

EN

EN

EN



COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 8.7.2009
COM(2009) 353 final

Proposal for a

COUNCIL RECOMMENDATION

On seasonal influenza vaccination

EXPLANATORY MEMORANDUM

INTRODUCTION

Influenza is a highly contagious respiratory infection of viral origin, which occurs epidemically most frequently during winter months. Influenza disease usually presents as rapid onset of a typical pattern of combined symptoms, in particular very prominent headache. Mild and asymptomatic cases also occur while recovery from the typical infection normally takes a week. However, many other respiratory infections of viral or bacterial origin will cause similar but rarely all combined symptoms.

Extensive disease often presents with severe or even fatal pneumonia. While these complications can occur in anyone they are far more common among the elderly or in people with chronic underlying medical conditions inducing higher rates of morbidity and mortality. These persons are considered as 'risk groups' (ECDC 2008¹).

This paper is based on two interlinked objectives:

- (1) to combat the burden of seasonal flu, and
- (2) to adjust the production capacity of flu vaccines in the EU in order that, in the event of a pandemic, the vaccine manufacturers can provide the amount of vaccines needed to cope with such a situation.

OVERALL DISEASE BURDEN

The burden from influenza is manifold. Firstly, there is severe disease that may be fatal. Secondly, there are large numbers of mild to moderate cases, which result in a multiplication of days called off sick and loss of productivity in the working population. Both effects are of great economic impact. The burden varies from year to year, which makes it hard to estimate the annual number of deaths. One estimate looking at excess deaths attributed to influenza found that, in milder influenza seasons, there were around 8 deaths per 100,000 population, while in more severe but non-pandemic years, the figure would be 44 per 100,000. Another independent estimate established similar data with average estimated excess deaths of 25 per 100,000 between 1989 and 1998. Extrapolating this data to an EU population of around 500 million in 2008 would result in between 40,000 deaths in a moderate year and 220,000 in a particularly severe influenza season, which however has not been seen recently.

These crude figures are not taking into account the variable levels of influenza vaccine use in vulnerable groups, or the rising proportion of the very old and vulnerable people in European countries. While much attention is paid to the potential impact of a pandemic many more people will regrettably die in the intervening years between two pandemics because of seasonal influenza epidemics than during a pandemic itself. Of additional and growing importance are large epidemics causing overflow of emergency medical services and high intake of hospital admissions, which together with flu-induced staff shortages in hospitals create extensive dysfunctions in the health care sector.

Estimates of disease associated costs

The costs caused by an illness are mostly calculated by computing the sum of all direct, indirect and intangible costs. Direct costs result from the use of medical and non medical

¹ http://ecdc.europa.eu/en/files/pdf/Publications/priority_risk_groups_forinfluenza_vaccination.pdf

resources. Indirect costs are due to productivity loss and absenteeism from work; and intangible costs relate to impaired performance and quality of life.

Direct costs are influenced by chronic underlying conditions and other risk factors (e.g. age), which may lead to increases in hospital admissions and prolonged treatments. Influenza constitutes a substantial socioeconomic burden for society in terms of medical treatments (increase in consultations, hospitalisations, clinical complications, drug use) and work absenteeism. There are different estimates on the total economic impact of an influenza epidemic. For example, the total impact of an influenza epidemic (total estimated direct and indirect costs) in industrialised countries may reach 56.7 million € per million people.

Several studies have estimated costs using a variety of methods. A WHO paper reported that for Germany, the estimated total costs of the 1996-1997 influenza epidemic amounted to approximately 987.8 million €; a French study estimated the total cost of influenza at more than 1,796 million €. In the United States, the yearly total costs have been calculated at approximately 10,000–17,000 million €. Extrapolating these costs to a standard EU population of around 495 million would give a level of costs shown in Table 1 with variations explained above.

Table 1: Estimated annual costs of influenza epidemics (million €)

Country	Population (million)	Annual costs (million €)	Extrapolated to EU population (495 million)
France	63.4 (2007)	1,796	14,022
Germany	82.3 (2007)	988	5,942
United States	303.8 (2008)	10,000 – 17, 000	27,699

Nevertheless, the precise cost/benefit relationship of a targeted vaccination of risk groups is difficult to evaluate.

