

# WHO activities in avian influenza and pandemic influenza preparedness

January - December 2006





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## Introduction

The World Health Organization (WHO), its Member States and its partners have been monitoring the possibility of a new pandemic of human influenza since 1968 when the last of the previous century's three pandemics began. Concerns were raised in early 2004 following reports that a new highly pathogenic strain of avian influenza, H5N1, was spreading across Asia, infecting both poultry and people. Although the virus has not yet gained the capacity for sustained human-to-human transmission, it continues to undergo genetic changes and has the potential to develop this capacity. By the end of December 2006, the virus had infected 263 people in ten countries from eastern Asia to Turkey<sup>1</sup> and a total of 158 people had lost their lives, almost half of whom died in the last 12 months.

These events have given the world its first advance warning that a pandemic may be near and an unprecedented opportunity to undertake appropriate protective actions. Pandemic influenza is a global threat from which no country is immune and the actions required are a shared responsibility of the whole international community. The experience of SARS has demonstrated that in the 21st century a pandemic virus could spread throughout the world in a matter of months, if not weeks.

The principal tasks facing the international community are twofold: (1) reduce the opportunities for the H5N1 virus to improve its pandemic potential and (2) be prepared for a pandemic should these efforts fail.

In November 2005, a meeting was convened by WHO, the Food and Agriculture Organization (FAO), the World Organisation for Animal Health (OIE) and the World Bank to review the current status of highly pathogenic H5N1 avian influenza in animals and to assess the risks it posed to humans including the likelihood of the virus developing pandemic potential.

The meeting agreed that solutions should be based as far as possible on existing infrastructures and mechanisms at both the country and regional level. Any additional emergency measures that would be needed should be combined with longer-term measures aimed at strengthening institutional capacities that would equip the world to protect itself in the long term against other emerging and epidemic-prone infectious diseases.

A 12-point action plan was drawn up. WHO is taking the lead in the five key areas that concern human health: to reduce human exposure to the H5N1 virus, to strengthen the early warning system, to put in place measures that might contain an emerging pandemic influenza at its source, to increase the capacities of countries and the international community to prepare for and cope with a global pandemic of influenza and to encourage all possible efforts into research and development of pandemic vaccines and antiviral medications and into improving global production capacity.

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<sup>1</sup> Countries in which confirmed human cases of avian influenza H5N1 have been reported to WHO: Azerbaijan, Cambodia, China, Djibouti, Egypt, Indonesia, Iraq, Thailand, Turkey, Viet Nam.

In early 2006, WHO developed and issued its Strategic Action Plan for Pandemic Influenza 2006–2007. The plan outlines the rationale and the key interventions needed in each of the five priority areas. It is accompanied by a budget for the biennium totalling USD 99.40 million dollars.

Since the Action Plan was issued, WHO headquarters, regional offices and country offices have been initiating and undertaking activities within the framework of the strategic objectives. The Global Influenza Programme, housed within the Department for Epidemic and Pandemic Alert and Response at WHO headquarters has overall responsibility for providing technical leadership as well as having a central coordinating function of the activities taking place across the organization. However, a wide range of departments and teams beyond the Department are bringing a wealth of different expertise to bear in what is multi-disciplinary endeavour. WHO is working closely with partners in ministries of health and agriculture of Member States, national and regional laboratory technicians, colleagues in UN agencies, other international organizations and non-governmental organizations as well as the wider scientific and research community.

#### WHO strategic action plan for pandemic influenza

	<b>Strategic action</b>	<b>Goal</b>
1	Reduce human exposure to the H5N1 virus.	Reduce opportunities for human infection and, in so doing, reduce opportunities for a pandemic virus to emerge.
2	Strengthen the early warning system.	Ensure that affected countries, WHO, and the international community have all data and clinical specimens needed for an accurate risk assessment.
3	Intensify rapid containment operations.	Prevent the H5N1 virus from further increasing its transmissibility among humans or delay its international spread.
4	Build capacity to cope with a pandemic.	Ensure that all countries have formulated and tested pandemic response plans and that WHO is fully able to perform its leadership role during a pandemic.
5	Coordinate global scientific research and development.	Ensure that pandemic vaccines and antiviral drugs are rapidly and widely available shortly after the start of a pandemic and that scientific understanding of the virus evolves quickly.

WHO has welcomed the generous financial support provided by the donor community as well as the in-kind contributions and donations that have been received from other partners, including the private sector. Donors have generously provided funding to WHO in its efforts to assist Member States totalling USD 68 million as at the end of 2006. Of the funding received by WHO, at least 77% has been allocated to WHO regional and



country offices to support the efforts of Member States. Further financial support and contributions in kind are being provided on a bilateral basis by donors to Member States.

A list of partners providing financial support is provided at the back of this document.

This report provides an update on progress made by WHO in each of the five strategic areas of the two year Action Plan.

## **I. Reduce human exposure to the H5N1 virus**

H5N1 is an avian influenza virus that has been circulating among bird populations for over three years. In that time, it has shown itself to be both highly contagious as well as pathogenic for poultry. Tens of millions of birds have contracted the virus over a large geographical area stretching from South-East Asia, to Africa and across Europe.

For now, the virus is not easily transmitted to humans. Most infections in humans have occurred as a result of close contact with birds in environments where families live alongside their backyard poultry stocks. Nevertheless, H5N1 is a significant threat to global public health. Firstly, the severity of the symptoms in humans is raising concerns. Unlike seasonal influenza, most patients who become infected with H5N1 develop life threatening conditions such as multiple organ failure and pneumonia. Over half of all laboratory-confirmed cases have died. However, it is the possibility that this virus could alter its genetic structure to become more easily transmissible among the human population that has caused the greatest concern. If that were to happen, a global pandemic of human influenza could be triggered.

It is essential that all efforts are made to reduce the amount of exposure humans have to the H5N1 virus. Not only will this lessen the risk of infection and mortality among those who come in contact with infected poultry, but it will also limit the opportunities for the virus to adapt its genetic structure to suit human transmission either through mutation or by sharing its genes with another seasonal human influenza virus in circulation.

WHO's strategic approach in this area is focused on several concurrent areas of activity. Firstly, any outbreak of avian influenza in humans demands an immediate response to investigate its source and minimize the risk of others also being infected. A greater understanding is also needed of the factors that increase the risk to humans of contracting H5N1 from infected birds. Collecting evidence from actual events of the transmission from birds to humans as well as the environmental and behavioural factors that can exacerbate the risk can provide valuable information to reduce human exposure.

This information is also critical for the development of policies to bring about behavioural change, providing the public with advice on the risks to health associated with close contact with poultry and how to protect themselves. Likewise, countries need to understand how to protect particular groups that could be most at risk, such as poultry cullers, laboratory workers or health-care providers. They need to know what measures to take to limit the amount of exposure these groups may have to the virus as well as the equipment and supplies that should be provided to protect them.

### **Investigating outbreaks and assessing risk**

WHO's operational activity in this area is focused on responding to and investigating actual instances of human infection with the H5N1 virus. Multi-disciplinary international teams are deployed as rapidly as possible to areas in which cases have been reported.

In 2006, over 200 experts took part in field investigation and assessment missions. National staff from ministries of health, agriculture and environment were accompanied by staff from WHO headquarters, regional and country offices as well as members of the

Global Outbreak Alert and Response Network (GOARN), the Global Influenza Surveillance Network, FAO and OIE. The teams include experts in epidemiology, infection control, logistics, social mobilization and communication. GOARN has played a central role in mobilizing these experts needed to participate in the missions.

In 2006 WHO mobilized a total of nine rapid response missions to investigate actual confirmed cases of avian influenza in human populations. These missions took place in Azerbaijan, Djibouti, Egypt, India, Indonesia, Iraq, Romania, Turkey and the West Bank and Gaza. A further 30 missions were conducted by teams from WHO headquarters, regional and country offices with the support of experts from GOARN and other international agencies to countries across all five regions of WHO. These missions assessed the capacity of national and local authorities and facilities to detect and respond to potential cases of human avian influenza.<sup>1</sup> They provided a better understanding of the alert and response mechanisms in place including the capacities for national early warning and verification. The missions assessed the local health infrastructure, availability of resources, clinical management and containment measures in place and the capacity of local laboratories to sample, handle and diagnose the H5N1 virus.

