Draft

WHO pandemic influenza draft protocol for rapid response and containment

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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 through preparedness, rapid response and containment. The rapid response and containment strategy aims to stop, or at least slow the spread of pandemic influenza at the source of its emergence in order to minimize global morbidity and mortality.

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 administration 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. Further modelling study published in May 2006 using data from previous pandemics illustrates the effectiveness of timely implementation of these pharmaceutical and non pharmaceutical interventions locally within the outbreak area, in significantly reducing the rate of global spread. This provides a window opportunity for attempting rapid containment, aimed at minimizing high morbidity and mortality as documented in previous pandemics.

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 a manufacturer, WHO has a global stockpile of the antiviral drug, oseltamivir, amounting to 3 million treatment courses. These drugs have been reserved strictly 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 the understanding of this virus and its pandemic potential. Recommended actions in this protocol are expected to evolve as knowledge about this virus in particular, and pandemic influenza in general, continues to improve.

Although most attention is focused currently 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.

Annex 1 sets out a flow chart depicting the different elements of the protocol which has four main parts. The first part 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 operations. The fourth part provides guidance on requesting use of the global antiviral stockpile and its deployment to support containment operations. Precise roles and responsibilities of countries and WHO in ensuring successful implementation of the different aspects of the protocol are set out in annex 4.

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. 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 timely detection of the first case representing improved human-to-human transmission of the virus. The immediate implementation of standard measures gives the strategy a greater chance of success.

The feasibility of early detection, rapid response and 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. External assistance for investigation and response is quickly requested when needed. In order to assist in a timely manner, WHO will immediately be informed

as mandated by the International Health regulations (2005), so that the international community can be alerted and further support mobilized as required.

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.

An epidemiological signal may manifest itself as an increase in the number of persons with unexplained respiratory illness in a defined area over a short period of time. This 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 constitute a signal.

To date, cases of human infection with the H5N1 virus have been sporadic and rare events, even in areas where the virus is widespread in poultry. Any transition in the behaviour and epidemiology of the virus indicating improved human-to-human transmissibility will most likely result in a visible event sufficiently "unusual" to be picked up by alert clinicians or the public health system.

Against this background, WHO proposes that clusters with the following features should trigger immediate investigation for evidence of infection caused by a novel influenza A virus:

Three or more persons, geospatially or socially linked (as evidence of efficient and sustained human-to-human transmission) with unexplained[1] moderate-to-severe acute respiratory illness[2] (or who died of an unexplained acute respiratory illness) and with onset of illness within 10 days of each other

AND

At least one of the cases exhibiting 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

[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 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^{o}C, cough, shortness of breath or difficulty breathing with or without evidence (clinical or radiological) of pneumonia.

– A possible occupational exposure, including employment as an animal culler, veterinarian, laboratory worker, or health care worker.

Virological signals

While epidemiological signals are likely to be the most reliable indicator of a change in transmission patterns, studies and analyses of virus isolates may 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 of suspicion, and notify national authorities as soon as preliminary information suggests that the cluster of cases is "unusual" or "different". Receipt of the notification 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. 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

   – Characterize the illness in terms of clinical presentation, the spectrum of disease, the proportion of cases requiring hospitalization, clinical outcomes, and case fatality ratio.

   – 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.

- 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.

2. Conduct laboratory tests

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

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, immediate investigations should be initiated, including search for possible source and reservoir and 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 agencies 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. However, subsequent investigations in all such instances have confirmed 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, active case finding, tracing and monitoring of contacts 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.

If the preliminary investigation of any of the signals establishes and characterizes the outbreak (influenza alert), efforts should be made to do a preliminary assessment of risks and immediate control needs. These should be followed immediately with implementation of control interventions to curtail further spread and reduce mortality.

Reporting to WHO

In line with the International Health Regulations (2005), the national health authority should notify WHO, using the fastest possible means of communication, within 24 hours of detection of an epidemiological or virological signal suggestive of sustained human-to-human transmission of a novel influenza virus. 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, and this should trigger further assessment of the emerging virus sub-type. Likewise, countries should report the actions undertaken to contain the outbreak.

Countries should provide details about the geographical location 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.

Following the initial notification, the affected country should continue to report to WHO timely, accurate and detailed public health information regarding the evolution of the outbreak and response and containment measures, and seek further support and guidance as needed.

II Verifying the event: Event assessment, immediate control measures and deployment of international field teams

Risk assessment

Upon receipt of notification and relevant information, WHO will support countries in assessing the risk further. If this assessment concludes that the signal requires further investigation, several activities should follow immediately.

1. Diagnostic confirmation., Laboratory specimens should be sent to a WHO H5 reference laboratory for identification, verification and confirmation of the causative agent, even when prior cases have been confirmed in the affected country.
2. Burden assessment. WHO, together with the national authorities, will use the available data generated during the signal investigation to characterize the disease pattern, determine the population at risk, and identify factors affecting transmission pattern and control activities (such as geographical location of outbreak, movements in an out of the area). Where feasible, modelling should be undertaken to help predict spread, and anthropological investigation should be undertaken to examine socio-cultural factors that may have implications for control interventions.

3. Needs assessment. Based on the analysis of the burden and the available national resources for rapid response and containment, WHO and the national authorities should 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.

4. Request for antiviral. Should the assessment establish a need to deploy a portion of the antiviral drug (oseltamivir) from the global stockpile, the appropriate government official should send an immediate request to WHO headquarters using the "WHO Global Stockpile Antiviral Request Form". (A SOP for requesting and distributing drugs from the WHO global stockpile is set out in annex 3)

5. Outbreak communications. The country and WHO will agree on a communication plan to ensure that all information relevant to outbreak assessment and response is communicated to the general public, international community and partners in the most expedient way possible and in a coordinated manner. Risk communication, including key messages to the public, should be developed and disseminated swiftly.

Immediate control measures

Routine control measures aimed at reducing opportunities for further transmission to occur should be initiated as soon as preliminary investigations of the detected clusters of cases confirm an existing epidemic. These measures should be strengthened and intensified concurrently as the risk assessment is being conducted in order not to loose time.

Recommended measures include traditional, standard interventions used during outbreak control. At present, many of these measures are being applied routinely 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.

Immediate measures include:

1. Isolation of clinical cases of moderate-to-severe respiratory disease in respiratory isolation rooms or single rooms.

2. Identification and voluntary home quarantine of persons who have had close contact with a case, and their 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 during the delivery of health care in health care facilities managing cases.

5. Intensive promotion of hand and cough hygiene.

6. Domestic cleaning, using household cleaning products, to reduce transmission via fomites and from infectious respiratory secretions on surfaces.

7. Appropriate waste management and disposal.

8. Informing the public of the outbreak and initiating social mobilization measures.

Deployment of international field teams

International field teams, drawn from institutions in the WHO Global Outbreak Alert and Response Network (GOARN), can be deployed rapidly following receipt of a request from the affected country. Such teams may be deployed to assist in the risk assessment and verification of the pandemic alert. Experience shows that expertise in laboratory diagnostics, epidemiology, clinical management, infection control, veterinary medicine, medical anthropology, social mobilization, logistics, media communications, and data management will be required.

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 additional supplies of information, educational and communication (IEC) materials for creating awareness in the general public.