An overall, comprehensive study has been established by the ECDC listing the different elements of the burden of disease of seasonal influenza in Europe and promoting the basis of cost/benefit evaluations in different risk groups classified according to their conditions.

VACCINE EFFICACY AND EFFECTIVENESS

Estimates of vaccine efficacy and effectiveness vary depending on the match between vaccine and the circulating viral strain, the age group and the clinical category. Generally, seasonal influenza vaccines tend to work less well in the elderly and those with underlying chronic disease. In trials, influenza vaccines have consistently been shown to prevent laboratory-confirmed illness in 70% to 90% of healthy adults. Despite the on average benign course of the disease, reduction in hospital admissions and deaths is still highly significant: 21 to 27% reduction in risk of hospitalisations attributable to influenza vaccination in the elderly and 12 to 48% reduction in risk of death attributable to influenza vaccination.

While for example cost benefit effectiveness for groups above 65 of age is well established in nearly all locations, this may vary from demographic and economic setting to setting. For example, cost benefit effectiveness is well established also for groups from 60-64 years of age in the Netherlands but might be less so in other countries.

RATIONALE FOR THIS PROPOSAL

Health benefits for seasonal influenza and the link to pandemic influenza preparedness

Every year, seasonal influenza causes considerable morbidity and mortality. Currently available antivirals are of limited use if any in the prevention or treatment of influenza, as they need to be administered in a very timely fashion after the onset of the first clinical symptoms. Furthermore, there are significant concerns about the development of resistance in influenza viruses that tend to limit their use with the view to preserving their value in the event of a pandemic. The best way therefore to mitigate seasonal influenza is vaccination. Since the genome of the influenza virus is prone to frequent mutations and re-assortments, WHO expert panels recommend for each season the three most appropriate antigens for inclusion in the formulations for industrial vaccine production. Although the immune response elicited by a single shot could last and protect longer, the antigenic variations impose that vaccinations need to be renewed every year.

Despite the well recognized merits of seasonal flu vaccination, actual vaccination coverage is low: twenty countries measured influenza vaccine uptake among those aged above 65 years, findings range from 1.8%-82.1%. Only seven countries assessed the coverage in persons with underlying medical conditions and found a range between 27.6% and 75.2%. Studies point at several reasons for this low coverage. The disease or condition associated with the risk (e.g. heavy smoking, asthma) is not always perceived as severe enough to justify vaccination, or vaccines are not considered as effective enough (mainly due to the confusion between influenza and other "influenza like" illnesses that might affect a person even when vaccinated).

Persons at risk could possibly be brought to accept a vaccination if their physicians or nurses tried to convince them harder. Lack of training on the disease and vaccines in the general public has also been pointed out. Evidently, stronger commitment of public health authorities and better organisation of vaccination campaigns and reimbursement of costs incurred would entail higher coverage rates. On the other hand, measurements of precise coverage rates of specific risk groups has its problem since the correct size of risk groups in Member States might be difficult to establish. This is the reason why in turn increasing coverage rates of risk groups has proven to be elusive. However, efforts by the ECDC on developing a robust monitoring tool are ongoing and have provided initial consensus on the identity of these groups (Eurosurveillance, October 2008²).

The need for action from Member States has already been emphasized in several documents adopted by the World Health Assembly, the Commission and the European Parliament.

In 2003, the World Health Assembly recommended in its resolution 56.19³ to increase seasonal influenza vaccination coverage of all people at high risk with the goal of attaining a vaccination coverage of the elderly population of at least 50% by 2006 and 75% by 2010. As this deadline is more and more elusive, we propose, following consultation with the WHO, 2015 or the best possible target by default⁴

² <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19018>

³ World Health Assembly. Prevention and control of influenza pandemics and annual epidemics. Fifty-sixth World Health Assembly; Resolution WHA56.19. 28 May 2003

⁴ The WHO recommendation was adopted in 2003 and seven years were given to countries worldwide to reach the 75% coverage objective. This objective has not been reached in the EU so far and the increase of coverage remains modest. Based on this recommendation a similar time-frame has to be envisioned to meet a similar target, however taking into account the specificity of the EU in terms of both demography and economic development.