In September 2006, WHO and GOARN partners met for an operational workshop to review the avian influenza response operations that had taken place in 2006. Participants included 12 GOARN institutions, 3 WHO regional offices, the WHO Mediterranean Centre for Vulnerability Reduction (WMC) and the departments at WHO headquarters concerned with avian influenza risk reduction. The workshop reviewed the operational and technical aspects of the missions, identified strengths and weaknesses in planning and deployment as well as post-mission follow-up. The workshop provided an opportunity to strengthen the participation of GOARN partners and regional networks in future international response operations and identified issues concerning the safety and security of team members that needed further attention.

### **Coordinating the response teams**

For each major outbreak of human avian influenza, an avian influenza response group was established at WHO Headquarters to coordinate all outbreak response activities across the world. In 2006, the response group conducted 360 teleconferences and 55 videoconferences from its base within the JW Lee Centre for Strategic Health Operations with over 30 country offices in response to the increasing number of reports of cases in humans and animals of avian influenza. The response group mobilized members of the investigation teams and coordinated and supported their activities in the field.

### **Investigation kits**

To enable WHO country offices to conduct investigations of avian influenza at the national level, Avian Influenza Investigation Kits have been assembled and are being dispatched to 116 country offices, as well as regional offices and partner organizations. Each kit contains Personal Protective Equipment, face masks, material to collect and transport virus samples safely and quickly, courses of antiviral drugs to be used in the event of exposure or infection with the virus and guidelines to help the national teams

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<sup>1</sup> Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Burkina Faso, Cambodia, Cameroon, Côte d'Ivoire, Cyprus, Egypt, France, Georgia, Iran, Italy, Jordan, Lao People's Democratic Republic, Lebanon, Moldova, Myanmar, Niger, Nigeria, Pakistan, Romania, Russian Federation, Sudan, Syria, Tajikistan, Turkmenistan, Ukraine.

conduct the investigation. A total of 14 000 sets of Personal Protective Equipment and 30 000 courses of the antiviral oseltamivir have been sent to countries at the frontline of avian influenza outbreaks. In the anticipation of possible larger-scale field investigations and outbreak response, strategic stockpiles of additional investigation kits are pre-positioned with the alert and response logistics mobility platform at Geneva and Dubai, United Arab Emirates.

### **Alert and response to animal outbreaks**

Experts in animal health from FAO and OIE have joined the WHO investigation teams in helping to assess the risk to people from the outbreaks in animals. Every animal outbreak presents an increased risk of infection to humans who come into contact with the infected animals. WHO is continuing to work very closely with FAO/OIE operations and procedures are now in place to ensure close inter-agency collaboration and cooperation between the animal and human health sectors.

### **Training and guidelines**

Training modules have been developed for ministries of health, health professionals and national laboratories in preparing for and managing investigations into possible cases of human avian influenza. In June 2006, a sub-regional training course on avian influenza was held in Harare, Zimbabwe organized jointly by WHO headquarters and the WHO Regional Office for Africa. The course was provided for epidemiologists, laboratory experts and clinicians from six southern African countries. Additional sessions were also held for West African countries in French.

Two sessions of the WHO/GOARN Outbreak Response Training were organized in Geneva in 2006, in February and in October. Overall, 51 participants from GOARN institutions and WHO headquarters, regional offices and country offices received training on the various components of international outbreak response, including that of avian influenza.

## **Infection control**

While reducing the chance of close contact with infected poultry is an important aspect of public health measures, there are certain occupational groups whose work will inevitably involve direct and close contact with the H5N1 virus. These include outbreak investigators, health-care providers who are caring for sick patients, veterinarians responding to animal outbreaks and laboratory technicians who handle the live virus strains. Adhering to rigorous biosafety procedures is critical to control the spread of infection and reduce the risks to which these workers are exposed.

WHO experts on infection control and case management have accompanied field outbreak and assessment missions to provide advice to the teams in the use of Personal Protection Equipment and other procedures that should be followed when operating in affected areas. As part of the missions, on-site visits were carried out to hospitals, provincial and district health authorities, laboratories and to ministries of health. Health-care workers and other hospital staff were provided with advice and training on infection control when caring for patients infected with avian influenza and in following the appropriate biosafety procedures when handling samples.

Additional technical guidelines and information notes have been developed for health-care staff on measures they should be taking to protect themselves when working with patients infected with H5N1 and in controlling the spread of the virus within the hospital facilities. Guidelines have also been produced for laboratory technicians in gathering, sampling, analysing and transporting live avian influenza viruses to ensure their procedures comply with all biosafety requirements. In April 2006, the WHO Regional Office for the Western Pacific updated comprehensive guidelines on infection control within health-care facilities. A series of posters in Bahasa Indonesia is also under preparation for distribution to hospitals and health departments across Indonesia. A three-day course in infection control and basic hygiene principles was piloted in Azerbaijan and has now taken place in Bulgaria, Armenia and the Russian Federation. The course is available on request to other countries.

## **Managing human cases of avian influenza**

Although human cases of avian influenza remain sporadic, the disease is severe and the case fatality rate is high. In March 2006, WHO assembled an international panel of experts to develop measures to be taken by health-care workers to alleviate patients' symptoms and improve their chances of survival.

In May 2006, WHO published guidelines on the pharmacological management of humans infected with H5N1. The guidelines include recommendations on the use of currently available formulations of antiviral medications and other appropriate treatments for patients with suspected avian influenza infection. It also has recommendations on the use of antivirals for prophylaxis according to the level risk to which members of the community may have been exposed.

## **Averting high-risk behaviour**

In many countries in which H5N1 is thriving, poultry is a prime source of food. Many rural and periurban households have backyard flocks of chickens and ducks and slaughter their birds at home. Live poultry is sold in local markets close to where food is being prepared and consumed. Understanding how the virus spreads from animals to humans can help to identify what measures people should take on their own to reduce the risk of exposure to the virus before and during an outbreak. Well planned public awareness and social mobilization initiatives are effective in reaching a wide number of people.

In March 2006, the WHO Mediterranean Centre for Vulnerability Reduction (WMC), FAO and the United Nations Children's Fund (UNICEF) came together in an ad hoc meeting on behavioural interventions for avian influenza risk reduction. The meeting identified the four highest priority behaviours that would have most impact and feasibility i. reporting unusual sickness or death among birds or animals in the vicinity and seeking treatment immediately should fever develop after contact with a sick bird ii. separating poultry stocks from other species, from wild birds and from children iii. washing hands after contact with birds and disinfecting cages, clothes and vehicles regularly, and iv. handling, preparing and consuming poultry meat safely.

The WMC is providing technical input into a research project being conducted by the West Africa Regional Office of UNICEF. The project aims to study and document the impact of H5N1 on livelihoods and explore community coping mechanisms in Burkina

Faso and Nigeria. It is hoped that the results will help agencies develop more targeted and appropriate communication strategies for the region. The WMC is also working with UNICEF to produce chapters on avian influenza and pandemic influenza for the UNICEF publication series *Facts for Life*. The chapters are designed to deliver technical information through simple key messages that will inform households and communities on how best to protect themselves from the risk of infection of H5N1.

The WMC has also been working closely with food safety experts at WHO headquarters, country offices and ministries of health to develop a series of easily accessible food safety messages in print and in DVD format for schools and communities. Technical support has been provided to Cambodia, Egypt, Iraq, Niger, Nigeria and Turkey.

