the use of adjuvanted vaccines for pregnant women. Europe has been using inactivated adjuvanted vaccines for at least two years. To date, their experience suggests no risk to pregnant women being vaccinated with adjuvanted vaccines. However, no controlled studies have been performed. SAGE recommends that inactivated nonadjuvanted vaccines similar to most seasonal influenza vaccines be considered the preferred option given the extensive safety data on their use in pregnant women. However, if such a product is not available, pregnant women should be vaccinated with another pandemic influenza

vaccine available at that time, for example, an adjuvanted inactivated influenza vaccine or a live attenuated influenza vaccine.

PAHO's Regional Plan for Pandemic Vaccination

As part of PAHO's technical cooperation activities with Member States in response to the influenza A(H1N1) pandemic, a Regional Vaccination Plan for Pandemic Vaccination was developed and distributed to Member States in May 2009. Ensuring equitable access to vaccine, the two main objectives of this plan are to (a) strengthen seasonal influenza vaccination in the Region and (b) assist Member States in their preparation for the introduction of influenza A(H1N1) pandemic vaccine.

As of December 2008, 35 Member States and territories administered the seasonal vaccine in the public sector, vaccinating a variety of risk groups, compared to 13 in 2004. Most countries purchase vaccine through PAHO's Revolving Fund. While there is no evidence that seasonal influenza vaccines confer cross protection against influenza A(H1N1), strengthening vaccination with the seasonal vaccine is essential to reduce the seasonal disease burden and to prevent the co-circulation of both seasonal and influenza A(H1N1) strains.

As of 21 August, the majority of country and territories had estimated the need to vaccinate approximately 200 million people. As more information becomes available concerning dose requirements and finalized target groups, this consolidation will need to be revised. Because intense public demand for influenza A(H1N1) vaccine is expected to be coupled with initial vaccine shortages, messages will have to be elaborated carefully to clearly communicate national target groups, in essence suppressing the public turnout for vaccination. This presents a unique communication situation in the Region that will need to be handled carefully.

Considering that influenza A(H1N1) vaccine supply will be limited, countries will need to prioritize risk groups. On 7 July 2009, WHO's Strategic Advisory Group of Experts in Immunization (SAGE) recommended that countries should consider three objectives (and associated population groups) when deciding upon vaccination priorities: protecting essential health infrastructure (vaccinating health care workers), reducing morbidity and mortality (vaccinating individuals with chronic disease), and reducing virus transmission (vaccinating school children). After considering the current context, SAGE recommended the following population groups (edited to reflect age ranges more commonly managed in the Region):

- Health care workers
- Pregnant women
- Population older then 6 months of age with chronic disease
- Healthy young adults aged 19-49 years
- School children aged 5-18 years
- Children aged 6 months to 4 years
- Healthy adults older than 50 years.

As with all new vaccines, the detection of events supposedly attributable to vaccine or immunization (ESAVIs) will be essential. The main objectives of ESAVI surveillance are:

- Detection of triggers and known events from previous use of pandemic vaccines and events possibly associated with adjuvants.
- Rapid, transparent, and efficient communication of investigation results to the public and parents.

Neurological ESAVIs are one specific concern. Guillain–Barré Syndrome (GBS) is a rare condition with an annual incidence of 10–20 cases per one million adult population and has been associated with many respiratory and gastrointestinal illnesses. During the swine influenza vaccination campaigns of 1976 in the United States, the increase in the GBS cases above the background rate was approximately one case per 100,000 persons vaccinated. Through the surveillance of acute flaccid paralysis (AFP) from 2000-2008 in the Americas, approximately 10,500 GBS cases were diagnosed, resulting in an average incidence of 0.82/100,000 aged less than 15 years.

Protocols to evaluate the impact of influenza A(H1N1) vaccine in the Region of the Americas will be developed and implemented through the ProVac initiative, once the vaccine is introduced.

Recommendations:

Considering the current dynamic epidemiological situation of the influenza A(H1N1) virus and the current SAGE recommendations concerning the use of an influenza A(H1N1) vaccine, TAG makes the following recommendations, which may need to be updated based upon evolving information.

- The national objectives for vaccination against pandemic influenza should be to reduce morbidity and mortality and keep health services functioning. Therefore, priority groups for vaccination should be health care workers, pregnant women, and persons aged >6 months with chronic diseases (heart disease, diabetes, respiratory conditions, immunodeficiency, obesity). Depending on the epidemiological situation, availability of resources, and EPI capacity, TAG suggests the following additional risk groups to be prioritized: children aged 6 months to 4 years, healthy children aged 5-18 years, and healthy adults aged 19-49 years.
- Due to the annual high morbidity and mortality caused by seasonal influenza viruses, vaccination with the seasonal vaccine should be continued. Technical recommendations regarding the simultaneous administration of both influenza vaccines should be followed, when applicable. Continued epidemiological monitoring of the circulating influenza strains should be continued to inform decisions regarding the future composition of influenza vaccines.
- Countries should conduct retrospective studies to calculate baseline rates of GBS in different populations so that potential changes in the incidence of GBS associated with influenza A(H1N1) virus circulation, and potentially with influenza A(H1N1) vaccines can be detected.
- Countries should monitor the following events during the introduction of the vaccine: (1) serious events (require hospitalization, life-threatening, cause disability, fatal), (2) new events, (3) rumors, (4) events that occur in groups of people, and (5) programmatic errors.
- Countries should prepare social communication strategies to:
    - Maintain public trust by informing in a clear and transparent fashion;
    - Ensure that individuals and their families are using mitigating interventions for prevention;
    - Ensure that the public fully understands the recommendations and the reasons for vaccination of priority groups; and
    - Understand the general benefits and risks of events associated with vaccination when they occur.

- PAHO and WHO should continue to strengthen and prioritize the global regulatory network and national regulatory bodies that comply with WHO policy.
- In unique emergency situations, TAG endorses the SAGE recommendation which allows for countries to buy unlicensed vaccine. In these situations TAG also recommends that national regulatory authorities fast track their licensing procedures.
- In order to ensure comparability, countries should follow PAHO/WHO guidelines to strengthen and standardize surveillance systems.
- Ministries of Health should continue strengthening national influenza centers and influenza laboratories by allocating more resources.
- Countries should conduct retrospective hospital-based studies to more accurately determine morbidity and mortality of influenza A(H1N1).
- To promote dose-sparing and ensure equitable access to the limited pandemic vaccine supply, adjuvanted vaccine should be used whenever possible.
- Industrialized countries in the Region of the Americas with abundant pandemic vaccine access are encouraged to contribute vaccine supplies to countries with considerable less access. To do this, they should consider limiting their vaccine interventions to priority groups, as seconded by SAGE and TAG.
- Recognizing that Brazil and Mexico are embarking on influenza vaccine production, TAG encourages PAHO to develop a Regional strategic plan that will ultimately lead to Regional vaccine self-sufficiency.
- PAHO should revitalize the supply chain alliance that in the past successfully identified unused oversupply of vaccine in some countries that could be used in other resource-poor countries.
- To assure equitable access to an influenza A(H1N1) vaccine, countries should use the PAHO Revolving Fund for Vaccine Procurement to buy vaccine.