While the seasonal influenza virus is different from the pandemic influenza virus, the initiatives for both cases are closely linked. In the case of an influenza pandemic one of the main tools to fight the pandemic will be – in addition to the use of antivirals, masks and the implementation of social distancing measures – vaccination of the population with the strain responsible for the pandemic. Pandemic vaccines will be produced using the same manufacturing facilities as for seasonal flu vaccines. Regarding pandemic preparedness, we can note the following initiatives at the EU level:

On 22 April 2005 the Commission published a paper called ‘Towards sufficiency of pandemic influenza vaccines in the EU’⁵. This paper sets out recommendations for a strategy for creating conditions of sufficiency in such vaccines and outlines a public-private partnership (PPP) between public bodies and the vaccine industry. One of the proposed public sector contributions is a firm commitment ('pull') by all EU Member States to increase inter-pandemic influenza vaccine uptake in line with the World Health Assembly (WHA) Resolution 56.19. On the other hand, the significance of linking increase of seasonal vaccine coverage, i.e. use of inter-pandemic vaccines to current vaccine production capacity that is not deemed sufficient to meet the demands of the Community in the event of a pandemic ('push') has already been reiterated by the Commission in the reviewed version of the Community Pandemic Influenza Preparedness and Response Plan adopted on 28 November 2005⁶.

On 26 October 2005 the European Parliament adopted a resolution on the strategy against an influenza pandemic⁷ stating that:

- the potential threat of the avian influenza virus recombining with seasonal influenza would be reduced by ensuring that all those at high risk of exposure to the avian influenza virus are immunized against seasonal influenza;
- there is a substantial risk of inadequate, inequitable and delayed supply of vaccines in countries, which do not produce them;
- Member States are responsible for taking the necessary measures to prevent and prepare for an influenza pandemic but the Commission plays a coordinating role;

Furthermore, the European Parliament

- urges Member States to take all necessary steps to prevent recombination of H5N1 into a virus that can be transmitted from person to person, and, therefore, insists that workers in and connected to the poultry sector be vaccinated as a matter of priority;
- urges Member States to increase vaccination coverage during the inter-pandemic period in accordance with WHO recommendations, which will also encourage industry to expand production capacity to meet the expected pandemic demand for vaccines;
- calls on Member States to target poultry farmers as a high priority group for vaccination in order to reduce the chances of recombination of human and avian

⁵ http://ec.europa.eu/health/ph_threats/com/Influenza/influenza_key03_en.pdf

⁶ Communication from the Commission to the Council, the European Parliament, the European Economic and Social Committee and the Committee of the Regions on Pandemic Influenza Preparedness and Response Planning in the European Community, COM(2005) 607 final: http://eur-lex.europa.eu/LexUriServ/site/en/com/2005/com2005_0607en01.pdf,

⁷ European Parliament. Strategy against an influenza pandemic. European Parliament resolution P6_TA(2005)0406. 26 October 2005

influenza viruses at one of the most important potential interfaces. While this point is reaching less and less scientific consensus (many species can serve as a mixing vessel, not only humans) it should be kept under scrutiny in respect of the principle of precaution.

In addition, on 14 June 2006, the European Parliament adopted another Resolution on pandemic influenza preparedness and response planning in the European Community⁸, recalling that:

- particular attention should be paid to developing further the capacity to produce pandemic vaccines;
- the Commission should take steps to ensure that sufficient antivirals and vaccines are available;
- Member States should increase orders of seasonal influenza vaccines in line with WHO recommendations to assist the pharmaceutical industry in increasing the production capacity of influenza vaccines, in order to cope with the substantial increase in demand in the event of a pandemic.

In the event of a pandemic the EU27 would need at least 495 million doses of pandemic vaccine (monovalent). The annual seasonal flu vaccine production in the EU is estimated to be 223 million doses, of which about 105 million doses are marketed in the EU. Seasonal vaccines are, however, trivalent (i.e. contain three different seasonal vaccine strains). In terms of vaccine production capacity this means that each seasonal vaccine dose requires as much capacity as three pandemic vaccine doses and that the amount of vaccine necessary to vaccinate one person for seasonal flu is the same as that which is needed to vaccinate three persons for pandemic flu. Accordingly, in order to cover the whole EU population, we will need to increase the production of trivalent seasonal flu vaccine for the EU to 165 million doses, to reach the capacity of 495 million monovalent pandemic vaccine doses. This increase from 105 million to 165 million doses represents a 57% increase (i.e. 60 million doses) in the use of trivalent seasonal flu vaccines. Such an increase would enable the industry to have the capacity to produce enough pandemic vaccines for the entire EU population. The target of increased seasonal vaccination coverage for high risk groups, as mentioned above, will help the EU attain this objective regarding pandemic vaccines.