WHO will ensure that field teams are in place within 48 hours following receipt of the request. National authorities will need to facilitate the speedy arrival of teams through, for example, the rapid approval of visa applications and customs clearances.

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

Any attempt to contain an emerging pandemic virus at its source will be a demanding and 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 towards more efficient human-to-human transmission. Such evidence will be drawn from a combination of clinical, epidemiological, and virological findings as guided by the following criteria:

1. Clustering of cases of moderate-to-severe respiratory illness (or deaths) with two generations of transmission in a health care facility, and laboratory confirmation of H5N1 infection in at least one of them. The cases could be three or more health care workers who have no known exposure other than contact with ill patients, or just one health care worker and additional patients with evidence of nosocomial transmissions.

2. Moderate-to-severe respiratory illness (or deaths) in 5 to 10 persons with evidence of human-to-human transmission in at least some as determined by temporal sequencing of onset dates of cases and opportunity among cases for exposures to one another consistent with respective infectiousness and incubation period. At least 2 of these persons should have a laboratory-confirmed H5N1 infection.

3. 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 the time of detection that it renders containment impracticable for logistical 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

The feasibility of rapid containment will depend further 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, 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, isolation of cases, 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, surveillance activities should be intensified in the outbreak zone and the surrounding areas to guide the continued implementation of public health measures and monitor their impact. Geographically surrounding countries, or those that are linked through communication routes, may need to be on the alert for possible introduction of potential cases.

Phase one: standard measures to reduce transmission

Activities in this 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, appropriate management of cases in a safe environment, implementation of infection control measures within the health care setting, contact tracing and monitoring, use of antiviral drugs for the treatment of cases and targeted prophylaxis, intensified surveillance and the real-time reporting of data. The 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.

Case management

In the initial phase, when a manageable number of cases is assumed, clinical cases should be hospitalized and managed in single rooms if possible. Once laboratory confirmation of infection is available, and the number of cases exceeds the available number of single rooms, patients may be cohorted and managed in group isolation rooms. Depending on local circumstances and feasibility; group isolation rooms could be adapted to have negative pressure facilities.

When the number of cases exceeds the capacity of existing health care facilities, ill persons should be isolated in other designated areas or in individual homes, depending on the severity of their illness. National governments should identify potential isolation facilities as part of their preparedness planning 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 mild, moderate or severe respiratory illness must 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

Within the health care setting, infection control measures should be adhered to strictly. Recently, WHO has 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. They are available online, and can be accessed at:
http://www.who.int/csr/disease/avian_influenza/guidelines/infectioncontrol1/en/index.html

Antiviral treatment and targeted prophylaxis

In the containment zone, 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 define jointly (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.

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.

Intensified surveillance

Once the reported signal is confirmed to be an influenza alert requiring immediate intervention, surveillance activities should be intensified immediately within the initial outbreak zone. The surrounding area, and the geographically “at risk” areas, should also intensify their surveillance and remain on alert for possible introduction of the virus.

Within the outbreak zone, enhanced detection and reporting of individual cases and clusters of human-to-human transmission can be achieved through institution of active surveillance to identify all potential cases, and increased diagnostic suspicion. This is essential to:

– Manage the outbreak and monitor its evolution

– Evaluate the success of containment measures and the potential need to modify the strategy

All cases identified during this activity should be referred for appropriate case management. Attempts should be made to investigate as many cases as possible using the case investigation form. The initial investigation of cases 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 facilitate surveillance for cases in the outbreak zone and elsewhere, WHO will develop case definitions that include clinical, epidemiological, and laboratory criteria.

Contact tracing

During investigation and response, contact tracing must be implemented to 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 after last contact. If the number of contacts requiring investigation is large, follow up should be prioritized 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.

Monitoring contacts for signs of illness

Case contacts and the community at large should:

1. Be familiar with the risks factors and risk behaviours of exposure, and the signs and symptoms of the illness. The public should be informed of the most common symptoms which are fever and/or cough. They should receive instructions on how to self-monitor for fever post exposure, which should be performed for at least 7 days following the last contact with a possible case of influenza.
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 during the duration of self monitoring.
3. Be visited or telephoned daily by a member of the public health team to ascertain their clinical status. In remote and inaccessible areas, community focal points could be identified, trained and facilitated to monitor, report on clinical status and appropriately refer contacts who show symptoms.

Prompt investigation and treatment must be provided when symptoms are reported. Investigations can be undertaken at home, locally at an appropriate health care facility or in a designated field hospital.

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

Voluntary quarantine

Experience during the SARS outbreak suggests that quarantine, applied on a voluntary basis, may be as effective as enforced quarantine. 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. However, for voluntary quarantine to succeed, the public will need to be informed and sensitized on benefits.

National, sub-national, and local governments should be prepared to enforce, legally and operationally, 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 between 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 documented fully in scientific studies. They are, nonetheless, included here as some element of national pandemic preparedness plans. These may include:

– The closing of schools and workplaces

– Cancellation of mass gatherings and public transportation

– Border controls

Mass antiviral prophylaxis

Modelling studies also suggest that a pandemic might successfully be contained through geographically targeted prophylaxis with antiviral drugs, also known as “ring” prophylaxis. If mass prophylaxis is attempted, 90% coverage of the target populations should be the goal for successful containment.

Mass antiviral prophylaxis can be achieved in two ways:

– Mass prophylaxis of the affected population within a radius of 5–10 km from each detected case;
– Targeting administrative areas to cover the “at risk” population (10,000–50,000).

Each of the individuals is given a single course of oseltamivir (for a duration of 10 days). In the event that more cases arise among the targeted population, a second round of prophylaxis is administered.

Mass antiviral prophylaxis ceases automatically ten days after the date of symptom onset in the last reported case.

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, except in circumstances where the foreseeable benefits outweigh the risks. Such use should be undertaken only after adequate counselling and informed consent of the case or parents of the case.

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. All people reporting adverse events should be given advice on management of the event. National authorities should examine their responsibility for liability in their respective public health and legal systems should severe adverse events occur. WHO will not be responsible for liability concerning any adverse events.

IV Deployment of the antiviral stockpile for containment operation

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 made the request for the global stockpile. This authorization will be guided by the needs assessment and the decision to launch containment operations 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 be calculated to cater for treatment courses sufficient to treat 25% of the population and prophylactic courses for 10 days for the remaining 75% of the population in the containment zone. 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 delivery to the nearest international airport, where direct handover to WHO will take place. Officials in the affected country should be ready to authorize any package type and composition, and to waver liability. National authorities are also responsible for customs release and compliance with importation requirements.

Requesting and distributing the WHO global stockpile of antivirals.

Annex 2.1, presented in the form of a checklist, spells out the preparedness activities being undertaken by WHO and Roche in greater detail. WHO activities aimed at improving capacities within countries are also described.

Annex 2.2, devoted to activities within countries, suggests some preparedness activities for those countries wishing to include use of the global stockpile as a component of their preparedness plans.

Annex 3 sets out a standard operating procedure, developed by WHO, for use when requesting and distributing antiviral drugs from the global stockpile (annex 3).

Annex 3 is further supported by an activity checklist for stockpile deployment (annex 3.1), a timeline for deployment (annex 3.2), and a model form for use by countries when requesting oseltamivir for a containment operation (annex 3.3).

