
WHO pandemic influenza draft protocol for rapid response and containment

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**World Health
Organization**

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Background

Recent experiences with highly pathogenic H5N1 avian influenza have given the world its first advance warning that another influenza pandemic may be imminent. Given the serious consequences of past pandemics, this advance warning has stimulated a search for ways to prevent such an event from occurring.

In 2005, two research groups published studies based on the mathematical modelling of transmission patterns that might be seen near the start of a pandemic. These studies suggested that an initial outbreak caused by an emerging pandemic virus might be contained provided several demanding conditions were met within a very short timeframe. In both studies, mass administrative of antiviral drugs within the outbreak zone was the cornerstone of the containment strategy, supported by additional non-pharmaceutical measures, such as area quarantine and social distancing, aimed at reducing transmission within the area and minimizing spread beyond it. The studies further concluded that, should the containment strategy fail to prevent the emergence of a fully transmissible pandemic virus, it could nonetheless delay international spread.

Several international consultations on pandemic influenza asked WHO to explore the feasibility of this containment strategy further. On 12 December 2005, WHO convened an informal meeting to gather views on the proposed use of antiviral drugs and other interventions to contain an emerging pandemic virus at its source or delay its international spread. This initial exploratory meeting was followed by further discussions during a second meeting, held from 12 to 13 January 2006 in Tokyo. One result was the development of an initial draft protocol for early containment of pandemic influenza.

In a parallel development, an international stockpile of antiviral drugs has been established. Following a donation by industry, WHO will have a stockpile of the antiviral drug, oseltamivir, amounting to 3 million treatment courses by May 2006. These drugs have been strictly reserved for use during an operational intervention aimed at containing an emerging pandemic virus at its source.

From 6 to 8 March 2006, WHO convened a global technical meeting to finalize the early containment protocol for pandemic influenza. The meeting was attended by more than 70 international experts and WHO staff experienced in the areas of operational planning, outbreak response, logistics, epidemiology, laboratory diagnosis, infection control, health legislation, ethics, social mobilization, and public and media communications. This document is a result of their deliberations.

No attempt has ever been made to alter the natural course of a pandemic near its start. Moreover, given the unpredictable behaviour of influenza viruses, no one can know in advance whether the start of a pandemic will begin gradually, following the emergence of a virus not yet fully adapted to humans, or be announced by a sudden explosion of cases, thereby precluding any attempt at containment.

International concern about the threat posed by the H5N1 virus has stimulated intense research efforts aimed at improving understanding of this virus and its pandemic potential. Recommended actions in this draft protocol are expected to evolve as knowledge about this virus in particular and pandemic influenza in general continues to improve.

Although most attention is currently focused on the H5N1 virus, scientists are well aware that the next pandemic might be caused by a different influenza virus.

Recommendations within the protocol are frequently specific to the present H5N1 situation, but could equally apply to other influenza viruses demonstrating pandemic potential.

The protocol has three main parts. The first describes the steps needed to recognize the signal or “triggering” event. The second part describes the immediate actions that should follow recognition of the signal. The third part describes the actions that should be undertaken once the event has been verified, the overall situation has been assessed, and a decision has been made to launch the rapid containment operation.

I Recognizing the event

Detection, investigation, and reporting of early signals

The success of a strategy for containing an emerging pandemic virus is strictly time dependent: modelling studies suggest that mass administration of antiviral drugs must begin within 21 days following detection of the first case representing improved human-to-human transmission of the virus. The feasibility of early detection and rapid containment depends on several assumptions:

1. The emerging virus causes moderate to severe acute respiratory illness, thus making the event visible and increasing the likelihood that it will be detected.
2. The detection of clusters of such cases immediately triggers the appropriate clinical, epidemiological, and laboratory investigations.
3. Notification and assessment of the event occur rapidly, moving from the local, to the intermediate, to the national level.
4. WHO is immediately informed, so that the international community can be alerted and further support gathered, if needed.
5. External assistance for investigation and response is quickly requested when needed.

Epidemiological signals

Epidemiological signals are likely to be the most sensitive and reliable indicators of a transition from inefficient, non-sustained human-to-human transmission of the virus to efficient and sustained transmission. The detection of clusters of cases, closely related in time and place, is likely to be the most important epidemiological signal of such transition.

