BACKGROUND BRIEFING

PREPARING FOR A HUMAN INFLUENZA PANDEMIC VACCINE

EVM members* are addressing the challenges posed by the threat of a human influenza pandemic worldwide by developing and manufacturing pandemic vaccines. In this respect, EVM has been working closely with the European Commission and EU Member States to set up a coordinated EU strategy for influenza pandemic preparedness and efficient response planning (EVM proposal for an action plan on flu pandemic preparedness available at: http://www.evm-vaccines.org/pdfs/evm_pap.pdf).

Advance planning to get sufficient pandemic vaccines in time is critical. These plans should cover:

1. acceleration of the development of prototype pandemic vaccines;
2. anticipation of the production demands required to produce pandemic vaccines in extremely large quantities;
3. addressing liability issues;
4. ensuring equitable distribution.

1. Accelerate the development of prototype pandemic vaccines

For optimal effectiveness, a vaccine needs to be based on the strain of flu it is to protect against. Vaccines used to protect against seasonal flu will not work against a pandemic strain. However, a tailored pandemic vaccine cannot be made until the pandemic strain is identified and it will therefore be a race against time to make that vaccine before the virus begins to spread.

- An accelerated regulatory approval has been established

The EMEA issued guidelines in March 2004 on the submission of marketing authorization applications and dossier structure and content for pandemic influenza vaccine. These guidelines provide a route for accelerated regulatory approval through the submission of the prototype pandemic vaccine files in advance of a pandemic. The EMEA has agreed to waive the registration fees of the prototype pandemic vaccine files, since they may never be commercialized. International harmonised procedures may help to ensure the optimal availability of vaccines around the world.

- Flu vaccine manufacturers are engaged in the development of "prototype" vaccines

EVM member companies are engaged in the development of influenza pandemic prototype vaccines, based on potential pandemic-like flu strains. Some target avian strains, like H5N1 and H9N2, while others target human strains, like H2N2. These "prototypes" are being submitted for registration to the EMEA.

Making pandemic vaccines is a new development for flu vaccine manufacturers, whose experience has been built on seasonal flu vaccines. Developing prototype vaccines involves upgrading manufacturing facilities to meet regulatory requirements on the use of genetically modified vaccines strains. These vaccines are based on avian strains and consist of specific monovalent formulations, and have to undergo clinical testing before approval.

* EVM Members are: Baxter, Berna Biotech, Chiron Vaccines, GlaxoSmithKline Biologicals, Sanofi Pasteur, Sanofi Pasteur MSD, Solvay Pharmaceuticals, Wyeth Vaccines.

- Long term R&D activities

Vaccine manufacturers are not only committed to the short/medium term development of prototype vaccines but also to long-term efforts to improve the performance of existing influenza vaccines using new technologies and concepts.

The 7th EU framework R&D programme or a specific designed flu pandemic programme should incorporate projects aimed at encouraging research into new influenza pandemic vaccines concepts.

- Public-Private Partnership is needed to prepare prototype vaccines

The Commission has issued a document entitled "Towards sufficiency of pandemic vaccines in the EU", outlining Public Private Partnership (PPP) between the EU Member States, the Commission and the European Vaccine Manufacturers (22 April 2005). The PPP is based on a two-tiered approach: financial support for pandemic vaccines ("push") and a sustainable increased interpandemic influenza vaccination uptake, aimed at adapting production capacities to meet pandemic needs ("pull"). The EVM considers that the push mechanisms are still too limited and Europe remains far behind the policies developed by the USA, Canada, Australia and Japan to support the development of pandemic vaccines. These include contractual arrangements with manufacturers to develop vaccine formulations and increase manufacturing capacity.

