

AVIAN FLU: ADDRESSING THE GLOBAL THREAT

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AVIAN FLU: ADDRESSING THE GLOBAL THREAT

WEDNESDAY, DECEMBER 7, 2005

HOUSE OF REPRESENTATIVES,
COMMITTEE ON INTERNATIONAL RELATIONS,
Washington, DC.

The Committee met, pursuant to notice, at 10:34 a.m. in room 2172, Rayburn House Office Building, Hon. Henry J. Hyde (Chairman of the Committee) presiding.

Chairman HYDE. The Committee will come to order.

On the morning of March 11, 1918, while World War I was raging overseas, a young private reported to the infirmary at Fort Riley, Kansas complaining of a headache, sore throat, and fever. By noon, more than 100 other servicemen were hospitalized, a number that swelled to 500 by week's end.

Although no one knew it at the time, it was the beginning of the great influenza pandemic of 1918, which caused tens of millions of deaths around the world, infected one quarter of the U.S. population, and killed over 600,000 Americans, more than all the wars of the 20th century combined.

Since the so-called Spanish flu pandemic of 1918, there have been two others of lesser magnitude: The Asian flu pandemic in 1957, and the Hong Kong flu pandemic in 1968. Many experts believe that we are overdue for another one. It is not clear that humanity is any less vulnerable than we were during the last century. Indeed, the same currents of progress that have improved our capacity to fight disease have also enhanced its ability to spread. International travel and commerce, which have brought us so many benefits, also increased our shared vulnerabilities.

The flu strain that has been the focus of so much recent attention, the H5N1 virus, is already endemic to vast poultry and bird populations, particularly in Southeast Asia. If, and some insist when, the virus mutates into a form easily transmitted between people, the effect on human health will be explosive.

In contrast to the mortality rate in the 1918 epidemic, which was somewhere around 2.5 percent, more than half of those affected with H5N1 have died, including the young and fit. So far we have been spared a pandemic by chance, and the inefficiencies of viral mutation. We cannot responsibly depend on those two uncertainties for our future protection.

Because infected people are contagious before they display visible symptoms and migratory birds do not carry passports, an Avian flu pandemic cannot be halted at our airports, borders, or custom checkpoints. It is a global threat that requires proactive inter-

national attention. For that reason, it is a key concern of this Committee.

I applaud the President for assembling the National Strategy for Pandemic Influenza to help catalyze federal, state, local, and private planning to meet the pandemic threat. I strongly agree with its assertion that “the most effective way to protect the American population is to contain an outbreak beyond the borders of the U.S.”

However, given the unprecedented dangers we face, the 3.5 percent of the President’s \$7.1 billion emergency funding request earmarked for pandemic influenza might not be adequate to the task. I am confident the panel of distinguished witnesses before us today will apprise us of our efforts to detect and combat Avian flu outbreaks, and help us to better comprehend the level of financial and other resources we will need if we are to annihilate on distant shores the forces of a devastating and pitiless invasion, that even now are amassing for an assault.

Let me now turn to my friend and esteemed colleague, Mr. Lantos, the Ranking Democratic Member, for any remarks he may wish to make before we hear from our witnesses. Mr. Lantos.

Mr. LANTOS. Thank you very much, Mr. Chairman. And as is so often the case, I never cease to wonder at the degree to which our opening statements parallel each other, despite the total lack of coordination between our preparation of these statements.

Mr. Chairman, the 1918 flu pandemic was a bolt out of the blue. Without warning, the deadly virus spread quickly, extinguishing the lives of some 50 million human beings. Nearly 40 years later, the 1957 Asian flu pandemic rocketed around the world, taking nearly two million lives. And in 1968, the Hong Kong flu struck down one million without warning.

Our nation faces a new emerging threat, the Avian flu, that could take hundreds of thousands of American lives. But this time, Mr. Chairman, we have been warned. The world’s preeminent medical specialists and public health professionals have loudly proclaimed the potentially enormous consequences to the world’s population if we fail to detect and contain the Avian flu pandemic.

We must take bold and decisive steps to act on this advance warning, Mr. Chairman. If we do not, we will be no better off than the previous three flu pandemics, when our nation was caught flat-footed and unprepared to protect its citizens.

Our top priority must be to make every effort humanly possible to detect and contain an Avian flu outbreak before it hits the United States. In that regard,—and I am delighted you raised this same issue, Mr. Chairman—I am singularly unimpressed by the Administration’s proposal to spend only 3 percent of its \$7 billion Avian flu budget on tackling the virus where it is already emerging, in markets and small villages across the continent of Asia.

We should be channeling our funds to reducing the chance that Avian flu will mutate into a highly transmittable form, detecting outbreaks when they occur, and controlling the spread of outbreaks to avoid a global pandemic. Dedicating only \$250 million, which is a pitiful 3 percent of our budget, for this purpose to this critically important task is woefully insufficient, and I recommend that we, minimally, double this amount.

Mr. Chairman, it is imperative that the United States strongly support the indispensable work of the United Nations and the World Health Organization, both of which are working feverishly to build up the capacity of local authorities to monitor and to respond to any disease outbreak.

While we must make every effort to stop a pandemic at its source, these efforts may fail. And if they do, we must have concrete plans to protect the front lines in the potential battle against Avian flu.

Mr. Chairman, in my district, at the heart of my Congressional district is the San Francisco International Airport. Last year, my airport handled over 32 million passengers, three million of whom stepped off planes from Asia. A similar number landed at the Los Angeles International Airport. In fact, each year California receives nearly 60 percent of the airline traffic from Asia to the United States.

It is imperative that the Administration have specific plans to deal with the most likely initial points of entry, with respect to the detection of infected individuals.

After the 9/11 tragedy, this country made the horrendous mistake of assuming that Laramie, Wyoming is as likely to be hit as New York or San Francisco. We provided funding and made preparations on a nationwide basis, as if we were dealing with highway funds, disregarding the fact that some areas are dramatically more likely to be targets of terrorist attacks than others.

We cannot make the same mistake again, as our nation prepares to battle a potential Avian flu pandemic. Resources for this battle cannot be allocated uniformly across the nation, as if they were school funds. We have to concentrate on the most vulnerable places. A swift response, Mr. Chairman, will be the only way to save untold numbers of lives.

The 1918 flu epidemic circled the globe several times in 18 months, which was an amazing feat given that we were a generation away from commercial air travel. Just consider what kind of devastation such a virus could unleash given the enormous presence of global air travel today.

Finally, Mr. Chairman, it will be my pleasure to join with Nancy Pelosi, my colleague representing San Francisco, in the near future in announcing a comprehensive Avian flu legislative package. Our bill will dramatically scale up our nation's efforts to stop an Avian flu pandemic at its roots, and boost our Government's ability to save lives here at home should a pandemic occur.

Mr. Chairman, I thank you again for calling a hearing on this critically important and timely matter. I look forward, as always, to working with you closely to ensure that our Government's response to the potential Avian flu pandemic is as strong and robust and effective as possible. I look forward to listening to our witnesses.

Chairman HYDE. Thank you, Mr. Lantos. The Chair will entertain 2-minute opening statements from those Members desiring to make them. This is not mandatory, I suggest, but nonetheless, I will call the roll in the order in which the people showed up.

Mr. Smith of New Jersey.

Mr. SMITH. Thank you very much, Mr. Chairman. And I, too, want to thank you and Ranking Member Lantos for your very eloquent statements in summarizing and setting the stage for what I think is a very important hearing. We need to hear from our very distinguished panel what is being done, what is being accomplished, and how quickly it is happening.

I just returned yesterday from a 4-day trip in Vietnam primarily focused on human rights, religious freedom issues, health issues and HIV/AIDS. Of course Avian flu was something discussed. I was struck by how every restaurant we went to along the roadside, there was a lack of poultry on the menu, so there seems to be a very significant effort to go after the source of this terrible disease.

But it would be very, very helpful to know how quickly this work is being done. In reading the testimony I see that an HHS person is going to be assigned, or maybe more than one personnel. Vietnam certainly is bearing the brunt of not only the incidents of sickness, but also the number of fatalities, with 93 cases so far causing 42 deaths, far exceeding any other country in the region.

I would also note for the record that our Ambassador, Ambassador Marine, is very much focused on this issue. And I think we are being very well-served by his work there. So I look forward to hearing the testimony.

I was in Hanoi, Hue, and Ho Chi Minh City during the course of those 4 days, again mostly on the religious freedom issue, which is an ongoing serious problem in Vietnam. But when it comes to collaborating and working with the Government of Vietnam in mitigating and hopefully preventing an outbreak, no matter how bad their record is on human rights, we need to work with them.

So I again look forward to hearing from our very distinguished panel on the strategy and how quickly it will be implemented. Thank you. I yield back.

Chairman HYDE. Mr. Blumenauer of Oregon.

Mr. BLUMENAUER. Thank you, Mr. Chairman. I just hope that in the course of this discussion we can also—while obviously we are interested in the international perspective, and I appreciate the leadership that you and our Ranking Member have brought forward—think about what is happening here in this country; for example, with live poultry markets we have in the United States. I would hope that there are opportunities for us to take some simple common sense steps that deal—not just with China, this is not just Vietnam, this is Philadelphia, New York, where there are potential breeding grounds for this vector, and the potential to spread it very quickly.

I have worked in the past with Mr. Tancredo on animal fighting: Dog fighting, cock fighting. We have continued in this country an illicit trade in fighting animals that have proven in the past to be a vector for disease. I would hope that this is an opportunity, with the professionals that we have here, with the Administration, to get serious about something that continues to be both an international problem where these fighting birds are involved with international traffic. And domestically here in the United States, where Congress has been asleep at the switch and has not established meaningful penalties for the illegal transport. And so it continues, and it could cost the lives of millions of people.

Last, but by no means least, we have started to take some steps in terms of the foreign importation of exotic birds. I hope that the work of this Committee, and with our witnesses, that we can spotlight things that go beyond animal welfare, but things that can actually threaten human lives.

Thank you very much.

Chairman HYDE. Thank you. The gentleman from Iowa, Mr. Leach.

Mr. LEACH. Perspective is always difficult to bring to any issue, but self-evident to the greatest foreign policy issue of our time is neither the problem of war and peace between nation states or our other problem with terrorism, but rather the human vulnerability to disease that we all share.

The tragic global spread of the HIV virus and the mounting threat of the first Avian flu pandemic of the new century have begun to focus public attention on this fact. It may be that the magnitude of disease-inflicted death is so awesome that we cannot envision changing our budgetary and policy priorities to match the challenge. Yet what is self-evident is that we do have the capacity to act, and the failure to do so could be the single greatest failure of public policy and public duty in our lifetime.

Thank you.

Chairman HYDE. Ms. Watson of California.

Ms. WATSON. I want to thank the Chairman for bringing the issue, and the panelists for coming this morning.

I think this is a timely, and a very necessary, discussion. I am looking forward to hearing from you as to how we are advancing with the knowledge of how this bird epidemic will then spread to humans, and are we prepared, not only in this country, but our neighboring countries, particularly those to the south and in the Caribbean area.

So I look forward to the information. I would like to correspond with some of you to specifics, and I won't take the time now, but I will look to you to answer some of the questions I have.

Thank you very much, and thank you, Mr. Chairman.

Chairman HYDE. Thank you. Mr. Rohrabacher of California.

Mr. ROHRABACHER. First and foremost, I want to thank you, Mr. Chairman, for again demonstrating leadership in the arena of international affairs and international relations. This hearing today reflects that type of depth of understanding that you have of the importance of various issues that other people might think would be the purview of other Committees. This is vitally important to the United States of America, vitally important to the world, and you are providing leadership here today.

One little note I would like to put in the discussion as we start. If there is anything that suggests to me that the United States should have been in control of its borders to a much greater degree than we have been, it is the fact that infectious diseases threaten in such an incredible way the well-being of the people of the United States.

In California, because we have had an influx of illegal immigrants who have come, and a system that is a broken system, we have seen diseases emerge that were cured in the United States

decades ago. Our own children now are being now made susceptible to these diseases again.

So as we look at this issue today, I hope that—and I don't want to preempt Mr. Tancredo here—but I hope that we consider that illegal immigration and our out-of-control situation at the border may be putting us in jeopardy to a much greater degree than we ever thought.

Thank you very much, Mr. Chairman.

Chairman HYDE. Thank you. Mr. Chandler, Kentucky. Thank you.

Ms. McCollum of Minnesota.

Ms. MCCOLLUM. Thank you, Mr. Chairman. Thank you for holding this hearing.

The International Global Health Caucus held a hearing in which we understood, and which the way this very deadly, potential deadly disease could evolve and really cause some major challenges for not only our public health, but our economy and our international relations.

In today's hearing I hope I hear from some of the panel members on some questions that have occurred to me since learning more about this issue in traveling abroad recently.

