

Chapter III. The Second European Influenza Conference—Lessons learnt and actions to take

The urgent need for a European Influenza Task Force[☆]

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1. Introduction

Founded in 1992, The European Scientific Working Group on Influenza (ESWI) is a multidisciplinary group of key opinion leaders and representatives of several organisations in influenza. ESWI aims to reduce the impact of epidemic and pandemic influenza in the European population by identifying and communicating with stakeholders and by facilitating interactions between them. Targeted communication and well-chosen projects help ESWI to reach this objective.

One such project is the establishment of Integrated National Influenza Stakeholder Networks (see textbox). A second project, consistent with the success of the National Influenza Networks, was the organisation of the Second European Influenza Conference (SEIC) in Malta in September 2005. This conference brought together -about 850 scientists, opinion leaders in healthcare work, government representatives and policy makers. As part of the influenza stakeholder community, representatives of influenza vaccine and antivirals manufacturers were also present. The different target groups worked together during the 3-day conference to look for ways both to reduce the impact of annual epidemic influenza and to prepare Europe for pandemic flu.

The conference concept was highly innovative. Indeed, for the first time ever, influenza was not only discussed

from a scientific perspective. Opinion leaders in healthcare work, government representatives and policy makers were also recognised as influenza stakeholders and were offered separate programme tracks. These included tailor-made lectures and workshops on all relevant aspects of the disease. Moreover, many participants attended sessions from different programme tracks, allowing them to look at influenza from other perspectives. In addition, specific sessions brought together the entire influenza stakeholder community. These sessions focussed on information exchange and interaction among all participants. The result was highly interesting new visions on how best to combat epidemic and pandemic influenza in Europe. These visions are documented in this chapter. The main conclusion of the meeting is that coordination in Europe is insufficient and therefore a European Influenza Task Force should be established in order to accelerate Europe's preparedness for a pandemic outbreak.

The establishment of Integrated National Influenza Stakeholder Networks

National experts can achieve influenza control more directly and effectively. In many countries, however, the available infrastructure and influenza expertise is insufficient to either recognise the need for, or undertake, this kind of activity. To bridge the gap between national influenza stakeholders – including GP's, healthcare workers, policy makers and government representatives – and national institutions, ESWI has developed the concept of Integrated National Influenza Stakeholder

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Networks (INISN). In 2003, ESWI established such networks in Germany, Poland and Sweden. Since then, considerable progress has been made in the control of influenza as the individual INISN implement their jointly developed action plans, i.e. they are realising the various objectives that the national influenza stakeholder community agreed upon. ESWI continues to play a role as catalyst and facilitator, and is ready at any time to assist stakeholders with its specific expertise. Based on this experience, ESWI intends to establish cooperation with the national Influenza networks with several other EU countries.

2. The European pandemic response: establishing a European Influenza Task Force

The threat posed by a possible pandemic influenza outbreak is high on the social and political agenda. This is because outbreaks of avian influenza, which might eventually lead to a pandemic influenza outbreak in humans, seem to be looming over Europe like a sword of Damocles. However, the recent influenza H5N1 infections in Turkey and in Romania may not significantly increase the risk of a pandemic influenza outbreak in humans. According to Prof. Dr. Albert Osterhaus, Chairman of the European Scientific Working Group on Influenza (ESWI): “Isolated outbreaks of avian influenza in Europe are, of course, a problem in terms of economy, animal welfare and biodiversity, but the threat to public health will probably be manageable, largely due to the lessons learned during the 2003 bird flu outbreak in The Netherlands; if the proper measures for animal and public health are taken, such outbreaks may be contained with limited consequences for human health”.

Nonetheless, ESWI believes that a human influenza pandemic that kills several million people may be imminent. The highly pathogenic avian H5N1 influenza virus continues to circulate in Asia. If this avian influenza virus further adapts to humans and develops the capability to spread efficiently from human to human, a new influenza virus strain may emerge against which the vast majority of the world’s human population has no immunity. Such a pandemic virus can be expected to spread worldwide with unprecedented speed given the high level of global traffic and trade. No country would be spared and there would be little or no time to react.

The participants in the Malta meeting urge governments and the international community to create a European Influenza Task Force (EIT). The Task Force would accelerate Europe’s preparedness and would also play an important role in the international coordination that is essential in dealing with an outbreak that affects countries worldwide.