The use of clusters of cases as an epidemiological signal is context dependent. In general, the signal is expressed as an increase in the number of persons with unexplained respiratory illness in a defined area over a short period of time. In addition, the pattern of unexplained respiratory illness should be different from that usually seen in the area. Observations with H5N1 infections to date suggest that a cluster of five closely related cases (including the index case) in which human-to-human transmission is suspected would be an unusual event. Experience has, however, shown that it is often difficult, during the investigation of such clusters, to determine whether people acquired their infection from each other, from some shared animal or environmental exposure, or from a combination of the two.

Experience to date has further shown that cases of human infection with the H5N1 virus are rare events, even in areas where the virus is widespread in poultry kept in close contact with households. The rarity of human infections in the present epidemiology of this disease makes it likely that a transition in the behaviour of the virus, moving towards improved transmissibility, will result in a visible event sufficiently “unusual” to be picked up by alert clinicians.

Against this background, WHO proposes that clusters with the following features be immediately investigated for evidence of infection caused by a novel influenza A virus:

Three or more persons with unexplained¹ moderate-to-severe acute respiratory illness² (or who died of an unexplained acute respiratory illness) and with onset of illness within 7 to 10 days of each other

AND

With a history strongly suggesting potential exposure to the H5N1 virus, including:

- Travel to or residence in an area affected by avian influenza outbreaks in birds or other animals
 - Direct contact with dead or diseased birds or other animals in an affected area
 - Close contact with an H5N1 patient (living or deceased) or a person with unexplained moderate-to-severe acute respiratory illness
 - A possible occupational exposure, including employment as an animal culler, veterinarian, laboratory worker, or health care worker.
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Virological signals

While epidemiological signals are likely to be the most reliable indicator of a change in transmission patterns, comparative studies of virus isolates can also yield useful clues. Such studies of H5N1 viruses, isolated from both humans and animals, are presently being conducted by the WHO network of H5 reference laboratories as part of routine investigation of H5N1 outbreaks. Although the exact mutations that would result in efficient and sustained human-to-human transmission are not precisely understood, two types of virological changes would be considered cause for concern: detection of a virus with new genetic and antigenic features (such as a “reassortant” virus containing both human and avian genetic material), and isolation of a virus from a human case showing a number of mutations not seen in avian isolates.

Notification of national health authorities

Detection of a cluster of unexplained moderate-to-severe acute respiratory disease showing the features described above should trigger immediate notification of the national health authorities. Local health authorities should respond with a high level

¹ Unexplained: clinical, epidemiological, or laboratory evaluation does not determine a cause or etiological agent, such as a routine community-acquired pneumonia. Countries that do not have adequate diagnostic or diagnostic capacity to establish a probable diagnosis within 48 hours of cluster identification should request immediate support from WHO.

² Moderate-to-severe respiratory illness: lower respiratory tract illness (temperature greater than 38°C, cough, shortness of breath or difficulty breathing with or without evidence (clinical or radiological) of pneumonia.

of suspicion, and notify national authorities accordingly, as soon as preliminary information suggests that the cluster of cases is “unusual” or “different”, and should not wait until all information described above has been collected. Receipt of this alert by national authorities should immediately trigger further assessment and the provision of support for the investigation, as needed.

Steps in the initial investigation of epidemiological signals

1. Conduct laboratory tests

Given the need for speed, laboratory testing of clusters (as for example by RT-PCR) to identify the causative agent should ideally be completed within 48 hours following detection of the cluster.

2. Initiate the epidemiological investigation

Following detection of a cluster of cases of moderate-to-severe unexplained respiratory disease, an investigation should be launched to characterize patients by person, place, and time. This should be undertaken through interviews of cases, their relatives, and health care workers as well as through a review of medical and any other relevant records. More specifically, these investigations should

- Undertake descriptive epidemiology, including determination of demographic information, occupational data, and possible exposures to ill persons, birds, animals, contaminated environments, and other risk factors. Epidemiologists should estimate the incubation period, describe transmission patterns, and seek to differentiate between person-to-person transmission and a common- or continuing-source outbreak.
- Characterize the illness in terms of clinical presentation, the spectrum of disease, the proportion of cases requiring hospitalization, pathophysiology, clinical outcomes, and the case fatality ratio.
- Undertake the tracing and follow-up of contacts, and gather as much detail as possible on the number of immediate contacts (at the household, school or workplace), their social networks, and any history of recent travel.
- Initiate intensified case finding to detect additional persons with moderate-to-severe respiratory illness, especially persons closely associated in time and place with the initial cluster of cases. Of critical importance is monitoring to detect unexplained rapid increases in the number of persons and the number of clusters.