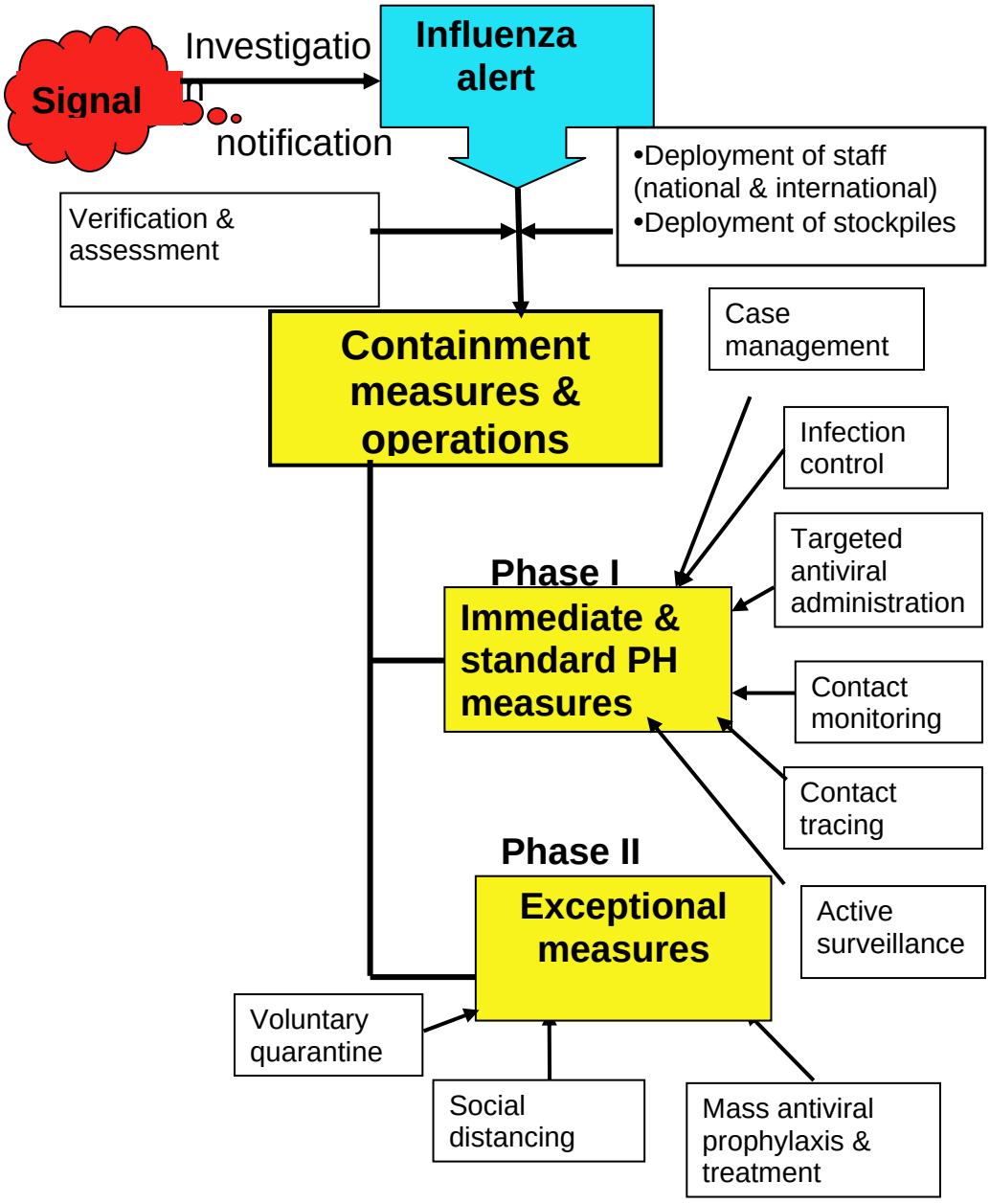
The remaining annexes describe the responsibilities of countries and WHO and explain the role of operational communications.

The activities, timelines, checklists, and roles and responsibilities set out in these annexes are considered the “ideal” prerequisites for success – the essential elements that, if in place early enough, will give the containment operation the greatest chances of success.

Further consultations with countries and partners will be held in the near future to review these activities, assess their feasibility, and work out ways of overcoming obstacles that may be identified. The results of these consultations will be used to develop country-specific protocols.

Work is also under way to develop training curricula and training materials for health workers, staff currently engaged in surveillance, and teams that will be deployed to investigate and contain the outbreak.

Annex 1: Flow chart for influenza response and containment operations



Annex 2: Overview of essential planning, preparedness and reporting activities

Background:

Member States of the World Health Organization (WHO) are looking to WHO to lead the effort to stop a novel strain of influenza virus from starting a pandemic. WHO has developed a Rapid Response and Containment Protocol to document its concept for accomplishing this goal.

Rapid response and containment of a novel influenza virus with pandemic potential is a complex, multifaceted operation that will employ numerous public health measures. The use of antiviral drugs is, however, a key component of the overall strategy.

F. Hoffmann-La Roche, Ltd. (hereafter referred to as Roche) has reserved 3 million therapeutic courses of its antiviral medication, oseltamavir, for use by WHO in a containment operation. These 3 million courses form the WHO global stockpile. Once a country, in close coordination with WHO, determines that a novel influenza virus has begun to spread from one person to another with increasing efficiency, the country or countries experiencing the outbreak may request quantities from the global stockpile to augment their own capabilities to contain the virus and prevent a pandemic or delay its spread.

Purpose: For oseltamivir to be an effective containment measure, all stakeholders, including WHO, Roche, and countries, need to plan now to ensure that several operational procedures can be undertaken with sufficient speed and efficiency. Such procedures involve the ways in which drugs in the global stockpile are requested, received, secured, distributed, stored and dispensed. Suggested preparedness measures are introduced below and then described in greater detail in subsequent annexes. This overview describes the actions that WHO headquarters, regional offices, country offices and countries should take in order to be prepared to request, receive, store, and distribute antiviral drugs.

Stockpile planning and preparedness

To ensure the timely delivery of drugs from the stockpile to an outbreak site, WHO and Roche need to have well developed, synchronized, and rehearsed plans available well in advance. Such plans help ensure that essential activities are launched as soon as a country's request has been approved. Many additional preparedness measures, that can be put in place in advance, can expedite delivery of oseltamivir to a country, once a request has been made. Annex 2.1 provides a checklist of these WHO and Roche preparedness actions.

Of equal importance, each country's national influenza preparedness plan should ideally have well developed and rehearsed executable plans that will enable them to receive,

store, transport/distribute, and dispense the drugs from the global stockpile rapidly to protect their populations and fulfil their role in the containment effort. For example, the plan should state “how” antivirals will be moved to the site of the outbreak, “who” will accomplish the movement, “what” transportation assets will be used, and “when” the antivirals will be moved following its arrival at the airport. The plans need to be backed up with contingency contracts with commercial partners or documented agreements with supporting governmental or non-governmental agencies.

Annex 2.2 provides a checklist of preparedness measures countries can take and a checklist for use in ensuring their national influenza preparedness plan includes necessary elements to request drugs and properly manage them upon receipt.