3. Duties and composition of a European Influenza Task Force: overview

The conclusion of the closing session of the conference was clear: Europe is not ready for the next pandemic. Scientists, healthcare workers, government representatives and policy makers were all in agreement on this point.

The broad consensus is that a worldwide outbreak of influenza is just a question of time. Only by placing this issue at the top of Europe’s health agenda now, will member states take the necessary steps towards preparing infrastructure, citizens and the community at large for the threat.

“Failure to act now to introduce proper pandemic preparedness, including early warning systems, will leave us empty-handed when a pandemic strikes and will cause needless deaths,” stressed Prof. Dr. Albert Osterhaus, ESWI Chairman.

If Europe is to protect its citizens and its economy, it must act now. European policy on influenza pandemic preparedness is scattered. Europe needs a single voice to focus governments and the European population on accelerating preparations for an influenza pandemic.

Only the rapid creation of a European Influenza Task Force can ensure an adequate and timely European response to a pandemic. ESWI wishes to play a facilitating role in the creation of such a Task Force.

In the EIT leading specialists from the following disciplines should be brought together:

- human and animal health experts;
- specialists in virology, epidemiology, pathology, ecology and agriculture;
- communication experts;
- experts in translating science into policy at a global level;
- representatives of European and global governments, institutions and NGO’s;
- representatives of UN organisations.

Representatives of the European influenza vaccine and antiviral industries should also be included in the EIT in order to facilitate the establishment of preparedness and intervention strategies for influenza outbreak situations in animals and humans in Europe.

The duties of the Task Force would be:

1. To gain insight into the European influenza situation, taking into account temporal and geographical variation of influenza viruses in Europe and in those areas that may pose a direct threat to Europe. Besides human influenza viruses, those of several animal species such as wild birds, poultry, pigs, horses and cats should also be taken into account.
2. To prioritise research and integrate knowledge from different disciplines on human and animal influenza.
3. To further develop early warning systems and intervention strategies for influenza outbreaks in humans and animals. Participation of industrial partners in this area is crucial.

4. To translate knowledge into policy advice, emphasising the integration of human and animal health strategies.
5. To increase the percentage of the human population vaccinated against annual influenza to one-third in all EU member states.
6. To create public–private partnerships between European authorities and vaccine manufacturers for the research and development of potential pandemic influenza vaccines and antivirals.
7. To establish adequate stockpiles of antiviral compounds for pandemic influenza preparedness in all the EU member states.

The role of ESWI in the establishment of the Task Force will be to help identify the respective participants and representatives, to stimulate communication among them and to help generate the political will and funding needed for this initiative.

In the following paragraphs, the major duties of this Task Force are elaborated upon with respect to:

- The expansion of annual influenza vaccination programmes to cover one-third of the human population in all EU member states, and adequate stockpiling of antivirals.
- The creation of public–private partnerships between European authorities and vaccine manufacturers.
- Bird flu monitoring to gain insight into the European influenza picture.

4. The expansion of annual influenza vaccination programmes to cover one-third of the human population in all EU member states

4.1. Grounds for 30% EU vaccination

4.1.1. Annual vaccination: cornerstone for combating epidemic and pandemic flu

Annual vaccination of one-third of the EU population against epidemic influenza is medically justified and will greatly improve the availability of pandemic influenza vaccine in Europe. Annually occurring influenza is an important public health problem in Europe, and the cornerstone for combating both epidemic and pandemic influenza is the use of vaccines. Also, antivirals constitute a useful adjunct to vaccines. According to the WHO's Global Agenda on Influenza Surveillance and Control, the enhanced utilisation of influenza vaccines and antivirals in the inter-pandemic period will contribute to pandemic preparedness.

4.1.2. Stockpiling of antivirals as an intermittent solution

At the start of an influenza pandemic, a pandemic vaccine will probably not be available and it will take considerable time to produce sufficient amounts of a vaccine once one has been developed. To bridge this period, stockpiling of antivirals (e.g. the neuraminidase inhibitors) to cover at least

20% of the population should be seriously considered by EU member states.

The neuraminidase inhibitors have few adverse side effects, and the virus only rarely develops resistance. Stored in bulk form, antivirals have a shelf-life of 15 years. An important downside to antivirals, however, is their relatively high cost.

Simulations showed that a stockpile of antivirals covering 20% of the population and universal treatment during the Spanish Flu pandemic of 1918–1919 would have reduced the number of deaths by 53 percent—or about 25 million people [1].