3. Investigate the source or reservoir

If the initial investigation suggests a relationship in time and place with unusual deaths in poultry or other animals, an urgent veterinary investigation should be initiated or intensified. This investigation should include the collection of appropriate animal specimens for laboratory evaluation. If in-country capacity to conduct such investigations is not available, external assistance should be sought immediately in consultation with FAO and OIE, as these agency maintain a network of reference laboratories for animal diseases and can assist in field assessments. In several instances, human H5N1 infections have been confirmed in areas with no reported outbreaks in animals. In all such instances, subsequent investigations have identified outbreaks in poultry.

Steps in the initial investigation of virological signals

If the sole signal arises from a virological isolate from one or more persons, contact tracing and active case finding should be initiated in the geographical area where the isolates were collected. This activity should include a thorough investigation of persons from whom the isolate was obtained and tracing of close contacts in households, schools, and workplaces. As the exact mutations associated with improved transmissibility in humans are not fully understood, virological signals should always be interpreted in line with epidemiological evidence indicating whether an actual change in transmission patterns has occurred.

Reporting to WHO

The national health authority should notify WHO immediately following detection of a credible signal. The national authority is expected to provide WHO with all relevant information, including clinical, epidemiological, and laboratory data. Priority should be given to information indicating an increase in the size of the cluster following its initial detection, a high proportion of persons with evidence of severe respiratory illness, or a high case fatality ratio. Laboratory results indicating a novel virus subtype or a non-typable virus should also be reported. Countries should likewise report the actions undertaken to contain the outbreak.

Countries should provide details about the geographical locality where cases are occurring, population size and density, the size and level of health care facilities within the outbreak area, accessibility by road and air, possible security concerns, and in-country epidemiological and laboratory resources available to continue the investigation and implement initial control measures. Such information will help WHO plan appropriate support should external assistance be requested.

II Verifying the event

Event assessment and immediate control measures

Initial risk assessment

Upon receipt of notification and relevant information, WHO, supported by its regional and country offices, will carry out an initial assessment. If this assessment concludes that a signal event has occurred, several activities should follow immediately.

1. Diagnostic confirmation. Laboratory specimens should be sent to a WHO H5 reference laboratory for identification or verification of the causative agent.
2. Needs assessment. WHO, together with national authorities in the affected country, will assess the need for additional support, which may include personnel (such as epidemiologists, clinicians, logisticians, laboratory experts, or experts in communications and social mobilization), supplies (such as personal protective equipment and antiviral drugs), and other logistics needs.

3. Continuous communications. The country and WHO will agree on a communication plan to ensure that all information relevant to outbreak assessment and response is shared in the most expedient way possible.
4. Control measures. Measures to control the outbreak within the community should then be launched immediately.

Immediate control measures

Routine control measures aimed at reducing opportunities for further transmission to occur should be initiated as soon as clusters of cases are detected. Immediately following signal detection, local authorities, supported by national resources if needed, should apply the measures, aimed at reducing transmission, outlined below.

Recommended measures include traditional, standard interventions used during outbreak control. At present, many of these measures are being routinely applied in H5N1 outbreaks characterized by sporadic human cases with no evidence of efficient human-to-human transmission. These measures should be introduced immediately and should not await laboratory confirmation of the causative agent.

Since the onset of human cases of H5N1 infection in the current outbreak, which began in December 2003, WHO has acquired considerable experience in assessing needs, applying control measures, and arranging for rapid support when requested.

Immediate measures include:

1. Isolation of clinical cases of moderate-to-severe respiratory disease and other patients under investigation in respiratory isolation rooms or single rooms.
2. Identification and voluntary home quarantine of asymptomatic close contacts and daily monitoring for symptom onset
3. Administration of antiviral drugs for the treatment of cases and, if domestic supplies permit, for the targeted prophylaxis of close contacts
4. Strict infection control and the use of personal protective equipment in health care facilities caring for cases during the delivery of health care
5. Intensive promotion of hand and cough hygiene.
6. Domestic cleaning, using household cleaning products, to reduce transmission via fomites (infectious respiratory secretions on surfaces)

Deployment of international field teams

International field teams, drawn from institutions in the WHO Global Outbreak Alert and Response Network (GOARN), can be rapidly deployed following receipt of a request from the affected country. Such teams may be deployed to assist in the initial assessment of pandemic signals. Based on recent experience, teams may require expertise in laboratory diagnostics, epidemiology, clinical management, infection control, veterinary medicine, medical anthropology, logistics, communications, and database management.