An assessment of the day-to-day activities in Indonesia's live markets was undertaken in January 2006 by experts in food safety from WHO headquarters and from the WHO Regional Offices of South East Asia and the Western Pacific. The assessment has provided valuable information on the potential risks of exposure to the virus. Guidelines and information notes have now been developed for workers in the poultry production industry, including those working in live markets, to help reduce those risks of contracting the virus should they come into contact with infected bird stocks. The material has now been compiled into an information kit and distributed to 51 countries directly affected by avian influenza.

Training modules in social mobilization and food safety have been developed to be included in standardized WHO training packages for ministries of health in H5N1 control and preparedness. The modules have been field tested in countries in the Region of Africa and in the Russian Federation.

## **The role of communications in reducing risk**

Communications can play a significant role in reducing the risk to human beings of contracting H5N1 during an outbreak as well as informing the population of investigation and containment measures that may be necessary in their communities. It is also essential for developing a relationship of trust between government authorities and communities who may be fearful for their safety and livelihoods.

WHO has developed training modules and guidance material for media professionals and communications staff working within national authorities. A comprehensive toolkit is being developed in collaboration with UNICEF that addresses all aspects of the development of a communications strategy in the event of widespread outbreaks of avian influenza in humans. Communications experts supported outbreak investigations teams in Azerbaijan, Egypt, Indonesia, Iraq, Romania and Turkey.

## **Dissemination of technical information**

WHO has a central role to play in making technical information and guidance widely and promptly available that reflect the rapidly evolving level of understanding of the nature of the H5N1 avian influenza and the risk it poses to human beings.

Information concerning the number of human cases of H5N1 around the world is posted on the WHO web site and is updated whenever a new case is confirmed. Maps that reflect

the spread of the virus within bird populations are available. Reports on the results of investigation and assessment missions to countries are published in all six of the official WHO languages and new guidelines, recommendations and other technical resources are published on the web site as soon as they become available. New findings into the epidemiology of H5N1 are published when available in the *Weekly Epidemiological Record* [www.who.int/wer](http://www.who.int/wer)

Advice for persons who may be considering travel to regions and countries affected by avian influenza is available on the WHO web site and is reflected will be reflected in the updated 2007 edition of *International Travel and Health*.

## **II. Strengthen the early warning system**

Early warning of the emergence of a pandemic influenza virus is essential if the international community is to be able to mobilize all necessary efforts to contain its spread. Countries affected by outbreaks need to be able to detect and manage cases quickly while WHO and the international community must obtain the epidemiological data and clinical specimens needed for accurate risk assessment, to determine the level of pandemic alert and to develop pandemic influenza vaccines. This requires strong and effective surveillance and reporting systems at the national and international level. Existing surveillance systems in many of the countries on the frontline of avian influenza remain inadequate, particularly in rural areas where many cases have occurred. This limitation undermines the accuracy of risk assessment and leads to gaps in our epidemiological understanding of the evolution of the virus.

The newly revised International Health Regulations ("IHR(2005)") are designed to provide a standardized way for the international community to detect, report and respond to signs that a public health emergency of international importance may be developing. Once the IHR(2005) come into force in June 2007 and countries work towards improving their own national capacities that will be needed under the revised Regulations, the international health community will have a clearer early warning should pandemic influenza appear.

In 2006, the World Health Assembly (WHA) called upon Member States to comply immediately on a voluntary basis with some of the general provisions of the IHR(2005) that are considered particularly relevant to the current risks posed by avian and pandemic influenza. The WHA also instructed WHO to upgrade its own capacity in line with IHR(2005) to meet the demands of avian and pandemic influenza alert and response.

Over half of Member States have already nominated a National IHR Focal Point. WHO has established a database to register all relevant information concerning the Focal Points and has published guidance on their roles and responsibilities. WHO has designated IHR Contact Points in all six of the WHO regional offices and at WHO headquarters and they are available on a round-the-clock basis, seven days a week.

### **Improving influenza surveillance**

Samples of the virus need to be collected and analysed rapidly and accurately to ascertain the presence of H5N1 as well as to detect any significant shifts in its genetic structure. The WHO Global Influenza Surveillance System is founded on the participation of local laboratories across the world. It has served the international community for well over 50 years in the detection and analysis of seasonal influenza virus strains. However the emergence of the highly pathogenic influenza virus H5N1 with pandemic potential is presenting the system with significant technical challenges which will be amplified during the demanding conditions of a large scale outbreak. National laboratories need to be provided with up-to-date information and material for the safe collection and shipment of virus specimens. Other laboratories that have the expertise and facilities to work with the H5 virus strain may require further training and support to reliably diagnose H5N1 and any other novel virus subtypes that may emerge.



### **At the national level**

The capacities of the existing surveillance systems have been assessed in over 30 countries across all WHO regions.<sup>1</sup> National surveillance systems are being strengthened and improved to enable the rapid detection, confirmation, investigation and reporting of suspected human cases of H5N1. Field epidemiology capacity in all regions is being improved through training programmes and workshops. Training workshops were held in the South-East Asia region and in south-eastern Europe and support was provided to the ministries of health of Viet Nam, Cambodia, China and Lao PDR to develop their national field and hospital surveillance capacities. WHO is also providing technical support for rapid mapping assessments in high risk areas as well as guidance, training and tools to enable the integration of Geographic Information System (GIS) into national surveillance systems.

New early warning systems have been established and existing surveillance mechanisms have been enhanced in several countries in Asia and Africa.<sup>2</sup> In the Region of the Americas, the Regional Office has been working to expand surveillance targets and strengthen the existing surveillance network. A new generic protocol for influenza surveillance is being developed in collaboration with the US Centers for Disease Control and Prevention (CDC) to ensure that influenza surveillance is harmonized and comprehensive throughout the region.

The National Influenza Centres (NIC) at the country level are frequently the first stage in the global process of collection and sampling of influenza viruses. They play a crucial role in ensuring that influenza virus strains collected from patients together with analytical information on their genetic structure are provided to vaccine producers. The WHO diagnostic kits for seasonal influenza have been updated and distributed to all National Influenza Centres. Recent advancements in diagnostic and surveillance systems have been reviewed and recommendations on introducing new systems and procedures have been provided to countries. The WHO manual of laboratory diagnosis of influenza infections is currently under review and will be updated in 2007.

Not all countries however, have a recognized National Influenza Centre able to participate in global influenza surveillance, particularly the low income countries at the frontline of avian influenza. WHO has been working with many of these countries to help establish NICs. New centres are now planned for Georgia, Ukraine, Azerbaijan, Estonia, Lithuania and Kyrgyzstan.

Even in countries that have an established NIC, few are equipped with the necessary expertise and facilities to work with H5N1. These laboratories must be provided with all the necessary information, guidance and materials to allow them to recognize, store and safely transport samples of deadly H5N1 to more specialized laboratories. WHO is providing equipment and training to staff working within national laboratories as well as deploying experts to provide hands-on support.

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<sup>1</sup> Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Burkina Faso, Cambodia, Cameroon, Côte d'Ivoire, Cyprus, Egypt, France, Georgia, Iran, Italy, Jordan, Lao People's Democratic Republic, Lebanon, Moldova, Myanmar, Niger, Nigeria, Pakistan, Romania, Russian Federation, Sudan, Syria, Tajikistan, Turkmenistan, Ukraine.

<sup>2</sup> Burkina Faso, Cambodia, Cameroon, China, Côte d'Ivoire, Lao PDR, Niger, Nigeria, Viet Nam

### **At the regional level**

The network of specialized laboratories with the particular expertise and facilities required to analyse H5 virus strains is also being enhanced to ensure every country has access to a regional H5 laboratory facility. The Terms of Reference for these specialized centres are under review and other laboratories in areas without this capacity are being upgraded to meet the requirements of H5 designation. The H5 Reference Laboratory network provided support to several countries in shipping specimens and providing rapid confirmation of suspected cases of human infection with avian influenza.<sup>1</sup> In December 2006 WHO published the criteria by which the diagnostic results of H5N1 submitted by a laboratory to WHO will be accepted.

