



## **Questions and answers on vaccines for the H1N1 ('swine flu') pandemic**

The European Medicines Agency has started reviewing data on pandemic flu vaccines received from vaccines manufacturers. This follows the strategy that the Agency established in 2003, which was designed to allow the rapid authorisation of vaccines to be used during a pandemic. The Agency's goal is to ensure that the data are reviewed as early as possible, before the autumn and the beginning of the flu season in the Northern hemisphere.

### **What is the 'swine flu' pandemic?**

The 'swine flu' outbreak started in April 2009 in Mexico, and was officially declared a pandemic by the World Health Organization in June 2009. A pandemic is an outbreak of influenza due to a new type (strain) of flu virus that is spreading easily from person to person. It is different from the normal 'seasonal' flu, because the strain is new, and because most people have no protection (immunity) against it. Because of the lack of immunity, the virus can spread widely.

### **Which vaccines can be used during the pandemic?**

Normal flu vaccines, which are prepared to protect against seasonal flu, are not effective in this pandemic. Instead, special pandemic flu vaccines need to be used. They will be used to build up protection against the pandemic virus in people who have not yet been exposed to it. This is expected to lessen the overall impact of the pandemic.

### **How will pandemic flu vaccines be made available?**

Now that the virus strain causing the current pandemic has been identified, manufacturers can start to develop pandemic vaccines. Before these vaccines can be made available, they will need to be authorised. Because of the urgency for pandemic vaccines and the need to speed up the assessment, the data presented by the manufacturers are assessed as and when they become available.

There are two ways vaccine manufacturers can obtain an authorisation:

- Using the 'mock-up' vaccine approach. A mock-up pandemic influenza vaccine is a vaccine that is prepared in advance of a future pandemic influenza, using a strain that could cause a pandemic, but before knowing the actual virus strain that will cause the pandemic. Companies carry out full studies of the quality, safety and efficacy of the mock-up vaccine with the original virus strain. Once the pandemic virus strain is known, it is used to replace the original strain in the vaccine. The original studies can be used to predict how people will react to the vaccine once the flu strain causing the pandemic has been included.
- Developing a new vaccine 'from scratch'. This will require a new, full marketing authorisation and therefore more data than the mock-up approach. The Agency is currently working with two manufacturers towards the authorisation of new pandemic vaccines.

### **Which mock-up vaccines have been authorised?**

The European Commission has granted marketing authorisation to four mock-up vaccines:

- Celvapan, from Baxter AG;
- Daronrix, from GlaxoSmithKline Biologicals S.A.;
- Focetria, from Novartis Vaccines and Diagnostics S.r.l.;
- Pandemrix, from GlaxoSmithKline Biologicals S.A..

Three of these vaccines, Daronrix, Focetria and Pandemrix, contain 'adjuvants'. These are compounds that are included with the vaccine strain to help stimulate a better response. All mock-up vaccines have been prepared with an H5N1 strain of flu virus that needs to be changed now to the H1N1 strain that is causing the current pandemic.

#### **What is happening now with the mock-up vaccines?**

The companies are now growing the novel flu virus and preparing the pandemic vaccines by including the new strain into their mock-up vaccines. Because this is a change to the vaccine's composition, the companies will need to apply for a 'variation' to the marketing authorisation. Because data are assessed as soon as they become available, this variation will be processed quickly, normally within five days. Once the Agency's scientific committee, the Committee for Medicinal Products for Human Use (CHMP), has given a positive opinion, the variation can then be approved by the European Commission and the vaccine can be made available for use.

Manufacturers of mock-up vaccines have indicated that they intend to submit the necessary variations to produce pandemic vaccines. The Agency has been informed that the first of these may be filed in September 2009.

Clinical trials in adults and children are starting. Data from clinical trials in adults and older subjects are expected first, followed by data from clinical trials in children. Manufacturers have indicated that initial results will become available from September 2009 onwards.

#### **How will the Committee assess the variation to a mock-up vaccine?**

The CHMP will review data on the methods used to make and test the final vaccine. This review, in conjunction with the review previously carried out for the mock-up vaccine, will allow the Committee to issue an opinion on whether the vaccine can be authorised for use in the European Union. The results from the ongoing studies of the final H1N1 vaccine tested in people will be assessed once the studies have been completed. These results will add to the information on safety and efficacy that was reviewed when the original mock-up vaccines were authorised. These data included the results of studies in over 8,000 people, including adults, older subjects and children.

The CHMP is of the opinion that the inclusion of the H1N1 virus strain will not have a major impact on the final vaccine's safety and efficacy. This is based on past experience with 'seasonal' flu vaccines. The composition of these vaccines is adjusted on a yearly basis, according to international recommendations, by including the seasonal flu strains that are expected to cause the upcoming seasonal flu outbreak. Experience has shown that the change of strain does not have an impact on the safety and efficacy of the seasonal vaccine.

#### **What will happen once pandemic vaccines have been authorised?**

Once the vaccines have been authorised, the CHMP will continue to evaluate all the further data that will be generated from the clinical trials the companies are carrying out.

While the final vaccine is expected to have the same safety profile as the mock-up vaccine, it is only with the widespread use of the vaccines that all side effects can be detected. The Committee is therefore requiring that vaccine manufacturers carry out further safety studies and put special pandemic risk management plans in place. These will ensure that the safety of the vaccines can be monitored very closely, by both companies and regulatory authorities, once they are used in the general population.

After the final vaccines are ready, decisions on which groups should receive the vaccines, and when they should receive them, will be made by the government in each EU Member State.

The EMEA will update this document as new information becomes available.