Stockpiling drugs in advance is presently the only way to ensure that they will be available when needed for at least 20% of the population. Only a small, well-informed and wealthy part of the population will build their own personal stockpile. Most of the general population will rely on coordinated action by public authorities. Hence, a European stockpile should be built.

4.1.3. 30% capacity for trivalent vaccines equals 100% capacity for monovalent vaccines

Given the current production technology and capacity of trivalent vaccines for inter-pandemic use, one can conclude that if one-third of the EU-25 population is vaccinated annually with a trivalent vaccine, then sufficient monovalent pandemic vaccine could be produced to vaccinate the entire EU-25 population at least once.

Although more research is needed before an effective and safe prototype pandemic vaccine can be produced, annual vaccination of one-third of the EU-25 population within 5 years will contribute significantly to the availability of a pandemic vaccine when it is most needed.

4.1.4. 150 million doses required annually

During influenza epidemics in developed countries, attack rates of 1–5% are most commonly observed, but the attack rate is often higher among high-risk groups, and the annual mortality rate among such groups can be as high as 7.5–23 deaths per 100,000 [2]. Vaccination may significantly reduce respiratory illness and sick leave among healthy adults, and reduce severe disease and premature death in the elderly and in persons with underlying ailments or diseases during influenza outbreaks. In fact, appropriate influenza vaccines achieve protection rates against clinical disease of about 50–80% in healthy adults, and reduce the risk of serious complications or death by 70–85% among the elderly. Successful vaccination campaigns in the EU have targeted the elderly and other risk groups over the past decades, providing protection to an increasing number of susceptible individuals. Despite this, during the influenza season, this high-risk group can still place additional pressure on healthcare services [3].

The ESWI recommendation that by the year 2010, one-third of the total population of the European Union 25 Member States (EU-25) be vaccinated annually against epidemic influenza, equates to about 150 million of the 455

million population of the EU-25. Current epidemic vaccination rates vary between countries due to differences in compliance rates, population size, the number of elderly per country, those with chronic medical conditions, and the number of healthcare workers in each country.

4.1.5. *Even high risk groups are insufficiently vaccinated*

Although vaccines have proven to be safe and efficacious, influenza vaccination is currently usually restricted to people in high-risk groups. These typically include the elderly (>65 years), and people with chronic medical conditions such as diabetes, heart, lung, or kidney disease.

Health authorities restrict reimbursement of influenza vaccination to those in high-risk groups. The current risk groups represent about 28% of the EU population. Of these, it is estimated that less than 62% are being vaccinated with the current vaccine supply, the equivalent of 17% of the EU-25 population. This suggests that a large proportion of those traditionally assumed to be most at risk from influenza are not being vaccinated.

Recent evaluations have identified the population across EU-25 that could most benefit from influenza vaccination. These groups include all persons aged 50 and above, healthcare workers and the remaining population who are in the current high-risk groups such as those who suffer from respiratory disease, cardiovascular disease or diabetes. A substantial amount of recent data indicates that vaccination of young children would also be beneficial, but more research is needed on the vaccination of healthy children.

Across the EU-25, these groups were found to represent 44%, the equivalent of 200 million, of the total EU-25 population. Since it is well known that in reality a maximum of 75% of the recommended groups are vaccinated, ESWI has adopted an annual vaccination target of one-third of the European population within 5 years.

The implication of ESWI's recommendation would be an annual vaccine usage of 150 million doses, compared to the 79 million doses currently consumed [4] across Europe. Thus, today, no more than 40% of ESWI's recommended target population is being vaccinated in the EU-25. This not only leads to more influenza cases, but also to more influenza-related morbidity and mortality, and results in substantial social and economic costs that could otherwise be avoided.

4.1.6. *Indirect flu costs significantly higher than vaccination cost*

The most significant cost of influenza to society is the indirect cost of lost productivity and absenteeism. In Europe, influenza accounts for around 10% of sick leave, while estimates of the cost in lost productivity in France and Germany range from £5.6 billion to £8.5 billion per year [5]. There is, therefore, an immediate need for EU-25 member states to make plans to increase vaccination coverage in the next 5 years. Public-private partnerships between health authorities, industry and target groups should be established to reach this goal within this time period.