Reporting requirements

Ensuring that antiviral drugs are available when and where they are needed is critical to the success of a containment effort. At present, however, drug supplies to support country, regional, and global needs for containment are limited. The finite supply of drugs makes it important for WHO to include, as one of its preparedness objectives, the maintenance of good visibility on all antiviral assets that could conceivably be made available to support containment efforts and thus maximize the chances of success. This asset visibility can be achieved only through the reporting of all quantities of antivirals available for containment and the reporting of all antivirals distributed by owners (preferably following prior coordination with WHO) of the various regional stockpiles in support containment efforts. Without such visibility there is a significant risk that quantities shipped to the site of an initial outbreak may vastly exceed the containment requirement, while quantities available for subsequent outbreaks will be insufficient to be effective.

To obtain visibility on antiviral stocks available for containment efforts, countries should ideally provide a quarterly report of the amount of antivirals they have available for containment purposes in their country or for use by other countries or regions. Annex 2.3 provides a suggested reporting format. Reports should be submitted to WHO country offices on the 15th day of March, June, September and December and reflect containment inventory on hand as of the 14th day of that month. WHO Country Offices will submit reports to Regional Offices for compilation and submission to the WHO SHOC.

International organizations/associations that have acquired antivirals for containment purposes are also requested to submit quarterly reports directly to the WHO SHOC. Countries and international organizations/associations should submit their initial reports on 15 June 2006.

At the same time, however, WHO recognizes that quantities of drugs held in national or other stockpiles may constitute politically sensitive information. Disclosure of this information, though highly desirable, remains at the discretion of countries.

Annex 2.1: WHO and Roche Recommended Preparedness Actions Checklist (for discussion)

Item #	Requirement	Completed		Comments
		Yes	No	
WHO HQ Preparedness actions:				
2.1.1	Identify priority countries for a gap analysis of logistics capacity			
2.1.2	Conduct gap analysis of country logistics capacities in coordination with WHO Regional Offices, Country Offices, countries, Roche and partner UN agencies			
2.1.3	Develop contingency plans to mitigate gaps identified in countries			
2.1.4	Develop deployment decision criteria			
2.1.5	Develop global asset visibility of antivirals in coordination with WHO Regional Offices, Country Offices, countries, and Roche			
2.1.6	Implement 24 hour on-call duty officer system			
2.1.7	Compile list of Country Office representatives, and country representatives designated to sign for global stockpile			
WHO Regional Office Preparedness actions:				
2.1.8	Collaborate with WHO HQ, Country Offices, countries, and partner UN agencies to conduct a logistics capacity gap analysis for each country within the region			
2.1.9	Collaborate in development of contingency plans to mitigate capacity gaps in logistics identified in countries at highest risk for an outbreak			
2.1.10	Develop asset visibility of antivirals available to the region for purposes of containment and provide quarterly status reports to the WHO SHOC by fax or email.			

Annex 2.1: WHO and Roche Recommended Preparedness Actions Checklist (for discussion)

Item #	Requirement	Completed		Comments
		Yes	No	
2.1.11	Compile updated status information from Country Offices and submit quarterly to WHO SHOC by fax or email, including status of: • oseltamivir registration/ licensure/ waiver • Expedited landing rights procedures • Expedited procedures to process antivirals through customs • Identification of Country Office and country representatives to sign for oseltamivir • antiviral assets available for containment			
WHO Country Office Preparedness actions:				
2.1.12	Collaborate with the Regional Office, WHO HQ, countries, and partner UN agencies to conduct a logistics capacity gap analysis for each country within the region			
2.1.13	Collaborate in development of contingency plans to mitigate logistics capacity gaps identified in countries at highest risk for an outbreak			
2.1.14	Develop asset visibility of antivirals, available to the country for purposes of containment and provide quarterly status reports to the Regional Office.			
2.1.15	Identify the Country Office representative who will accept the oseltamivir from Roche and provide contact information to Regional Office.			
2.1.16	Validate the country has registered/licensed oseltamivir for use and advise regional office.			

Annex 2.1: WHO and Roche Recommended Preparedness Actions Checklist (for discussion)

Item #	Requirement	Completed		Comments
		Yes	No	
2.1.17	Validate country has developed procedures to expedite approval of landing rights to enable delivery of antivirals within 24 hours and advise regional office.			
2.1.18	Validate country has developed procedures to expedite antivirals through customs and advise regional office.			
2.1.19	Validate and understand the process the country will use to expedite the issuance of visas to WHO HQ staff arriving in conjunction with the oseltamivir			Visitors will require immediate entry
2.1.20	Obtain the name and contact information for the country representative that will sign for antivirals from the Country Office representative			Name and contact information:
Roche Preparedness actions:				
2.1.21	Develop capability to deploy oseltamivir to arrive at the international airport nearest the site of an outbreak, but within the country of the outbreak within 24 hours of a decision to deploy			
2.1.22	Assess the supply chain between Roche storage locations and the international airports with highest probability of becoming a designated delivery point to determine their suitability for product receipt and handoff			
2.1.23	Coordinate security of oseltamivir at storage site and during transport from the storage site to the destination airport			
2.1.24	Rotate WHO designated oseltamivir to ensure product deployed has a minimum of 6 months remaining on its shelf life			

Annex 2.2:
Recommended Member State Preparedness Checklist (Global Stockpile)

Item #	Requirement	Completed		Comments
		Yes	No	
2.2.1	The country has developed a national influenza preparedness plan that is consistent with the WHO global influenza preparedness plan, the WHO Rapid Response and Containment Protocol and contains the recommended content in Tab A			
2.2.2	The plan has been fully exercised--including the portions related to requesting, receiving, storing, and dispensing of the global stockpile of antivirals.			Date of last exercise:
2.2.3	oseltamivir is registered/licensed or a waiver for licensure been granted			This information must be provided to WHO with request for oseltamivir. If registration/licensure is waived, a copy of the waiver must accompany the request.
2.2.4	An adequately sized and environmentally controlled storage location for oseltamivir has been identified and a contract or agreement to use the space is in place (see Tab B for storage requirements)			
2.2.5	The storage location (if utilized) has loading docks and forklifts and operators are available			Number of loading docks: Number of forklifts: Number of licensed operators:
2.2.6	The country has the capacity to distribute (transport) antivirals to a containment site within 12 hours			If not, specify additional requirements:
2.2.7	The necessary/appropriate arrangements/agreements/contracts have been made to ensure transportation resources will be available when required			
2.2.8	Processes/procedures have been established to rapidly grant landing rights to aircraft delivering antivirals			
2.2.9	Arrangements have been made to expedite antivirals through customs.			