In Africa, two national reference laboratories in Nigeria, one in Cameroon and one in Côte d'Ivoire have been upgraded with the support of Institut Pasteur to enable them to conduct H5 diagnosis and another reference laboratory in the Russian Federation is currently being considered for H5 diagnostic capacities.

WHO is developing a training programme in partnership with the WHO Collaborating Centres to improve regional influenza diagnostic capacity and the coverage of influenza surveillance.

A series of Best Practices for Sharing Influenza Viruses and Sequence Data has been developed that will provide guidance and will outline the responsibilities of members of the global influenza surveillance community. The Best Practices cover the process by which viruses and their genetic structure are shared as soon as they are obtained, the importance of making critical findings publicly available as soon as possible and the principles of ensuring that countries from which the viruses originate are able to share in the benefits and are recognized for their contribution to the system.

### **Tracing contacts**

Anyone who has had contact with a patient exhibiting symptoms of avian influenza must be traced as quickly as possible. Not only may they also have contracted the virus from the same source, but any indication of human-to-human transmission would raise significant alarms that a pandemic could be imminent. Mounting a contact tracing operation in the densely populated and impoverished areas in which many avian influenza cases are occurring presents significant challenges for under resourced health authorities.

WHO has developed a Field Information Management System (FIMS) to manage the information generated at the field level during an outbreak investigation, including information on contacts. Data concerning case contacts can be stored easily and analysis generated to facilitate further investigation. The FIMS model is now being introduced in several WHO country offices and is currently being used by the WHO Country Office in Jakarta as well as by the Ministry of Health in Indonesia to manage the ongoing cases in the country. Other countries are field testing the system and adapting the modules to their national needs.

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<sup>1</sup> Azerbaijan, Egypt, Indonesia, Iraq, Nigeria, Turkey.

## Animal outbreak surveillance

The geographical spread of H5N1 in animals in 2006 has been the fastest and most extensive of any pathogenic avian influenza virus recorded since the disease was first detected. The animal health and agricultural authorities are actively tracking and verifying animal outbreaks. Collaboration between these authorities and the human health sector is essential.

In July 2006, the Global Early Warning and Response System (GLEWS) for animal diseases that are transmissible to humans was launched by FAO, OIE and WHO. GLEWS is the first joint early warning and response system conceived with the aim of tracking and responding to animal diseases including avian influenza. Up-to-date and detailed maps that show the spread of the disease in animals are available on the WHO web site. In September 2006 WHO convened a working group of senior scientists and laboratory directors involved in research on the animal and human interface. The discussions focused on improving diagnosis of the disease in humans and the genetic and environmental factors that may increase human vulnerability to the virus. Control strategies including culling and the use and quality of existing animal vaccines, virus activity in areas of dense human population such as live urban markets and backyards flocks and the role of migratory birds and other animal species in the generation of pandemic viruses were also discussed.

## Enhancing connectivity

In addition to strong surveillance systems, reliable global telecommunications connectivity is needed to ensure rapid reporting and exchange of information. This will be particularly important in the early stages of a pandemic when existing information channels are likely to become rapidly overloaded. WHO is establishing connections for its country offices that are based on a Global Private Network that will be able to continue to operate when external communication systems may be compromised.<sup>1</sup> Upgrades in equipment are ongoing for some country offices and satellite communications hubs are being improved to absorb the network overload during pandemic situations.<sup>2</sup>

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<sup>1</sup> Cambodia, East Timor, Fiji, Kiribati, Lao PDR, Malaysia, Samoa, Solomon Islands, Tonga, Turkmenistan, Uzbekistan, Vanuatu, Viet Nam

<sup>2</sup> Bangladesh, Bhutan, East Timor, Indonesia, Mongolia, Thailand.

### **III. Intensify rapid containment operations**

In 2005, two research groups published studies<sup>1</sup> based on mathematical modelling indicating that rapid intervention at the earliest sign of the emergence of pandemic influenza could be effective in containing the outbreak and stopping it from spreading beyond the immediate area. The studies also suggest that even if the strategy ultimately failed to contain the virus at its source, valuable time would be gained before the outbreak could spread internationally providing countries and the international community with a window of opportunity to intensify preparedness activities and minimize the scale of mortality and illness.

No attempt has ever been made to alter the natural course of a pandemic at its start and the behaviour of influenza viruses is hard to predict. Nevertheless, the rapid containment approach is considered one of the key elements of pandemic influenza preparedness. The strategy is based on rapid detection and reliable reporting of outbreaks, immediate availability of the necessary antiviral medications for large numbers of people and the restriction of movement of people in and out of the area affected. It will require excellent surveillance and logistics mechanisms as well as an ability to ensure compliance with policy directives.

Activities towards strengthening the national and international surveillance mechanisms to ensure the rapid detection and verification of an outbreak are a central part of WHO's efforts to improve early warning systems. What is needed in addition, however, is an agreement and common understanding on how a rapid containment operation should be launched and conducted in the event of a significant outbreak and what the key roles and responsibilities would be of all actors, including international agencies and national governments throughout. In parallel, there is also a need to establish a stockpile of the necessary drugs and equipment that would be required.

#### **Rapid response and containment strategy**

In January 2006, a meeting was convened jointly by WHO and the Government of Japan in Tokyo at which more than 130 participants from more than 14 Asian countries, donor governments and international organizations discussed the elements of a draft protocol that would guide a rapid response and containment operation.

Two months later, in March 2006, WHO brought together 70 international experts in epidemiology, virology, logistics, outbreak response, health legislation, social

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<sup>1</sup> Ferguson NM et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. *Nature*, 2005, 437: 209–214

Longini IM et al. Containing pandemic influenza at the source. [Sciencesexpress/www.sciencexpress.org/](http://www.sciencexpress.org/) 3 August 2005: 1–5

mobilization, communications, laboratory and public health issues in a three day consultation to discuss the operational details of such a rapid response and containment operation. The meeting focused on three areas: the operations and logistics required to mount such an effort, surveillance and epidemiology issues and the public health measures that would be needed including quarantine, social distancing and the distribution of antiviral medication.

A draft protocol was published on 30 May 2006. Since then WHO has been planning a series of workshops to raise awareness and understanding of the containment strategy and to develop further the operational aspects of the draft protocol.

The protocol covers all stages of a rapid response and containment operation. At the outset, detecting, investigating and reporting early signals that human-to-human transmission has taken place is central if the strategy is to have any chance of success. That will be dependent upon efficient and effective surveillance and early warning mechanisms as foreseen under the revised IHR (2005).

A series of investigations would then be needed to characterize the disease and to understand its transmissibility. International teams would be deployed to scene of the outbreak to assess the circumstances of the outbreak, the risk to the population and the feasibility of immediate control measures such as isolation and infection control as well as the use of antivirals from the stockpile. At the same time, the country concerned would work with WHO to agree a communication plan to ensure all relevant information is made available to the public and the international community in the most expedient way possible.

The protocol also covers the decision-making process needed to launch a rapid containment operation and to release supplies from the antiviral stockpile, particularly given the finite supplies of material and human resources available. It also looks at the different phases that would be likely to occur during the early days of a pandemic and the implications for containment interventions at each phase.

## **Rapid response and containment training**

The first International Workshop for Rapid Response and Containment of Potential Pandemic Influenza took place in Jakarta, Indonesia from 27 November to 1 December 2006. A total of 58 participants attended from 12 countries as well as WHO staff members from headquarters and regional offices. This first workshop aimed to establish a cadre of people based in Asia and to train them to be ready to implement a rapid response and containment operation. It also aimed to refine some of the concepts in the draft protocol and to identify any gaps in countries' national strategies.

A second workshop is now under preparation and is scheduled for March 2007. Training modules on containment and pharmaceutical and non-pharmaceutical interventions are also being developed in collaboration with the regional offices.

## **Antiviral stockpiles for rapid response and containment**

In parallel to the development of the draft protocol on rapid response and containment, WHO has been discussing the establishment of an antiviral stockpile with Hoffman LaRoche, producers of the antiviral drug oseltamivir which is marketed under the name Tamiflu®.