For example, monitoring in Asia. In the twin cities area we have a great diversity of people who have chosen to live in our frozen tundra—people from Africa, people from Laos, people from all over the world—who go back and forth visiting and traveling with friends and neighbors. So the monitoring that we are doing in country there becomes critically important to the people who come to the St. Paul/Minneapolis Airport.

Having recently been in Africa, what policies are we putting forward to really understand the devastation that something such as the Avian flu pandemic will have on a very vulnerable population with food insecurity, lack of clean water, and HIV on top of it.

Dollars in some of the poorest countries of the world. What is the international community doing to replace the protein value of chickens? Sometimes something that is critically important, one egg a week to a child or to a family, can make a huge difference in the way that child develops. If those are culled, where does the family get the dollars to replace, and how do they go about doing that?

So I have a great many questions about international monitoring, and how we are working on that, just for our own perspective as people come back here in the United States, and for our brothers and sisters around the world.

But the other thing I am very interested in hearing is what is the plan for Embassies and for Americans abroad should warnings or a pandemic take place.

Mr. Chairman, thank you very much for having this hearing.

Chairman HYDE. Thank you. Mr. Faleomavaega.

Mr. FALEOMAVAEGA. Thank you, Mr. Chairman. As usual, I want to commend you and our Ranking Member, Mr. Lantos, for calling this hearing. I think it is very important and appropriate.

I want to share with the Members and my colleagues that recently reported in the *New York Times* and the *Washington Post* inaccurately suggesting that American Samoa, and I believe one

other country, were not affected by the influenza pandemic that occurred in 1918.

I wanted to share with my colleagues an experience. My own father at that time had 10 brothers and sisters, and only three survived, because of influenza. My grandfather had 15 brothers and sisters, and only five survived.

So to suggest that our little place there in the South Pacific was not affected by the pandemic that occurred in 1918 was not true. It affected the entire world. I think what we are faced with now, I do not know if the President's proposal of having to suggest that \$7 billion might be able to cure this problem I think is far from it. And I certainly am looking forward to hearing from our distinguished members of our panel to give us some insight on what we need to do as far as the Congress is concerned.

And Mr. Chairman, I look forward to hearing from our panelists. Thank you.

Chairman HYDE. Thank you. Mr. Ackerman of New York.

Mr. ACKERMAN. Thank you very much, Mr. Chairman, to you and the Ranking Member for conducting a hearing on this very important matter.

I have just returned with some of our colleagues with a delegation led by Mr. Issa and Mr. Engel of our Committee as part of the Trans-Atlantic legislative dialogue. And as part of that we visited Geneva, and had the opportunity to meet with people from WHO and some of our colleagues in the European Parliaments. And this is an issue that is of paramount global concern.

One of the side issues that ties into this, that I am very interested in, and causes me some great concern, is the issue of distribution of whatever antidotes, whatever drugs, whatever it is going to take to fight this, as well as other diseases, should there be an outbreak. And it is the same shared concern that has to do with being responsive to a chemical or a biological attack on the United States.

Not too widely reported was the fact that shortly after September 11 there landed in New York's LaGuardia Airport, within a day, a massive supply of medicines and drugs to respond to whatever it is people suspected might be going on. Of course, we did not know at that point. And those pallets and pallets and pallets filled with emergency supplies sat there and sat there throughout the entire process, because nobody knew what to do with them.

I have received numerous complaints to date concerning the distribution of the current flu virus injections from medical societies and individual physicians complaining about the uneven distribution. I think the distribution network in our country is somewhere between lacking and non-existent. Physicians continuously complain that big box stores get huge supplies to conduct clinics, and physicians in various places, spotty though it is, are left without. I think that we have to address the issue of a major quick-response distribution network, and figure out exactly how to do that.

Thank you, Mr. Chairman.

Chairman HYDE. Thank you. We have two very distinguished panels of witnesses appearing before us today. Mr. Anthony Rock is Acting Assistant Secretary of the Bureau of Oceans and International Environmental and Scientific Affairs at the Department of

State. A career member of the Senior Foreign Service, Mr. Rock has served with distinction in numerous posts overseas. Previously as Chief for International Health Policy in the OES Bureau he oversaw the development of U.S. plans for international surveillance of emerging infectious diseases.

We also have Dr. Kent Hill, Assistant Administrator for Global Health at USAID. Dr. Hill is responsible for a bureau which currently manages or co-manages over \$2 billion worth of health programs all over the world. Dr. Hill also serves as USAID Assistant Administrator for Europe and Eurasia.

Dr. Anne Schuchat is Acting Director of the National Center for Infectious Diseases at the Centers for Disease Control and Prevention of the Department of Health and Human Services. She joined colleagues from across the agency during emergency response activities for the 2001 anthrax bioterrorism response, as well as the 2003 SARS outbreak, where she headed the Beijing City epidemiology team for the World Health Organization, China Office.

Dr. Anthony Fauci has been the Director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health since 1984. He oversees an extensive research portfolio of basic and applied research to prevent, diagnose, and treat infectious and immune mediated illnesses. Dr. Fauci also serves as one of the key advisors to the White House and the Department of Health and Human Services on global AIDS issues, and on initiatives to bolster medical and public health preparedness against possible future bioterrorist attacks.

Thank you for being here today. Without objection, the full written statements of all witnesses, as well as the text of an article by Mr. Todd Buchanan, will be made a part of the record. And if members of the panel could condense their statements somewhere in the range of 5 minutes, we will be grateful, as your full statement will be made a part of the record, and we will have questions for you.

Mr. Rock, we look forward to hearing your testimony. Please proceed.

STATEMENT OF MR. ANTHONY F. ROCK, ACTING ASSISTANT SECRETARY, BUREAU OF OCEANS AND INTERNATIONAL ENVIRONMENTAL AND SCIENTIFIC AFFAIRS, U.S. DEPARTMENT OF STATE

Mr. ROCK. Mr. Chairman, Members of the Committee, thank you for the opportunity to be here today to discuss U.S. efforts to engage in international coalition against a possible outbreak of pandemic influenza.

The current outbreak of H5N1 highly pathogenic Avian influenza is, as you have noted in your opening statement, a truly global challenge. No country can fight a potential pandemic alone. An outbreak anywhere risks an outbreak everywhere.

Nations must join together now to prevent an outbreak, preparing to contain and respond if Avian flu becomes a pandemic among people. Dealing with a novel influenza virus with pandemic potential before it reaches our border is a necessary form of forward defense.

H5N1 is not just a health matter, but an economic, security, and social issue, as well. The social, economic, and political impacts of a virulent human flu pandemic, whether sparked by the strain that is currently circulating in birds or by any other new strain, could be devastating.

The 2003 SARS outbreak cost more than 700 lives and some \$80 billion worldwide. The issue requires the involvement not only of ministries of health and agriculture, but also ministries of foreign affairs and the senior executive leadership of all countries.

The U.S. framework for international action is organized around three principal goals: Effective surveillance, national preparedness, and coordinated response and containment wherever possible. Recognizing the importance of coordinated international effort, President Bush announced the establishment of an international partnership on Avian and pandemic influenza on September 14, 2005 during the high-level segment of the UN General Assembly.

The President's speech focused the world's attention on the need for timely and sustained high-level political leadership, and concrete cooperative action. Specifically the partnership's aims are to combat the threat of Avian flu, and improve global readiness by elevating the issue on national agendas. Through the partnership, countries have agreed to work together to develop the capacity to plan for, detect, prevent, and rapidly respond to an epidemic.

They agree to coordinate efforts among donor and affected nations, to mobilize and leverage resources, to increase transparency, the quality of surveillance and sharing of data and samples. To build local capacity, to identify, contain, and respond to a pandemic, and to work in close cooperation with key international organizations, including the World Health Organization, the Food and Agricultural Organization, the World Organization for Animal Health, and the World Bank.

Mr. Chairman, I am pleased to report that the partnership is off to a good start. In early October the State Department hosted a well-attended meeting of the partnership member countries. Senior officials from 88 countries and nine international organizations participated actively in plenary sessions and roundtables. In these sessions partners acknowledged that many countries lack the capacity to prepare for and respond to a pandemic, and capacity building must be a priority.

The partners stressed the need for communication and education strategies to raise public awareness and change behavior. Participants also emphasized the need for prompt reporting of suspected cases, and they urged that we must prepare not only for the health impacts, but for the economic and social effects.

The partners also identified three priority areas for continued discussion and coordination. Building stockpiles of drugs and supplies, speeding vaccine development and distribution, and implementing rapid response and containment measures. Significantly, a number of countries have supported the partnership by taking leadership roles in several of these key areas.

Following the senior officials' meeting, Canada agreed to spearhead discussions on international stockpiling. We held discussions in the context of the WHO and with representatives of the European Union on strategies for vaccine research development and

production. Australia and Japan agreed to collaborate in the context of APEC on rapid response and containment.

One issue to be more fully addressed is donor coordination. In the recent discussions in Geneva we proposed that WHO, World Bank, and other major donors coordinate on assessment of country needs. This will allow us to come to a more common understanding of what financial and technical assistance is necessary.

The partnership is a cooperative effort. It works with regional organizations as well. The Asian Pacific Economic Cooperation Forum, the Association of Southeast Asian Nations, the African Union, the European Union, the Summit of the Americas, and the Bush Administration has taken every possible bilateral and multilateral opportunity to stress the seriousness of the threat posed by Avian influenza, and the need for rapid action.

The President is personally engaged, and has raised the issue with the Presidents of China, Indonesia, and Russia, as well as the Prime Ministers of Canada and Thailand. President Bush also joined APEC leaders last month in Korea, where the topic of Avian influenza was the centerpiece of those discussions, and the United States chaired the APEC Health Task Force.

Secretary Rice expressed our concerns to ASEAN countries during the meetings at the UN General Assembly, and devoted time in her recent trip to Canada for briefings on possible stockpiles.

In mid-October, Undersecretary of State Dobrionski joined Secretary of Health and Human Services Mike Leavitt and representatives of NIH, CDC, USAID, USDA, on a visit to seven countries in Southeast Asia. And the delegation was joined by WHO Director General Lee and representatives of FAO and the World Organization for Animal Health.

We were pleased that these delegations met with Foreign and Prime Ministers of these countries, indicating the success in raising the political profile of the issue. The President has charged the State Department with leading the international activities of the U.S. National Strategy for Pandemic. And in so doing, we closely collaborate with colleagues at HHS, AID, USDA, and other technical agencies.

Our activities are underway to meet the three key areas of our strategy: Surveillance, preparedness, response and containment. We are reaching out to help national veterinary facilities worldwide, national public health staff, ministries of health, and to help conduct preparedness training and simulations. We are working to establish rapid response teams, and working with all of the international organizations to help conduct containment measures in animal populations, and prepare for human reaction.

In conjunction with the President's November 1 announcement of the national strategy, he called for an additional \$7.1 billion in emergency funding. And this request does include \$251 million to detect and contain outbreaks before they spread around the world.

In conclusion, Mr. Chairman, let me say that in the few months since its creation, the International Partnership has already made a dramatic difference in heightening international awareness, and made addressing this issue a priority for nations. We are seeing closer collaboration among agriculture, health, economic, and foreign ministries. We are seeing more rapid placement of monitors

in high-risk countries. We are seeing strengthening of surveillance networks, and increased donor commitment and coordination. But there is still more that needs to be done.

Countries are only now beginning to recognize that the cost of taking action now is significantly less than the cost of the pandemic itself.

Thank you, Mr. Chairman, and I welcome any questions.

[The prepared statement of Mr. Rock follows:]

PREPARED STATEMENT OF MR. ANTHONY F. ROCK, ACTING ASSISTANT SECRETARY,
BUREAU OF OCEANS AND INTERNATIONAL ENVIRONMENTAL AND SCIENTIFIC AFFAIRS,
U.S. DEPARTMENT OF STATE

Introduction: Mr. Chairman, thank you for the opportunity to discuss our efforts to engage the international coalition to improve global readiness against a possible outbreak of pandemic influenza. The current outbreak of H5N1 highly pathogenic avian influenza (HPAI) virus is a truly global challenge. No country can fight a potential pandemic alone; an outbreak anywhere risks an outbreak everywhere. Nations must join together now to prevent an outbreak, while preparing to contain and respond if avian flu becomes a pandemic among people. Indeed, dealing with any novel influenza virus with pandemic potential before it reaches our border is a necessary form of forward defense.

The H5N1 highly pathogenic avian influenza virus is not just a health matter but an economic, security and social issue. The social, economic and political impacts of a virulent human flu pandemic, whether sparked by the strain that is currently circulating in birds or by any other new strain, could be devastating. The 2003 SARS outbreak cost more than 700 lives and some \$80 billion worldwide. This issue requires the involvement of not only Ministries of Health and Agriculture but also Ministries of Foreign Affairs and Executive Offices of Presidents and Prime Ministers. Our framework for action is predicated on measures in support of surveillance, preparedness, and response and containment.