In addition, the logistics of vaccinating rapidly the entire EU population are not to be underestimated: the higher the coverage rate, the higher the vaccine dispensing capacity in case of emergency needs to be. Member States have already taken measures to increase the dispensing capacity, for example by allowing nurses to give flu shots. Nevertheless, this capacity increase cannot be planned but has to be tested incrementally. Indeed, doubling the current level of coverage of flu vaccines in the general population would mean reaching about 30 % overall coverage. This means that in most cases the vaccination workload would double in the time window foreseen between the release of the season's vaccine and the start of the caseloads. At the level of an individual General Practitioner, this would mean that flu vaccination could take up the entire week. Logistical problems of bringing vaccines to point of care delivery are already encountered year after year.

⁸ European Parliament. Pandemic influenza preparedness and response planning in the European Community. European Parliament resolution P6_TA(2006)0259. 14 June 2006

It is estimated that the present insufficient capacity to produce and dispense vaccines will lead to difficult choices in terms of vaccination targets and will create discrepancies among the Member States.

NEED FOR BEHAVIOURAL AND ORGANISATIONAL CHANGES AND RESEARCH NEEDS

Some Member States have already high vaccination coverage and a good organisation to achieve high coverage levels (communication, reimbursement, administration of the vaccine). But for some other Member States the target is still very far to reach and they step up efforts to address health professionals and at risk groups in order to ensure better vaccination coverage.

Member states as well as successive Commission Framework Programmes (FP) for Research have made significant investments into influenza research and have funded a number of vaccine development projects. While the majority of these projects were focused on pandemic vaccines, they also include novel concepts like intranasal delivery, cell-based vaccine production methods and the testing of new adjuvants, which are relevant for seasonal vaccines. However, more social and behavioural sciences research, epidemiological studies of vaccine effectiveness and efficacy as well as continued research into the above mentioned biological and technological innovations is necessary in order to reach the goal of a better protection of the population. Funding for these needs should come from vaccine manufacturers as well as from public sources.

WORKING TOGETHER IN EUROPE

The health of EU citizens depends on having an agreed approach to the mitigation of seasonal influenza, a disease responsible in recent times for several severe pandemics. The 1918 "Spanish" Flu pandemic, for instance was responsible for more deaths than the WW I military operations. Given the large scale of movements of people in the EU a pandemic influenza virus can spread very rapidly through the population and take advantage of weaknesses in vaccination preparedness. The great discrepancies among Member States in vaccination coverage against seasonal influenza indicates that there is an important potential for reducing the burden of the disease in Europe in at risk groups that would be most beneficial to those Member States with lower vaccination coverage. In addition, the well being of the EU as a whole would benefit by ensuring that spread of disease is reduced, with significant savings in health terms but also in terms of economic loss avoided.

In case of a pandemic access to sufficient doses of pandemic vaccine will be difficult. This will lead to difficult choices to determine the target population to be vaccinated.

DEFINITION OF RISK GROUPS

The European Centre for Disease Prevention and Control (ECDC) has provided a scientific opinion on the at risk groups, which most benefit from vaccination. The analysis of literature indicates that there are two at risk groups where routine annual immunisation with seasonal influenza vaccine is justifiable on scientific and public health grounds in Europe:

- (1) older age groups, usually 65 years and older; and
- (2) people with chronic medical conditions, particularly diseases of the following categories:
 - chronic respiratory diseases;

- chronic cardiovascular diseases;
- chronic metabolic disorders;
- chronic renal and hepatic diseases;
- persons with deficient immunity (congenital or acquired);
- young people taking long-term salicylate therapy; and
- persons with conditions, which compromise respiratory function.