Hoffman LaRoche has donated 3 million courses of oseltamivir specifically for the use of WHO in the event of a launch of a rapid containment operation. Stockpiles are now held in WHO facilities at Geneva, Dubai and in regional offices.

In addition, Hoffman LaRoche has donated a further 2 million courses of oseltamivir for stockpiling at the national level to assist countries in their efforts to respond to local outbreaks of avian influenza as they occur. A total of 116 countries have been identified as needing stockpiles and treatment courses from these supplies have already been used to treat patients infected with avian influenza.

A series of Standard Operating Procedures (SOP) is being finalized to guide the use of antivirals for outbreak investigations at the national level as well as the circumstances under which stocks from locally held stockpiles can be deployed.

## **IV. Build capacity to cope with a pandemic**

In the event of an outbreak of pandemic influenza spreading outside of the immediate vicinity and across international borders, countries will face unprecedented strains on their health services and are likely to experience high levels of mortality, morbidity and social and economic disruption. The ability of countries and the international agencies that support them to cope with the arrival of a pandemic and mitigate its impact will depend greatly on the accuracy and comprehensiveness of their preparedness plans.

Experience and knowledge from past experience has provided WHO with an understanding of the likely impact of a pandemic and is working with all countries in helping them to formulate and test their national pandemic preparedness plans and to identify gaps in their core capacities. Furthermore, as the leading international agency for human health, WHO will need to assume a global leadership role should the pandemic develop and spread across the world.

National pandemic preparedness plans need to address how best health authorities can protect their citizens from becoming infected with the virus and how best to treat patients who do fall ill with pandemic influenza. It is unlikely that sufficient quantities of vaccines and antivirals will be available in any country at the outset of a pandemic. Authorities will therefore need to make the most of non-pharmaceutical measures to reduce morbidity, mortality and social economic disruption.

The planning process must also take into account the fact that health and social services will quickly become overwhelmed by the sudden surge in demand. Absenteeism in all sectors due to illness will exacerbate the situation. Plans therefore need to foresee ways to ensure the continuity of essential services and availability of basic needs such as food, water and sanitation.

### **National pandemic preparedness plans**

WHO is providing technical support to countries as they develop their national preparedness plans and has prepared generic guidance on their content and structure. Tools and exercises have also been developed to enable countries to evaluate and test their plans in advance. Over 178 countries across all WHO regions have now drafted or finalized a national preparedness plan. A training package is also being developed in collaboration with technical partners that will comprise a core curriculum and materials that can be used by all regions and adapted locally as needed. The package will include basic information about influenza, preparation, surveillance, detection, alert and reporting, investigation and verification, response and control and clinical management.

Guidelines are also under way for national health services to help plan their response to the clinical impact of pandemic influenza both in terms of treatment and infection control. An international training workshop on emergency preparedness and response for health-care facilities was launched by WHO in collaboration with the Asian Disaster Preparedness Center. The course covers hospital infection control procedures, hospital infrastructure and the organization of teams and community services during a pandemic situation. The first session of the workshop was held in Bangkok, Thailand in September



2006 and included the participation of health-care professionals from countries across the South-East Asia region.

## **Regional pandemic preparedness plans**

WHO Regional Offices are also engaged in regional preparedness and response plans and are initiating regional and sub-regional training sessions.

In the WHO Region for Africa, a region-wide preparedness and response plan has been developed and endorsed by 42 Member States and partners. The plan is serving as a reference for the health sector component of countries' own national multi-sector plans. The WHO Regional Office has also developed a package of training material designed for national health officers and two workshops were held in June and July 2006.

In the WHO Region of the Americas, a multidisciplinary Task Force on Epidemic Alert and Response has been established to advise, coordinate and monitor all activities of the organization related to the planning and implementation of influenza pandemic preparedness and response. All its activities are framed within the requirements of the IHR (2005). The Task Force has developed a strategic and operational plan to guide the organization's technical cooperation activities in preparing the region for a pandemic and in supporting countries to develop their own national capacities.

Sub-regional workshops have been held in the use of modelling software to develop estimates of the country-level impact of a pandemic in terms of morbidity, mortality and in direct economic costs. The software also provides estimates of surge capacity requirements for health services. The Regional Office is also helping countries to assess their core capacities needed to implement national plans and is developing an influenza surveillance protocol for the Region of the Americas. National rapid response teams are being provided with training and are working with staff from the WHO Regional Office on simulation drills and table top exercises.

In December 2006, WHO held a rapid response training workshop in Cairo, Egypt. The workshop aimed to develop qualified teams of professionals responsible for the investigation of outbreaks of human avian influenza and prepare them to conduct further training of rapid response teams in their own countries. Thirty-one epidemiologists, clinicians, virologists, laboratory staff, veterinarians, nurses and health administrators from ministries of health and agriculture from 8 countries in the Eastern Mediterranean Region participated in the 4-day workshop. The training was facilitated by WHO headquarters and the Regional Office for the Eastern Mediterranean, the Centers for Disease Control and Prevention, Atlanta USA and Kenya and the US Naval Medical Research Unit No. 3.

The WHO Regional Office for Europe has been working closely with the European Commission and the European Centre for Disease Prevention and Control to update the current level of understanding of avian influenza and to review lessons learned from joint missions in the Region. A workshop was held that brought together 52 Member States of the European Region which assessed the state of preparedness in the Region and identified areas that required further strengthening. Further sub-regional training workshops are also taking place and the Regional Office is providing assistance directly to individual countries upon request.



A regional preparedness plan has been developed for the South-East Asia Region and table top exercises are being organized by the Regional Office for countries to assess their national plans. The table top exercises will be packaged with a compilation of material from other pandemic influenza exercises executed at the international, national, provincial and local levels including a lessons learned session. In November 2006, WHO staff observed table top exercises carried out in Seoul, Republic of Korea and in Brisbane, Australia. The Korean exercise testing inter-ministerial coordination and effectiveness of measures in their pandemic preparedness plan revealed that local health authorities would play an increasingly critical role in managing the pandemic as it progressed. The Australian exercise, including simulated quarantine procedures, also tested coordination and communications at all levels. Modelling scenarios in the exercise showed that while containment measures could have an impact on delaying the virus spread in Australia, they may not be able to contain the virus.

The WHO Regional Office for the Western Pacific has produced guidelines on creating and validating pandemic preparedness plans. Direct technical assistance has been provided to over 8 countries in the Region and to the secretariat of the Pacific Community in the development of the Pacific Regional Influenza Pandemic Preparedness Project.

## **Ethical concerns in pandemic planning**

In the early stages of an influenza pandemic it is likely that the demand for vaccines, prophylaxis and therapeutic care will be far higher than the supply available at the national as well as the international level. Governments and authorities will therefore be forced to take difficult and sometimes politically uncomfortable decisions over access. In addition, some of the control measures that may be needed could come into conflict with the rights and freedoms of individuals and communities. At the heart of many of these choices lie ethical concerns which when identified, discussed and agreed by key stakeholders can not only help to guide decision-making, but equally importantly can help to make difficult choices more understandable and palatable.

WHO is working with ethical experts and human rights specialists to help Member States identify those areas in pandemic planning and response in which ethical issues may arise and to begin the process of rooting their decisions within their own national ethical framework. In May 2006, WHO convened a global consultation and four technical working groups comprising experts within and outside of WHO were established to consider four distinct focus areas; equitable access to therapeutic and prophylactic measures, the ethics of public health measures such as quarantine and social distancing initiatives, the responsibilities and obligations of public health authorities and health-care workers and the issues that may arise between governments in a multilateral response. The working groups presented their findings to a second global consultation held in Geneva in October 2006 at which a series of recommendations for Member States were developed. The full report of the meeting together with the recommendations is scheduled to be published in early 2007.

## **Developing communications strategies**

The development of a comprehensive communications strategy is an integral part of pandemic preparedness. Effective communications, both prior to the start of a pandemic and during the different phases of its spread can play a significant role in reducing human exposure and mitigating the impact of the pandemic.