The Partnership: Recognizing this threat can only be averted through coordinated international effort, President Bush seized the mantle of global leadership, announcing the establishment of the International Partnership on Avian and Pandemic Influenza on September 14, 2005 during the high-level segment of the UN General Assembly meeting. The President's speech focused the attention of the world community on the need for timely and sustained high-level political leadership and concrete, cooperative action. Specifically, the Partnership's aim is to combat the threat of avian flu and improve global readiness for human pandemic influenza by elevating the issue on national agendas; coordinating efforts among donor and affected nations; mobilizing and leveraging resources; increasing transparency and the quality of surveillance; and building local capacity to identify, contain and respond to a pandemic influenza.

The Partnership is a voluntary coalition built on a set of ten core principles, which call for enhanced preparedness, surveillance, transparency in the form of rapid reporting and the sharing of data and samples, and cooperation among Partners and with several key international organizations, including the World Health Organization (WHO), the Food and Agriculture Organization (FAO), and the World Organization for Animal Health (OIE). Through the Partnership, countries have agreed to work together to develop the capacity to plan for, detect, prevent, and rapidly respond to an incipient epidemic. The Partnership is working closely with the international organizations that have led global efforts to heighten surveillance in poultry and die-offs in migratory birds and rapid introduction of containment measures. Members have developed, or are in the process of developing, national preparedness plans, setting up surveillance networks and working closely with the WHO, FAO, and OIE in the detection of outbreaks.

I am pleased to report that the Partnership is off to a good start. In early October, the State Department hosted a well-attended meeting of the Partnership member countries. Senior officials from 88 countries and nine international organizations participated actively in the plenary sessions and roundtables, and identified three priority areas for collaboration: building stockpiles of drugs and supplies; speeding vaccine development and distribution; and implementing rapid response and containment measures. Several conclusions also emerged from these productive discussions: recognizing that many countries lacked the capacity to prepare for or respond to a pandemic, capacity building is a priority. A number of participants stressed the need for communication and education strategies to raise public awareness and

change behavior. Participants also emphasized the need for prompt reporting of suspected cases and for a coordinated international effort. They stated that, in addition to the health impacts of the pandemic, we must prepare for the economic and social effects, ensuring continuity of business operations, for instance.

The Partnership is truly a cooperative effort. It includes not only key U.N. agencies and international organizations such as the World Health Organization, the Food and Agriculture Organization, the World Organization for Animal Health, and the World Bank, but also regional organizations such as the Asia Pacific Economic Cooperation (APEC) forum, the Association of Southeast Asian Nations (ASEAN), the African Union, the European Union, and the Summit of the Americas. Significantly, a number of countries have supported the Partnership by taking leadership roles in several key areas. As a result of the Senior Officials Meeting, Canada agreed for example, to spearhead follow-on discussions on international stockpiling of vaccines and anti-viral medicines as an important component of readiness. We held discussions with representatives of the European Union on a comprehensive strategy for vaccine research, development and production. Australia and Japan agreed to collaborate on rapid response and containment, including the economic and social impacts of a pandemic. Since the October Senior Officials Meeting, work is progressing on the issues of stockpiles, rapid response and containment, and vaccines. Much of this work was carried forward at a meeting co-hosted by the WHO, FAO, OIE and the World Bank in Geneva on November 7–9, 2005, and at the annual Ministerial meeting of the Global Health Security Action Initiative (GHSI), in Rome on November 17–18, 2005, which brought together the Health Ministers of Canada, France, Germany, Italy, Japan, Mexico, the United Kingdom, and the United States, along with the Commissioner of Health and Consumer Protection of the European Commission and the Director-General of the WHO.

Stockpiles: In late October, Canada held a meeting of health ministers in Ottawa and put on the agenda the topic of stockpiles of anti-viral medicines and vaccines. At the conclusion of the Ottawa meeting, the ministers endorsed a communiqué stressing the urgent need for strengthening surveillance, a global policy on vaccine development, and coordinated risk communication. HHS Secretary Leavitt told the assembly that the involved countries and relevant international organizations would need to agree on a proper doctrine to govern rapid response and containment as a prelude to getting national commitments to the creation of an international stockpile of anti-virals. In addition, he called for holding a tabletop exercise, including simulated drug delivery, to enhance international understanding and communication on this important topic, to be followed, by the end of calendar year 2006, with a full dress-rehearsal to test the international response to a cluster of human cases of a novel influenza virus with pandemic potential in Southeast Asia. Discussion of stockpiling of anti-virals continued at the GHSI Ministerial, where the eight Ministers of Health endorsed the creation of mechanisms to supplement the three million treatment courses of Tamiflu that Hoffman-La Roche has donated to the WHO Secretariat for containment of an incipient outbreak. The Ministers made it clear, however, that they conditioned their support on the production by the WHO staff of a clear and coherent concept of operations and doctrine of deployment for stockpiled anti-virals.

Rapid Response and Containment: Australia used the Asia Pacific Economic Cooperation (APEC) forum's avian influenza preparedness meeting on October 31 through November 1 to make progress on response and containment strategies. In addition to the 21 APEC members, WHO, FAO, ICRC and the World Bank attended the meeting. Participants agreed to establish communication and information-sharing networks among experts in the region, build an inventory of regional resources and capabilities that could be provided to expert multilateral organizations for rapid response in the event of an outbreak, and conduct a regional desktop simulation in the first half of 2006 to test regional communication during a potential pandemic outbreak. Given that a human influenza pandemic is most likely to emerge from Southeast Asia, the work begun at this meeting in Brisbane to enhance a regional rapid response capability is essential. The Global Health Security Action Initiative (GHSI) Health Ministers also committed to work with the WHO Secretariat to produce a doctrine of deployment for international containment efforts and a clear concept of operations for international stockpile(s) of anti-virals and medical supplies for presentation to the WHO Executive Board at the end of January 2006.

Vaccines: On November 4–5, the World Health Organization hosted an experts meeting on the development of vaccines for pandemic influenza. This meeting afforded an opportunity for all countries working on a vaccine against avian influenza to share their progress and establish a way to share technical information in order to speed the development of a safe and effective human vaccine. In the first quarter of calendar year 2006, HHS and the WHO Secretariat will be co-hosting a meeting

of international drug regulators to begin the process of harmonizing, to the greatest extent possible, the requirements for marketing approval of vaccines against a pandemic strain.

On November 7–9, 2005, in Geneva, the WHO, FAO, OIE, and the World Bank hosted a Partners meeting on avian influenza and human pandemic influenza. Specifically, as an outgrowth of our Partnership’s Senior Officials Meeting, there were detailed discussions on focusing international efforts on short-term animal monitoring, surveillance, antiviral stockpiles, expanding vaccine production capacity, contingency planning to ensure continuity of operations if an outbreak occurs, and communications strategies. In addition there was agreement on the importance of working to help African countries—particularly those already overwhelmed by HIV/AIDS.

Partnership’s Next Steps: One issue to be more fully addressed is donor coordination. In the recent discussions in Geneva, we proposed that the WHO, the World Bank and other major donors, coordinate with us their assessments of country needs. This will allow us to come to a common understanding of what additional financial and technical assistance is necessary. A subsequent conference to be co-sponsored by the European Commission and the Chinese in mid January will provide an opportunity for donors to outline what they are, and will be, doing to help countries affected with avian influenza. And we will hold another meeting of the Senior Officials of the International Partnership on Avian and Pandemic Influenza early next year to take stock of the progress being achieved and to determine what additional steps should be taken.

Diplomatic Engagement: The Bush Administration has taken advantage of every possible bilateral and multilateral opportunity to stress the seriousness of the threat posed by avian influenza and the need for rapid action. The President is personally engaged and has raised this issue with the Presidents of China, Indonesia, and Russia as well as the Prime Ministers of Canada and Thailand. Secretary Rice reiterated our concerns to ASEAN countries, meeting on the margins of the September High-Level Segment of the UNGA. She also devoted time on her recent Ottawa trip to a briefing on the progress of the Canadian health ministerial discussion on possible stockpiles of anti-viral medicines and vaccines.

We are also advancing this issue at the highest levels in Asia. President Bush attended the APEC Leaders meeting last month in Korea and the topic of avian influenza was a centerpiece of those discussions. As the Chair of the APEC Health Task Force, the U.S. Government is working with our key partners in APEC to strengthen the region’s commitment to prepare for and prevent an influenza pandemic. In the ASEAN Regional Forum (ARF), we are encouraging participants to consider the security implications of a pandemic. Deputy Secretary Zoellick raised the threat of avian influenza and the need for preparation and planning in the ASEAN and ARF meetings in Laos this past July.

In addition, we are reaching out to the private sector to improve their regional capacity to respond and prepare for a pandemic. We are urging the APEC Business Advisory Council (ABAC) to look into using private sector health facilities to enhance epidemic surveillance and detection capabilities. We are also recommending that ABAC consider establishing a set of business community ‘best practices’, including a checklist for emergency preparedness, paying special attention to small and medium sized enterprises.

During mid-October, Under Secretary Dobriansky traveled to Southeast Asia—Thailand, Cambodia, Laos, Vietnam, Indonesia, Singapore and Malaysia—with Secretary of Health and Human Services, Mike Leavitt (and members of his staff from the National Institutes of Health and from the Centers for Disease Control and Prevention), and representatives from USAID and the U.S. Department of Agriculture, as well as Dr. Lee, the Director-General of the World Health Organization (WHO), and representatives of the Food and Agriculture Organization (FAO) and the World Organization for Animal Health (OIE). We were very pleased that these countries had their Foreign or Prime Ministers meet with the U.S. delegation—an indication that we were succeeding in our efforts to raise the political profile of this issue. Malaysia, for instance, named a senior point of contact in its Foreign Ministry to enhance bilateral and multilateral communication. Vietnam offered for the first time during the U.S. visit to accept international monitors to augment their national surveillance efforts.

As a result of the U.S. delegation visit, and additional assessments done by U.S. experts, we learned more about the needs of those countries. For example, Vietnam, Laos, Cambodia, and Indonesia are particularly in need of capacity building in technical areas such as laboratory training and vaccine development. The U.S. delegation stressed our desire to work with the public and private sectors in these nations

to address these shortcomings and the Administration has, in fact, already begun to fill these critical needs.

I'd like to emphasize that this is truly an unprecedented interagency effort by the United States. The President has charged the State Department with leading the international activities of the U.S. National Strategy for Pandemic Influenza and, in doing so, we collaborate closely with our dedicated colleagues at HHS (including CDC and NIH), USAID, USDA and other technical agencies. With that in mind, let me provide some concrete examples of U.S. assistance in three key areas of our strategy—surveillance, preparedness, and response and containment. Our assistance targets the needs of the most affected countries with the least capacity such as Laos, Cambodia, Vietnam and Indonesia. These activities are being designed and funded by USAID, HHS and USDA as part of a coordinated interagency process.

On *surveillance*, we are providing training, financial, technical and commodity support for national veterinary and other staff to monitor H5N1 in domestic and wild birds. We are increasing the capacity of national public health staff to detect new human infections of this and other novel strains of influenza and ensure timely and accurate diagnoses. We are working with the FAO on strengthening “early warning systems” in the agricultural sector and the ability to communicate rapidly about concerning cases. To give a country-specific example, we have provided the support of the U.S. Naval Medical Research Unit (NAMRU-2) to strengthen surveillance efforts in Indonesia.

On *preparedness*, we are supporting Ministries of Health as they develop national pandemic preparedness plans. We are helping Ministries in Asia to conduct pandemic preparedness training and simulations. We are purchasing equipment for experts in the region to test samples. With the FAO and WHO, we are engaging Agriculture, Health and other ministers to increase regional and international coordination. To give a country-specific example, the Vietnamese Ministry of Health has received support from HHS (including CDC) for vaccine development and clinical trials and has solicited our assistance in monitoring its response to human and animal infections of H5N1.

Finally, on *response and containment*, we are establishing, training, and supporting rapid response teams through FAO to conduct containment measures in animal populations and through Ministries of Health to react quickly to attempt to contain cases of H5N1 or other novel flu strains in humans. We are building local capacity to cull and dispose of infected or exposed animals, and setting up in-country and regional emergency stockpiles of essential commodities. We are, for example, pre-positioning protective gear in Southeast Asian countries to be used in case of an avian flu emergency.

Funding: Efforts are already underway for HHS and USAID to use \$25 million in emergency Tsunami supplemental funds and \$5.8 million of reprogrammed USAID Fiscal Year '05 funds for this emerging policy priority. In addition, USAID plans on reprogramming another \$6.3 million of Tsunami funds for this purpose. This is, of course, only the start. In conjunction with his November 1st announcement of the National Strategy, the President called for an additional \$7.1 billion in emergency funding. This request includes \$250.8 million to detect and contain outbreaks before they spread around the world; as the President rightly noted: “early detection is our first line of defense.” Of the \$250.8 million, the Department of State would receive a total of \$8.3 million for international response coordination, involving foreign governments and non-governmental organizations, diplomatic outreach, exchanges of U.S. and foreign medical personnel, and health support and protection of U.S. Government employees and families at U.S. missions overseas. The Department of State would also receive \$20 million to fund the potential evacuation of U.S. Government personnel and dependents from overseas missions.

