



ACTION PLAN IN CATALONIA IN THE EVENT OF A POSSIBLE FLU PANDEMIC

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1. INTRODUCTION

Influenza is an infectious disease caused by the viruses of the *Orthomyxoviridae* family, which includes the *Influenzavirus A and B* and *Influenzavirus C* genres. From the epidemiological standpoint, the influenza A virus is the main cause of winter flu that occur every year (epidemic influenza), whereas the influenza B virus generally presents in more localised epidemic outbreaks. The influenza C virus has been studied little; it seems to produce only sporadic cases.

From the clinical standpoint, influenza is generally speaking a self-limiting disease that affects the general population.

Its morbidity and mortality are particularly important in certain population groups known as "risk groups" (above 65 years and below this age with a base condition that may be decompensated by the flu infection). It is calculated that epidemic influenza, the one that occurs every year, has an attack rate of approximately 30-50%; nevertheless, only 10-20% of the people infected develop a clinical disease that requires medical care. The usual mortality of influenza ranges from 0.06% to 0.18% of the people that fall ill, although it depends on the flu strain causing the epidemic process.

The annual influenza epidemics occur as a result of the small antigenic *drifts* that take place in the different epitopes of the surface glycoproteins called haemoagglutinin (HAS) and neuraminidase (NA). These minor changes are responsible for the need to reupdate the antigenic composition of flu vaccines every winter. The current vaccines, generally inactivated, are trivalent and are comprised of two strains of the influenza A virus (subtypes H3 and H1) and one strain of the influenza B virus.

The appearance of an antigenically new strain (antigenic *shift*), i.e. with an HAS and/or NA belonging to a previously undetected subtype in the human species, has only happened three times in the course of the 20th Century. The main biological mechanism responsible for this phenomenon was genetic exchange (regrouping) between human and swine strains, which in turn come from the avian strains (natural reservoir of all subtypes).

The last three flu pandemics were caused by type A influenza virus and correspond to the appearance of the H1N1 subtype (1918, Spanish influenza), H2N2 (1957, Asian influenza) and H3N2 (1968, Hong Kong influenza). The common characteristics of the main flu pandemics described are:

- Emergence or appearance of a new virus of the influenza type A, with regard to the haemoagglutinin and/or neuraminidase antigen, with regard to the human strains that have circulated previously.
- Existence of a high proportion of the world's unprotected population, i.e., without previous immunity or non-protective titres in the face of the new emerging strain.
- High capacity of the emerging strain to be transmitted from person to person and to produce clinical disease.

Nevertheless, from 1998, the possibility that the human being can catch the disease directly from infected birds without a period of adaptation to the swine being required has been detected (epidemic outbreak by type A H5N1 and H9N2 flu strains). Before the appearance of antigenically new strains capable of infecting the human being, and the existence of favourable ecological conditions for the genetic exchange processes, the experts agree on the theoretical possibility that within a not very far-off time, albeit evidently unpredictable frame, a new influenza virus will appear to which the human being will not be immune and a new pandemic will be caused which could affect the world's population within months.

For this reason, there is a need to develop national plans to fight a flu pandemic. In 2003, the Ministry of Health and Consumer Affairs drafted the document *Action Plan in the event of a possible influenza pandemic*, which we took as a guide to work on the version before this document. In May 2005, the Ministry approved the document *National Plan for the preparation and response to an influenza pandemic*, that features the new classifications of the pandemic phases defined by the WHO.

Following the same criteria of these documents, but taking into account the reality of the health, social and political structure of Catalonia, we have developed a plan whose objective is to reduce, as far as possible, the mortality, morbidity and social and health care impact of this infectious process in Catalonia.

2. NEED FOR AN ACTION PLAN

The need for this plan is based on the social and healthcare impact of actual flu infection and must take the following approaches into account:

1. Most of the experts in influenza consider that the appearance of a pandemic is probable, but they also agree that its impact may be reduced if suitable surveillance, control and follow-up systems are established. Moreover, even if we accept that this pandemics may take place, at the moment nobody is capable of predicting when it will happen.
2. There is now a growing concern and interest in the question of pandemic influenza. Following the guidelines of the WHO, Spain and most of the countries of our environment have developed national pandemic plans, and the European Union has drawn up a community plan that coordinates actions between countries.
3. It is very likely, in a country, that the outbreaks would take place initially in different points and subsequently spread, and that there would be regional or local disequilibriums in health needs and human resources at different times.
4. The effects and the consequences of an influenza pandemic in people may be prolonged (from weeks to months), unlike other natural disasters, which are not prolonged for more than a few days.
5. The impact of the possible flu pandemic may be very important for health and the health services of a country.

This impact, nevertheless, is very difficult to define and will depend on the antigenic characteristics of the new strain (level of divergence with regard to the previous ones), of its degree of virulence (for example, major virulence associated with the appearance of mutations in the area of proteolytic cut of the haemoagglutinin) and the capacity to be transmitted from person to person (secondary cases). As an example of a highly virulent strain, attention must be drawn to the one that caused 18 cases of Avian influenza in Hong Kong in 1997 (influenza A, H5N1) with 6 deaths and more than one hundred cases in Thailand, Vietnam, Cambodia and Indonesia in 2004 and 2005, and recently Turkey with dozens of deaths. A strain of these characteristics and which also presented facility of transmission between human beings would have devastating health and medical effects; Nevertheless, we must think that if the strain adapted to man and could be transmitted from person to person its lethal nature would be notably reduced.