4.2. *Factors supporting and hindering achievement of 30% EU-vaccination: healthcare workers, policy makers and government representatives make an inventory during conference workshops*

During the conference, healthcare workers, government representatives and policy makers collaborated in several workshops to identify the factors supporting and hindering the achievement of the goal advanced by ESWI: the vaccination of one-third of the EU population by 2010 and the stockpiling of antiviral drugs for 20% of EU citizens.

Annual vaccination of one-third of the EU population against epidemic influenza is medically justified and will greatly improve availability of pandemic influenza vaccine in Europe. Annually occurring influenza is an important public health problem in Europe. It is associated with increased visits to general practitioners, increased hospital admissions [6], and excess deaths [7]. It also leads to increased days lost due to absences from work and school, decreased productivity, and extra pressure on healthcare services during the winter season.

4.2.1. *Attitudes and misconceptions with healthcare workers identified as main barriers to increased influenza vaccination*

The current vaccine usage in Europe of 79 million doses equates to coverage of only 17% of the total population. Moreover, while the EU's current risk groups represent about 28% of the total population, it is estimated that fewer than 62% of such people are being vaccinated with the current vaccine supply.

At the ESWI conference, healthcare workers from all over the world worked together to identify factors that support or hinder an increase in the vaccination rate of risk groups on a European scale.

Healthcare workers play a crucial role in raising public awareness and increasing vaccination rates at the local level. They constitute both the problem and the solution to a more effective influenza vaccine effort in Europe; they have first-hand knowledge of the institutional obstacles to progress such as lack of resources and poorly focused public information campaigns, but their own work practices and attitudes can be misguided, as well.

The main obstacle to higher vaccination rates in Europe appears not to be limited financial resources, but rather the attitudes of healthcare workers. Their misconceptions about vaccine side effects, and their general emphasis on treatment over prevention, are a bigger problem than limited financial resources or inconsistent policy across EU countries regarding influenza reimbursement.

Misconceptions about flu and flu vaccination are still widespread among nursing personnel, or even GP's. For example, many believe that a flu shot could have severe side effects, could provoke an outbreak of the disease itself, that flu is just "a common cold", or that a flu shot can cause sinusitis or ear infections in children. Due to these and other

misconceptions, a large group of healthcare workers is not supporting – or is even discouraging – the vaccination of their patients, even those in risk groups [8].

To reach ESWI's goal of immunising 30% of Europe's population (and 75% of the high risk groups), the healthcare workers participating in the conference workshop defined a list of solutions. They identified well-targeted and consistent communication via appropriate channels to high-risk groups, general practitioners (GPs) and patient associations as playing a key role in this process. Opinion leaders can be used to communicate messages and generate trust. Creating consistent messages between spokespersons and between countries is another crucial factor. And, of course, communicating with healthcare workers via continuous education and clear guidelines is essential [9].

4.2.2. *Public misconceptions are greater barrier than insufficient vaccine supply*

The government representatives and policy makers participating in the conference workshop identified far more obstacles than supporting factors in achieving the objective advanced by ESWI, the vaccination of 30% of the EU population by 2010. Four basic groups of obstacles were defined: public confusion, political inertia, vaccine supply and distribution, and economics.

Misconceptions in the minds of the general public and even healthcare workers undoubtedly are the biggest obstacle to better flu control and vaccination uptake.

A consistent communication strategy should clarify misunderstandings about, for example, the real risks of flu complications or the difference between pandemic and epidemic flu. As healthcare workers, especially GPs, play a key role in raising awareness and implementing national guidelines, a special focus must be placed on them [10].

The currently inadequate levels of vaccine production and available antivirals, and the fact that 99% of all vaccine production is concentrated in only nine countries, are additional major obstacles. Equally important are the logistics of organising the vaccinations. Vaccine centres or "one stop shops" for vaccinations are a possible remedy.

Finally, political inertia should be remedied. Governments should make clear analyses of the public health and economic benefits of annual vaccination, make investments in clear communication (especially to high risk groups), and increase reimbursement for the vaccine.

5. **Creation of public–private partnerships between European authorities and vaccine manufacturers**

ESWI calls upon the European authorities to stimulate and establish public–private partnerships in order to develop prototype pandemic vaccines, and test them for safety and efficacy in clinical trials as soon as possible.

