



Influenza Pandemic Preparedness

EVM Proposal for an Action Plan to ensure availability of effective vaccines in the event of an influenza pandemic

October 2008

EXECUTIVE SUMMARY

Significant progress has been made in pandemic preparedness at EU and member state levels since last update of the EVM proposal for action plan issued in 2006. This included sustained industry efforts at both R&D and production levels. Key elements have also been identified that should be addressed to ensure timely and equitable access of vaccines to European citizens in case of an influenza pandemic.

Through this updated proposal, EVM members re-emphasize their strong commitment to meet these objectives and call for an increased partnership with the European institutions and member states.

EVM expects the European Commission to:

- Support and encourage member states in defining effective vaccination strategies for protection of their populations in case of a pandemic;
- Set up processes to secure development, acquisition and deployment of pre and pandemic vaccines;
- Take forward its proposal for a Council recommendation regarding seasonal vaccination coverage rates;
- Support ongoing work on technical issues (regulatory procedures and standardization of assays to evaluate candidate vaccines);
- Continue its strong support of the WHO Global Action Plan and the Global Influenza Surveillance Network

EVM asks that member States continue to support further increases in vaccine development and manufacturing capacities by:

- Encouraging Research & Development in EU through public/private partnerships;
- Defining operational approaches to pre- and pandemic vaccination strategies;
- Increasing usage of seasonal influenza vaccines, in accordance with the 2010 WHO target, and by extending current recommendations for seasonal vaccination.

Since publishing its first Proposal for Action Plan (PAP) in 2004, updated in 2006, the European vaccine industry has made significant progress towards the overall objective of ensuring the availability of sufficient volumes of safe and effective vaccines in the event of a pandemic

Industry's Contribution has followed through on the commitments made in the previous plans and has:

1. Strengthened R&D activities

- Developed and obtained regulatory approval for several prototype vaccines for use during the pandemic vaccine (see definitions 1). These are based on egg and cell culture technologies. (http://www.emea.europa.eu/htms/human/pandemicinfluenza/moc_kup.htm)
- Developed several H5N1 vaccines, for stockpiling in advance of the pandemic and potential use before the first pandemic wave (see definition 2). One pre-pandemic vaccine has been approved by the EMEA http://www.emea.europa.eu/pdfs/human/opinion/PrepandemicVaccine_36644608en.pdf
- Continued R&D into new antigens, adjuvants and delivery technologies [http://www.evm-vaccines.org/pdfs/ipd table R&D projects Europe update october2008.pdf](http://www.evm-vaccines.org/pdfs/ipd_table_R&D_projects_Europe_update_october2008.pdf)

2. Adapted and prepared influenza vaccines production to address a pandemic situation

- Industry has made significant progress in adapting facilities to enable avian/pandemic Influenza vaccine manufacture – for example to enable the use of seed viruses produced from reference strains by reverse genetics (Genetically Modified Organisms (GMOs)).
- Significant capacity increases have also occurred, using both egg and cell culture technologies. http://www.ifpma.org/Influenza/content/pdfs/Presentations/2007_10_19_WHO_GAP_meeting.pdf.
- This has been further assisted by the development of pandemic and H5N1 vaccines using antigen sparing approaches (such as novel adjuvants or whole virus).
- Industry has also identified the timing problems involved in the supply of pandemic vaccines. It will take 3 to 6 months to supply the first vaccine doses, during which time the first pandemic wave could strike globally. Pandemic vaccines will most likely arrive too late for the first pandemic wave. Industry has therefore invested heavily in finding solutions to the timing issue, through the development of improved H5N1 vaccines, which could be manufactured and stockpiled in advance

3. Contributed to evaluate of alternative or complementary vaccination strategies

As foreseen in the 2006 PAP, scientific evaluation, particularly in relation to the optimal use of pre-pandemic vaccination has included (but is not limited to):

- Administration of pre-pandemic H5N1 vaccine at the start of the pandemic if the pandemic strain is an H5N1 strain.