6. The preventive and therapeutic measures available at the moment, including vaccines and antiviral drugs, might be insufficient, particularly in non-producing countries. It should also be mentioned that Spain at the moment does not produce anti-flu vaccines or specific antivirals against influenza and therefore depends on the importation of these resources.

3. BENEFITS OF THE ACTION PLAN

At this time, the development of an action plan for the influenza pandemics will not only facilitate an effective response at the time of the pandemic, but moreover will provide important planning and logistics benefits:

1. Better systems of communication between the health systems and the sectors of response to the emergency.
2. Participation of the different administrations and social and community structures in the preparation of the plan to facilitate its deployment and application. Moreover, throughout its planning, the role of the parts involved will be clarified, possible errors in the responses will be detected and it will be possible to make sure that there are no regulatory imperatives or difficulties (distribution of powers) that might hamper its deployment and application. The actions that must be conducted will be coordinated with those of the National Plan and the European Plan.
3. The increase in epidemiological surveillance activities and the emergency response services will facilitate (creating awareness in the members) the routine actions that must be developed during the annual flu epidemics that cause the estimated death of about 400 people in Catalonia, approximately.
4. The current improvement of all the infrastructures and health and administrative intercommunication plans are the main elements for facing up to an influenza pandemic. These improvements will provide benefits, immediate and future, regardless of whether or not the flu pandemic occurs (general improvement in infrastructure for social and health care and emergency in the event of natural disasters).
5. Finally, most of the elements and infrastructures developed for the prepandemic phase may be used, to a greater or lesser extent, in other health emergency risk situations.

4. PHASES OF AN INFLUENZA PANDEMIC

To guarantee maximum efficacy, coordination and functionality of the Action plan the different pandemic stages or phases (figure 1) must be identified and declared in accordance with the following WHO recommendations:

Interpandemic period

Phase 1. No new ^A subtype of the virus has been detected in human beings. The subtype that causes human infection may be present in animals. If this is the case, the risk of human infection or disease is regarded as low.

Phase 2. No new subtype of the influenza virus has been detected in human beings. Nevertheless, the existence of a new subtype in animals entails a substantial risk of disease for human beings^b

Pandemic warning period

Phase 3. Detection of human infection(s) by a new subtype without reliable evidence of person-to-person transmission, although it may rarely be transmitted through intimate contact^c.

Phase 4. Detection of small clusters of cases with scant person-to-person transmission and high local dissemination, which suggests that the virus has not yet adapted well to the human being^c.

Phase 5. Detection of major clusters of cases; despite person-to-person transmission, it still has to be considered local, and suggests that the virus is adapting better to the human being but as yet does not present a total transmissibility (substantial pandemic risk)^c.

^a The new subtype is defined as a subtype that has not circulated in human beings for several decades, so that most of the population has no protection against it.

^b The distinction between Phase 1 and Phase 2 is based on the potential risk of human infection or disease resulting from the circulation of a new subtype in animals.

^c The distinction between Phase 3, Phase 4 and Phase 5 is based on establishing the possibility of pandemic risk of a new subtype. That is why different factors and their relative importance must be considered according to current scientific knowledge. These factors must include: transmission rate; geographical localisation and dissemination; seriousness of the disease; presence of human origin genes in the new subtype (if from an animal strain); other information on the viral genome; and other relevant information.

Pandemic period

Phase 6. Pandemic phase: substantial increase in transmission among the general human population. This phase is divided into 4 subphases:

- Subphase 6.1: Spain is not affected
- Subphase 6.2: the pandemic is declared in Spain
- Subphase 6.3: end of the first wave in Spain
- Subphase 6.4: the end of the pandemic is declared

Postpandemic period

Return to the interpandemic period.

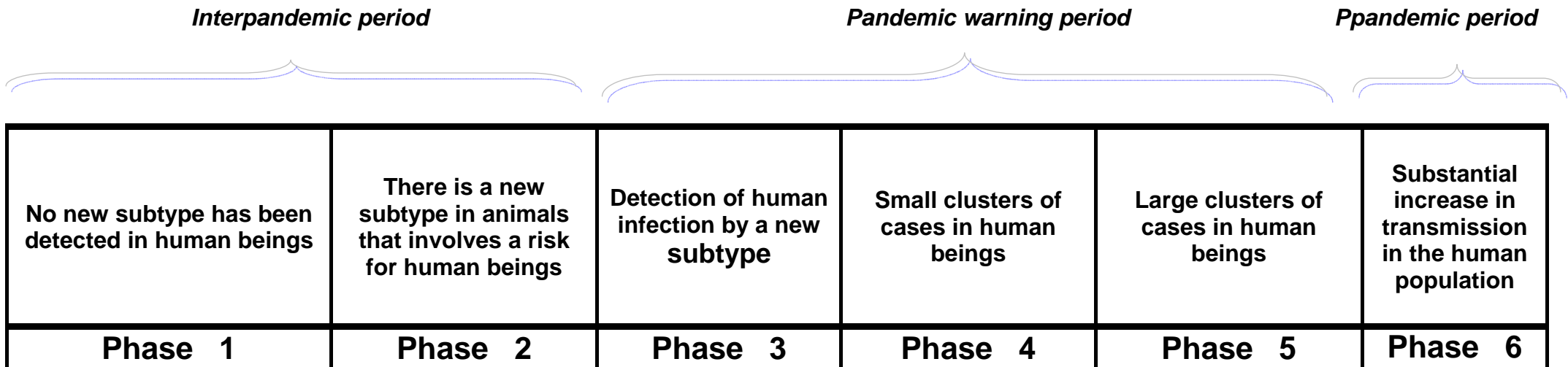


Figure 1: Phases of an influenza pandemic.