Conclusion: In the few months since its creation, the International Partnership on Avian and Pandemic Influenza has already made a dramatic difference in heightening international awareness and made addressing this issue a priority for nations; fostered closer collaboration among Agriculture, Health, Economic and Foreign Ministries; accelerated the placement of monitors in high-risk countries; catalyzed the development and deployment of comprehensive surveillance networks; and increased donor commitment and coordination. But there is still more that needs to be done.

We believe that our message of cooperation and common cause has resonated with many countries, particularly those most affected in Asia. Countries that lack the capacity to prepare for, and respond to, an influenza pandemic are showing growing understanding and increasing willingness to confront the problem. They realize that the cost of taking action now is significantly less than the cost of a pandemic. At the recent meeting in Geneva, WHO Director General Lee estimated that 120 countries now have, or have begun preparing some form of avian flu preparedness plans; this is twice the number estimated just two months ago. Those plans will serve as

the foundation on which national and regional surveillance networks will be built and strengthened. We are also hearing from the FAO and OIE that at-risk countries are becoming increasingly transparent, sharing information and samples more readily than in the past. These international organizations credit countries and their leadership for making this issue a priority and laud the United States for helping to make this progress possible through the International Partnership on Avian and Pandemic Influenza and sustained high-level diplomacy. Even as we work with our partners to coordinate assistance, the United States has begun to assist the highest risk countries in the key areas of surveillance, preparedness, and response and containment. We will build on this solid foundation as the Partnership progresses. We look forward to working with you on avian flu and I thank you again for this opportunity to testify before this Committee.

I welcome any questions you may have.

Chairman HYDE. Thank you, Mr. Rock. Dr. Hill.

STATEMENT OF KENT R. HILL, PH.D., ASSISTANT ADMINISTRATOR FOR GLOBAL HEALTH, U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT

Mr. HILL. Chairman Hyde, distinguished Members of the Committee, thank you so much for this opportunity to address this important issue.

Thankfully, right now the H5N1 mainly affects animals, more specifically birds. As you have stated, there is no efficient transmission from animals to humans or human to human at this point. But the impact could be significant.

Indeed, if it hit in the way that the 1918 influenza hit, it would be devastating in terms of the millions who would die. And the World Bank has estimated that it could cost as much as \$800 billion in terms of that impact alone.

The key, of course, is early and rapid response to preparedness, dialogue with political leaders, political commitment, and transparency. We know that the death toll right now is something like 68 that have been confirmed by WHO is relatively small, but we know that the fatality rate of those that get sick is very, very high. So there is something to be concerned about.

And if I could just add this one point at the very beginning. There are those who say since there is no guarantee that H5N1 will in fact achieve efficient human-to-human transmission, that we are gambling and spending a lot of money when we don't even know if it is going to be necessary.

The key point that we have to keep reminding ourselves about, our constituents about, is this. The record over 300 years is that pandemics do come, 10 in 300 years, three in the last century. Whether it is H5N1 or not, it will be a pandemic. All the steps that we are taking internationally now will guard not just against H5N1, but any other pandemic that may come in the next few months or years.

Our approach at USAID is to quickly detect a virus, to, once it is identified, to cull the birds, when possible to vaccinate birds in that vicinity. We work closely with the State Department. As my colleagues in the State Department stated, they are in the lead on international development issues in terms of the overall strategy in working with governments. The USAID has headed the interagency working group that is worked on this since last April with all the other colleague agencies for the field operations to help do the con-

tainment, the surveillance, the response, et cetera, the communication related to this.

We also work extremely closely with our international organizations that we funnel a lot of money through and work very closely with: WHO and FAO. That is a key part of what we are trying to do.

I want to touch on, if I could, some of the key things that USAID has been doing recently that I think are very helpful. There are 107 countries in the world that we are eligible to give assistance to. We have done a survey of those 107 countries. We know what their level of response is. We are preparing a global analysis of that that we will be reporting out, that will help us to identify the gaps in priorities for coordination that we must focus on.

As you know, this is no longer something that just has to do with Southeast Asia. In August 2005, the H5N1 strain was confirmed in Russia, in Kazakhstan. It has since been found in Eastern Europe and Romania, Turkey, Croatia. It will follow the migratory flyways and end up in Africa and elsewhere in the world. This seems unavoidable.

We have expended, USAID, \$10 million of the \$25 million that the Congress gave us in the supplemental a few months ago. We have also reprogrammed about \$5.8 million. We are working with OMB and the State Department to find an additional \$6.3 million from the supplemental that was for the tsunami. We have got good plans for this money, and none of this even has to do with the President's most recent proposal that has to do with both domestic and international preparation.

I do want to say just a word about the importance of national communication campaigns to promote safe behavior in terms of contacts with animals. This is a key part of our strategy and what we are trying to produce by early this year, early next year. Early warning systems will be fully moving forward in all of the major countries where the risk is greatest, but we have been working to prepare for this for a number of months.

By February compensation options for farmers should be identified for Vietnam, Indonesia, Cambodia, and Laos. If we don't succeed in persuading the farmers who have the first access and know about the deaths of the birds, if we don't communicate to them how they can tell the difference between whether a bird dies of Newcastle's Disease or H5N1—and by the way, it is clear, you can explain it; that is why you have to use NGOs to help you get the message out—H5N1 kills very quickly, and in bunches. Newcastle's, for example, will take a few days longer. So if you know what you are looking for, you can report it. If it is reported, the steps for containment can take place quickly.

Just a word about the President's plan announced on November 1, the \$7.1 billion plan and the \$251 million for international, USAID will be taking care of about \$131 million of that money. It will expand on the work that we have been doing in cooperation with international organizations in Southeast Asia, and we will work with our partner agencies on that.

I think the last point I want to make is simply this. The United States should understand that it is not the only player in trying to deal with this. The \$251 million is not the only money going into

this. We are trying to coordinate with other bilateral donors, with other international organizations. USAID's work that has to do with health infrastructure that is an ongoing process all has to do with increasing the capacity, the capability of countries to deal with any kind of a health threat that comes up.

So this is just a part of an overall international and even national plan to deal with the international needs of these countries as they try to prepare to deal with what is, in fact, a very significant health threat to them, and to us, as well.

Thank you.

[The prepared statement of Mr. Hill follows:]

PREPARED STATEMENT OF KENT R. HILL, PH.D., ASSISTANT ADMINISTRATOR FOR
GLOBAL HEALTH, U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT

Chairman Hyde, Representative Lantos and other distinguished Members of the Committee, I would like to thank you for convening this important hearing on avian influenza (AI) and for inviting me to testify.

USAID has closely followed the rise and spread of the H5N1 strain of avian influenza for nearly two years. On February 6th, 2004, USAID provided \$250,000 to the World Health Organization (WHO) to assist in the response to the outbreak of avian influenza in Asia. USAID also provided personal protection equipment (PPE) to Vietnam to be used in handling and culling of infected poultry.

More than six months ago, in April, 2005, USAID staff began having regular interagency AI planning meetings with U.S. government partners at the Departments of State, Health and Human Services, Agriculture and Homeland Security to coordinate our efforts to help nations respond to this threat and prevent the spread of avian influenza.

Also in April, USAID set aside \$1.25 million to purchase additional PPE and to strengthen surveillance and laboratory capacity in SE Asia, and improve rapid response, including \$300,000 transferred to the World Health Organization (WHO). Our Office of Foreign Disaster Assistance also procured 10,000 sets of personal protective equipment for health workers and animal cullers, and pre-positioned it in five SE Asian countries.

Our technical experts in Washington and the field are working with nations, as well as regional and international organizations to contain the spread of the AI virus and, in case it is needed, prepare for a potential human influenza pandemic. USAID has reached out to all of the countries where we have missions as well as to non-presence countries to assess the readiness of regional programs to respond to avian influenza. USAID has completed rapid assessments of the state of preparedness to respond to avian and pandemic influenza in 107 countries eligible for USAID assistance. Assessments cover a full range of essential capabilities, including pandemic planning, surveillance and diagnosis, communications, rapid response, and emergency stockpiles. The information is being compiled in a global analysis that will enable agency health experts to identify gaps, establish priorities and provide strong coordination. By mid-December, the global analysis will be available for use by other U.S. Government agencies.

Our response strategy is guided by the level of the threat in each country. For instance, a country with animal infections but no human infections is at a lower level of threat than one with both animal and human infections. Countries with neither animal nor human infections are at the lowest level of threat. Lower priority is given to countries that can meet their own needs and receive significant contributions from other donors.

Under the leadership of Secretary Rice, USAID is helping countries prepare for a potential pandemic and respond to current animal outbreaks. Working in close coordination with U.S. government partners, USAID is supporting case detection among birds and tracking animal outbreaks so that we may act as rapidly as possible to aggressively contain the illness. In this regard, it is imperative that we raise the profile of avian influenza to host governments so that we can help them undertake efforts to prevent and contain the spread of the virus.

In support of the President's *National Strategy on Pandemic Influenza*, the Agency is focused on the following key principles:

- Preparedness
- Surveillance

- Diagnostics and Response
- Public Communication and Education

STATUS OF THE DISEASE

As of today, highly pathogenic avian influenza [HPAI] H5N1 virus is an avian disease. There is, as yet, no evidence of efficient human-to-human transmission. Nevertheless, mounting an effective response at this stage is essential to halting the spread of this virus in Asia and preventing a potential pandemic.

With the first human death in China linked to the H5N1 avian influenza virus on November 16th, five Asian countries have confirmed fatalities from the disease. H5N1 influenza has been responsible for 133 confirmed human infections with 68 fatalities. More than 200 million domestic poultry in Asia and Eastern Europe have died as a result of avian influenza or been culled or killed.

In each country with outbreaks, it will be vital to quickly detect the virus in birds and contain it there by culling and vaccinating all infected and exposed animals. Some countries such as Indonesia and Vietnam use a combined approach of both culling and vaccination of poultry to reduce the chances of the virus passing to humans.

The present threat mainly stems from animal-to-human transmission and has been mostly confined to Southeast Asia and southern China. But trends are worrisome.

Migratory birds are the natural reservoir of all 16 H subtypes of avian influenza viruses; these viruses exist in the bird in a lowly pathogenic form. However, in Asia and parts of Europe, it appears that migratory birds may actually be harboring HPAI H5N1 virus and disseminating it along their migratory pathways.

The recent expansion of AI into Russia and the Eurasia region underscores the sobering fact that the whole world is potentially at risk. During August 2005, the highly pathogenic H5N1 strain of avian influenza was confirmed in poultry in parts of Siberia, Russia and in adjacent parts of Kazakhstan. Both countries have reported deaths of migratory birds in the vicinity of poultry outbreaks. In October 2005 the presence of H5N1 avian influenza was confirmed in samples taken from domestic birds in Turkey, Romania, Croatia, Kazakhstan and Russia.

The migration of infected birds may have already carried the virus to Africa, as it follows migratory flight paths southwest from northern Russia to east Africa.

USAID Missions in Romania, Ukraine, Georgia, West Bank/Gaza, Tanzania and Ethiopia have been quick to respond to this spreading threat by reprogramming FY 2005 funds to support outbreak containment. To date USAID Missions have reprogrammed \$5.8 million, which is in addition to the \$10 million emergency supplemental funds, bringing the total USAID commitment for AI in FY 2005 to \$15.8 million.

It is important to note that no human cases have been reported in any of these newer outbreaks, although it is possible that suspect human cases have gone unreported. At the present time, the risk to humans is generally low because avian influenza viruses do not usually infect humans.

Despite the limited spread of the virus from animals to humans, there is growing concern that this strain of the Influenza A virus could evolve and spread efficiently from human-to-human, placing millions of lives at risk. If sustained human-to-human transmission occurs, our effectiveness in responding and containing the spread of the virus will be key to minimize death and suffering.

SPECIFIC CHALLENGES

Success in containing AI requires limiting animal infections. However, it is extremely difficult to contain animal infections since 70 to 80 percent of poultry raised in Southeast Asia live on small, "backyard" farms. We are facing a lack of awareness about the threat the virus poses to animals and humans alike in the communities that raise these animals. The fact that 50 to 80 percent of poultry deaths in Asia are from non-AI infections poses a further problem in getting small farmers to recognize and report die offs. Farmers who live at subsistence levels are also reluctant to report sick birds for fear of losing their entire flock to culling without compensation.

The economic consequences of a tardy response could be devastating. The Asian Development Bank estimates that the SARS epidemic cost the global business community some \$60 to \$80 billion in industries, hitting the airlines, manufacturing, and financial sectors particularly hard. The United Nations Food and Agriculture Organization (FAO) estimates that AI has already cost private business as much as \$10 billion. Should the circulating influenza strains become easily transmissible between humans, the effects on business around the world would be disastrous.

To effectively meet these challenges, USAID is working in partnership with international organizations and governments to bolster disease surveillance and testing capacity, draw up preparedness plans, and take other preventive actions to contain outbreaks.