Teams will be equipped with supplies required for the initial investigation and response. Depending on the situation within the country, such supplies may include kits for the collection and transportation of specimens, antiviral drugs and other medical supplies, personal protective equipment, and information and educational materials for communicating essential messages to the general public.

WHO will ensure that field teams are in place with 24 to 48 hours following receipt of the request. National authorities will need to facilitate this rapid arrival as, for example, through the rapid approval of visa applications.

The field team will assist local and national authorities in their investigation and assessment of the disease event and in the gathering of critical information required for the operational response. Examples of information useful in such an assessment include the identification and characterization of chains of human-to-human transmission and of situations that could potentially lead to large numbers of additional cases. Such information will be used when deciding whether the launching of a rapid containment operation is both justified and feasible.

III Containing the event

The rapid response and containment operation

The decision to launch a containment operation

An attempt to contain an emerging pandemic virus at its source is a demanding exercise and a resource-intensive operation. Moreover, supplies of antiviral drugs reserved for use to support such an operation are finite and not easily replenished, and must therefore be used judiciously.

For these reasons, the decision to initiate activities aimed at rapid containment should be triggered by compelling evidence that the situation represents a transition in the behaviour of the virus likely to result in efficient and sustained human-to-human transmission. Such evidence will derive from a combination of clinical, epidemiological, and virological findings as guided by the following criteria:

1. Moderate-to-severe respiratory illness (or deaths) in three or more health care workers who have no known exposure other than contact with ill patients, and laboratory confirmation of H5N1 infection in at least one of these workers.
2. Moderate-to-severe respiratory illness (or deaths) in 5 to 10 persons with evidence of human-to-human transmission in at least some, and laboratory confirmation of H5N1 infection in more than 2 of these persons.
3. Compelling evidence that more than one generation of human-to-human transmission of the virus has occurred.
4. Isolation of a novel virus combining avian and human genetic material or a virus with an increased number of mutations not seen in avian isolates from one or more persons with moderate-to-severe respiratory illness (acute onset), supported by epidemiological evidence that transmission patterns have changed.

Rapid containment measures should not be attempted in the following circumstances:

1. Laboratory studies fail to confirm H5N1 or another novel influenza A virus
2. The number or geographical distribution of affected persons is so large at time of detection that it renders containment impracticable for logistic reasons.
 - The number of persons requiring prophylactic administration of antiviral drugs exceeds available supplies
 - The size of the affected community makes it impossible to ensure adequate supplies of food and shelter, and the provision of medical care and emergency services during a containment operation
3. More than 4 to 6 weeks have passed since detection of the initial cluster, thus decreasing the likelihood that containment would be successful.

The feasibility of rapid containment will further depend on the number of contacts of the initial cases and the ability of government authorities and international teams to ensure basic infrastructure and essential services to the affected population. Such services include shelter, power, water, sanitation, food, security, and communications with the outside world.

A two-phased containment response

The rapid containment strategy is implemented in two phases

1. Immediate implementation of standard measures aimed at reducing further transmission. In this phase, active case finding and contact tracing are undertaken and antiviral drugs are administered, in a targeted way, to persons identified during these activities.
2. Implementation of exceptional measures, including wider prophylactic administration of antiviral drugs, quarantine, and (possibly) the introduction of social distancing measures.

During both phases, enhanced surveillance at national and international levels is important to guide the continuation of measures and monitor their impact.

Phase one: standard measures to reduce transmission

Activities in the phase are based on the assumption that an emerging pandemic virus will not immediately cause the explosive increase in the number of cases seen during a full-fledged pandemic. Assuming that the number of new cases is still manageable, activities should concentrate on investigation and laboratory confirmation of cases, contact tracing, and the real-time reporting of data. The main interventions at this phase aim to reduce opportunities for further transmission to occur and thus, ideally, prevent the virus from becoming well adapted to humans.

These measures must be implemented immediately. Mathematical models have indicated that a containment strategy, based on the mass administration of antiviral drugs, has a chance of success only when drugs are administered within 21 days

following the detection of the first case. The immediate implementation of standard measures gives the strategy a greater chance of success.

Active surveillance

Detection of a signal event should result in active surveillance both within the initial outbreak zone and internationally.

Within the outbreak zone, enhanced detection and reporting of individual cases and clusters of human-to-human transmission is essential to:

- Manage the outbreak and monitor its evolution
- Pick up signs of further geographical spread
- Evaluate the success of containment measures and the potential need to modify the strategy

Active surveillance in the initial outbreak area should also gather information about recent travel histories that may have placed other areas or countries at risk, thus signalling the need for intensified surveillance elsewhere.