5. CONTENTS OF THE PLAN

5.1. Surveillance

5.1.1. Animal surveillance

Avian influenza is a highly contagious viral disease that affects mainly chickens, as well as turkeys, geese and ducks. It is caused by a virus of the *Influenzavirus* gender, type A, and is characterised by signs that range from a slight reduction in the number of eggs, greenish diarrhoea, cyanosis and oedema of the head, crest and wattle, to a fulminating infection that affects the central nervous system. In poultry farms it usually causes a mortality of 90% of the animals in 4 days.

It is a disease that must be declared according to the International Office of Epizooties (IOE). The measures applied by the DARP for avian influenza are framed within a *Surveillance Programme*, a *Warning Plan* and an *Emergency Plan*.

The Surveillance Programme is applied annually by means of analyses of samples from birds taken at random according to a general distribution that the European Union establishes for every member state and the Spanish Ministry of Agriculture, Fisheries and Food (MAPA) redistributes among the Autonomous Communities. It includes the control of birds from poultry farms and wild birds, particularly ducks. The Programme particularly seeks to detect possible avian influenza viruses of low pathogenicity, since they are susceptible to transform into high pathogenicity viruses.

In Catalonia, the Poultry Surveillance Programme has been implemented, since 2003, by the Poultry Health Centre of Catalonia (CESAC) according to the instructions issued by the Animal Health Service of the DARP, which is based on community regulations, and in coordination with the MAPA. Over these three years, improvements have been made in the selection criteria of the farms to be sampled according to the type of farms and their location rather than an overall increase in the number of samples taken.

In wild birds, the DARP has established a Surveillance Programme by means of an agreement with the Animal Health Research Centre (CReSA) that collects samples from different wild birds from the four wild animal recovery centres. The surveillance is conducted with the collaboration of the Department of the Environment and Housing, that facilitates the samples collected from hunting campaigns, from ring-placing operations and specific captures made for this purpose. The 2005 wild bird programme is much more specific than that of 2004 and the type of birds to be analysed was diversified to include water birds, marine and other birds. The number of wild birds sampled in 2005 quadrupled the initial number forecast.

The Surveillance and Prevention Programme also includes all the transversal measures that are useful for fighting all diseases. These are the biosafety measures for animals and for people, the control and restriction of bird movements, if necessary, and people training.

The Warning Plan is applied when there are outbreaks of cases in other countries with a risk for birds from Catalonia, and it comprises the following actions:

- Review and control of movements: all batches of birds and eggs that arrive in Catalonia from countries with a risk of transmitting the disease are checked.
- Immediate and continuous information and dissemination: the communication mechanism established rapidly notifies all the sectors involved (official veterinary services, CESAC, Catalan Poultry Federation, Association Poultry Slaughterhouses, Public Health and Food Safety Agency) As well as by means of the DARP web and the RURALCAT site for general information.
- Emphasis is placed on reinforcing the measures established in the Surveillance and Prevention Programme: biosafety measures and movement control.
- Urgent sampling and analysis of birds coming from risk areas. The CESAC laboratory is prepared to perform the necessary analyses rapidly.
- Handling of suspected cases. The protocol established to rule out or confirm the disease as quickly as possible is applied.

The Emergency Plan is implemented when there is a reasonable suspicion of positivity to avian influenza. It provides for the action and organisation procedures and the basic objectives of the struggle, namely: A) early detection of the locus; b) rapid elimination of the locus and c) minimisation of the risk of dissemination. The actions to be performed are visits, confirmation of suspicion, delimitation of protection and surveillance areas, and slaughter and destruction of dead bodies.

5.1.2. Surveillance in human beings

Due to the continuous antigenic changes in the influenza virus , a rigorous and constant integral surveillance of the disease is required, including virological and epidemiological aspects. The virological surveillance must include the detection and isolation of viruses, in community and hospital cases, and the conduct of antigenic and genetic studies, whereas the epidemiological surveillance will focus on knowledge of the dissemination and the clinical impact of possible new antigenic strains detected. Although the detection of major variants (antigenic shift) are the maximum objective of virological surveillance, minor antigenic variations (*drifts*) that occur in every annual epidemic should not be mimimised. As these minor changes occur continuously, they must be followed up and their prevalence and impact on the frequency of appearance of the disease and its clinical consequences (morbidity and mortality) established. The new strains that gradually

appear must also be available to be able to include them as standard strains in the annual vaccination programmes for the influenza epidemic. In our country, the WHO reference centres for influenza send them to their corresponding European reference centre. At the moment, in Spain there are three WHO reference centres for influenza (National Microbiology Centre of Majadahonda; Influenza Centre of Valladolid and the Microbiology Laboratory -Hospital Clínic / University of Barcelona-).