THE USAID RESPONSE

On May 11, 2005, President George W. Bush signed an emergency supplemental appropriations bill, which contained \$25 million to prevent and control the spread of avian influenza. USAID was allocated a significant portion of this funding and is working in conjunction with the Department of Health and Human Services (HHS) and the U.S. Department of Agriculture (USDA) in developing nations around the globe to address the current H5N1 outbreaks within poultry and to prepare for a possible pandemic.

The Agency, in partnership with other USG agencies, has moved quickly to operationalize programming in the field. In July, 2005, USAID led an interagency assessment team with HHS and USDA to Laos, Cambodia, Vietnam, and Thailand to develop country-specific action plans for emergency assistance.

We expect that by the end of January, the start of the flu season in Southeast Asia, multi-sector country preparedness plans will be developed with USAID assistance in Vietnam, Cambodia, Indonesia and Laos. USAID targeted these countries because they have the most serious animal outbreaks and cases of human infection, and therefore are in most need of immediate external assistance. In addition, national communication campaigns promoting safe behavior will be underway in the high-risk countries. By the end of February, early warning systems and national response teams should be in place in the four countries to report human and animal outbreaks within one week of onset and to confirm these outbreaks no later than one additional week.

We project that a national program to vaccinate chickens and ducks will be completed by then in Vietnam. Indonesia will benefit from the presence of an emergency team of experts as well as from the establishment of local disease control centers in hot-spot areas. In addition to offering up-to-date information, these centers will train animal health technicians and veterinarians in how to expedite disease surveillance and control in birds. With Indonesian authorities, they will help decide upon appropriate control measures such as culling, vaccination, and bio-security. They also provide support for animal health teams in their systematic, house to house search for diseased birds.

By February, compensation options for farmers should be identified in Vietnam, Indonesia, Cambodia and Laos. These options will be for national governments, multilateral organizations and other sources to examine as it is critically important to reduce their financial burden from losses to their flocks. Simply put, they are our first line of defense and without farmers quickly reporting suspected deaths or cases of AI, our efforts are handicapped from the outset at one of the most critical points.

Pandemic preparedness training in the affected countries is slated to begin in February. This will have local officials gain a better understanding of the importance of transparency and responsiveness in handling reports of disease.

Also, by early to mid 2006, the training of active case detection teams will have occurred in Vietnam, Cambodia, Indonesia and Laos. They will provide logistical support and ensure quality control for sample collections from animal populations and, in cooperation with work funded by HHS, in humans. Health workers will have completed technical education on identifying cases and minimizing their own risks. This will strengthen disease surveillance and laboratory diagnosis capacity.

USAID is working closely with private sector partners as well as international organizations, including the World Health Organization (WHO) and the FAO. This includes providing the first bilateral support to the new Office of the Global Coordinator for Avian and Human Influenza at the United Nations who will lead the efforts of the WHO, FAO and other United Nations agencies. We are helping assure that this global threat is met with a well coordinated and strategically appropriate global effort.

The capacity we are building in surveillance, laboratories, epidemiology and disease control measures and response to infectious disease outbreaks will help countries to better respond to new threats from natural diseases like SARS, measles, and cholera, as well as deliberately-caused diseases of bio-terrorism.

As a concrete demonstration of this inter-agency and collaborative approach to our work on this crucial subject, I joined Under Secretary of State for Global Affairs and Democracy Paula Dobriansky, Deputy Under Secretary of Agriculture Jim Butler, and HHS Secretary Mike Leavitt in September on a fact-finding mission to Southeast Asia that included stops in Thailand, Cambodia, Laos, Viet Nam and Indo-

nesia. The delegation saw first-hand the challenges we face on the ground, and urged national government leaders at the highest levels to work with us, in a spirit of transparency and open sharing of information, to contain the H5N1 virus in animals and prepare for an eventual human influenza pandemic. They also saw programs that are beginning to be the beneficiaries of our recent investments.

In total, USAID obligated \$15.8 million in FY 2005 to help prevent and contain avian influenza in Southeast Asia, where the largest impact of this epidemic has been felt. Ten million dollars were from the FY 2005 Emergency Supplemental and \$5.8 million were redirected from other programs.

USAID's Office of Foreign Disaster Assistance (OFDA) has pre-positioned personal protective gear for local health and agricultural staff in Cambodia, Laos, Vietnam, Indonesia and Thailand to be used in the case of an AI emergency. Agency experts are also working with FAO and WHO to help strengthen planning for AI control and pandemic preparedness, and working with the business community to increase the resources, expertise and financing available for this effort.

In addition, USAID is an active supporter of the International Partnership on Avian and Pandemic Influenza, which was announced by President Bush at the United Nations in September.

At USAID's headquarters, Administrator Natsios chairs the Agency's Avian Influenza Preparedness and Response Task Force that meets weekly to consider urgent policy and budget issues. It includes representation from all Agency bureaus.

In early October, Mr. Natsios personally wrote to all of USAID's missions to signal avian influenza as the top agency priority, calling for each mission to engage national government and local partners on country-level preparedness and readiness.

Administrator Natsios also established the Avian and Pandemic Influenza Management and Response Unit located in the Bureau for Global Health. This unit is responsible for day-to-day management and oversight of the Agency's AI activities, including providing direct technical and program support to the regional bureaus and field missions, liaising with other U.S. government and international partners on AI, and identifying and reporting to the Task Force on key policy and budget issues that require senior level action.

In the field, USAID Missions around the globe are moving ahead rapidly with plans to address AI. Many are supporting U.S. Government and ministerial task forces, collaborating with international organizations, and working with FAO on animal surveillance.

In addition to the multi-sector plans for Southeast Asia, USAID is also closely working with ministries of health and agriculture and international organizations in Africa, Latin America and the Caribbean, and Europe and Eurasia to draft preparedness plans to include: establishing sentinel surveillance sites for poultry flocks and wild birds; strengthening monitoring and reporting of human respiratory illnesses to rapidly identify unusual cases; reinforcing laboratory capacity to enable detection of AI, or identify labs in nearby countries that can do testing.

USAID is working aggressively to address imminent risks in Africa, especially the East African countries of Ethiopia, Kenya, and Tanzania to increase surveillance for H5N1 among birds especially along trade routes. In addition, in collaboration with HHS, USAID is redirecting its existing human disease surveillance program in East Africa to include a strong focus on detecting and diagnosing AI. And while the threat in West Africa is marginal now, it will increase in the spring when wild birds from East Africa travel and meet with birds from Europe.

USAID missions are providing assistance to host governments to assemble donors, establish task forces, and develop pandemic preparedness plans in cooperation with other U.S. Government agencies, FAO, and WHO. In addition, countries with USAID support are strengthening disease surveillance programs to include a strong focus on detecting, diagnosing, and responding to avian influenza.

USAID has a person designated as point of contact for avian influenza in every Mission and regional office and, through their efforts, has received assessments from 40 African countries detailing country activities, preparedness level, and potential role of USAID. These assessments are currently being analyzed to use in the planning and resource distribution process. In addition, several African countries, including Ethiopia, Uganda, Senegal, Tanzania, and Nigeria, have provided detailed plans for avian influenza preparedness activities. Many countries are building upon existing SARS and Influenza preparedness plans and task forces and focusing on strengthening existing surveillance and laboratory capacity.

Tanzania, for example, has moved ahead quickly to address the potential threat of avian influenza. The USAID Mission has reprogrammed \$75,000 of existing surveillance funds to focus on wild bird surveillance, and has been asked to write the wild bird risk assessment section of the health sector National Preparedness Plan. The Mission has also supported multi-sectoral work on avian influenza, including

the convening of a multi-sector task force with participation of the Ministries of Health, Water and Livestock Development, and Natural Resources and Tourism.

On October 31st, Under Secretary of State for for Global Affairs and Democracy Paula Dobriansky joined USAID Africa Bureau Assistant Administrator Lloyd Pearson, Avian and Pandemic Influenza Management and Response Unit Director Dr. Dennis Carroll and myself at a USAID-sponsored meeting with 12 African Ambassadors to provide an update on AI and discuss responses.

USAID's 16 missions in Latin America and the Caribbean are working with host governments and other partners to raise awareness and plan for a potential AI outbreak. This involves assessments of the pandemic preparedness of host countries, and technical consultations in cooperation with other U.S. government agencies and the Pan American Health Organization (PAHO).

In recent weeks, USAID quickly responded with our other U.S. Government counterparts to AI outbreaks in animal populations in Eastern European and Eurasian countries. We are providing technical assistance to develop and strengthen preparedness plans, conduct disease surveillance among animals, and determine immediate needs to head off further outbreaks in the region.

We are also beginning to work with the private sector on possible public-private partnerships. USAID's Global Development Alliance (GDA) is reaching out to corporations and talking to consumer product companies that employ community health advocates to incorporate AI information into their curriculum. USAID's GDA Secretariat has met with approximately 25 companies to date. In addition to meetings in the United States, GDA recently hosted a series of discussions in Indonesia, Vietnam and Thailand with potential private sector partners as well as American Chamber of Commerce and Embassy representatives.

Businesses can play an important role by bringing the message beyond the workplace, by educating communities where their facilities are located, and promulgating the message through their distribution channels. USAID is also in contact with companies in the poultry and animal feed industry to help them improve bio-security measures and establish improved surveillance and control measures within their supply chains.

NEXT STEPS

On November 1st 2005, President George W. Bush requested \$7.1 billion from Congress to fund a comprehensive response to avian and pandemic influenza. The request includes \$251 million in support of international efforts to detect and contain outbreaks of novel influenza strains with pandemic potential before they spread around the world.

The budget request reflects a national strategy that is designed to meet three critical goals: first, detect and contain outbreaks of novel influenza strains that occur anywhere in the world; second, protect the American people by stockpiling vaccines and antiviral drugs, and improve the U.S. ability to rapidly produce new vaccines against a pandemic strain; and, third to prepare for an effective response at the federal, state and local levels in the event that a pandemic reaches our shores.

The first part of our strategy is to detect outbreaks among animals before they spread across the world. In the fight against avian and pandemic flu, early detection is our first line of defense. USAID, in partnership with HHS, USDA and the Department of State has been charged to lead the international effort. One hundred and thirty-one million dollars of the request to Congress is for USAID programs to help our foreign partners expand their surveillance and testing capacity for possible H5N1 outbreaks, draw up preparedness plans, and take other critical actions to detect and contain outbreaks.

Specifically, USAID, in close cooperation with HHS and USDA, will strengthen animal and human surveillance, behavior change communications, and response capacity in the most-affected countries—Cambodia, China, Indonesia, Laos, and Vietnam. Because of endemic animal infections and confirmed human cases, these countries represent the greatest risk for human health. China is a significant poultry producer which increases the risk for human infections, and they are on a major flyway for migratory birds.

USAID will also improve pandemic planning and animal surveillance in countries where H5N1 has been recently introduced or those at high-risk of introduction because of bird migration patterns. These activities would be focused in Eastern Europe, Eurasia, the Near East, and Africa. Activities in Central and South America will focus on pandemic planning.

The Administration's request for supplemental FY 2006 funding will allow, USAID, in partnership with HHS and USDA to create a stockpile, to be managed by the Office of Foreign Disaster Assistance, of key medical supplies that will be

pre-positioned in high-risk regions of the world to contain potential outbreaks of H5N1 among humans. We are presently working out the details, in concert with our U.S. Government and international partners, on the stockpiles composition, quantities and strategies for their use.

CONCLUSION:

The first principle of good disaster preparedness and management is: we may be allowed to hope for the best but we must be prepared for the worst. This principle has guided our preparedness planning for the challenge of a potential outbreak of avian influenza.

It should be underscored that as of today there is no evidence of efficient human-to-human AI transmission. This is not a moment for complacency, however, as the distinguished members of this Committee well know. We may be allowed to hope for the best but we must be prepared for the worst. This has been an operating principle at USAID since Administrator Natsios made the issue of avian influenza the number one priority at the Agency in September.

Chairman HYDE. Thank you. Dr. Schuchat.

**STATEMENT OF ANNE SCHUCHAT, M.D., ACTING DIRECTOR,
NATIONAL CENTER FOR INFECTIOUS DISEASES, CENTERS
FOR DISEASE CONTROL AND PREVENTION**

Dr. SCHUCHAT. Good morning. Thank you for the invitation to testify on influenza pandemic planning.

CDC and other agencies within HHS are working together to prepare the United States for this potential threat to our nation, and we are also working with colleagues at the Department of State, USAID, and other Federal and international organizations to ensure close collaboration in the global efforts.

In order for an influenza virus to cause a pandemic, it must be a virus to which there is little or no preexisting immunity in the human population. It must be able to cause severe illness in humans, and it must have the ability for sustained human-to-human transmission.

So far the H5N1 virus circulating in Asia meets the first two criteria, but not yet the third.

In the current H5N1 outbreaks in Asia, since January, 2004, 134 human cases have been confirmed by the World Health Organization. These have resulted in 69 deaths, a fatality of around 50 percent.