To assist surveillance for cases in the outbreak zone and elsewhere, WHO will develop case definitions including clinical, epidemiological, and laboratory criteria.

Contact tracing

Contact tracing must be aggressively implemented when the signal is received and must include the identification of extended social networks and the travel history of all cases and contacts during the preceding 14 days. Contacts of cases should be traced and followed up for evidence of respiratory illness for at least 7 days. If the number of contacts requiring investigation is large, priority groups should be established based on:

1. Heightened probability of infection, such as contact with a laboratory-confirmed case
2. Duration and closeness of this contact
3. A high-risk exposure, such as unprotected patient care
4. Exposure in settings that could accelerate spread to large numbers of contacts, such as when a confirmed case worked in a school or attended a large gathering

Whenever possible, cases should be isolated in health care facilities to maintain strict infection control. Contacts should be advised to remain at home (voluntary home quarantine) for at least 7 days after the last contact with a person under investigation.

Should evidence of spread beyond the initial containment zone emerge, the containment areas designated for antiviral prophylaxis should be re-defined. This decision will be made in collaboration with local and national authorities and WHO.

Targeted antiviral prophylaxis

Antiviral drugs should be administered to cases of moderate-to-severe respiratory illness, to reduce morbidity and mortality, and to their contacts to reduce ongoing spread. Priority access to antiviral drugs and other medical interventions is expected to work as an incentive that increases the willingness of patients and their contacts to comply with recommended public health measures under what are likely to be stressful and demanding conditions.

Local and national authorities, with support from WHO, will jointly define, within the outbreak zone, the households, schools, workplaces, health facilities or other settings where the delivery of antiviral drugs, personal protective equipment, and other medical supplies should be targeted.

Monitoring contacts for signs of illness

Contacts of patients and the community at large should:

1. Know the symptoms of concern. People should be informed that the most consistent first symptoms are fever and/or cough, and instructed on how to self-monitor for fever. Fever monitoring should be performed for at least 7 days following the last contact with a person under investigation. Self-monitoring for fever is a community-based intervention that gives individuals responsibility for their own health care.
2. Report the onset of symptoms. People should immediately report the onset of fever and other symptoms to the health authorities and remain in voluntary home quarantine pending medical care. Prompt testing and treatment must be provided when symptoms are reported.
3. Be visited or telephoned daily by a member of the public health team to ascertain their clinical status.
4. Be investigated locally at an appropriate health care facility should symptoms develop.

Case management

In the initial phase, when a manageable number of cases is assumed, clinical cases should be hospitalized and managed in respiratory isolation rooms or single rooms depending on the local circumstances. Once laboratory confirmation of infection is available, patients can be cohorted if sufficient numbers of single rooms are not available.

When the number of cases exceeds the capacity of existing health care facilities, ill persons should be isolated in homes, field hospitals, or other designated areas depending on the severity of their illness. National governments should identify potential isolation facilities as part of their preparedness planning or identify the need for field hospitals during discussion with WHO. Patients should be transported to these facilities by trained staff wearing appropriate personal protective equipment and using designated vehicles.

To minimize the risk of nosocomial transmission, persons showing signs of influenza-like illness should, wherever possible, be assessed in premises separated from those where confirmed cases are being managed. Options for doing so include

the establishment of fever clinics, home visits by medical staff, drive-through consultation services, and other methods of triage and diagnosis that limit opportunities for exposure.

Infection control in health care settings

WHO has recently issued detailed infection control guidelines for avian influenza, including information specific to H5N1 infection. The [guidelines](#) (Avian influenza, including influenza A (H5N1), in humans: WHO interim infection control guidelines for health care facilities) were issued in February 2006 and are available online.

Topics covered range from standard precautions for health care facilities, through respiratory hygiene and cough etiquette, isolation precautions for suspected or confirmed cases, and recommendations for family members and visitors, to waste disposal, linen and laundry management, cleaning and disinfection, and the prioritized use of personal protective equipment when supplies are limited.