The surveillance of influenza in Catalonia started in the 1988-1989 season and was modified as of the 1999-2000 season in order to accomplish greater geographical representativeness and wider coverage in the obtainment of samples for virological study. At present, the number of sentinel doctors involved is 44, distributed over 24 centres in different regions of Catalonia. The sentinel doctors collect pharyngeal and nasal samples throughout the season (weeks 40 to 16). The viruses studied, besides the influenza virus, are the syncytial respiratory virus, the parainfluenza viruses 1, 2, 3 and 4, adenovirus, coronavirus, rinovirus and enterovirus. The search for these different viruses from the influenza viruses helps to distinguish between outbreaks with an flu aetiology from other cases and outbreaks of acute respiratory processes caused by other viruses. The morbidity indicators collected from the sentinel centres and the virological indicators are obtained daily. Moreover, and since it is a well-known fact that mortality increases during influenza epidemics, fundamentally among the elderly, every week the number of deaths occurred in the city of Barcelona and other 6 municipalities of the province of Barcelona (l'Hospitalet de Llobregat, Manresa, Mataró, Terrassa, Sabadell and Santa Coloma de Gramenet) is collected. The mortality data are monitored according to the Box-Jenkins time series methodology; the ARIMA model (3,0,0) is used for the city of Barcelona and the 6 municipalities of the province of Barcelona.

The virological and epidemiological data obtained are compiled in the Information Sheet that is published and distributed weekly, and are sent to the National Epidemiology Centre, which in turn compiles all the data from Spain and sends them to the EISS (*European Influenza Surveillance Scheme*). This surveillance system is highly useful and is the cornerstone of surveillance activities to be developed in Catalonia to face up to a possible pandemic.

Since the flu vaccination programmes were started in the 50s, it has been demonstrated that they are a key element, indispensable and essential in the prevention and control of this infection.

For the last 20 years, and in the course of the year, the international collaborating centres of the WHO detect and monitor the new antigenic variants of the influenza virus that appear, with the objective of assessing their inclusion in the flu vaccination of the following season. In the northern hemisphere, the vaccine strains selected are published at the end of February in the Weekly Epidemiology Record of the WHO; the pharmaceutical laboratories work on the preparation of the vaccines during spring and summer and are distributed generally in September and October (beginning of the immunisation campaign). The influenza vaccine is given and recommended in

Catalonia in people aged above 60 years, people of any age with predisposing base condition and people in regular contact with these high-risk patients and pregnant women.

In case of the possibility of an influenza pandemic, a series of questions pertaining to the administration and application of the vaccination programme must be considered:

- Importance increase in the target population to be vaccinated beyond the risk groups considered, and ideally covering the whole of Catalonia.
- The warning period before the expansion of the pandemic will probably be very short (2-3 weeks), so the fastest possible distribution and administration system must be prepared.
- Since the pandemic strain may appear at any time and the minimum need of the pharmaceutical laboratories for the preparation of the new vaccine is 6 to 8 months, it is very likely that this time must be shortened, eliminating some of the final phases of effectiveness to be given quickly. It is also possible that there is no efficacious vaccine or that the amounts of the existing one will be insufficient to attend to the needs of the population.
- In general terms, the immune response to a vaccine in seronegative the people is rather poor; thus, the emergence of a new strain with an antigenically different haemoagglutinin (H) and/or neuraminidase (N) would require the administration of a second dose 30 days after the first to guarantee the maximum protective efficacy.

As a consequence of the questions addressed, it must be considered that in the case of a flu pandemic there will not be enough vaccine and for this reason it is very important to guarantee the legal mechanisms that permit, by means of national agreements, and within the framework of the European Union, a fair supply of vaccines. It will be important to control and distribute stocks to the groups regarded as requiring priority protection, efficaciously and rapidly replace and redistribute the unused dosed and guarantee the second dose if it is finally regarded as necessary for optimal protection.

5.3. Antiviral drugs

For some years now a group of antiviral drugs (amantadine and rimantadine) with proven efficacy in the prophylaxis and treatment of the type A influenza infection has been on the market. These antivirals can prevent the development of the disease in 70-90% of adolescents and adults; similarly, they have shown great efficacy in the reduction of the seriousness and the clinical manifestations 48 hours after administration (therapeutic efficacy). Nevertheless, these antivirals

present a series of side effects (associated with individuals with deficits in their renal functionalism) that have limited their use.

The recent appearance of a new group of antiviral drugs, known as the neuraminidase inhibitors (zanamivir and oseltamivir), with proven efficacy in the treatment and the prophylaxis of infections by the influenza A and B virus, and with fewer side effects, opens up the gate for a potential massive use as therapy and/or prophylaxis of pandemic influenza.

At the moment in the Spanish state the antiviral drug *Amantadina Level* 100 mg, 20 capsules is marketed with the indication for prevention and treatment of type A influenza, which is marketed by the ERN Manufacturer (Barcelona). Nevertheless, the studies carried out by the laboratories of the WHO influenza network have shown that the most recent strains of the influenza A (H5N1) virus, responsible for the cases of Avian influenza in men, and most recently in South East Asia, are resistant to amantadine.

Similarly, the marketing of the new antiviral drugs in the treatment of influenza that belong to the group of the neuraminidase inhibitors (zanamavir and oseltamivir) with the trade names of Relenza® and Tamiflu®, marketed, by GlaxoSmithKline and Roche Pharma, respectively, is authorised. In any case, only Relenza is available on the market, although at the moment there are problems of supply. These drugs, when given in the first 48 hours of the appearance of the symptoms, reduce the duration of the disease by approximately 2 days and reduce respiratory and cardiac complications, as well as mortality. The studies that may be carried out hitherto have proven their efficacy in the prophylaxis of the infection.