We cannot predict the severity and impact of an influenza pandemic, whether from the H5N1 virus currently circulating in Asia and Europe, or the emergence of another influenza virus of pandemic potential. Modeling studies suggest that a medium-level pandemic in the U.S. alone could result in 89,000 to 207,000 deaths here. But a more severe pandemic, as happened in 1918, could have a much greater global and domestic impact.

There are several important points to note about influenza. First, as has been mentioned, pandemics happen. There were three in the past century; we can expect more.

Second, the capacity to intervene and control spread of the virus once it gains the ability to have sustained person-to-person transmission will be extremely limited. An outbreak anywhere in the world increases the risk everywhere.

Third, the H5N1 Avian influenza strain that is circulating in Asia is currently considered the leading candidate to cause the next pandemic, but it is possible another influenza virus which could originate anywhere in the world could cause the next pandemic.

This uncertainty is one reason we need year-round laboratory surveillance of influenza viruses that infect humans.

And fourth, because early detection means having more time to respond, it is critical for the U.S. to collaborate with domestic and global partners to expand and strengthen the early warning surveillance activities.

In October, Secretary Leavitt led a delegation of United States and international health experts to Southeast Asia. They learned several key lessons.

First, international cooperation is essential. Second, surveillance, transparency, and timely sharing of information are critical. Third, it is vital to strengthen preparedness and response capabilities in Asian countries and other parts of the world.

As you know, the fiscal year 2005 emergency supplemental appropriations included \$25 million in international assistance funds for HHS, USDA, and USAID to prevent and control the spread of Avian influenza in Asia. With these funds, HHS and its agencies are working to assist in developing regional capacity in Southeast Asia for epidemiology and laboratory management of pandemic flu.

Strategies include developing and implementing an Avian influenza curriculum for epidemiologists and laboratorians, training for public health leaders to develop a national network of public health field staff, and training for local allied health personnel to detect and report human cases of influenza.

We are assigning HHS staff to Vietnam, Cambodia, and Laos to improve the detection of influenza cases, and to provide technical assistance for case investigation, and for developing national preparedness plans.

Here in the U.S., the HHS pandemic influenza plan is a blueprint for pandemic influenza preparedness and response, and provides guidance to national, state, and local policymakers and health departments, with the goal of achieving a national state of readiness and quick response.

Among CDC's roles in preparation for a pandemic, we are working to ensure that states have sufficient epidemiologic and laboratory capacity, both to identify novel viruses throughout the year, and to sustain surveillance during a pandemic. We are improving reporting systems so information needed to make public health decisions is available quickly, and we are enhancing monitoring of resistance to current anti-viral drugs to guide policy for their use.

In conclusion, although much has been accomplished, more preparation is needed for a possible human influenza pandemic. As the President mentioned during the announcement of the national strategy for pandemic influenza, our first line of defense is early detection. CDC is closely monitoring the international situation, in collaboration with the World Health Organization, currently affected countries, and other partners. We are using our extensive networks of partners to enhance pandemic influenza planning.

Lastly, the national response to the annual domestic influenza seasons provides a core foundation for how the nation will face and address pandemic influenza.

Thank you for the opportunity to testify, and I am happy to answer questions.

[The prepared statement of Dr. Schuchat follows:]

PREPARED STATEMENT OF ANNE SCHUCHAT, M.D., ACTING DIRECTOR, NATIONAL CENTER FOR INFECTIOUS DISEASES, CENTERS FOR DISEASE CONTROL AND PREVENTION

Mr. Chairman and members of the Committee, I am pleased to be here today to describe the current status of avian influenza around the world; the consequences of a possible human influenza pandemic; and international and domestic efforts to prepare for, and respond to such a pandemic, including the *HHS Pandemic Influenza Plan*. Thank you for the invitation to testify on influenza pandemic planning and preparedness which Department of Health and Human Services (HHS) Secretary Mike Leavitt has made a top priority. The Centers for Disease Control and Prevention (CDC) and other agencies within HHS are working together formally through the Influenza Preparedness Task Force that Secretary Leavitt has chartered to prepare the United States for this potential threat to the health of our nation. We are also working with other federal, state local and international organizations to ensure close collaboration.

As you are aware, the potential for a human influenza pandemic is a current public health concern with an immense potential impact. Inter-pandemic (seasonal) influenza causes an average of 36,000 deaths each year in the United States, mostly among the elderly, and more than 200,000 hospitalizations. In contrast, scientists cannot predict the severity and impact of an influenza pandemic, whether from the H5N1 virus currently circulating in Asia and Europe, or the emergence of another influenza virus of pandemic potential. However, modeling studies suggest that, in the absence of any control measures, a "medium-level" pandemic in which 15 percent to 35 percent of the U.S. population develops influenza could result in 89,000 to 207,000 deaths, between 314,000 and 734,000 hospitalizations, 18 to 42 million outpatient visits, and another 20 to 47 million sick people. The associated economic impact in our country alone could range between \$71.3 and \$166.5 billion. A more severe pandemic, as happened in 1918, could have a much greater impact.

There are several important points to note about an influenza pandemic:

- A pandemic could occur anytime during the year and could last much longer than typical seasonal influenza, with repeated waves of infection that could occur over one or two years.
- The capacity to intervene and prevent or control transmission of the virus once it gains the ability to be transmitted from person to person will be extremely limited.
- Right now, the H5N1 avian influenza strain that is circulating in Asia among birds is considered the leading candidate to cause the next pandemic. However, it is possible that another influenza virus, which could originate anywhere in the world, could cause the next pandemic. Although researchers believe some viruses are more likely than others to cause a pandemic, they cannot predict with certainty the risks from specific viruses. This uncertainty is one of the reasons why we need to maintain year-round laboratory surveillance of influenza viruses that affect humans.
- We often look to history in an effort to understand the impact that a new pandemic might have, and how to intervene most effectively. However, there have been many changes since the last pandemic in 1968, including changes in population and social structures, medical and technological advances, and a significant increase in international travel. Some of these changes have increased our ability to plan for and respond to pandemics, but other changes have made us more vulnerable.
- The current threat of a human pandemic due to HPAI H5N1 should be addressed at both the human and animal levels, recognizing that this is currently an animal disease. But because pandemic influenza viruses will emerge in part or wholly from among animal influenza viruses, such as birds, it is critical for human and animal health authorities to closely coordinate activities such as surveillance and to share relevant information as quickly and as transparently as possible.

THE CURRENT STATUS OF H5N1 VIRUS IN ASIA

Beginning in late 2003, new outbreaks of lethal highly pathogenic avian influenza A (HPAI H5N1) infection among poultry and waterfowl were reported by several countries in Asia. In 2005, outbreaks of HPAI H5N1 disease have also been reported among poultry in Russia, Kazakhstan, Turkey, and Romania. Mongolia has reported outbreaks of the H5N1 virus in wild, migratory birds. In October 2005, outbreaks of the H5N1 virus were reported among migrating swans in Croatia. In 2004, sporadic human cases of avian influenza A (H5N1) were reported in Vietnam and Thai-

land. In 2005 additional human cases have been reported in Cambodia, China, Indonesia, Thailand, and Vietnam. Cumulatively, as of December 6, 2005, 134 human cases have been reported and laboratory confirmed by the World Health Organization (WHO) since January 2004. These cases have resulted in 69 deaths, a fatality rate of approximately 51 percent. Almost all cases of H5N1 human infection appear to have resulted from some form of direct or close contact with infected poultry, primarily chickens. In addition, a few persons may have been infected through very close contact with another infected person, but this type of transmission has not led to sustained transmission.

For an influenza virus to cause a pandemic, it must: (1) be a virus to which there is little or no pre-existing immunity in the human population; (2) be able to cause illness in humans; and, (3) have the ability for *sustained* transmission from person to person. So far, the HPAI H5N1 virus circulating in Asia meets the first two criteria but has not yet shown the capability for sustained transmission from person to person.

The highly pathogenic avian influenza A (H5N1) epizootic (or animal) outbreak in Asia that is now beginning to spread into Europe is not expected to diminish significantly in the short term. It is likely that H5N1 infection among birds has become endemic in certain countries in Asia and that human infections resulting from direct contact with infected poultry will continue to occur. So far, scientists have found no evidence for genetic reassortment. Reassortment can occur when the genetic code for high virulence in an H5N1 strain combines with the genetic code of another influenza virus strain resulting in a new virus that is more easily transmitted. However, the animal outbreak continues to pose an important public health threat, because there is little preexisting natural immunity to H5N1 infection in the human population.

In October 2005, CDC Director Julie Gerberding accompanied HHS Secretary Mike Leavitt when he led a delegation of U.S. and international health experts on a 10-day trip to five nations in Southeast Asia. The purpose of this trip was: 1) to learn from countries that have had first-hand experience with avian influenza; 2) to emphasize the importance of timely sharing of information in fighting the disease; and, 3) to determine the best use of our resources abroad to protect people in the United States. They learned several important lessons. First, international cooperation is absolutely essential; an outbreak anywhere increases risk everywhere. Second, surveillance, transparency, and timely sharing of information are critical. The ability of the United States and the world to slow or stop the spread of an influenza pandemic is highly dependent upon early warning of outbreaks. Finally, it is vital to strengthen preparedness and response capabilities in Asian countries and other parts of the world. The delegation also concluded that pandemic preparedness and preparation must be both short- and long-term in scope. These critical elements form the basis of the Administration's diplomatic engagement strategy through the International Partnership on Avian and Pandemic Influenza, launched by the President in September, and drive our efforts with the international health community to prepare effectively for a pandemic. As I stated earlier, there is no way to know if the current H5N1 virus will evolve into a pandemic. However, we do know that there have been three pandemics in the past 100 years, and we can expect more in this century.

HHS ROLE IN INTERNATIONAL PREPAREDNESS

The Secretary's trip reaffirmed the value of several actions undertaken by HHS and its agencies over the last few years. It is vital to monitor H5N1 viruses for changes that indicate an elevated threat for humans, and we are continuing to strengthen and build effective in-country surveillance, which includes enhancing the training of laboratorians, epidemiologists, veterinarians, and other professionals, as well as promoting the comprehensive reporting that is essential for monitoring H5N1 and other strains of highly pathogenic avian influenza. In collaboration with international partners and other U.S. Government Agencies, HHS is also pursuing a strategy of active, aggressive international detection; investigation capacity; international containment; and laboratory detection support.

In the past year, working with the World Health Organization (WHO), other U.S. Government and international partners, HHS and its agencies have made significant progress toward enhancing surveillance in Southeast Asia. However, this initiative needs to continue at both national and international levels if we are to sustain our progress, expand geographic coverage, and conduct effective surveillance. These efforts to build international and domestic surveillance are essential for detecting new influenza virus variants earlier and for making informed vaccine decisions about inter-pandemic influenza. With the ever-present threat of a newly

emerging strain that could spark a human pandemic, we need to know what is happening in commercial poultry farms and the family backyard flocks found in Southeast Asia, as well as migrating birds and animal populations elsewhere throughout the world.

Earlier this year, Congress passed and the President signed the Fiscal Year 2005 Emergency Supplemental Appropriations Act for Defense, the Global War on Terror, and Tsunami Relief. This legislation includes \$25 million in international assistance funds for HHS, the U.S. Department of Agriculture (USDA), and the United States Agency for International Development (USAID) to prevent and control the spread of avian influenza in Asia. With these funds, HHS and its agencies are working to assist in developing regional capacity in Southeast Asia for epidemiology and laboratory management of pandemic influenza. Strategies include developing and implementing an avian influenza curriculum for epidemiologists and laboratorians, training for public health leaders to develop a national network of public health field staff, and training for local allied health personnel to detect and report human cases of influenza. HHS staff are being assigned to Vietnam, Cambodia, and Laos to facilitate improvements in the detection of influenza cases and to provide technical assistance in investigating cases and in developing national preparedness plans by the Ministries of Health, with the assistance of WHO and other partners.

We are also working with USAID, WHO Secretariat, WHO's Regional Offices and Ministries of Health in these countries to increase public awareness about the human health risks associated with pandemic influenza, and to advise countries concerning prevention or mitigation measures that can be used in the event a pandemic occurs.

HHS, through CDC, is vigorously working to increase laboratory capacity in the region and to provide laboratory support for outbreak investigations, including: a) testing clinical samples and influenza isolates, b) diagnosing the presence of avian influenza in humans by supplying necessary test reagents to the region and globally, and c) developing vaccine seed stock to produce and test pandemic vaccine candidates. HHS's National Institutes of Health (NIH) and Office of Public Health Emergency Preparedness are also providing technical assistance to the government of Vietnam as it proceeds with the development of a human H5N1 vaccine, including support for clinical trials.