- Priming with pre-pandemic H5N1 vaccine during the inter-pandemic period;

Partnership at European and national levels

The European vaccine industry (EVM) recognizes and welcomes the increased level of collaboration it has experienced at the EU level. This includes working with:

- EMEA on regulatory procedures and risk management plans;
- ECDC on pre-pandemic and pandemic vaccination strategies;
- European Institutions and individual member states in response to specific requests for information on the industry position in relation to seasonal and pandemic vaccination issues

Nevertheless EVM should underline the low level of R&D support in EU compared to other countries outside Europe. This is especially true in the USA where more \$7.9 billion has been dedicated to flu pandemic preparedness, including support industry efforts to develop production technology for pandemic vaccines. Recently, the Biomedical Advanced Research and Development Authority (BARDA) has been created to manage the development and purchase of medical remedies for biodefense and infectious diseases, including pandemic flu vaccines (<http://www.hhs.gov/aspr/barda/index.html>). To a lesser extent, but still above all EU efforts, the Japanese and the Australian governments have significantly contributed to their national industry efforts to develop and produce pandemic flu vaccines. In comparison, none of the limited EC investment in pandemic preparedness has been dedicated to support the European vaccine industry, despite its prominent role in the influenza vaccine R&D and production.

EVM acknowledges the progress made by some member states in encouraging and taking up developments, and in clarifying their future supply needs for pandemic and H5N1 vaccines. This is essential to EVM members in planning their future manufacturing capacities.

- Following the European Parliament resolution [P6_TA(2005)0406] on the strategy against an influenza pandemic of 26 October 2005, many Member States continue to announce Advance Purchase Agreements (APAs) for the supply of pandemic vaccines covering their populations. To date these include Austria, Denmark, Finland, France, Germany, Italy, the Netherlands, Norway, the UK, and Sweden.
- Several EU member states and nearby European countries have also announced purchases of H5N1 vaccine stockpiles to cover part or all of their populations. These include Finland, France, Ireland, Switzerland and the UK.

These efforts should be followed by all the EU member States to help lower the impact of an influenza pandemic. According to a study on “How prepared is Europe for pandemic influenza?,” conducted by the London School of Hygiene and Tropical Medicine: *“Considerable variations exist between countries, with important implications for the entire European region and individual nation states. Different national and regional responses, and the failure to reconcile them, could create considerable ethical and political tensions as well as very varied effectiveness in reducing the impact of a pandemic”* (reference 2).

Next Steps from 2008 onwards

1) Industry’s Commitments

EVM members will continue to contribute to pandemic preparedness in the key areas defined in the 2006 PAP:

1.1 Strengthen R&D Activities

Progress will continue in areas of concern identified:

- Strong immune responses have been obtained with vaccines containing low amount of antigen (antigen sparing approach) (Ref.1)
- Several vaccines have demonstrated good immune responses against drift variants of the H5N1 strain (e.g. an H5N1 Vietnam strain vaccine shows cross protection against Indonesia, Turkey & Anhui). (Ref. 3)
- Development of avian/pandemic Influenza vaccines. ([http://www.evm-vaccines.org/pdfs/ipd table R&D projects Europe update october2008.pdf](http://www.evm-vaccines.org/pdfs/ipd_table_R&D_projects_Europe_update_october2008.pdf))
- In parallel, R&D efforts are dedicated to improve the efficacy of seasonal flu vaccines through recently developed related to antigen content, use of adjuvants, alternative administration routes, live attenuated influenza vaccines, and new production technologies, or on new immunological approaches, such as those using antigens common to all influenza virus species.

1.2 Adapt & Prepare vaccine production for Pandemic

As explained above, industry will continue to adapt and significantly increase its industrial flu vaccine production capacity to be ready in case of pandemic.

1.3 Assess Vaccination Strategies

Scientific evaluation will continue, particularly in relation to the optimal use of pre-pandemic vaccination.

2) EVM call for increased Partnership at EU and member state level

2-1At European Union level

As pointed out in the 2006 update of the PAP, EVM is concerned about allocation of vaccine supply in the event of a pandemic, as it considers that it is not its role to allocate vaccines doses beyond contractual agreements. Therefore, looking ahead, and as part of EU Bio-preparedness plans, the industry calls on the European Commission to:

- Support and encourage member states in defining effective vaccination strategies for protection of their populations in case of a pandemic.
- Set up processes to secure development, acquisition and deployment of pre-and pandemic vaccines, including:
 - brokering agreements with vaccine manufacturers for securing vaccine supply in those member states currently with no such arrangements
 - assessing the value of a European H5N1 vaccine stockpile for containment of an initial outbreak wherever it occurs in Europe
- Continue its support to WHO in establishing a global H5N1 vaccine stockpile and pressing for measures to ensure procurement and supply, such as the establishment of advance purchase agreements for pandemic vaccines, for low income countries. This would include the provision of much needed financing mechanisms.
- Continue its strong support of the WHO Global Action Plan, the Global Influenza Surveillance Network and the free and timely sharing of viruses,

without which vaccine development and manufacture will be adversely impacted.