The indication of antivirals in the event of an influenza pandemic must be established according to the vaccine supply and distribution programmes, since the use thereof would target the treatment of people who have been infected to avoid subsequent complications, as well as protection in the case of the lack of vaccine or during the period in which it was still not available, i.e. in the first week of the pandemic.

5.4. Response to the emergency

An action plan in the case of a possible influenza pandemic presents certain very specific aspects, generally not included in other action plans. One of the main differences between an influenza pandemic and other natural disasters is the broad extent of the health effects that it would produce affecting both the people from the health service (doctors, nurses and other personnel) as well as the users that need these services (health collapse), determining the loss of the most critical infrastructure (human and health). This all makes it necessary to extend the team of people in charge that normally configure the different natural risk prevention plans.

If the disease caused by the pandemic strain is very serious, the local health services may collapse rapidly, giving rise to the following immediate consequences:

- Scarcity of beds in hospitals and in ICUs, with lack of ventilators and life support systems.

- Shortage of antiviral drugs and antibiotics for the treatment of secondary bacterial pneumonias.
- Need to open and prepare additional admission and medical treatment centres.
- Increased demand for funeral mortuary services.
- Increased demand for the different social and health services and health logistics.

5.5. Communication

The dissemination of suitable information rapidly and efficaciously among health managers, medical service providers, media (radio, press and television) and the general public, are one of the key and essential points in any response plan in a natural emergency, and particularly in the case of a possible influenza pandemic. Therefore, it is very important to guarantee that the different communications networks operate smoothly, particularly during the prepandemic period.

The main objectives of all the communication activities that must be performed following at all times the guidelines of the Secretaria Tècnica Col·legiada, must be:

- To provide communication support and tools to health professionals in contact with the public to promote safety.
- To create a favourable state of opinion and broad knowledge on the social and health impact of an influenza pandemic, and avoid overlapping efforts that may reduce human resources at the time of the action.

6. ORGANISATIONAL STRUCTURE OF THE PLAN

To render it possible to update the action plan as required by the epidemiological situation and for it to be implemented, a suitable organisational structure is necessary.

6.1. Executive Committee

An Executive Committee of Catalonia for the prevention, control and surveillance of the evolution of a possible influenza pandemic, reporting to the Department of Health, will be set up.

The functions of the Executive Committee of Catalonia for the prevention, control and follow-up of the evolution of a possible pandemic of the influenza will be as follows:

- a) The design of the organisational structure and the determination of the levels of responsibility in decision-making to face up to a possible influenza pandemic in Catalonia, including the approval of the Pandemic Plan.
- b) The follow-up and assessment of the response plans of the health-care centres and of all the areas involved.
- c) The approval of specific guidelines for every phase of the pandemic, following the recommendations of the WHO and of the Ministry of Health and Consumer Affairs.
- d) The coordination of the information that has to be supplied to organisations and institutions of Catalonia, national and international.
- e) Any another action related to the influenza pandemic.

The Executive Committee of Catalonia for the prevention, control and follow-up of the evolution of a possible influenza pandemic will be comprised of the following members:

The autonomous minister of health, who is its chairman/woman.

The secretary general of the Department of the Presidency, who is the first vice-chairman/woman.

The secretary general of the First Autonomous Minister, who is the second vice-chairman/woman.

The secretary or secretary general of the Department of Health.

The secretary or secretary general of the Department of Agriculture, Livestock and Fisheries.

The secretary or secretary general of the Department of Health.

The secretary or secretary general of Public Safety of the Department of the Interior.

The secretary for Mobility of the Department of Territorial Policy and Public Works.

The secretary or secretary general of the Department of Justice.

The secretary or secretary general of the Department of the Environment and Housing.

The secretary or secretary general of the Department of Governance and Public Administrations.

The director of the Servei Català de la Salut [Catalan Health Service].

The manager of l'Institut Català de la Salut [Catalan Health Institute].

The director or director general of public health.

The director or director general of Health Resources.

The director or director general of Planning and Assessment.

The director of Strategy and Coordination.

The director of the Health Studies Institute.

The director or director general of Emergencies and Civil Safety.

The director or director general of the public company Sistema d'Emergències Mèdiques, SA.

The head or the head of Cabinet of the Autonomous Minister of Health.

The chairman/woman of the Federació Catalana de Municipis [Catalan Federation of Municipalities].

The chairman/woman of the l'Associació Catalana de Municipis i Comarques [Catalan Association of Municipalities and Regions].

This Executive Committee of Catalonia for the prevention, control and follow-up of a possible influenza pandemic meet with the frequency required to accomplish its aims.

6.2. Technical Secretariat

With a view to making the decisions adopted by the Executive Council of Catalonia for the prevention, control and follow-up of the evolution of a possible influenza pandemic operative, and manage the plans and actions determined for every pandemic phase, a Technical Secretariat will be set up.

This Technical Secretariat is comprised of the following members:

The director or director general of public health, who is its chairman/woman.

The assistant director of the Catalan Health Service, who is the chairman/woman.

The directors or technical directors of the Pandemic Plan.

The directors of the territorial services of the Department of Health.

The managers of the health regions of the Catalan Health Service and the directors of the territorial Health services if they are not the same.

The manager of the Public Health Agency of Barcelona.

The technical staff appointed by each one of the departments represented on the Executive Committee.