Annex 2.2:
Recommended Member State Preparedness Checklist (Global Stockpile)

Item #	Requirement	Completed		Comments
		Yes	No	
2.2.10	The country has established procedures to ensure immediate approval of visas for WHO staff supporting the transfer of oseltamivir to the receiving country			
2.2.11	The country has the capability to secure the antivirals while at airport, being transported, or in storage			What security measures will be used and are they currently available?
2.2.12	International airports have appropriate equipment to rapidly off load antivirals from aircraft and upload them onto trucks			Mobile loading platforms and forklifts
2.2.13	The country focal point who will accept the antivirals from the WHO Country Office representative has been identified			Specify name and contact information (phone, fax, e-mail) on request for antivirals
2.2.14	Communications equipment required to support operational needs has been identified and is on hand			
2.2.15	A public information plan has been developed that includes notifying the public of receipt of antivirals			
2.2.16	The country has the capability and capacity to produce product information sheets for recipients of antivirals			

Tab A to Annex 2.2:
Recommended Member State Preparedness Plan Checklist (Global Stockpile)

Item #	Requirement	Completed		Comments
		Yes	No	
2.2A.1	The plan is updated annually			
2.2A.2	The plan includes procedures for evaluating the need to request antivirals from the global stockpile			
2.2A.3	The plan includes procedures for requesting global stockpile antivirals from WHO			
2.2A.4	The plan includes procedures for managing antivirals received from the global stockpile for containment purposes, including:			
2.2A.5	• Expediting antivirals provided for containment through customs			
2.2A.6	• Receiving antivirals from the WHO Country Office representative			
2.2A.7	• Transporting antivirals to the containment site to arrive within 12 hours			
2.2A.8	• Dispensing of antivirals to priority groups			
2.2A.9	• Security of the antivirals from its arrival in the country through dispensing			
2.2A.10	• Provision of antivirals product information sheets in the appropriate language for recipients of the pharmaceutical			
2.2A.11	The plan been shared within the Ministry of Health and with other stakeholder ministries			
2.2A.12	The plan is clear in defining:			
2.2A.13	• The chain of command			
2.2A.14	• Who will make decisions regarding the use of the antivirals			
2.2A.15	• Reporting requirements			
2.2A.16	The plan delineates jurisdictional responsibilities in countries with			

Tab A to Annex 2.2:
Recommended Member State Preparedness Plan Checklist (Global Stockpile)

Item #	Requirement	Completed		Comments
		Yes	No	
	multiple jurisdictional regions?			
2.2A.17	The plan provides for a method to gather information about the situation to assist WHO in making a decision to deploy global stockpile assets			
2.2A.18	The plan identifies the key information needed to assist the WHO in making a decision to deploy global stockpile assets			
2.2A.19	The plan lists key people and agencies to notify once a decision to deploy global stockpile assets has been made			
2.2A.20	The plan has a sequence to activate the distribution system including all the functions of:			
2.2A.21	• Command and Control			
2.2A.22	• Communications			
2.2A.23	• Security			
2.2A.24	• Distribution			
2.2A.25	• Warehouse management			
2.2A.26	• Dispensing			

Tab B to Annex 2.2:
Storage Requirements/Planning Factors (Global Stockpile)

Oseltamivir in the global stockpile is packaged in strip packs of 10 capsules each. Each strip pack comes in an individual box (Figure 1).

Figure 1

Individual boxes are packaged in intermediate packages of 10 individual boxes, and 44 intermediate packages (440 strip packs) are in one shipping box.

Each shipping box measures 595mm long*390mm wide*360mm high and weighs 7.8 kg

Shipping boxes are configured on pallets measuring 120cm*80cm. The height of the pallet depends on the number of layers of boxes as displayed in Figure 2 below:

Layers	Height of Pallet (cm)	Number of Shipping Boxes per Pallet	Weight of Product on Pallet (kg)
2	87	8	62.4
3	120	12	93.6
4	160	16	124.8
5	196	20	156.0

Figure 2

Based on a 3 layer configuration (12 boxes/pallet), each pallet will contain 5280 treatment/prophylaxis courses (10 capsule strip packs). Figure 3 depicts the number of pallets countries should plan to receive based on the number of people requiring treatment/prophylaxis courses.

Number of People to Treat/Prophylaxis	Number of Shipping Boxes	Number of Pallets
10,000	23	2
25,000	57	5
100,000	228	19
250,000	569	48

Figure 3

Storage temperature: 25°C (77°F) with permitted excursions between 15° and 30°C (59°- 86°F)

Annex 2.3
Antiviral Reporting (Rapid Response and Containment)
(Requested Reporting Frequency: Quarterly on 15th day of March, June, September, December)

1. Date of Report:_____

2. Country or International Organization Name:_____

3. oseltamivir for containment (specify number in terms of 10 capsule packages)

    a. Quantity for use within my country: _____ packages
    b. Quantity for use in other countries: _____ packages.
    Identify any restrictions your government (or governing body) has established for use of this oseltamivir by other countries (for example, it is only available to countries in a specific region)
    Restrictions: _____
    _____
    _____

4. Other antivirals available for containment:

    a. Name of antiviral: _____
    b. Manufacturer: _____
    c. Quantity for use within my country: _____ treatment courses.
    d. Quantity for use in other countries: _____ treatment courses.
    Restrictions: _____
    _____
    _____

Report submitted by: _____

Annex 3: SOP for requesting and distributing the WHO global stockpile of antivirals

1. **Background:** F. Hoffman-La Roche, Ltd. (hereafter referred to as Roche) has reserved 3 million therapeutic courses of the antiviral medication, oseltamivir, for use in containment efforts. These 3 million courses form the WHO global stockpile. Once a country, in close coordination with WHO, determines that a novel influenza virus has begun to spread from human to human, the country or countries experiencing the outbreak may request quantities from the global stockpile to augment their own and regional capabilities to contain the virus and prevent a pandemic.

2. **Purpose:** This SOP specifies:

   2.1. processes and procedures that countries will use to request antivirals (paragraph 3 and Annex 3.1);
   2.2. the processes and procedures WHO will use to evaluate country requests and notify Roche of the decision to deploy (paragraph 4 and Annex 3.1);
   2.3. WHO and Roche responsibilities and steps for deploying oseltamivir (paragraph 5 and Annex 3.1);
   2.4. steps and responsibilities for receiving, storing, distributing, dispensing, reporting and monitoring use of antivirals within the recipient country (paragraph 6 and Annex 3.1).

3. **Country requests for antivirals from the global stockpile and the deployment decision.** Time is a critical factor to the success of a rapid response and containment effort. It is therefore essential to streamline the process of reporting a signal and requesting antivirals from the global stockpile by encouraging direct communications between countries and WHO HQ.

   3.1. Once a country determines the need for antivirals from the global stockpile, the Minister of Health or other appropriate government official will:
      3.1.1. immediately notify the WHO duty officer;
      3.1.2. immediately notify the WHO Country Office;
      3.1.3. complete the "WHO Global Stockpile Antiviral Request Form" (Annex 3.3) and fax or email it to the WHO SHOC providing the following information:
         - Geographical location of cases
         - Population size and density in the outbreak area
         - Size and level of healthcare facilities within the outbreak area
         - Accessibility by road and air
         - Possible security concerns
         - In-country stocks of antivirals and PPE
         - antiviral requirements
      3.1.4. Provide WHO Country Office with a copy of the request.

4. WHO evaluation of country requests and notification of Roche.

4.1. Upon receipt of the telephone notification and subsequent fax/e-mail submission of the completed "WHO Global Stockpile Antiviral Request Form", the WHO duty officer will:

4.1.1. Confirm receipt of the notification/request/worksheet via fax/e-mail to the requesting country;

4.1.2. Coordinate a conference call among key personnel (specific positions TBD) within WHO HQ, WHO Regional and Country Offices, selected external partners and the requesting country. The call will occur ASAP following receipt of the "WHO Global Stockpile Antiviral Request Form" to develop a recommendation on deployment of the requested antivirals from the global stockpile.

4.1.3. Notify the Roche focal point of the potential deployment, providing:

- the geographical location of the cases;
- current status of the country's antiviral stocks, and;
- the quantity of antivirals the country is requesting.