WHO has developed tools to assess the current communications situations in the regions and the preparedness actions that should be taken. These include table top exercises for health workers, ministries of health and journalists, attitude surveys on the current level of knowledge of pandemic influenza among health-care workers and the public. A tool to conduct rapid assessment of public trust as the pandemic evolves has also been developed.

Outbreak communication workshops, including journalist-specific workshops are being planned in regional and country offices and Standard Operating Procedures for communications during a pandemic have now been produced. A training-of-trainers workshop took place in July 2006 in Washington DC for 80 participants from 37 countries in the Region of the Americas. Several workshops have been held in the Caribbean with a special emphasis on outbreak and crisis communication. In Argentina, a training workshop brought together communication specialists from ministries of health, agriculture and education of seven countries in the Region. Training sessions in outbreak communications have also been provided to officials within the Ministry of Health in the Russian Federation and to members of GOARN on two occasions.

A journalist's handbook on pandemic influenza has been developed and is available on the WHO web site. It has now been translated into the six official UN languages plus Bahasa Indonesia, Dutch, German, Hebrew, Hindi, Khmer, Turkish and Vietnamese. A training workshop in outbreak communications took place in November 2006 in Bangkok and included the participation of FAO, UNICEF and ministries of health and agriculture from 16 countries in the WHO Region of South East Asia.

WHO is contributing to the development of the common UN communication strategy for avian and pandemic influenza. Work is under way in collaboration with UNICEF, FAO and the Centers for Disease Control and Prevention (CDC) to develop an interagency communication toolkit. The toolkit will be a simple, succinct and easy-to-use, standardized approach that helps programme managers responsible for communication plan strategic communication interventions for highly pathogenic avian influenza and pandemic influenza.

In July 2006, a meeting was convened by the WHO Regional Office for the Americas that brought together United Nations agencies, including UN Information Centres, and officials of the Government of the United States of America to develop an Inter-Agency Communication Framework for Avian and Pandemic Influenza in the Americas.

## **Enhancing WHO's capacity to lead**

When the next human influenza pandemic occurs, the international community will look to WHO to lead countries under the IHR (2005) through the crisis from its emergence through each subsequent wave. WHO headquarters, regional offices and country offices

will need to carry out greatly expanded functions, around the clock, in coordinating the global response to the pandemic. The recent experience with SARS provided WHO with valuable lessons in how its operations, its structure and its expertise should be improved and scaled-up to meet the demands of a pandemic of influenza.

As part of the implementation of the IHR (2005) WHO has established Contact Points that are available on a 24 hour basis at headquarters and in the regional offices to receive reports of any indication of possible cases of pandemic influenza. An Influenza Pandemic Task Force has been established and met for the first time in September 2006. The Task Force is a temporary measure until the IHR (2005) come into force in June 2007 and is designed to provide the Director-General of WHO with advice on the current state of pandemic alert as well as on areas in which further WHO technical guidance and leadership is needed.

WHO is also strengthening its own internal systems of alert and response. A new Event Management System (EMS) is being established that will function as the official repository of all information relevant to any event that may constitute a public health emergency of international concern, including an outbreak of pandemic influenza. The EMS will facilitate global communications and updates on the outbreak and the evolving pandemic within WHO and with all key partners and Member States. It will greatly increase the efficiency, timeliness and inclusiveness of WHO's decision making process and maintain an historic record of operational activities and decisions.

WHO is addressing the likely increases in human resource requirements during a pandemic. A human resources plan for avian influenza and pandemic influenza preparedness has been developed. Additional staff members have been seconded to WHO programmes tasked with avian influenza and pandemic influenza preparedness and the process of recruitment and selection of additional required staff has been intensified. Surge capacity plans are under way for key areas of the avian influenza response in headquarters and in the regions.

## **Preparedness planning with non-state actors**

While the principal responsibility for pandemic planning lies with governments and health authorities, there is a wide range of non-state actors who either hold responsibility for the health and well-being of groups of people within their care, or who could potentially have a significant role to play in preventing the spread of the virus during a pandemic. The global nature of an influenza pandemic demands that all stakeholders, some of which may be beyond the scope of WHO's traditional partners are identified and brought into preparedness planning at an early stage.

The international and regional development banks will have essential roles to play in helping resource stretched countries finance their pandemic response activities. The Asian Development Bank has become a major partner of WHO in providing significant financial assistance to support its activities. WHO has also been holding a series of discussions with the African Development Bank. A briefing was provided to the IMF at a seminar held for European countries.

WHO has also been working closely with the humanitarian community to address pandemic influenza control issues in refugee and displaced populations. Non-

governmental organizations (NGOs) are frequently the principal health-care providers in humanitarian emergencies and in March WHO was requested by the NGO community to hold an interagency technical meeting to address pandemic influenza preparedness and mitigation specifically for refugee and displaced populations. Overcrowding, poor access to basic health-care services, malnutrition, and a high prevalence of diseases such as HIV are only a few of the risk factors for increased morbidity and mortality from influenza in these populations.

Participants included UN agencies, such as the Office of the United Nations High Commissioner for Refugees (UNHCR) and UNICEF as well as leading humanitarian NGOs and other international organizations such as the International Organization for Migration and the International Committee of the Red Cross who work on a regular basis with refugee and displaced populations. The European Commission's Humanitarian Aid Office, the Centers for Disease Control and Prevention and Epicentre also participated. Discussions focused on practical preparedness steps field staff can take to reduce impact of pandemic influenza on refugees and displaced populations and to protect agency staff. The meeting reached agreement on a list of supplies to be pre-positioned, the importance of public health measures and the necessary interventions that would apply in a camp setting. WHO has now published the guidelines on its web site.

Training material for first-line health and essential services staff working with refugee and displaced populations has been field tested in two refugee camps in Kenya and is currently being finalized before broad distribution to partners in the field. Technical information and updates are being provided to NGO partners, UN agencies and donors.

## Continuity planning

International organizations, based in Geneva, have been developing plans dealing with business continuity and health and safety of staff. A pandemic preparedness plan for "International Geneva" is currently being elaborated, with UN agencies meeting regularly to exchange information regarding their own internal preparedness plans. The overall plan aims to support the harmonization of pandemic preparedness activities by UN agencies and other international organizations, serving as a model for other international capitals. Issues being addressed for each phase of a pandemic include travel policies, international meetings, preventive measures, the scaling-down of non-essential functions, increases in teleworking and possible in-office quarantine measures for essential staff during a phase 6 pandemic situation. A contingency plan has been developed for the UN Medical Services to respond to the needs of UN staff members during a pandemic. A set of recommendations on measures to protect staff and their dependants will be included. WHO has also been liaising with the New York based United Nations System Influenza Coordinator on preparedness planning for the global UN system as a whole.

Briefings were provided to the Financial Stability Forum, a high level global committee of finance ministry officials, central bankers and financial regulators on pandemic risk and public health response measures. WHO participated in seminars organized by the International Monetary Fund for central banks and financial sector supervisors on preparedness planning for the financial sector in the event of an influenza pandemic.

WHO has also met with the International Civil Aviation Organization (ICAO) to discuss preparations for a possible influenza pandemic from the perspective of airlines, airports

and aviation authorities. Technical guidance from WHO has contributed to the plans under preparation by ICAO as well as the World Tourism Organization, the International Air Transport Association and the Airport Council International.

## **V. Coordinate global scientific research and development**

Vaccines are potentially the most effective intervention for reducing morbidity and mortality during a pandemic. If available early enough and in sufficient quantities, they can provide population-wide protection against infection. However, existing global manufacturing capacity for influenza vaccines falls far below expected demand during a pandemic and supply and access is inequitably distributed.

At present 90% of the global manufacturing capacity for all influenza vaccines is concentrated in Europe and North America in countries that account for only 10% of the world's population. The present maximum manufacturing capacity - at around 420 million doses of trivalent vaccine per year - falls far below the expected demand during a pandemic. Moreover, the manufacturing process is relatively fragile and technical problems can significantly disrupt supply.