The Technical Secretariat will meet whenever the agreements of the Executive Council of Catalonia for the prevention, control and follow-up of the evolution of a possible influenza pandemic must be implemented, and with the frequency established by or for epidemiological risk situations.

6.3. Advisory Scientific Council

An Advisory Scientific Council of the Influenza Pandemic Plan will be set up to guide the decisions of the Executive Committee of Catalonia for the prevention, control and follow-up of a possible influenza pandemic, in accordance with the scientific knowledge and experience of the professionals related to this matter.

This Advisory Scientific Council of the Influenza Pandemic Plan will report to the Executive Committee of Catalonia for the prevention, control and follow-up of a possible influenza pandemic, and will be comprised of the following members:

The chairman/woman, who will be appointed by the Autonomous Minister of Health from the experts designated by the Department of Health.

The assistant director or assistant director general of Surveillance and Response to Public Health Emergencies of the General Board of Public Health, acting as secretary.

A representative of the Department of Universities, Research and the Information Society.

A representative of the Catalan Society of Infectious Diseases and Clinical Microbiology.

A representative of the Catalan Society of Family and Community Medicine.

A representative of the Catalan Society of Paediatrics.

A representative of the Catalan Society of Public Health.

A representative of the Catalan Society of Emergency Medicine.

A representative of the Catalan Society of Geriatrics.

A representative of the Spanish Society of Preventive Medicine and Public Health.

A representative of the Spanish Society of Epidemiology.

A representative of the Catalan Association of Nursing.

A representative of the Catalan Association of Family and Community Nursing.

A representative of the Catalan Association of Infection Control Nurses.

A representative of the Catalan Society of Clinical Pharmacy.

A representative of the Council of Colleges of Physicians of Catalonia.

A representative of the Council of Colleges of Pharmacists of Catalonia.

A representative of the Council of Colleges of Veterinary Doctors of Catalonia.

A representative of the Council of Colleges of Nursing Diploma Holders of Catalonia.

A representative of the Agency of Health Technologies and Research.

up to an undetermined number of experts in the topic appointed by the Autonomous Minister of Health.

The Advisory Scientific Council of the Influenza pandemic Plan will be summoned whenever the Executive Committee of Catalonia for Prevention, control and follow-up of the evolution of a possible influenza pandemic or its Technical Secretariat needs its assessment.

7. ACTIONS IN THE DIFFERENT PANDEMIC PHASES

Of the phases described above, we are now in the pandemic warning phase 3, since a new virus (AH5N1) that has infected different people has appeared, although it is not capable of being transmitted from person to person. The actions to be conducted as of this moment, in accordance with the public health objectives:

7.1. Pandemic warning period (phase 3)

The fundamental health objectives for this phase are to guarantee the rapid characterisation of the new virus subtype, as well as the early detection and notification of new cases in human beings.

7.1.1. Animal surveillance

At the moment we are in this phase, although the virus that infects birds does not exist in Catalonia. Therefore, in this phase, surveillance (as long as it does not affect birds from Catalonia), warning (when there is a definite risk in Catalonia) or emergency measures (when the virus affects the birds of Catalonia) must be applied.

When the virus affects the birds of Catalonia (DARP emergency situation), early notice of new human cases must be given. Thus, a warning for the urgent communication of symptomatology susceptible of being avian influenza will be issued to all people in the DARP intervening in actions to combat avian influenza.

7.1.2. Surveillance in human beings

The objective during the pandemic warning period is the rapid diagnosis of clinical manifestations with suspected infection by avian influenza virus.

In this phase it will be necessary:

- To disseminate the action protocol in imported cases among health professionals. This protocol is available on the Department's web (www.gencat.net/salut).
- To perform a study of contacts of the important cases.
- To draft a protocol for the prevention of infection by pandemic virus in health staff.
- To design a study to assess the effectiveness of vaccines and antivirals during the pandemic.

In the event of a suspected or probable case of avian influenza, for confirmation of the case, following consultation with the corresponding territorial epidemiological surveillance unit, the following samples will be collected:

- Nasal and pharyngeal exudate or aspirate: a specific swab must be used to obtain and transport the samples for virological studies to be carried out (ViralCulturette type). They

must be kept refrigerated (4°C) until transported to Microbiology Service of the Hospital Clínic, which must be immediate.

- 5 ml of whole blood in a tube without anticoagulant during the acute phase (0-7 days) and the convalescent phase (>14 days). It must be stored at ambient temperature until transported to the laboratory, which must be immediate.
- The samples will be transported at 4°C (nasal and pharyngeal exudate or aspirate) and in triple safety packaging. The transport of the sample from the hospital where the patient is located to the Hospital Clínic will be conducted by the corresponding epidemiological monitoring unit, or else the Emergency Epidemiological Monitoring System of Catalonia (SUVEC Tel. no. 627 480 828), if the suspicion takes place on a non-working day or on a holiday.
- Diagnosis of avian influenza:
 - Antigenic detection, viral typing and subtyping by indirect immunofluorescence (IIF)
 - Detection of nucleic acids, viral typing and subtyping by RT-PCR
 - Serology by complement fixing reaction
- If positive, the samples are sent to the National Microbiology Centre (Instituto de Salud Carlos III) and the WHO Influenza Center (National Institute for Medical Research, Mill Hill, London).

7.1.3. Vaccines and vaccination programme

In this phase, vaccination with the human anti-flu vaccine must be recommended for all people travelling to areas where there is avian influenza if contact with birds is envisaged. The objective of this measure is to prevent the appearance of the human virus and the avian virus in the same person, since this would facilitate the exchange of genetic material and the appearance of a new virus that could be transmitted from person to person.