The guidelines can be accessed at:

http://www.who.int/csr/disease/avian_influenza/guidelines/infectioncontrol/en/index.html

Phase two: exceptional measures, including use of the antiviral stockpile

Voluntary quarantine

The SARS experience suggests that quarantine, applied on a voluntary basis only, is preferable to enforced quarantine and may be equally effective. The use of voluntary quarantine is also consistent with modelling studies recommending the application of quarantine and other community-based measures as part of a containment strategy. At the same time, however, national, sub-national, and local governments should be legally prepared to enforce individual and community-based containment measures if warranted. This preparedness should include examination of the ethical dimensions of enforced quarantine or compliance with other recommended measures. Wherever possible, authorities should apply the principle of proportionality, whereby the least restrictive measures are applied first, followed by a graded application of more restrictive measures when evidence indicates their necessity.

Local authorities should apply quarantine in the following situations:

- Exposure has occurred in a defined group of persons as, for example, in a household setting, at the workplace or school, or at a well-defined and circumscribed public gathering
- Exposure has occurred in a defined site or building (such as a hospital or an apartment building)

Quarantine may involve confinement at home or in a designed facility with appropriate equipment.

Persons in home quarantine may need to be provided with food, access to communications, psychosocial support, and supplies of their usual medications, especially for chronic conditions.

Social distancing

Modelling studies have indicated that certain “social distancing” measures might increase the likelihood of successful containment. Such measures aim to increase the social distance among people in an outbreak zone and thus reduce opportunities for transmission to occur. Like quarantine, these measures are socially disruptive and some may cause considerable distress or discomfort in the affected population. Moreover, their actual impact on transmission patterns has not been fully documented in scientific studies. They are nonetheless included here as some feature in national pandemic preparedness plans. They include:

- The closing of schools and workplaces
- Cancellation of mass gatherings and public transportation
- Community-based confinement (within homes) of asymptomatic persons
- Border controls

Deployment of the antiviral stockpile

WHO will authorize F. Hoffmann-La Roche Ltd, the manufacturer and donor of oseltamivir, to deploy the WHO global stockpile for rapid containment in a country that does not have a national stockpile. This authorization will be based on assessment of the criteria described above.

As supplies in the stockpile are finite and not easily replenished, WHO recommends a “multiple-wave” approach to the deployment of drugs from the stockpile. While it is anticipated that mass prophylaxis will continue for several weeks, sufficient quantities of antiviral drugs should be shipped initially to cover a two-week period during which intensive monitoring for new signals outside the containment zone will be undertaken. Estimates of the quantity of drugs initially required should calculate treatment courses sufficient to treat 25% of the affected population and prophylactic courses for 10 days for the remaining 75% of the population. Further shipment of antiviral drugs for containment purpose will depend on evaluation of the success of containment efforts.

Drugs in the WHO stockpile are being stored in company warehouses located in Switzerland and the USA, with 1.5 million treatment packs to be stored at each site. Roche is prepared to mobilize all 3 million packs if so requested by WHO. Arrangements with airlines and courier services to ensure the fastest and safest possible shipment to the outbreak site are well advanced. Roche will be responsible for the logistics of delivery to the nearest airport, where direct handover to WHO will take place. Officials in the affected country need to be ready to authorize the use of any package make-up and to waver liability. National authorities are also responsible for customs release and compliance with importation requirements.

Current shipment plans also include several security precautions to guard against theft during transport, at stopovers, or at destination. Roche and WHO recognize the

need for clear procedures for handover of the drugs at the outbreak site, and for a secure storage capacity within the country.

Further development of operational guidelines for drug deployment and distribution

On 28 March 2006, WHO will convene a meeting with Roche officials to work out further procedures for delivery of the drugs and handover to WHO. A more detailed operational plan, in line with actions recommended in this protocol, is the expected outcome.

Additional meetings with countries and partners will be held in the near future to address such key questions as staff responsibility for actual distribution of the drugs within the outbreak zone.

The results of these meetings will be used to refine this section of the protocol.

Work is also under way to develop standard operating procedures and training curricula for health workers, staff currently engaged in surveillance, and teams that will be deployed to investigate the outbreak. Precise roles and responsibilities of WHO and countries, set out in annex 2, are being further refined.

Antiviral drugs: informed and voluntary consent

The mass administration of antiviral drugs as part of a containment strategy raises certain ethical questions about informed consent during a mass intervention. National governments need to decide how to provide information about contraindications to the target community. More specifically, antiviral drugs have not been approved for use in pregnancy or in infants younger than one year of age. Antiviral drugs can, however, be administered to such groups provided appropriate information on the risks has been provided and provision has been made for individual counselling, as through information hotlines or discussions with health care workers.