4.1.3.1.Upon notification of a potential deployment Roche will:

4.1.3.1.1. notify their logistics agent which will:

4.1.3.1.1.1.work with WHO SHOC to identify the nearest international airport within the country of the outbreak[3] for the shipment;

4.1.3.1.1.2.assess the supply chain (or validate previously conducted assessment) to the potential destination airports and the infrastructure available at the airports.

4.1.3.1.1.3.identify issues/concerns and provide to the WHO SHOC for discussion with the requesting country, and;

4.1.3.1.1.4.recommend the destination airport for final decision by the WHO SHOC in coordination with the rapid response and containment work group lead.

4.1.3.1.2. send a representative from its company or its logistics agent to the WHO SHOC to serve as a liaison facilitating communication and coordination. The liaison should arrive ASAP, but no later than 8 hours of the notification of the request to deploy the stockpile.

4.2. WHO HQ (Event Manager) will lead the teleconference and validate the following during the course of the conference call:

4.2.1. Evidence of an outbreak is sufficient to warrant deployment of a portion of the stockpile;

[3] While the nearest international airport to an outbreak may be in a different country, the risk associated with delays that may result from importation and exportation or possible nationalization of oseltamivir, may negate any advantages associated with proximity.

4.2.2. The size of the outbreak and the number of people at risk are consistent with the amount of antivirals requested
4.2.3. Information available indicates containment is feasible and should be attempted;
4.2.4. Antiviral is licensed in the country, or a waiver for its use is in place;
4.2.5. Arrangements are in place to expedite any approved shipment through customs;
4.2.6. The country has security measures in place to ensure all product will reach the containment area;
4.2.7. Adequate equipment for handling material is available and a secure storage site is available for any interim storage requirements, and;
4.2.8. Adequate resources are available to distribute/transport and dispense the antivirals to and within the containment area.

4.3. Based on analysis of technical, operational, and legal/policy information discussed in the WHO conference call with the country, a recommendation to deploy, or not deploy, antivirals from the global stockpile for containment purposes will be made to the Assistant Director-General, Communicable Diseases (ADG/CDS). Three possible recommendations may be made:
4.3.1. Deploy all or a portion of the global stockpile to the requesting country;
4.3.2. Do not deploy any portion of the global stockpile for containment purposes. Such a decision would be based on conditions defined in the WHO protocol for rapid response and containment that specify when containment measures should not be attempted.
4.3.3. Do not deploy at present, but continue preparatory actions to deploy until sufficient evidence is obtained to make a final decision. This decision would be interim until additional evidence was gathered or until necessary internal/external consultations with experts lead to a final decision.

4.4. The ADG/CDS will present the recommendations to the Director-General for final decision.

4.5. WHO HQ will communicate its decision to Roche, the requesting country, and the WHO Regional and Country Offices immediately after the decision is made.

5. **Deployment of oseltamivir from the global stockpile.** Annex 3.2 depicts the deployment timeline of the stockpile.

5.1. When the decision is made to deploy the global stockpile, WHO SHOC will:
5.1.1. Fax or send an email to Roche within one hour, providing the following:
5.1.1.1.A written order specifying the quantity to be deployed
5.1.1.2.A Donation Letter specifying the oseltamivir is a donation from WHO to the country (required for customs clearance)

5.1.1.3.Contact information of the WHO representative to accept delivery of the product from Roche, including:

- Name
- Telephone (work, mobile)
- Fax number
- Email address

5.2. The WHO Alert and Response Operations (ARO) will send a logistician to the departure airfield to:

5.2.1. accompany the shipment;
5.2.2. assist the WHO Country Office with customs clearance, and;
5.2.3. ensure transfer of oseltamivir to the WHO Country Office representative.

5.3. WHO HQ will immediately deploy a senior representative of the Director-General (DG) and a senior representative of the Rapid Response and Containment working group.

5.3.1. The DG representative will assist and support the WR in:
5.3.1.1. interfacing with the Ministry of Health and external organizations;
5.3.1.2. managing international aspects of exposure.
5.3.2. The containment working group representative will:
5.3.2.1. facilitate the receipt and transfer of oseltamivir;
5.3.2.2. help ensure the intent of the containment stockpile is being met by the recipient country through monitoring and providing/coordinating assistance.
5.3.3. To facilitate these deployments, the following actions will occur:
5.3.3.1.The SHOC will provide the names and necessary information to secure a visa to the appropriate Country Office
5.3.3.2.The Country Office will work with the country to ensure visas for urgently deploying HQ staff are approved

5.4. Roche will coordinate deployment of the requested quantity of oseltamivir, ensuring that:

5.4.1. product is palletized on non-wooden (e.g. plastic) or ISPM 15 compliant wooden pallets (with certificates)
5.4.2. necessary customs documentation for shipment is provided to the receiving WHO Country Office representative (consignee), the SHOC and to the WHO logistician accompanying the shipment, including:
5.4.2.1.Certificate of Origin for oseltamivir
5.4.2.2.Donation Letter (provided to Roche by WHO)
5.4.2.3.Certificate of Analysis for the lots being shipped
5.4.2.4.Invoice
5.4.2.5.Packing list
5.4.2.6.Airway Bill
5.4.2.7.ISPM 15 certification for wooden pallets

5.4.3. the objective is for the product to be airborne within 12 hours of the decision to deploy and delivered to the WHO designated representative within 24 hours of the decision to deploy

5.4.4. security is provided en route from the Roche distribution facility to the arrival airport.

5.4.5. WHO SHOC is kept informed of flight schedule and status of delivery

5.5. The Country Office will accomplish the following steps prior to arrival of antivirals:

5.5.1. Coordinate customs clearance with the appropriate country ministry;

5.5.2. Coordinate with the country to ensure preparations are made to provide for security, distribution, storage, and dispensing of antivirals;

5.5.3. Meet the shipment at the airport.

5.6. The WHO SHOC (Event Manager) will track and communicate the status of the deployment of the materiel through communication and coordination with the Roche POC and the WHO Country Office representative. The critical information points include:

5.6.1. Status of product and aircraft (prior to departure)

5.6.2. Departure of aircraft and estimated time of arrival (ETA)

5.6.3. Arrival of aircraft at destination

6. Receiving, storing, distributing, and dispensing antivirals.

6.1. The WHO Country Office will:

6.1.1. Accept delivery of oseltamivir from Roche

6.1.2. Monitor security, storage, distribution, and dispensing and report status of containment effort to the WHO SHOC (Event Manager)

6.2. Once antivirals has arrived at the designated airport, the receiving country will:

6.2.1. Expedite clearance of antivirals through customs

6.2.2. Provide security for antivirals at airport and while in-transit or storage

6.2.3. Provide rapid clearance for aircraft departure to return to airport of origin

6.2.4. Distribute antivirals to containment area

6.2.5. Dispense antivirals according to country plan and in accordance with recommendations and advice of rapid response and containment protocol, country and international technical experts

6.2.6. Allow WHO representatives to monitor security measures, storage, distribution, and dispensing

6.2.7. Report the status of antivirals stocks on a weekly basis to the WHO SHOC (Event Manager), until the containment effort is completed

6.2.8. Request additional antivirals from the WHO SHOC (Event Manager) as necessary to continue containment effort, allowing a minimum of one week for delivery.