- Take forward its proposal for a Council recommendation regarding seasonal vaccination coverage rates.
- Supporting ongoing work on technical issues, such as defining correlates of protection for pandemic influenza and standardization of assays.
- Continue to work with EMEA on regulatory procedures and risk-management plans.

2-2 at Member State level

EVM ask that member states, supported by the EU, take up these developments and continue to support further increases in vaccine development and manufacturing capacities as part of their seasonal flu vaccination policies and of their pandemic preparedness plans, by:

- Defining operational approaches to implement pre- and pandemic vaccination strategies, including vaccine forecasting for pandemic vaccines, pre-pandemic vaccine stockpiles and their regular replenishment, as well as defining procurement processes that will allow vaccine manufacturers to meet national and international demands;
- Increasing usage of seasonal influenza vaccines, in accordance with the 2010 WHO target of 75% vaccination in the 65 and over age group, as agreed by member states in the WHA resolution. EVM's own data on vaccine distribution suggests that - for EU as a whole, distribution increased from 16% in 2003/04 to nearly 20% in 2007/08 of the total population. However, in the last two years, this increase trend has not been followed in all of the countries. This is still well short of the level of vaccination required to cover all those directly at risk or susceptible to increase the viral transmission representing up to 49% of the total European population (Ref. 4).
- Extending the recommendations for seasonal vaccination by decreasing the age cut-off for universal vaccination to 55 or 50 years and by the inclusion of children, as already implemented in several EU member states. Such policies are supported by their medical, public health and economical values. They also result from the actual failure of risk-based vaccination strategies compared to universal age-based strategies, when risk factors are multiple and affect a significant proportion of the population in a given age group. Pediatric vaccination also represents an important step forward, and EVM wishes that their comments on the ECDC technical report of January 2007 would be seriously taken into consideration by the Commission (Ref.5).

Conclusion

EVM acknowledges the significant progress made in pandemic preparedness at EU and Member States level since last update of the EVM proposal for action plan issued in 2006. However, EU and national Governments effort should continue in order to ensure sufficient volume and timely access of pandemic vaccines to the European citizens in the event of a pandemic.

The members of the European Vaccine Manufacturers Group re-emphasize their commitment to address the challenges posed by the threat of influenza pandemic worldwide and call for an increase support of EU institutions and member States.

Reference 1:

Antigen sparing and cross-reactive immunity with an adjuvanted rH5N1 prototype pandemic influenza vaccine: a randomised controlled trial

Isabel Leroux-Roels et al

Lancet, Volume 370, Issue 9587, 18 August 2007-24 August 2007, Pages 580-589

Safety and antigenicity of non-adjuvanted and MF59-adjuvanted influenza A/Duck/Singapore/97 (H5N3) vaccine: a randomized trial of two potential vaccines against H5N1 influenza

Karl G Nicholson et al.

Lancet, Volume 357, Issue 9272, 16 June 2001, Pages 1937-1943

Reference 2:

<http://www.lshtm.ac.uk/ecohost/projects/pandemic/HowpreparedisEurope.pdf>

Reference 3:

Broad Clade 2 Cross-Reactive Immunity Induced by an Adjuvanted Clade 1 rH5N1 Pandemic Influenza Vaccine

Isabel Leroux-Roels et al

PlosOne, February 27th, 2008

Boosting immunity to influenza H5N1 with MF59-adjuvanted H5N3 A/Duck/Singapore/97 vaccine in a primed human population

Iain Stephenson et al.

Vaccine Volume 21, Issue 15, 2 April 2003, Pages 1687-1693

Cell culture (Vero) derived whole virus (H5N1) vaccine based on wild-type virus strain induces cross-protective immune responses

Otfried Kistner et al,

Vaccine Volume 25, Issue 32, 10 August 2007, Pages 6028-6036

Reference 4:

Establishing the health and economic impact of influenza vaccination within the European Union 25 countries

Ryan et al, Vaccine

Volume 24, Issue 47, 17 November 2006, Pages 6812-6822

Reference 5:

EVM comments on the ECDC Technical Report on infant and children seasonal immunisation against influenza on a routine basis during interpandemic period (13 February 2007)

Definitions

1. **Pandemic vaccine** - intended for the prevention of influenza during an officially declared pandemic influenza situation, once the pandemic viral strain has been included.
2. **Pre-pandemic vaccine** - prepared from influenza viruses with a pandemic potential that are intended for use before a pandemic is declared or during an officially declared influenza pandemic (<http://www.emea.europa.eu/htms/human/pandemicinfluenza/pre.htm>)