Reporting of adverse events

Adverse events will be monitored through use of telephone surveys or hotlines. Where such communication structures are lacking, adverse event reporting will be conducted during visits by mobile medical or public health teams, other surveillance networks, or by food and social welfare distribution networks. Adverse event reporting will target such high-risk groups as pregnant women, children, and persons with underlying medical conditions. Persons reporting adverse events should be simultaneously given advice on management of the event. National authorities should assume responsibility for liability should severe adverse events occur.

Annex 1: Roles and responsibilities for rapid response and containment

Roles and responsibilities of countries

1. Preparedness planning

Countries should ensure that their national pandemic preparedness and contingency planning consistent with the co-ordinating role of the international response by WHO and partners. National pandemic preparedness plans should address the issue of integration of national resources for rapid response and containment. National plans should be updated frequently to take account of international developments.

Countries have specific responsibilities in the following areas to:

- Plan rapid national response and containment, including agreement with other national emergency response agencies on the command, control and co-ordination structure that will be activated in the event of pandemic influenza emergence;
- Assess current clinical, laboratory, epidemiological, veterinary, logistics, communication and social mobilization expertise, among other disciplines, in anticipation for rapid response and containment. This should include identifying gaps in capacities that would require early requests for support from WHO and other international partners;
- Identify and test national capacity to transport critical specimens from the source location to one of four WHO H5 reference laboratories within 48 hours of specimen collection;
- Build or strengthen core capacities for epidemic alert and emergency response in accordance with the requirements of the International Health Regulations (2005);
- Establish or strengthen early warning and surveillance to rapidly detect unusual disease events or acute severe respiratory illness that could be the early signs of emerging pandemic influenza;
- Train clinicians, primary health care providers, traditional healers, primary care providers in other sectors e.g. animal health, and the wider community to handle respiratory illness cases appropriately and to report cases when appropriate to public health authorities.
- Include influenza in the list of notifiable diseases and establish mechanisms for the rapid investigation and reporting of potential pandemic influenza signals to the national public health authority and to WHO
- Strengthen laboratory capacity and infrastructure for the rapid confirmation of the virological agent within the country and make prior agreements and arrangements for the rapid shipment to an external or WHO collaborating centre;
- Build the national operational platform for the rapid deployment of response teams, supplies and field security;
- Facilitate rapid response and containment by identifying and modifying the legislative, administrative and other impediments to the implementation of rapid containment (national and international activities);
- Identify multidisciplinary teams for training in rapid response and containment;

- identify and train external partners required for successful containment operations; such as the providers of emergency services, water and sanitation, transport, catering, etc.
- develop a strategy for public communications and social mobilization;
- develop and implement a strategy for the identification and protection of critical infrastructure in the event of pandemic influenza emergence, including health care facilities, security, water and sanitation, public utilities (electricity, gas etc), the food supply, and operational and public communications technology.

2. During rapid response and containment

- Coordinate national rapid response and containment operations.
- Rapidly investigate potential pandemic signals as defined in this protocol, and facilitate the risk assessment for rapid response and containment by collecting the core dataset required for signal interpretation and decision making.
- Immediately seek support from WHO for assistance if national clinical, epidemiological and laboratory capacities are insufficient to characterize the event
- Mobilize national resources for rapid response and containment, including the provision of human, material (antiviral drugs and personal protective equipment etc) and logistics resources, and field security for personnel and stockpile materials and equipment. Work in close collaboration with WHO and international teams in the field.
- Establish or strengthen surveillance for cases of influenza-like illness within and outside the containment zone.
- Provide public communications and social mobilization expertise for rapid containment.
- Monitor adverse events following the administration of antiviral agents.
- In collaboration with WHO, evaluate the effectiveness of rapid response and containment operations.
- Ensure the safety and security of international staff who are assisting with rapid pandemic response activities

The roles and responsibilities of WHO

1. Preparedness planning

- Assist Member States on request with the development of national rapid response and containment plans as an integral part of the national preparedness plan. .
- Support country efforts to build core capacities and to coordinate efforts to build upon other existing WHO surveillance and response networks.
- Provide WHO 24-hour on-call system for reporting of potential pandemic influenza signals.
- Develop and implement training for national and international members of rapid response and containment teams. Use a "training of trainers" approach to provide training to in-country staff.
- Strengthen mechanisms for collection and transportation of clinical specimens for rapid testing.
- Identify WHO staff and experts from the Global Outbreak Alert and Response Network (GOARN) and regional response networks who can be on "stand by" for rapid deployment when needed and to make the necessary arrangements with countries to enable their rapid deployment.