CDC is one of four WHO Global Influenza Collaborating Centers. In this capacity, CDC conducts routine worldwide monitoring of influenza viruses and provides ongoing support for the global WHO surveillance network, laboratory testing, training, and other actions. HHS and USAID also support the WHO Headquarters in Geneva and the WHO Regional Offices in Manila and New Delhi for pandemic planning, expansion of global influenza surveillance, shipment of specimens, training, and enhancing communications with agricultural authorities. Several of the top flu specialists on the WHO staff are HHS personnel on loan, another demonstration of our strong commitment to international collaboration in the fight against the threat of a pandemic influenza.

In addition to our partnership with USAID under the Tsunami supplemental appropriation, HHS also partners with other U.S. Government departments in its international collaboration, such as with the Department of Defense Naval Medical Research Unit Two (NAMRU2) in Indonesia and Naval Medical Research Unit Three in Cairo (NAMRU3). These collaborations support training, the expansion of influenza surveillance networks to countries where none exists, the enhancement of the quality of surveillance in other countries to enhance outbreak detection, seroprevalence studies in populations at risk for avian influenza such as poultry workers, and enhanced outbreak response.

SCIENTIFIC RESEARCH

Federal agencies have been very active in scientific research on avian influenza. Scientists at HHS and USDA have collaborated to successfully reconstruct the influenza virus strain responsible for the 1918 influenza pandemic. The findings from this research will greatly advance preparedness efforts for the next pandemic. Previously, influenza experts had limited knowledge of factors that made the 1918 pandemic so much more deadly than the 1957 and 1968 pandemics. One of the most striking features of the 1918 pandemic was its unusually high death rate among otherwise healthy people aged 15 to 34. In reconstructing the virus, the researchers are learning which genes were responsible for making the virus so harmful. This is an important advance to strengthen preparedness efforts, because knowing which genes are responsible for causing severe illness can help scientists develop new drugs and vaccines that focus on the appropriate targets.

Additionally CDC researchers have conducted studies on the incidence of adamantane resistance among influenza A viruses isolated worldwide from 1994 to 2005. Adamantanes are antiviral drugs that have been used to treat influenza A virus infections for many years. However, their use is rising worldwide, and viral resistance to the drugs has been reported among influenza A viruses (H5N1) strains isolated from poultry and humans in Asia. This data raises questions about the appropriate use of antiviral drugs, especially adamantines, and draws attention to the importance of tracing emergence and spread of drug resistant influenza A viruses. It is important to note that, although the H5N1 viruses isolated from people in Asia during the past two years appear to be resistant to adamantanes, they remain sensitive to neuraminidase inhibitors such as oseltamivir (Tamiflu®).

DEVELOPMENT AND MANUFACTURE OF VACCINE

Another important research area is vaccines: seeking improved strategies to enhance their development, manufacture, distribution and delivery. The development and role of a pandemic influenza vaccine is a principal component of the HHS Pandemic Plan, which I will describe later in the testimony. During an influenza pandemic, the existence of influenza vaccine manufacturing facilities functioning at full capacity in the United States will be critically important. We assume the pandemic influenza vaccines produced in other countries are unlikely to be available to the U.S. market, because those governments have the power to prohibit export of the vaccines produced in their countries until their domestic needs are met. The U.S. vaccine supply is particularly fragile; only one of four influenza vaccine manufacturers that sell in the U.S. market makes its vaccine entirely in the United States; one other makes some of its vaccine in the United States.

Another important factor is that public demand for influenza vaccine in the United States varies annually. Having a steadily increasing demand would provide companies with a reliable, growing market that would be an incentive to increase their vaccine production capacity. In FY 2006, CDC will direct \$40 million through the Vaccines for Children (VFC) program to purchase influenza vaccine for the national pediatric stockpile as additional protection against annual outbreaks of influenza. These funds to purchase vaccine can be used if needed during annual influenza seasons or possibly in a pandemic situation. HHS has also signed a \$100 million contract with sanofi pasteur to develop cell culture vaccines. In addition, the President is requesting \$120 million in FY 2006, an increase of \$21 million, to encourage greater production capacity that will enhance the U.S.-based vaccine manufacturing surge capacity to help prepare for a pandemic and further guard against annual shortages.

Funds from the Strategic National Stockpile (SNS) have purchased approximately two million bulk doses of unfinished, unfilled H5N1 vaccine. This vaccine has not yet been formulated into vials, nor is the vaccine licensed by the HHS Food and Drug Administration. Clinical testing to determine dosage and schedule for this vaccine began in April 2005 with funding from NIH. Initial testing shows that, in its current form, a much higher dose of vaccine, up to 12 times as much as originally predicted, will be needed to produce the desired immune response in people. HHS therefore is supporting the development and testing of potential dose-sparing strategies that could allow a given quantity of vaccine stock to be used in more people. These strategies include developing adjuvants—substances added to a vaccine to aid its action—and the possibility of using intradermal rather than intramuscular injections. Such studies are currently underway, funded through the NIH. Additionally, HHS recently announced the award of a contract to the Chiron Corporation for the development of an H5N1 vaccine.

One of the main efforts by HHS in pandemic preparedness is to expand the nation's use of influenza vaccine during inter-pandemic influenza seasons. This increase will help assure that the United States is better prepared for a pandemic. Influenza vaccine demand drives influenza vaccine supply. As we increase annual production efforts, this should strengthen our capacity for vaccine production during a pandemic. We are also developing strategies to increase influenza vaccine demand and access by persons who are currently recommended to receive vaccine each year.

DOMESTIC PREPAREDNESS

HHS Pandemic Influenza Plan

On November 2, 2005, the *HHS Pandemic Influenza Plan* was released. The HHS Plan is a blueprint for pandemic influenza preparedness and response and provides guidance to national, State, and local policy makers and health departments with the goal of achieving a national state of readiness and quick response. The HHS plan also includes a description of the relationship of this document to other federal

plans and an outline of key roles and responsibilities during a pandemic. In the event of a pandemic and the activation of the National Response Plan, the CDC has a critical role to support the Department of Homeland Security in their role of overall domestic incident management and Federal coordination. The President is requesting additional FY 2006 appropriations for HHS totaling \$6.7 billion in support of the *HHS Pandemic Influenza Plan*. In seeking this funding, the goals are: to be able to produce a course of pandemic influenza vaccine for every American within six months of an outbreak; to provide enough antiviral drugs and other medical supplies to treat over 25 percent of the U.S. population; and to ensure a domestic and international public health capacity to respond to a pandemic influenza outbreak.

In addition to outlining the federal response in terms of vaccines, surveillance, and planning, the HHS Pandemic Influenza plan makes clear the role of individual Americans in the event of an influenza pandemic. The importance of such ordinary but simple steps as frequent hand washing, containing coughs and sneezes, keeping sick children (and adults) home until they are fully recovered are widely seen as practical and useful for helping control the spread of infection. The plan also describes options for social-distancing actions, such as “snow days” and alterations in school schedules and planned large public gatherings. While such measures are, ordinarily, unlikely to fully contain an emerging outbreak, they may help slow the spread within communities.

State and Local Preparedness and Planning

All states have submitted interim pandemic influenza plans to CDC as part of their 2005 Public Health Emergency Preparedness Cooperative Agreements. Key elements of these plans include the use of surveillance, infection control, antiviral medications, community containment measures, vaccination procedures, and risk communications. To support the federal and state planning efforts, CDC has developed detailed guidance and materials for states and localities, which is included in the HHS Plan. CDC will work with states to build this guidance into their plans. CDC has taken a lead role in working with the Advisory Committee on Immunization Practices (ACIP) and the National Vaccine Advisory Committee (NVAC) which recommend strategic use of antiviral medications and vaccines during a pandemic when supplies are limited.

CDC is working to: (1) ensure that states have sufficient epidemiologic and laboratory capacity both to identify novel viruses throughout the year and to sustain surveillance during a pandemic; (2) improve reporting systems so that information needed to make public health decisions is available quickly; (3) enhance systems for identifying and reporting severe cases of influenza; (4) develop population-based surveillance among adults hospitalized with influenza; and, (5) enhance monitoring of resistance to current antiviral drugs to guide policy for use of scarce antiviral drugs.

Collaboration with the Council for State and Territorial Epidemiologists (CSTE) has considerably improved domestic surveillance through making pediatric deaths associated with laboratory-confirmed influenza nationally notifiable, and by implementing hospital-based surveillance for influenza in children at selected sites. CDC will continue to work with CSTE to make *all* laboratory confirmed influenza hospitalizations notifiable. Since 2003, interim guidelines have been issued to states and hospitals for enhanced surveillance to identify potential H5N1 infections among travelers from affected countries, and these enhancements continue. Special laboratory training courses to teach state laboratory staff how to use molecular techniques to detect avian influenza have been held. In the past year, CDC trained professionals from all 48 states that desired training.

Healthcare System

If an influenza pandemic were to occur in the United States, it would place a huge burden on the U.S. healthcare system. Medical surge capacity may be limited, and could be vastly outpaced by demand. Healthcare facilities need to be prepared for the potential rapid pace and dynamic characteristics of a pandemic. All facilities should be equipped and ready to care for a limited number of patients infected with a pandemic influenza virus as part of normal operations as well as a large number of patients in the event of escalating transmission. Preparedness activities of healthcare facilities need to be synergistic with those of other pandemic influenza planning efforts. Effective planning and implementation will depend on close collaboration among state and local health departments, community partners, and neighboring and regional healthcare facilities. However, despite planning, in a severe pandemic it is possible that shortages in staffing, beds, equipment (e.g., mechanical ventilators), and supplies will occur and medical care standards may need to be adjusted to most effectively provide care and save as many lives as possible.

CDC has developed, with input from state and local health departments and healthcare partners, guidance that provides healthcare facilities with recommendations for developing plans to respond to an influenza pandemic and guidance on the use of appropriate infection control measures to prevent transmission during patient care. Development of and participation in tabletop exercises over the past two years have identified gaps and provided recommendations for healthcare facilities to improve their readiness to respond and their integration in the overall planning and response efforts of their local and state health departments. The healthcare system has made great strides in preparation for a possible pandemic, but additional planning still needs to occur.

Antiviral Drugs

A component of the HHS Pandemic Influenza plan is acquiring, distributing, and using antiviral drugs. CDC has been working to procure additional influenza countermeasures for the SNS. Because the H5N1 viruses isolated from people in Asia during the past two years appear resistant to one class of antiviral drugs but sensitive to oseltamivir (Tamiflu®), the SNS has purchased enough oseltamivir (Tamiflu®) capsules to treat approximately 5.5 million adults and has oseltamivir (Tamiflu®) suspension to treat nearly 110,000 children. The SNS also includes 84,000 treatment regimens of zanamivir (Relenza®). WHO recently announced that the manufacturer of Tamiflu®, Roche, has donated three million adult courses. These will be available to WHO by mid-2006.

Enhancement of Quarantine Stations

CDC has statutory responsibility to make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the United States. This effort includes maintaining quarantine stations. Quarantine stations respond to illness in arriving passengers, assure that the appropriate medical and/or procedural action is taken, and train Customs and Border Protection officers to watch for ill persons and imported items having public health significance. Currently, CDC's Quarantine Stations are actively involved in pandemic influenza preparedness at their respective ports of entry. CDC's goal is to have a quarantine station in any port that admits over 1,000,000 passengers per year. We are expanding the nation's Quarantine Stations; staff now have been selected for 18 Stations and are on duty at 17 of these Stations. HHS and the Department of Homeland Security (DHS) have recently established a Memorandum of Understanding setting out specific cooperation mechanisms to combat the introduction and spread of communicable diseases. These include DHS assistance with passive and, in certain instances, active surveillance of passengers arriving from overseas, as well as information sharing to assist in contact tracing of passengers with communicable or quarantinable diseases. HHS/CDC will provide training and other necessary support to prevent disease from entering the United States.

Informing the Public

Risk communication planning is critical to pandemic influenza preparedness and response. CDC is committed to the scientifically validated tenets of outbreak risk communication. It is vital that comprehensive information is shared across diverse audiences, information is tailored according to need, and information is consistent, frank, transparent, and timely. In the event of an influenza pandemic, clinicians are likely to detect the first cases; therefore messaging in the pre-pandemic phase must include clinician education and discussions of risk factors linked to the likely sources of the outbreak. Given the likely surge in demand for healthcare, public communications must include instruction in assessing true emergencies, in providing essential home care for routine cases, and basic infection control advice. CDC provides the health-care and public health communities with timely notice of important trends or details necessary to support robust domestic surveillance. We also provide guidance for public messages through the news media, Internet sites, public forums, presentations, and responses to direct inquiries. This comprehensive risk-communication strategy can inform the nation about the medical, social, and economic implications of an influenza pandemic, including collaborations with the international community. We are working through the International Partnership on Avian and Pandemic Influenza and with the WHO Secretariat to harmonize our risk-communication messages as much as possible with our international partners, so that, in this world of a 24-hour news cycle, governments are not sending contradictory or confusing messages that will reverberate around the globe to cause confusion.