7.1.4. Antiviral drugs

In this phase, anyone that may be a probable case of avian influenza according to the current protocols or presenting symptoms of influenza and in whom the Avian influenza virus H5N1 or any other influenza virus with pandemic potential has been isolated will be treated.

The preexposure prophylaxis for the personnel in charge of the control and slaughter of the infected birds will be carried out, as well as the personnel involved in the cleaning and disinfection of the place where these activities are carried out.

The preparation of the oral solution of oseltamivir phosphate will be made in the Pharmacy Service of a single hospital of Catalonia, which will keep a stock of this active ingredient. The preparation of the necessary units must be made in accordance with the established preparation procedure and the indications issued by the General Assistant Board of Pharmacy and Health Products.

The units prepared to carry out the treatments will be sent urgently to the places where the people to be treated are by means of transport by the Department of Health, with the collaboration of the Department of the Interior.

In this phase the following procedures will be implemented:

- A guide will be drawn up on the prescription of the treatment with oseltamivir phosphate in phases 3, 4 and 5.
- The protocol for the preparation of the oral solution of oseltamivir phosphate will be available, defining the conditions of storage, labelling, distribution, dispensing and recording of the activities conducted.
- The designation of the Pharmacy Service of the hospital centre of Catalonia that will prepare the necessary treatments (oseltamivir phosphate oral solution containers) during phases 3, 4 and 5 of the Pandemic Plan, and the implementation of the informative and training actions required for the staff involved.
- Preparation of the planning of the distribution of the containers of active ingredient and capsules of oseltamivir phosphate, in phases 4 and 5, among the different hospital centres of Catalonia that have a pharmacy service, taking into account the number of beds of each one and the population of their sphere of influence.
- Inform the hospital centres of Catalonia selected of the protocol for the preparation of the oral solution of oseltamivir phosphate, and the conditions of storage, labelling, distribution, dispensing and recording of the activities conducted.
- Drafting of a guide on the conditions for the prescription of the treatment with oseltamivir phosphate in patients attended to in the health centres with a view to their application in phase 6.
- The fractionation of part of the amount of oseltamivir phosphate currently available in 20 g containers to facilitate distribution to the pharmacy service designated to prepare the treatment in phases 3, 4 or 5.

7.1.5. Response to the emergency

In this phase, an action plan must be drawn up in each one of the hospitals, containing the actions envisaged from the organisational, structural and human resources standpoint to address a possible influenza pandemic. A guide will be drawn up by a commission of experts from the hospital setting to facilitate the preparation of the specific plans of every hospital.

The objectives of the plans would be:

- To provide an efficacious health-care response to the patients that reach the emergency services, interfering as little as possible in the work of the rest of the hospital
- To achieve maximum coordination/cooperation between the services of the hospital and extrahospital resources/services/mechanisms (primary health care centres, continuous health care centres and Medical Emergency Services)

The Plan must contain the following aspects:

- Definition of the management and operating coordination teams
- Definition of spaces and circuits
- Definition of the phases and/or levels of emergency
- Drafting of operating procedures and protocols for every phase
- Reinforcement of the supply of resources
- Coordination with other health-care areas and resources

7.1.6. Communication

In this phase it will be necessary to:

- Create the communication operating committee:
 - o Define its components
 - o Define its functions
- Draft the Communication Plan

A website must also be created with relevant information on avian influenza and human influenza, which will be updated constantly.

7.2. Pandemic warning period (phase 4)

The Health Department's fundamental objectives for this phase are to curb the transmission of the new virus in localized areas and delay its dissemination, with a view to gaining time for the application of the response measures.

7.2.1. Animal surveillance

In this phase, different hypotheses must be addressed depending on the pathogenicity and spreadability of the virus to people and/or birds. Different hypotheses will also be necessary according to transmissibility from people to birds and viceversa.

The actions in these phases will vary depending on the pattern of transmission followed by the virus.

7.2.2. Surveillance in human beings

The objective is the rapid diagnosis of suspicious clinical manifestations of infection by the avian influenza virus.

In this phase the following procedures will be implemented:

- The study of contacts of the important cases.
- Review and adjustment of the action protocol in the event of important cases.
- Assessment of the impact of the measures of contention and readjustment of the recommendations.

In the event of a suspected or probable case of avian influenza, the indications of section 7.1.2 must be followed to confirm the case.

7.2.3. Vaccines and vaccination programme

The procedure in this case will be the same as the previous phase (see sections 7.1.3).

7.2.4. Antiviral drugs

The criteria for carrying out the treatment with antivirals are the same as those indicated in the corresponding section of phase 3. (see section 6.1.4).

In this phase the following actions will be implemented:

- If drugs are available, the drums of available oseltamivir phosphate will be fractionated into containers of 1 kg and 500 g to facilitate distribution to the different hospital centres of Catalonia.

- Review and update the guidelines on the conditions for the prescription of treatment.

7.2.5. Response to the emergency

In this phase it will be necessary to:

- Make sure that the human and logistics resources have been fully deployed and are ready to initiate the functions assigned to them (health and community services).
- Coordinate the activities between the different institutions.