- Develop and implement the necessary administrative arrangements and operational platform for the rapid deployment of the international stockpile of antiviral drugs and other risk reduction materials.
- Develop specific protocols and standard operating procedures, including those for
 - Stepping down procedures following successful containment
 - Scaling up procedures if a larger response operation is indicated
 - Declaration of a phase change if containment fails.
- Finalize a media communications strategy in the event of pandemic influenza emergence.
- Develop communication materials for behavioural impact to be distributed in the containment zone and beyond.
- Continue to develop the critical elements needed to facilitate the rapid response and containment strategy.

2. Pre-identification and training of team members

Implementation of rapid response and containment activities requires the availability of a pool of highly trained and qualified staff who have been pre-identified and trained by WHO and who can quickly mobilize into teams. The international response teams will be drawn from a multi-disciplinary pool of experts in alert and response operations representing national and international organizations. Teams will be drawn from the large number of partner institutions in the GOARN and, if needed, other sources. The international field teams will integrate their efforts with national staff and provide direct day-to-day link between WHO and the country.

National governments are also expected to mobilize national staff including those focused on health care, local and national social mobilization, health promotion, risk communication, and mental health and social welfare of people and response staff in the containment zone and to provide "surge" capacity for critical positions. National teams will receive training in influenza, rapid response and containment goals, concepts and activities, and team roles and responsibilities.

WHO will establish a teaching curriculum and course materials, including "training of trainers" materials. Each training session will last approximately two weeks per group. The initial teaching venue will be at WHO in Geneva, Switzerland, but future courses will be held in regional venues.

3. During rapid response and containment

- Coordinate the international response to rapid response and containment, including deployment of international field teams to affected countries (upon request).
- Assist countries on request in their assessment of signals of the possible emergence of pandemic influenza.
- Undertake the initial joint risk assessment of the emergence of pandemic influenza with the affected country/area.
- Mobilize international technical partners to support countries in rapid response and containment if required.
- Dispatch the necessary logistics, material and technical resources for rapid containment.

Annex 2: WHO operational communications

WHO will adhere in all its public messages (such as press releases, press conferences) to the best practices set out in the *WHO Outbreak Communication Guidelines*.

Objectives

- To instill and maintain the publics' trust in the global and national public health system and to convey realistic expectations in its ability to respond to and manage the initial outbreak of an efficient transmission of a pandemic virus.
- To provide accurate, timely, consistent, and comprehensive information about containment activities.
- To identify and addresses rumors, inaccuracies, and misperceptions quickly and prevent stigmatization of affected groups.
- To promote compliance within the containment zone, to rapidly identify barriers to compliance, and to react with new approaches to increase compliance through a policy of transparent communication.

Activities

- Integrate communications staff into all discussions regarding the containment plan.
- Activate HQ's network of risk/outbreak communicators, for advice and deployment of communications officer(s) to affected region.
- Activate secure website as a means to share documents, updates, general public information, contact information, etc.

WHO communications with the media

- To be consistent and a part of WHO's overall pandemic communications, and adhere to WHO Outbreak Communication Guidelines.
- To instill and maintains the publics' trust in the global and national public health system and its ability to respond to and manage the initial outbreak of an efficient transmission of a pandemic virus.
- To provide accurate, timely, consistent, and comprehensive information about seasonal and pandemic influenza, and containment activities.
- To contribute to the maintenance of order, minimization of public fear, and facilitation of public protection.
- To quickly addresses rumors, inaccuracies, and misperceptions as quickly as possible, and prevent stigmatization of affected groups.
 - Wherever possible, WHO and the national government will attempt to integrate public communications. However, WHO will reserve the right to make independent assessments of the evolving situation as required.
 - HQ communications staff, together with Regional Office staff, to contact counterparts in the affected Ministry of Health, to discuss the announcement of containment strategy. The goal will be to announce this undertaking as soon as possible, particularly before it is reported in the media.
 - Three specific areas to be targeted: the initially affected outbreak zone, bordering regions, and the rest of the world. Each of these areas will have particular concerns, to be addressed by evolving technical assessments of the situation.
 - Communications surveillance to be enacted (in affected country and worldwide) to identify issues of concern for the public/media, and to allow WHO to respond as quickly as possible to rumours, negative press stories, etc.

- HQ communications staff to develop daily talking points based on evolving technical guidance and information from the field. To be shared within WHO and with external partners, as necessary.
- HQ communications, together with regional counterparts, to hold regular press briefings.
- The identification of at least two senior technical/policy WHO spokespeople – one at HQ and one in the field, to be available for regular media interviews.