Calculations made by ECDC suggest that on average about 25% of the EU population belongs to the two major risk groups.

Furthermore, the ECDC should be able to assist the Member States in developing standard operating procedures and surveillance methodologies to allow for better comparability of seasonal influenza vaccination uptake. The ECDC could help in monitoring the implementation of recommendation proposals and action undertaken by Member States.

AIM OF THIS PROPOSAL

In order to help Member States to reach a vaccination coverage of 75% of the "at risk groups" (elderly over 65 and people with specific health conditions/disease), the Commission hereby proposes to Council to adopt a Recommendation on seasonal influenza vaccination. This Recommendation proposes a set of specific measures to be implemented by the Member States to reach the target as early as possible, however, no later than by winter 2014/2015.

- Ensuring that a national action plan exists aimed at improving vaccination coverage in at risk groups. It should incorporate all the aspects of the policy.
- Description of the actions to be implemented to reach the 75% target by the winter of 2014/2015, which should cover the following:
 - Ways to improve vaccination coverage in at risk groups (e.g.: vaccination campaigns, reimbursement, etc.);⁹
 - Methodology used to measure coverage;
 - Training and information of health care professionals;
 - Communication targeting at the risk groups.
- Forecast of coverage to be reached from 2011 till 2012.
- Reporting to the Commission on the implementation of their national action plans every year before the 31st May after the adoption of this Recommendation. The report will include accurate data on the percentage of vaccination coverage achieved in at risk groups by means of uptake surveys and other methods developed by ECDC.

The lack of easily up-scalable manufacturing technology (such as cell-based production) is also a cause for insufficient (surge) capacity in manufacturing. Research on more efficient adjuvants would help immunize more people with less amount of antigen. Vaccine manufacturers should invest more on research in order to reach the target production capacity.

⁹ For the purpose of this Recommendation this set of risk groups will be used to benchmark the coverage of 75%. However, obviously nothing prevents the Member States from extending the benefit of vaccination to further groups.

Proposal for a

COUNCIL RECOMMENDATION

On seasonal influenza vaccination

(Text with EEA relevance)

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular its Article 152(4),

Having regard to the proposal from the Commission¹⁰,

Whereas:

- (1) Seasonal influenza is a highly contagious viral disease, which typically occurs as an epidemic during the cold months. It is one of the most significant and commonly occurring communicable diseases and is a frequent source of morbidity and mortality in all Member States of the European Union.
- (2) In some cases, complications go beyond a benign respiratory infection and encompass severe pneumonia with often fatal or debilitating outcome. These complications occur far more commonly among the older aged groups and in people with chronic medical conditions.
- (3) Seasonal influenza can be mitigated through vaccination but the virus changes frequently its antigenic composition and, therefore, vaccine composition need to be regularly updated.
- (4) The World Health Organisation (WHO) recommended, in 2003, in its resolution 56.19¹¹ to increase influenza vaccination coverage of all people at high risk with the goal of attaining vaccination coverage of at least 50% of the older aged groups of the population by 2006 and 75% by 2010.
- (5) In October 2005¹² and June 2006¹³ the European Parliament adopted Resolutions calling on the Member States to increase influenza vaccination in line with the WHO recommendations. These Resolutions also urged Member States to increase vaccination coverage during the inter-pandemic period in accordance with WHO recommendations, pointing out that it would also provide an incentive to the pharmaceutical industry to expand the production capacity in order to meet the expected demand for vaccines in case of a pandemic influenza as well as allow to increment the dispensing capacity of the health systems.

¹⁰ J.O.

¹¹ World Health Assembly. Prevention and control of influenza pandemics and annual epidemics. Fifty-sixth World Health Assembly; Resolution WHA56.19. 28 May 2003

¹² European Parliament. Strategy against an influenza pandemic. European Parliament resolution P6_TA(2005)0406. 26 October 2005

¹³ European Parliament. Pandemic influenza preparedness and response planning in the European Community. European Parliament resolution P6_TA(2006)0259. 14 June 2006