2. Anticipate the production demands required to produce pandemic vaccines in extremely large quantities

Within the EU we benefit from the presence of vaccine manufacturers. These manufacturers produce 70% of the influenza vaccines used worldwide (more than 50% of that production is distributed outside the EU). European vaccine manufacturers are, therefore, global suppliers. Today, the EU production is around 190 million doses (of trivalent seasonal flu vaccine) for the Northern hemisphere and consumption within EU is around 90 million doses. This means that only 20% of the European population (450 million) is vaccinated against seasonal flu.

- In the event of a pandemic, wider vaccination will be needed

The seasonal vaccination campaigns focus on selected target groups, primarily the elderly. Whilst the 1918-19 pandemic killed many people in all age groups, young adults experienced the highest mortality. This implies that pandemic vaccination would be required in much larger quantities, as the entire world population could be susceptible to the emerging pandemic strain.

- Pandemic vaccines will be made in the plants that make seasonal vaccine

Although a prototype vaccine, developed against a particular existing avian strain of 'flu, may offer some cross protection against the pandemic strain, a proper pandemic vaccine cannot be made until the pandemic strain has been fully identified. Very large quantities of it will then have to be made very quickly. Building additional production facilities purely to make pandemic vaccines, which may be needed only every 30 years, is not realistic. Pandemic vaccines will therefore have to be produced using facilities that normally make seasonal vaccines. Because of the large quantities of pandemic vaccines that will be required, manufacture of seasonal vaccines will have to cease for the duration of pandemic vaccine production.

- Manufacturing capacity is determined by demand for seasonal vaccine

Influenza vaccine capacity is linked to annual uptake of seasonal vaccines due to the fact that influenza vaccine composition must be reformulated

annually to match or "fit" the currently circulating strains. Influenza vaccines therefore cannot be stockpiled for subsequent years.

To avoid any shortage, the way to increase 'flu vaccine production capacity is to increase annual uptake of seasonal 'flu vaccination, as the WHO and the European Commission have repeatedly emphasized.

Today around 20% of the European population is vaccinated. In order to protect 50 to 100% of the population in case of a pandemic, vaccine production during the interpandemic period should be raised from current 90 million doses (20% of population) to about 150 million doses (33% of population). Thus, additional approaches are needed to increase coverage rates. The industry investments needed to increase production capacities can only be based on product demand and forecast.

Member States should anticipate their pandemic needs through National Advance Purchase Agreements and adapt proportionally their interpandemic use of influenza vaccines.

- Industry is working to stretch existing capacity as far as possible

Seasonal vaccine is "trivalent", providing protection against three different 'flu strains. Pandemic vaccines (and their prototypes, based on existing strains) are limited to one strain ("monovalent"), which theoretically triples the available capacity. However, two injections per person may be needed to provide adequate protection, because the pandemic virus will be totally new to our immune system. The characteristics of the pandemic vaccines (antigen dosage, adjuvanted versus non-adjuvanted, …) would have also an impact on final production capacities.

- There is a long lead-time for increasing vaccine manufacturing capacity

New vaccine manufacturing facilities are subject to rigorous regulatory approval procedures and it takes 3-5 years for them to become operational. It also takes a time for companies to train the skilled personnel needed to run them safely and effectively.

3. Addressing liability issues

Vaccine manufacturers are responsible for the legal liabilities arising from the use of vaccines that are manufactured and administered according to current safety, quality and efficacy requirements.

In the case of a flu pandemic, tight deadlines will need to be met, and it may be that health authorities in the Member States would urgently require pandemic vaccines for mass vaccination while clinical safety data will be limited or even not available during the first vaccination campaign. Provisions to provide compensation due to any unexpected vaccine injury in these exceptional circumstances should be put in place by the competent authorities (EU/MSs).

4. Ensure equitable allocation of pandemic vaccines

In the event of a pandemic, ensuring the equitable allocation of vaccines between countries is a crucial aspect of the control of the disease. European influenza vaccine manufacturers, the European Commission and the EU Member States should collaborate to ensure allocation of vaccine supplies in accordance with public health needs (epidemiology, local outbreaks), whilst respecting EVM members' commitments inside and outside the EU.

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