Greater research efforts are needed to accelerate the development of new vaccines and technology that could radically increase vaccine supplies and facilitate the delivery of the vaccines to all countries that need them. The time delay between the assessment of a new candidate vaccine and the granting of a marketing license needs to be reduced. This could be achieved through greater coordination of research initiatives and standardized assessment protocols.

Antiviral drugs are the only interventions available at present for the direct treatment of infection. However, only a small number of antiviral drugs are currently available and supplies remain limited.

At the start of a pandemic there will be an urgent need for epidemiological data to characterize the virus and to understand the principal age groups affected, the modes of transmission and its pathogenicity. Rapid gathering of clinical data will be needed to establish management protocols and to track possible changes in the virulence and severity of the illness during the second or possibly third wave of international spread. To ensure this research can take place in a timely and coordinated manner, networks of experts need to be established in advance.

In May 2006 WHO convened a consultation in Geneva and invited over 120 scientific experts from national immunization programmes, national regulatory authorities, vaccine manufacturers and the research community. The objective of the consultation was to identify and prioritize practical solutions to reduce the anticipated gap in vaccine supply. Participants drew up an Action Plan which outlined strategies for the short, mid and long term based on three main approaches: to increase the uptake of seasonal influenza vaccine; to increase production capacity and; to stimulate further research and development.

## **Global pandemic influenza action plan to increase vaccine supply**

The Global Pandemic Influenza Action Plan to Increase Vaccine Supply was published by WHO in September 2006. It describes the current situation of vaccine production, the estimated demand during a pandemic and the key challenges the scientific community is facing to close the gap. The plan presents the three main approaches to increasing vaccine availability and outlines the key activities needed within each.

### **Increasing the use of seasonal vaccines**

Increasing the uptake of the seasonal influenza vaccine would provide the vaccine industry with a solid demand forecast and stimulate it to increase production capacities. The most effective way to achieve this is to encourage countries that could afford to do so to introduce a standard seasonal influenza vaccination programme into their national health policies. WHO regional offices will develop plans for influenza vaccination programmes in consultation with their Member States and will provide technical assistance wherever needed in addressing the impediments countries may be facing in implementing such a strategy.

### **Increasing the global influenza vaccine production capacity**

The second approach concentrates on increasing production capacity for pandemic vaccines. If a pandemic were to emerge that appeared to cause high mortality, there would be calls to vaccinate the entire global population, currently estimated to be 6.7 billion. The Action Plan outlines a number of ways in which improved vaccine preparedness could be achieved; i. improving the production yields and immunogenicity of vaccines based on H5N1 influenza strains, ii. building new production plants in both developing and industrialized countries, iii. exploring other formulations of influenza vaccine than those commonly used for seasonal vaccination and iv. exploring alternative ways of administering the vaccine to lower the dosage required.

### **Promoting further research and development**

The third approach builds on the research and development efforts currently being undertaken by the research community including the vaccine industry to design more potent and effective vaccines. Efforts are focusing on developing vaccines that could provide sufficient protection after just one dose and, in parallel, on developing vaccines that would provide long-lasting immunity against a wide range of influenza virus strains, including pandemic strains.

WHO is working with the wider research community to explore all the options laid out in the Action Plan and to encourage the levels of financial investment that will be needed from all sources. Although none of these initiatives would be able to close the gap immediately, it is hoped that action taken now will bear fruit within three to five years.

## **Reducing the licensing time delay**

Finding ways to reduce the time delay between the emergence of a pandemic influenza virus and the availability of a safe and effective vaccine is a priority. Regulatory procedures and expectations concerning quality, safety and efficacy of vaccines vary between different national authorities. In 2006, WHO convened two workshops for



regulators and has issued a draft guidance note on regulatory preparedness for pandemic influenza vaccines which covers a range of issues from production and quality control through to post-marketing surveillance. The document is currently being finalized and further efforts are planned to bring the global vaccine regulatory community towards internationally agreed specifications that will accelerate the licensing of human pandemic influenza vaccines.

### **Assessing current vaccine clinical trials**

At present more than 30 vaccine clinical trials are in progress based on viruses collected by the National Influenza Centres in the countries experiencing human infections of H5N1. WHO has been holding information discussions with experts engaged in these trials and reviewing the progress. WHO Collaborating Centres and H5 Reference Laboratories have also been selecting, reviewing and developing several new recombinant H5N1 prototype vaccine strains. Five of the most promising strains have now been made available to interested manufacturers and institutions. In August 2006, WHO published a guidance document for national authorities and vaccine companies on the selection of candidate viruses for use in vaccine development.

Discussions have also been held in collaboration with FAO and OIE on the technical feasibility of producing human influenza vaccines during a pandemic in facilities normally used to produce animal vaccines.

### **Broadening research and development efforts**

While efforts to develop and produce an effective vaccine remain a high priority for WHO and the international research community, increased research efforts are also needed into improving risk assessment, prophylaxis, diagnosis and clinical management. WHO is participating in the development of a South-East Asian Clinical Influenza Network. The full implementation of the oseltamivir treatment protocol is under way with an anticipated enrolment period of 2 years.

The Regional Office for South-East Asia has compiled a bibliography of research undertaken into avian influenza to help identify research priorities and has participated in the Asian Research Partnership in Beijing.



## Conclusion

The first six months of 2006 saw an unprecedented rise in the number of human infected with H5N1 avian influenza as well as a dramatic spread of the disease in bird populations. This was inevitably accompanied by a rapid demand from all sources for information, guidance and support in dealing with the outbreaks.

While sporadic cases of human infection with avian influenza and outbreaks in animals continued to occur in the second half of the year, WHO was also presented with a valuable opportunity to consolidate and review its operations and policies and to identify gaps and plan new initiatives.

As countries prepare for the revised IHR(2005) to come into force in June 2007, great challenges still remain at all levels. WHO will continue to assist countries and to strengthen the international mechanisms to support global health security.

## Selected WHO information resources

### General

- *WHO Strategic Action Plan for Pandemic Influenza 2006–2007*  
[www.who.int/csr/resources/publications/influenza/WHO\\_CDS\\_EPR\\_GIP\\_2006\\_2c.pdf](http://www.who.int/csr/resources/publications/influenza/WHO_CDS_EPR_GIP_2006_2c.pdf)
- *Avian Influenza (Bird Flu): What people need to know, AFRO, March 2006*  
[www.afro.who.int/csr/epr/avian\\_flu/bird\\_flu\\_information.pdf](http://www.afro.who.int/csr/epr/avian_flu/bird_flu_information.pdf)
- *Influenza Pandemic Risk Assessment and Preparedness in Africa, AFRO, 2005*  
[www.afro.who.int/csr/epr/avian\\_flu/afr\\_avian\\_flu\\_31\\_10\\_05.pdf](http://www.afro.who.int/csr/epr/avian_flu/afr_avian_flu_31_10_05.pdf)

### Outbreak investigations

- *Collecting, preserving and shipping specimens for the diagnosis of avian influenza A(H5N1) virus infection: Guide for field operations, October 2006*  
[www.who.int/csr/resources/publications/surveillance/WHO\\_CDS\\_EPR\\_ARO\\_2006\\_1.pdf](http://www.who.int/csr/resources/publications/surveillance/WHO_CDS_EPR_ARO_2006_1.pdf)
- *Guidelines for case definitions for human infections with influenza A(H5N1) virus, August 2006*  
[www.who.int/csr/disease/avian\\_influenza/guidelines/case\\_definition2006\\_8\\_29/en/index](http://www.who.int/csr/disease/avian_influenza/guidelines/case_definition2006_8_29/en/index)