Today, vaccine manufacturers need at least 6–8 months to produce an effective vaccine. Intensive and expensive

research is needed to develop new methods for the faster production of pandemic flu vaccine [11]. Moreover, the current production capacity of vaccine manufacturers, which is adjusted to the demand of the annual flu vaccine, covers only 20% of possible pandemic vaccine demand. Given the unpredictability of flu pandemics, private companies will need strong incentives to invest in developing a new product that may never be needed, or that nobody is willing to pay for unless a pandemic occurs. Transparent agreements have to be made on how pandemic vaccine should be used, how much is needed, and who will pay for it.

A combination of "push" and "pull" mechanisms is needed to stimulate the development and production of pandemic flu vaccines. The objective of the push mechanisms is to reduce the costs and risks of pandemic vaccine development, whereas the pull mechanisms aim to address the perceived lack of viable markets for pandemic flu vaccines.

A first possible push mechanism is the development of a library of reference strains by the public sector. The development of a seed stock library to a level where it is usable by manufacturers as a master seed lot may significantly expedite vaccine production when a pandemic strain emerges.

A second possible push mechanism is the establishment by the public sector of serological and potency testing of candidate vaccines. Waiving regulatory licensing fees by governments and regulatory authorities could be a third important stimulating factor.

Pre-pandemic vaccination coverage is a major pull mechanism. Increased flu vaccine usage during the inter-pandemic years leads to increased production capacity and would give countries experience in the logistics of vaccine distribution and administration. It is also undoubtedly very useful from a public health perspective.

Advance purchase agreements and awards for licensing prototype vaccines are other pull mechanisms designed to share the financial risks. Indemnification from liability claims could be another important pull mechanism. Finally, ensuring equitable global distribution according to rational and evidence-based governmental plans, for the poorer countries as well as for the industrial countries, is a key element.

6. **Bird flu monitoring to gain insight into the European influenza picture**

Migratory birds appear to be the main carriers of avian influenza. An integrated network for the real time monitoring of influenza virus infections in migratory birds should therefore be established in Europe. Within this network, influenza virologists and ornithologists will work together to create an early warning system for the introduction of avian influenza viruses that could threaten poultry and, eventually, other animal species, including humans.

The mandate of this "FLUBIRD" network should be 3-fold. First of all, it should set up the necessary ornithological studies and sampling activities. Secondly, it should play a key

role in virus detection, isolation and characterisation. And finally, it should support data processing and analysis for the early warning systems and risk evaluation processes.

Currently, the highly pathogenic avian H5N1 influenza virus is circulating in Asia. Migratory birds spread the virus outside the Asian continent, and have already caused several outbreaks of avian influenza in Europe. These could eventually lead to a pandemic influenza outbreak in humans.

However, the current H5N1 influenza infections in poultry may not significantly increase the risk of a pandemic influenza outbreak in humans, if the proper measures for animal and public health are taken now. Only when this avian influenza virus further adapts to humans and develops the capability to spread efficiently from human to human, can a new influenza virus strain emerge against which the vast majority of the world's human population has no immunity. Given the high level of global traffic and trade, such a pandemic virus could spread worldwide with unprecedented speed.

7. Conclusion

In accordance with the views of the influenza community, ESWI urges the creation of a European Influenza Task Force in order to accelerate Europe's preparedness for the next pandemic outbreak of influenza.

Antiviral stockpiling is an important aspect of influenza pandemic preparedness, and many European countries have decided to build stockpiles. The rapid development and production of a human pandemic influenza vaccine, however, will be equally crucial when a pandemic emerges. ESWI, therefore, calls upon the European authorities to stimulate and establish public–private partnerships in order to develop prototype pandemic vaccines, and test them for safety and efficacy in clinical trials as soon as possible. In addition, an integrated network for the real time monitoring of influenza virus infections in migratory birds should be established in Europe, and influenza virologists and ornithologists should collaborate closely within this network. Such a network will act as an early warning system for the introduction of influenza viruses that may threaten poultry and eventually other animal species, including humans.

The Task Force will consist of human and animal health experts, scientists from all relevant disciplines, communication experts and representatives of the pharmaceutical industry.

The role of ESWI in the establishment of the EIT Task Force will be to help identify the respective participants and representatives, to stimulate communication among them and to help generate the political will and funding needed for this initiative. In so doing, ESWI's expertise in bridging the gaps between national influenza stakeholders will prove extremely valuable. Indeed, influenza control is a joint responsibility, both on a national and on a supranational level.

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