6.3. The WHO SHOC (Event Manager) will track and communicate the status of the distribution and dispensing of the materiel through communication and coordination with the WHO Regional and Country Office representatives. The critical information points include:

6.3.1. Clearance of product through customs

6.3.2. Status of product delivery to storage and/or containment area

6.3.3. Follow-on requests by the country for additional antivirals

Annex 3.1
Activity Checklist for Deploying the Global Stockpile of Tamiflu®

Task #	Activity	Accountable Entity	Timeframe
3.1.1	Country determines it has a requirement for antivirals to contain an outbreak	Country	
3.1.2	Telephone notification to: • the WHO duty officer • the WHO Country Office	Country	ASAP
3.1.3	Completed "WHO Global Stockpile Antiviral Request" (Annex 3.3) faxed or emailed to the following: • WHO SHOC • WHO Country Office	Country	Immediately following telephone notification
3.1.4	Confirm receipt of "WHO Global Stockpile Antiviral Request Form" with country via fax or e-mail	WHO Duty Officer	Immediately following receipt
3.1.5	Coordinate a conference call among key personnel (specific positions TBD) within WHO HQ, WHO Regional and Country Offices, selected external partners and the requesting country.	WHO Duty Officer	Immediately following confirmation to country
3.1.6	Notify Roche focal point of potential deployment of global stockpile, providing: • the geographical location of the cases; • current status of the country's antiviral stocks, and; • the quantity of antivirals the country is requesting.	WHO Duty Officer	Immediately following coordination of conference call
3.1.7	Roche notifies their logistics agent which: • Assesses the supply chain into the designated country • Identifies the in-country international airport nearest the outbreak area in coordination with WHO SHOC • Assesses the infrastructure at the airport, identify issues/concerns and make recommendation for use – WHO SHOC makes gives final approval • Begins initial coordination with their air carrier.	Roche	Immediately upon notification of a possible deployment
3.1.8	Roche sends a liaison officer to WHO SHOC to facilitate communication and coordination	Roche	ASAP after notification of potential to deploy

Annex 3.1
Activity Checklist for Deploying the Global Stockpile of Tamiflu®

Task #	Activity	Accountable Entity	Timeframe
3.1.9	WHO Event Manager leads teleconference with key personnel (TBD) to validate the following: • Evidence of an outbreak is sufficient to warrant deployment of a portion of the stockpile; • The size of the outbreak and the number of people at risk are consistent with the amount of antivirals requested • Information available indicates containment is feasible and should be attempted; • Antiviral is licensed in the country, or a waiver for its use is in place; • Arrangements are in place to expedite any approved shipment through customs; • The country has security measures in place to ensure all product will reach the containment area; • Adequate handling equipment is available and a secure storage site is available for any interim storage requirements, and; • Adequate resources are available to distribute and dispense the antivirals to and within the containment area.	WHO Event Manager	ASAP following receipt of request
3.1.10	WHO Event Manager makes deployment recommendation to ADG/CDS	WHO Event Manager	Immediately following teleconference
3.1.11	ADG/CDS makes recommendation to DG for final decision	ADG/CDS	ASAP
3.1.12	Final decision communicated to country, WHO and Roche	WHO Event Manager	Immediately following decision

Annex 3.1
Activity Checklist for Deploying the Global Stockpile of Tamiflu®

Task #	Activity	Accountable Entity	Timeframe
3.1.13	If decision made to deploy stockpile, notify Roche and provide a Donation Letter and an order document with the following information: • Quantity to be deployed • Contact information for the WHO representative to accept delivery of the product from Roche, including: o Name o Telephone (work, mobile) o Fax number o Email address	WHO/SHOC	Within one hour of decision
3.1.14	WHO HQ logistician sent to accompany shipment and coordinate customs clearance and transfer of oseltamivir to WHO Country Office representative at arrival airport	WHO/ARO	Immediately upon decision to deploy
3.1.15	Senior representative of Director-General and senior representative of rapid response and containment work group deploy to country receiving global stockpile • Names of WHO HQ representatives provided to Country Office by WHO SHOC • Country Office works with receiving country to obtain visas to enable immediate entry	WHO HQ Country Office/Country	Immediately upon decision to deploy

Annex 3.1
Activity Checklist for Deploying the Global Stockpile of Tamiflu®

Task #	Activity	Accountable Entity	Timeframe
3.1.16	Roche coordinates deployment of required quantity of oseltamivir to arrive at destination within 24 hours of decision to deploy oseltamivir[4] • Coordinates security from storage site to departure airport and in-flight requirements • Product palletized on non-wooden or ISPM 15 compliant wooden pallets • Generates the following documents: o Certificate of origin for oseltamivir o Donation Letter (provided to Roche by WHO) o Certificate of Analysis for lots being shipped o Invoice o Packing list o Airway bill o ISPM 15 certification for any wooden pallets • Keep WHO SHOC informed of status of shipment and scheduled delivery	Roche	Aircraft departure within 12 hours of decision, with target arrival at destination airport within 24 hours
3.1.17	WHO Country Office representative will: • Coordinate customs clearance with appropriate country minister • Coordinate with country to ensure preparations are made to provide for security, distribution, storage, and dispensing of antivirals • Meet shipment at airport • Accept delivery of oseltamivir from Roche • Monitor security, storage, distribution, and dispensing and report status of containment effort to WHO Event Manager	WHO Country Office	Upon notification of decision to deploy and throughout containment effort

[4] The objective delivery time for oseltamivir is 24 hours from the decision to deploy, however, availability of aircraft or finalization of legal documentation required by countries may result in a delay of up to 48 hours.

Annex 3.1
Activity Checklist for Deploying the Global Stockpile of Tamiflu®

Task #	Activity	Accountable Entity	Timeframe
3.1.18	Receiving country will: • Expedite clearance of antivirals through customs • Provide security for antivirals at airport, and while in-transit or storage • Provide rapid departure clearance for aircraft to return to airport of origin • Distribute antivirals to containment area • Dispense antivirals according to country plan, WHO rapid response and containment protocol, and recommendations from technical experts • Allow WHO representatives to monitor security, storage, distribution, and dispensing • Report the stock status of antivirals on a weekly basis to the WHO SHOC • Request additional antivirals to continue containment effort	Country	Dispensing of antivirals to begin within 12 hours of receipt
3.1.19	Track status of deployment, including: • Status of product and aircraft (prior to departure) • Departure of aircraft and estimated time of arrival • Arrival of aircraft at destination • Clearance of product through customs • Status of product delivery to storage and/or containment area • Asset visibility of antivirals in country • Follow-on requests for additional antivirals	WHO/SHOC in coordination with Roche	Ongoing

Annex 3.2: Oseltamivir deployment timeline

	Task	Lead	Timing (Best Case)
3.2.1	Member state informs WHO about possible outbreak. Samples sent to authorized laboratory for analysis. WHO sends assessment team	**Member State**	**H-48**
3.2.2	WHO informs Roche about potential need for rapid response	**WHO**	**H-48**
3.2.3	WHO officially informs Roche to proceed with shipment and informs about quantity, delivery place and name of WHO representative.	**WHO**	**H-48**
3.2.4	WHO faxes/e-mails written order stating complete addressee (name, tel, fax, e-mail) of contact at destination for handover of goods.	**WHO**	**H+1**
3.2.5	Roche forms global CMT and starts planning shipping activities	**Roche**	**H+1**
3.2.6	Roche informs WHO about flight schedule	**Roche**	**H+6**
3.2.7	Roche internal information about flight schedule to named persons	**Roche**	**H+7**
3.2.8	WHO informs member country office about flight schedules and ensures reception of goods	**WHO**	**H+8**
3.2.9	Shipment takes place	**Roche**	**H+12**
3.2.10	Shipment notification to WHO representative	**Roche**	**H+12**
3.2.11	Flight to destination	**Carrier**	**H+12 to 24**
3.2.12	Arrival at destination and unloading	**Carrier**	**H+24**
3.2.13	Roche informs WHO about arrival of goods at destination and handover to WHO representative	**Roche**	**H+24**
3.2.14	WHO and receiving country's authorities assume responsibility for security, transportation, storage, and dispensing of oseltamivir	**WHO and Member state**	**H+24**

Annex 3.3: WHO Global Stockpile Antiviral Request Form

Countries requesting antivirals from the WHO global stockpile for rapid response and containment must complete this request form, and fax or email the document to the WHO SHOC.