### Averting high risk behaviour

- *Avian influenza: protecting human health from farm to fork- public information film*
- *Questions and answers: A selection of frequently asked questions on animals, food and water*
- *Successful strategies in controlling avian influenza, August 2006*
- *Highly pathogenic H5N1 avian influenza outbreaks in poultry and in humans: food safety implications, November 2005*
- *Healthy food markets, April 2006*
- *Stop the spread: measures to stop the spread of highly pathogenic bird flu at its source, March 2006*
- *Public health interventions for prevention and control of avian influenza: a manual for improving biosecurity in the food supply chain, March 2006*
- *WHO/FAO/UNICEF ad hoc meeting on behavioural interventions for avian influenza risk reduction, Summary Report and Recommendations, March 2006*

#### All available at:

[www.who.int/foodsafety/micro/avian/en/index.html](http://www.who.int/foodsafety/micro/avian/en/index.html)

- *Advice for People Living in Areas Affected by Bird Flu or Avian Influenza, WPRO,*  
[www.wpro.who.int/NR/rdonlyres/04FA6993-8CD1-4B72-ACB9-EB0EBD3D0CB1/0/Advice10022004rev08112004.pdf](http://www.wpro.who.int/NR/rdonlyres/04FA6993-8CD1-4B72-ACB9-EB0EBD3D0CB1/0/Advice10022004rev08112004.pdf)

### **Infection control**

- *Avian influenza, including influenza A(H5N1), in humans: WHO interim control guideline for health care facilities*  
[www.who.int/csr/disease/avian\\_influenza/guidelines/infectioncontrol1/en/index.html](http://www.who.int/csr/disease/avian_influenza/guidelines/infectioncontrol1/en/index.html)
- *Aide-Memoire -Infection control recommendations for avian influenza*  
[www.who.int/csr/disease/avian\\_influenza/guidelines/EPR\\_AM\\_final1.pdf](http://www.who.int/csr/disease/avian_influenza/guidelines/EPR_AM_final1.pdf)
- *Avian Influenza, Including Influenza A(H5N1), in Humans: WHO Interim Infection Control Guideline for Health Care Facilities*, WPRO, April 2006  
[www.wpro.who.int/NR/rdonlyres/04FA6993-8CD1-4B72-ACB9-EB0EBD3D0CB1/0/Advice10022004rev08112004.pdf](http://www.wpro.who.int/NR/rdonlyres/04FA6993-8CD1-4B72-ACB9-EB0EBD3D0CB1/0/Advice10022004rev08112004.pdf)

### **Case management**

- *WHO Rapid Advice Guidelines on pharmacological management of humans infected with avian influenza A (H5N1) virus*, May 2006  
[www.who.int/medicines/publications/WHO\\_PSM\\_PAR\\_2006.6.pdf](http://www.who.int/medicines/publications/WHO_PSM_PAR_2006.6.pdf)

### **Epidemiological information**

- The WHO Weekly Epidemiological Record,
  - Human avian influenza in Azerbaijan, February–March 2006  
No. 18, 2006, 81, 5 May 2006  
[www.who.int/wer/2006/wer8118.pdf](http://www.who.int/wer/2006/wer8118.pdf)
  - Epidemiology of WHO-confirmed human cases of avian A(H5N1) infection  
No. 26, 81, 249–260, 30 June 2006  
[www.who.int/wer/wer8126.pdf](http://www.who.int/wer/wer8126.pdf)
  - Human cases of influenza A(H5N1) infection, in eastern Turkey, December 2005–January 2006  
No. 43, 2006, 81, 27 October 2006  
[www.who.int/wer/2006/wer8143.pdf](http://www.who.int/wer/2006/wer8143.pdf)

### **International Health Regulations (2005)**

- The designation or establishment of National IHR Focal Points  
[www.who.int/csr/ihr/nfp](http://www.who.int/csr/ihr/nfp)

### **Global influenza surveillance**

- *WHO criteria for accepting positive results of H5N1 infection in humans from national reference laboratories*, November 2006  
[www.who.int/csr/disease/avian\\_influenza/whoacceptancecriteria.pdf](http://www.who.int/csr/disease/avian_influenza/whoacceptancecriteria.pdf)

### **Rapid response and containment**

- *WHO pandemic influenza draft protocol for rapid response and containment*, May 2006  
[www.who.int/csr/disease/avian\\_influenza/guidelines/protocolfinal30\\_05\\_06a.pdf](http://www.who.int/csr/disease/avian_influenza/guidelines/protocolfinal30_05_06a.pdf)

## **Pandemic preparedness**

- *WHO global influenza preparedness plan, November 2005*  
[www.who.int/csr/resources/publications/influenza/GIP\\_2005\\_5Eweb.pdf](http://www.who.int/csr/resources/publications/influenza/GIP_2005_5Eweb.pdf)
- *Maintaining a Safe and Adequate Blood Supply in the Event of Pandemic Influenza*  
[www.who.int/bloodproducts/quality\\_safety/WHO\\_Guidelines\\_on\\_Pandemic\\_Influenza\\_and\\_Blood\\_Supply.pdf](http://www.who.int/bloodproducts/quality_safety/WHO_Guidelines_on_Pandemic_Influenza_and_Blood_Supply.pdf)
- *Pandemic influenza preparedness and mitigation in refugee and displaced populations, WHO guidelines for humanitarian agencies*  
[www.who.int/csr/disease/avian\\_influenza/guidelines/humanitariandoc2006\\_04\\_07/en/print.html](http://www.who.int/csr/disease/avian_influenza/guidelines/humanitariandoc2006_04_07/en/print.html)

## **Research and development**

- *Global pandemic influenza action plan to increase vaccine supply, September 2006*  
[www.who.int/csr/resources/publications/influenza/CDS\\_EPR\\_GIP\\_2006\\_1.pdf](http://www.who.int/csr/resources/publications/influenza/CDS_EPR_GIP_2006_1.pdf)
- *Influenza research at the human and animal interface: Report of a WHO working group, September 2006*  
[www.who.int/csr/resources/publications/influenza/WHO\\_CDS\\_EPR\\_GIP\\_2006\\_3C.pdf](http://www.who.int/csr/resources/publications/influenza/WHO_CDS_EPR_GIP_2006_3C.pdf)
- *Antigenic and genetic characteristics of H5N1 viruses and candidate H5N1 vaccine viruses developed for potential use as pre-pandemic vaccines, August 2006*  
[www.who.int/csr/disease/avian\\_influenza/guidelines/recommendationvaccine.pdf](http://www.who.int/csr/disease/avian_influenza/guidelines/recommendationvaccine.pdf)
- *Availability of new H5N1 prototype strain for influenza pandemic vaccine development March 2006*  
[www.who.int/csr/disease/avian\\_influenza/guidelines/avianinfluenzastrains2006/en/print.html](http://www.who.int/csr/disease/avian_influenza/guidelines/avianinfluenzastrains2006/en/print.html)
- *Availability of new H5N1 prototype strain for influenza pandemic vaccine development May 2006*  
[www.who.int/csr/disease/avian\\_influenza/guidelines/2strains2006/en/print.html](http://www.who.int/csr/disease/avian_influenza/guidelines/2strains2006/en/print.html)
- *Availability of new H5N1 prototype strain for influenza pandemic vaccine development June 2006*  
[www.who.int/csr/disease/avian\\_influenza/guidelines/2strainsJune2006/en/print.html](http://www.who.int/csr/disease/avian_influenza/guidelines/2strainsJune2006/en/print.html)
- *Availability of new recombinant H5N1 vaccine virus December 2006*  
[www.who.int/csr/disease/avian\\_influenza/guidelines/h5n1vaccinevirus/en/print.html](http://www.who.int/csr/disease/avian_influenza/guidelines/h5n1vaccinevirus/en/print.html)
- *Avian influenza: significance of mutations in the H5N1 virus, February 2006*  
[www.who.int/csr/2006\\_02\\_20/en/index.html](http://www.who.int/csr/2006_02_20/en/index.html)

**Further information resources are available at:**

[www.who.int/csr/disease/avian\\_influenza/en/index.html](http://www.who.int/csr/disease/avian_influenza/en/index.html)

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