- (6) Therefore, concerted action at the Community level should be taken to contain seasonal influenza by encouraging vaccination among at risk groups. The purpose of this Recommendation is to reach the target of 75% vaccination coverage of the older aged groups recommended by the WHO as far as possible by 2015 or the earliest possible target beyond 2010. This target of 75% should be extended to the at risk group of people with chronic conditions, in line with the guidance issued by the European Centre for Disease Prevention and Control (ECDC) in August and October 2008.
- (7) Increased vaccination rates among at risk groups would also contribute to higher vaccination rates in general and therefore to the expansion of the strategically important production capacity of vaccines within the European Union.
- (8) To bring about the changes a necessary first step is that all participants of the health care environment, at risk groups, health care workers, physicians, health care managers and policy makers need to be informed about the problem of seasonal influenza through public and professional awareness campaigns.
- (9) Measures taken by the Member States in this area and the way they have taken into account this Recommendation should be the subject of annual reports at the national level. It is notably essential to gather specific and comparable data as to the uptake rates in at risk groups in order to properly assess the situation in all the Member States. Such data was not always available before the adoption of this Recommendation. Based on this data the Commission and the Member States will be able to share information and best practices with third countries through the existing channels of international cooperation in the field of health.
- (10) Regulation N° (EC) 851/2004 of the European Parliament and the Council¹⁴ of 21 April 2004 establishing a European Centre for Disease Prevention and Control (ECDC) notably entrusted the ECDC with the mission to provide technical and scientific expertise to the Commission and to the Member States. The ECDC also operates the dedicated network established for the surveillance of seasonal influenza in accordance with Commission Decision N° 2000/96/EC¹⁵ of 22 December 1999 on the communicable diseases to be progressively covered by the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. The ECDC should therefore assist the Member States in developing guidelines in order to improve the comparability of seasonal influenza vaccination uptake.
- (11) In accordance with the principles of subsidiarity set out in Article 5 of the Treaty, any new measure taken in an area which does not fall within the exclusive competence of the Community, such as seasonal influenza vaccination, may be taken up by the Community only if, by reason of the scale or effects of the proposed action, the objectives proposed can be better achieved by the Community than by Member States. Seasonal influenza can lead to a pandemic and cannot be confined to a geographical region or Member State. Coordinated action at Community level is therefore required.

HAS ADOPTED THE FOLLOWING RECOMMENDATION:

1. Member States should adopt and implement a national action plan aimed at improving vaccination coverage, in order to reach, as early as possible, however, no

¹⁴ OJ L 142 of 30.4.2004, p. 1–11

¹⁵ OJ L 028 of 3.2.2000, p. 50 - 53

later than by the winter season 2014/2015, a vaccination coverage rate of 75% in all at risk groups referred to in point 2(a).

The action plan should take into account the gaps identified at national level and should allocate necessary resources to reach the target and to organise the activities referred to in point 2 (b) and (c).

2. In the framework of the national action plan referred to in point 1 Member States should :
 - (a). adopt and implement the following common definitions of "at risk groups" according to the guidance issued by the ECDC in August 2008¹⁶:
 - (i) "Older Age Groups" means population of 65 years and older;
 - (ii) "People with underlying Medical Conditions" means people with health conditions of the following categories:
 - chronic respiratory system diseases and dysfunctions ;
 - chronic cardiovascular diseases;
 - chronic metabolic disorders;
 - chronic renal and hepatic diseases;
 - immune system dysfunctions (congenital or acquired);
 - (b). organise annual uptake surveys in all at risk groups in accordance with guidelines to be issued by the ECDC, and to analyse the reasons why persons do not benefit from vaccinations;
 - (c). foster education, training, and information exchange on seasonal influenza by organising:
 - (i) information for health care workers;
 - (ii) information for persons at risk groups and their families about risks and prevention.
3. Member States should report to the Commission on the implementation of this Recommendation, notably on the coverage achieved among at risk groups, every year (before the 31st May) following the adoption of this Recommendation with a view to contributing to the follow-up of this Recommendation at Community level.
4. The Commission is invited to report to the Council on the implementation of this Recommendation, on the basis of the annual reports provided by the Member States, on an annual basis until 2015, and then every 3 years.

Done at Brussels,

*For the Council
The President*

¹⁶

http://ecdc.europa.eu/en/files/pdf/Publications/priority_risk_groups_forinfluenza_vaccination.pdf