Date of Request: _____ Country: _____
Primary Language:_____

Factors

1. Specify the geographical location and dispersion of the cases
   _____
   _____

2. Specify the population size and density (urban, rural) of the containment area: _____

3. Specify the number, size and level of healthcare facilities within the outbreak area:
   _____

4. What is the nearest in-country international airport to the outbreak area and have procedures to expedite granting of landing rights implemented?
   _____

5. Is the outbreak area accessible by air and/or road (paved, gravel or dirt)? Yes/No (circle one)
   5.1. How will product be moved from the international airport to the outbreak site?
   _____

6. What are the security arrangements for antivirals while in storage or being transported? Are there any security concerns? (if so, specify in comments).
   _____
   _____

7. Specify the amount of antivirals currently in-country for use in containment (treatment of prophylaxis)--state the amount in terms of 10 capsule packages: _____

8. What arrangements are in place to expedite processing of antivirals through Customs?
   _____
   _____

9. Will antivirals be stored after it is received in the country? Yes/No (circle one)
   9.1. Is the storage site climate controlled (15°C-30°C)? Yes/No (circle one)
   9.2. Is sufficient materiel handling equipment (MHE) available? Yes/No (circle one)

   Comments:
   _____
   _____
   _____
   Requested quantity of oseltamivir (number of packages of 10 capsules): _____

Name of local recipient:
_____
Address of local recipient (delivery address for oseltamivir):
_____
_____
Tel: _____ Fax:_____ E-Mail: _____

I certify that:
1. The above information is factual;
2. That the requested antiviral is registered/licensed in this country or the government has issued a waiver to allow for its import and use (a copy is attached).
3. That neither WHO nor Roche will be charged import duty for the oseltamivir donation;
4. That oseltamivir received from the WHO global stockpile will be used solely for the purpose of containment of an influenza outbreak caused by a novel virus.
5. That visas are available for the WHO HQ representatives associated with the shipment.
6. I am the designated authority of my country to request oseltamivir for containment purposes (documentation of this authority, signed by the Minister of Health or Minister of Foreign Affairs is attached)

Printed name: _____

Signature: _____

Position: _____

Annex 4: Roles and responsibilities of countries and WHO in rapid response and containment

Roles and responsibilities of countries

1. Preparedness planning

Countries should ensure that their national pandemic preparedness and contingency planning is consistent with the co-ordinating role of WHO and partners during international response. National pandemic preparedness plans should address the issue of integration of national resources for rapid response and containment. These plans should be made flexible and should continuously be updated to incorporate national and international developments.

Countries have specific responsibilities 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 (Annex 2 provides planning and preparedness checklists for obtaining and using antivirals from the WHO global stockpile);
- 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 detect unusual disease, or moderate-to-severe acute severe respiratory illness, that could be the early signs of emerging pandemic influenza rapidly;
- Train clinicians, primary health care providers, traditional healers, primary care providers in other sectors e.g. animal health, and the wider community to detect and manage clusters of moderate-to-severe acute respiratory illness, and to report these clusters to the appropriate public health authorities;
- Ensure rapid confirmation the etiological agent either within the country if the capacity exists, or at a WHO reference laboratory.
- Facilitate rapid response and containment by identifying and modifying the legislative, administrative and other impediments to the implementation of rapid containment;
- Identify multidisciplinary teams for training in rapid response and containment;
- Identify and train technical partners and NGOs that may be required to support implementation of containment operations. These could include 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;
- Investigate potential pandemic signals as defined in this protocol rapidly, and facilitate the risk assessment for rapid response and containment by collecting the core dataset required for signal interpretation and decision making;
- Seek support from WHO immediately 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;
- Intensify surveillance for cases of mild, moderate and severe respiratory illness inside 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 countries, on request, with the development of national rapid response and containment plans as an integral part of the national preparedness plan;
- Support countries in building core capacities for detection, response and containment of possible influenza pandemic, 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 and requesting antivirals from the global stockpile;
- Develop and implement training for national and international members of rapid response and containment teams.
- Strengthen mechanisms for collection and transportation of clinical specimens for rapid testing and confirmation at a reference laboratory or WHO collaborating centre;
- Identify and mobilize staff and experts from the Global Outbreak Alert and Response Network (GOARN) and the regional response networks for rapid deployment during containment operations;
- 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
    - Declaration of a phase change if containment fails
- Develop a media communications strategy in the event of pandemic influenza emergence;
- Develop information, education and communication (IEC) materials for distribution in the containment zone and beyond to encourage and reinforce positive behavioural change;
- 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 in rapid response and containment operations, and who can be mobilized into teams quickly. 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 a 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, social mobilization, health promotion, risk communication, mental health and social welfare of people and response staff in the containment zone, and to provide "surge" capacity for critical operations. The national teams should be trained in influenza rapid response and containment operations, activities and team dynamics.

WHO will establish a teaching curriculum and course materials, including "training of trainers" materials. Each training session will last approximately one to two weeks per group. The initial teaching venue will be at WHO in Geneva, Switzerland, but future training of trainers will be held at regional venues. Training for national staff may be conducted within an affected country.

3. During rapid response and containment

- Coordinate the international response to rapid containment, including the deployment of international field teams to affected countries (upon request);
- Upon request, assist countries 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;
- Mobilize and dispatch the resources (antiviral, other materials and logistics) for rapid containment operations;
- Mobilize financial resources for rapid response operations;

- Ensure appropriate control and accountability is in place for material and financial resources.

Annex 5: 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 Communications Guidelines*.

Objectives

- To instill and maintain public 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 the efficient transmission of a pandemic virus.
- To provide accurate, timely, consistent, and comprehensive information about containment activities.
- To identify and addresses inaccuracies, and misperceptions quickly and prevent stigmatization of affected groups.
- To promote compliance within the containment zone, to identify barriers to compliance rapidly, 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.
- Mobilise HQ's network of risk/outbreak communicators, to give advice where requested and to undertake the deployment of communications officer(s) to the 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 maintain public 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 on the "novel" influenza outbreak or emerging pandemic, and containment activities.
- To contribute to the maintenance of order, minimization of public fear, and the facilitation of public protection.
- To manage rumours rapidly, and handle inaccuracies, and misperceptions as quickly as possible, so preventing 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 effected (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.