7.2.6. Communication

- Activation of the information process defined for this phase in the Communication Plan to the internal targets.
- Activation of the information processes defined for this phase in the Communication Plan to the external targets: pedagogical discourse.
- Spokesperson training.
- Verification that all computing system work properly.
- Revision and permanent update of the web.

7.3. Pandemic warning period (phase 5)

In this phase the health objectives consist of maximising the efforts to contain, delay or prevent the dissemination of the pandemic and gain time to be able to apply the response measures.

7.3.1. Animal surveillance

As in the previous phase, the actions will vary according to the total transmittability of the virus.

7.3.2. Monitoring in human beings

In this phase the following procedures will be implemented:

- Review and adjustment of the adaptation protocol in the event of important cases.
- Review and updating of the management protocols of the patients and their contacts.

In the event of a suspected or probable case of avian influenza, the indications of section 7.1.2 must be followed to confirm the case.

7.3.3. Vaccines and vaccination programme

In this phase the same actions as those of phases 3 and 4 will be continued.

7.3.4. Antiviral drugs

The criteria for carrying out the treatment with antivirals are the same as those indicated in the corresponding section of phase 3 (see 6.1.4).

In this phase the following actions must be carried out:

- Distribute the containers of oseltamivir phosphate among the different hospital centres of Catalonia that have a pharmacy service according to the established planning (in phase 3).
- Review and update the guidelines on the conditions for the prescription of treatment.

7.3.5. Response to the emergency

In this phase the necessary actions would be:

- Place the response or action Plan for the influenza pandemic in the alert state.
- Coordinate all the activities among the different health-care levels.

7.3.6. Communication

- Adaptation of the communication contents
- Activation of the information process defined for this phase in the Communication Plan to the internal target.
- Activation of the information process defined for this phase in the Communication Plan to the external targets:wait-and-see or preventive discourse.
- Review and update ofthe website.

7.4. Pandemic period (phase 6)

In this phase, the health objective consists of minimising the impact of the pandemic.

7.4.1. Animal surveillance

In this phase animal surveillance will target identifying the viruses that cause avian influenza.

7.4.2. Monitoring in human beings

In this phase the surveillance system must be adapted to obtain information on the evolution of the pandemic and there will be a systematic collection of samples of nasal and pharyngeal exudate or aspirate (in the sampling and transport conditions specified above) of:

- suspected cases of pandemic influenza by means of the Sentinel Doctor Network of according to the PIDIRAC protocol for influenza surveillance.
- patients diagnosed with pandemic influenza and with criteria for admission in 5 hospital centres of Catalonia to a maximum of 5 weekly samples per centre.

In all these samples the following actions will be undertaken in the pandemic phase:

- Antigenic detection, viral typing and subtyping by indirect immunofluorescence (IIF)
- Detection of nucleic acids, viral typing and subtyping by RT-PCR
- Viral isolation in cell culture (if a biosafety laboratory with level II Plus or III is available)
- Phylogenetic analysis of the circulating strains
- Detection of resistance mutations in the anti-flu drugs
- Dispatch of isolated strains to the WHO Influenza Center (National Institute for Medicine Research, Mill Hill, Londres)
- Isolated strain archive

7.4.3. Vaccines and vaccination programme

If it were impossible to have sufficient quantities of pandemic vaccine, three operating eventualities must be provided for when designing the vaccination programmes:

- a) vaccination of the essential community services
- b) vaccination of the essential services and risk groups
- c) vaccination of the whole population.

These three eventualities will be considered in staggered fashion, according to the availability of pandemic vaccine.

7.4.4. Antiviral drugs

In this phase, and depending on the amount of treatments available, the following actions will be implemented:

- The treatment of infected hospitalised people.
- The post-exposure prophylaxis of the elderly hospitalised in health or closed social and health care institutions (residences) to control outbreaks.
- The treatment of the more vulnerable populations (children and the elderly) who are diagnosed in the primary health-care centres.

In this phase, the preparation of the oral solution of oseltamivir phosphate will be conducted by the pharmacy service of the hospital centres of Catalonia.

The distribution of the units of capsules available and of the active ingredient to the different Catalan hospital centres will be performed according to the number of beds in each one and the population in their sphere of influence.

In the case of the treatment of the patients diagnosed in the primary health care centres, the treatments prepared by the pharmacy services of the hospital centres will be sent to the corresponding primary health care centres for dispensing to patients, under the supervision of the corresponding primary care pharmacists.

Similarly, in this phase the following procedures will be implemented:

- To perform a continuous follow-up of oseltamivir phosphate in the different pharmacy services in which it has been distributed to make redistributions according to needs.
- Review and update the guidelines on the conditions for prescription of the treatment according to the epidemiological information and the amount of drug available.

7.4.5. Response to the emergency

Complete and total activation of the emergency plans in collaboration with the departments involved and in coordination with the state institutions.

7.4.6. Communication

- Total activation total of the Crisis communication Plan.
- Permanent review and update of the website.

7.5. Postpandemic period

The WHO is the only organisation in charge of deciding and establishing the termination of the pandemic period and therefore that of the flu pandemic. Epidemiologically it is very possible that a period of 2-3 years is needed after the termination of the pandemic flu activity and the return to the normal interpandemic situation or period, as it is considered that the pandemic stage has been overcome.

In the postpandemic period the situation reverts to normality. The emphasis will be placed on the assessment of the global impact of the pandemic and to analyse the actions carried out. Reports will be drafted and conclusions will be drawn that will serve to update the activities that will be conducted to prepare for future influenza pandemic threats.

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