CONCLUSION

Although much has been accomplished, from a public health standpoint more preparation is needed for a possible human influenza pandemic. As the President mentioned during the announcement of his *National Strategy for Pandemic Influenza*, our first line of defense is early detection. Because early detection means having more time to respond, it is critical for the United States to work with domestic and global partners to expand and strengthen the scope of early-warning surveillance activities used to detect the next pandemic. To monitor H5N1 viruses for changes indicating an elevated threat for people, we must continue to strengthen and build effective in-country surveillance. This must include continued enhancement of training for laboratorians, epidemiologists, veterinarians, and other professionals, as well as promotion of the comprehensive and transparent reporting that is essential to monitor H5N1 and other strains of highly pathogenic avian influenza.

The outbreaks of avian influenza in Asia and Europe have highlighted several gaps in global disease surveillance that the United States must address in conjunction with partnering nations. These limitations include: 1) insufficient infrastructure in many countries for in-country surveillance networks; 2) the need for better training of laboratory, epidemiologic, and veterinary staff; and, 3) the resolution of long-standing obstacles to rapid and open sharing of surveillance information, specimens, and viruses among agriculture and human health authorities in affected countries and the international community. The International Partnership the President established is also looking at how best to solve these challenges.

During an influenza pandemic, the presence of influenza vaccine manufacturing facilities in the United States will be critically important. The pandemic influenza vaccines produced in other countries are unlikely to be available to the U.S. market, because those governments have the power to prohibit export of the vaccines until their domestic needs are met. The U.S. vaccine supply is particularly fragile. Only one of four influenza vaccine manufacturers selling vaccine in the U.S. market makes its vaccine entirely in this country. It is necessary to ensure an enhanced and stable domestic influenza vaccine market to assure both supply and demand.

Although the present avian influenza H5N1 strain in Southeast Asia does not yet have the capability of sustained person-to-person transmission, we are concerned that it could develop this capacity. CDC is closely monitoring the situation in collaboration with WHO, the affected countries, and other partners. We are using its extensive network with other federal agencies, provider groups, non-profit organizations, vaccine and antiviral manufacturers and distributors, and state and local health departments to enhance pandemic influenza planning. Additionally, the national response to the annual domestic influenza seasons provides a core foundation for how the nation will face and address pandemic influenza.

Thank you for the opportunity to share this information with you. I am happy to answer any questions.

Chairman HYDE. Thank you, Dr. Schuchat. Dr. Fauci.

STATEMENT OF ANTHONY S. FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH

Dr. FAUCI. Mr. Chairman, Members of the Committee, thank you for giving me the opportunity to testify before you today about the preparedness for pandemic influenza.

As shown on the first overhead, you see a hard-copy reproduction of the national strategy for pandemic influenza that the President announced on November 1. And the day following that Secretary Leavitt made available the comprehensive HHS pandemic influenza plan that includes a number of items that are indicated on this visual, including international and domestic surveillance, communications, state and local preparedness, and the issue that I am going to briefly address with you this morning, vaccines and antivirals, or what we refer to as counter-measures. Next slide.

In 2004, with the situation as it was evolving in Southeast Asia, we isolated an H5N1 from a Vietnamese patient who had been infected from a chicken, and who got seriously ill. By a variety of mo-

lecular techniques, we made a vaccine for H5N1 that we began testing on this spring. Very briefly on the results that we have thus far, in looking at healthy young adults, we found that the vaccine was tolerated well, and that it induced an immune response that was capable of being predictive of being protective against that H5N1 virus.

That is the good news. The sobering news is that the concentration or dosage of the vaccine that would be required to induce that level of immunity was considerably higher than the dose that we use for seasonal influenza, which compounds an issue which I will get to in a moment about the problem that we have with the capacity to manufacture vaccines, and how this provides a daunting challenge in how we respond to the potential of a pandemic.

Also shown on this slide, that we have been doing studies, and we are continuing them on the use of an adjuvant, which is a substance which amplifies the immune response, and may allow us to, as it were, get away with a lower dose, rather than the dose that is so challenging now because of how high it is. Next slide.

When you think in terms of vaccines, you think of stockpile and strategy. And they are really quite different.

The stockpile for the H5N1 that I mentioned to you is relatively small. By the beginning of this coming year, we will have 8.6 million doses, which really is 4.3 million vaccine courses, of which two million are slated for the Department of Defense. So our stockpile will be very meager.

How we address that is by the strategy to have, within a reasonable period of time, about 20 million doses of what we call pre-pandemic vaccine. Pre-pandemic means you have a vaccine against a virus that you isolated some time ago, that first of all we hope we never have to use, and we hope we never get to the point of having human-to-human spread that is efficient. But if it does, that virus will likely change enough that the vaccine may not be optimally protective against it, which gets to the real critical issue regarding preparedness as to develop the capacity to manufacture, within a reasonable period of time measured in months, a vaccine against the virus that has actually achieved that capacity to go efficiently from human to human.

We are nowhere near that right now, but that is the bedrock of the plan at which \$4.7 billion of the \$6.7 billion to HHS is going to be devoted to trying to get the capacity to bring vaccine production to the point where we can efficiently respond.

Moving on to the next slide, the other area is antiviral therapy. We have two classes of antivirals that are effective against influenza in general. One is against the neuraminidase enzyme, and the other one is against the surface protein.

The one that we are concentrating on now is oseltamivir, or Tamiflu, which I am sure you have been hearing about in the media, as the antiviral that would most likely be utilized against H5N1. But I want to caution the Committee that we cannot equate stockpiling an availability of Tamiflu with preparedness, because in seasonal flu, what this antiviral does is diminish the duration of symptoms that you have if you have seasonal flu by approximately a day and a half.

We have no hard scientific data of how well this antiviral will perform under the conditions of a pandemic. Because, first of all, you have to give it within the 24 to 48 hours of onset of symptomatology in order for it to be effective. So we have a challenge not only in stockpiling and making the best of what we have, which is Tamiflu, but also directing our efforts of developing promising new antiviral candidates that we would feel more comfortable would be effective against a disease like influenza, particularly a pandemic flu. Next slide.

The strategy is ultimately to have 75 million treatment courses to cover 25 percent of the population. We have assurances from the company that we will get to 20 million treatment courses by December 2006, and the 75 million by the summer or spring of 2007. We obviously need to accelerate that if we were to have an imminent situation with pandemic flu.

And finally, on this last slide, I want to emphasize something that I think—next slide—that is really very important. We may not have an H5N1 pandemic, but as has been mentioned by several witnesses, in the future we certainly will. We don't know whether it will be a 1968 version or a 1918 version, but it will happen.

Our weakness is that we have considerable failings on how we handle seasonal influenza preparedness. So the strategy should be to build our capabilities from a public health standpoint, from the capacity to manufacture and equitably distribute vaccine in a situation that we face each year, because seasonal flu is, in fact, potentially, and in reality, a serious problem for us.

So if nothing comes of this except that it brings us closer to being able to respond in a more efficient way to seasonal flu, we will have succeeded and done a service for the American public.

Thank you, Mr. Chairman and Members of the Committee.

[The prepared statement of Dr. Fauci follows:]

PREPARED STATEMENT OF ANTHONY S. FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH

Mr. Chairman and members of the Committee, thank you for the opportunity to discuss with you the current global outbreak of avian influenza in birds, the threat of pandemic influenza in humans, and the activities of the Federal Government in preparing to meet this threat.

An influenza virus strain capable of causing the next human influenza pandemic could emerge with little or no warning in almost any part of the world. Three influenza pandemics occurred in the 20th century, in 1918, 1957, and 1968.

The pandemics of 1957 and 1968 were serious infectious disease events that killed approximately two million and 700,000 people worldwide, respectively. The 1918–1919 pandemic, however, was catastrophic: it is estimated that it killed more than 500,000 people in the United States and more than 40 million people worldwide. The possibility that a new influenza virus could emerge to cause a similar pandemic among human beings is a very real threat for which we must prepare.

Of known influenza viruses, the highly pathogenic avian influenza (HPAI) H5N1 avian influenza virus that is spreading in domestic and migratory birds in Asia and most recently in Eastern Europe currently is of greatest concern. The HPAI H5N1 virus is primarily an animal pathogen that has, however, infected more than 130 people in Asia. Approximately half of the people diagnosed with H5N1 avian influenza infection have died. At this point in time, the virus has not yet demonstrated the ability to spread efficiently from animals to humans and is very inefficient in spreading person-to-person. Because the virus is now widespread in many bird species in several countries in Asia and likely elsewhere, eradication is probably not feasible. The feared human pandemic could become a reality if the H5N1 virus mutates further, remains highly virulent, and acquires the capability to spread as efficiently from person to person as do the commonly circulating virus strains that

produce seasonal influenza epidemics. Even if H5N1 does not evolve into a pandemic strain, the possibility that a human influenza pandemic will occur at some time in the future is real.

On November 1, 2005, the President announced the *National Strategy for Pandemic Influenza*, and the next day U.S. Department of Health and Human Services (HHS) Secretary Michael O. Leavitt released an integral component of the *National Strategy*, the *HHS Pandemic Influenza Preparedness and Response Plan*. Together, these two documents provide a blueprint for a coordinated national strategy to prepare for and respond to a human influenza pandemic. The National Institutes of Health (NIH) within HHS, and the HHS/NIH National Institute of Allergy and Infectious Diseases (NIAID), in particular, have the primary responsibilities for conducting scientific research and clinical trials to foster product development to prepare our nation for a potential human influenza pandemic.

In my testimony today, I will tell you more about the scientific research and development efforts of the Federal Government, the academic community, and the private sector to counter the threat of pandemic influenza. In particular, I will focus on projects and programs that will help ensure that effective influenza vaccines and antiviral drugs will be available to counter any human influenza virus with pandemic potential that could emerge.

BASIC SCIENCE AND SURVEILLANCE

HHS/NIH/NIAID supports numerous basic research projects intended to increase our understanding of how animal and human influenza viruses replicate, interact with their hosts, stimulate immune responses, and evolve into new strains. These studies lay the foundation for the design of new antiviral drugs, diagnostics, and vaccines, and are applicable to seasonal epidemic and pandemic strains alike.

Each year, as influenza viruses circulate through the human population, their surface proteins undergo small changes. As these small changes accumulate, the influenza virus gains the ability to circumvent immunity created by prior exposure to older circulating influenza viruses or by vaccination.

This phenomenon, called “antigenic drift,” is the basis for the well-recognized patterns of human influenza disease that occur predictably every year, and is the reason that, working with the World Health Organization (WHO), we must update influenza vaccines each year. Influenza viruses also can change more dramatically. For example, viruses sometimes emerge that can jump species from natural reservoirs, such as wild ducks, to infect domestic poultry, farm animals, or humans. When an influenza virus jumps species from an animal, such as a chicken, to infect a human, the result is usually a “dead-end” infection that cannot readily spread further in the human population. However, mutations in the virus could develop that allow human-to-human transmission. Furthermore, if an avian influenza virus and another human influenza virus were to simultaneously co-infect a person or animal, the two viruses might swap genes, possibly resulting in a virus that is readily transmissible between humans, and against which the population would have no natural immunity. These types of significant changes in influenza viruses are referred to as “antigenic shift.”

H5N1 and H9N2 are two avian influenza strains that have jumped directly from birds to humans. In 1998, 1999 and 2003, H9N2 influenza caused illness in three people in Hong Kong and in five individuals elsewhere in China, but the virus did not spread further among humans, and caused no known deaths. At this time, H5N1 influenza appears to be a significantly greater threat than H9N2. In addition to the high fatality rate seen in people with H5N1 influenza, H5N1 viruses are evolving in ways that increasingly favor the start of a pandemic, including expanding their host-species range. Moreover, two highly probable cases of human-to-human transmission of the H5N1 virus have occurred, and it is possible that other such transmissions have occurred.

An understanding of the diversity of influenza viruses—in the wild, in domestic animals, and in humans—as well as close surveillance for the emergence of new strains are important components of the scientific program to prepare for a pandemic. HHS/NIH/NIAID supports major research programs that are important in this regard. One is a long-standing program based in Hong Kong to detect the emergence of influenza viruses with pandemic potential. Dr. Robert Webster of St. Jude Children’s Research Hospital and his team conduct extensive surveillance of influenza viruses in animals in Asia, analyze new influenza viruses when they are found, and generate candidate vaccines against them. Another effort, the Influenza Genome Sequencing Project, is a collaborative project of HHS/NIH (NIAID and the National Library of Medicine), the Institute for Genomic Research, the Wadsworth Center, the U.S. Department of Defense Armed Forces Institute of Pathology, St.

Jude Children's Research Hospital, and several other organizations. Its purpose is to rapidly provide complete genetic sequences of thousands of influenza virus isolates to the scientific community. This program has enabled scientists to better understand how influenza viruses evolve as they spread through the population, and to match viral genetic characteristics with virulence, ease of transmissibility, and other biological properties. A high priority of HHS is to further enhance international and domestic influenza surveillance systems so they can reliably detect an outbreak and to determine accurately the lethality and transmissibility of influenza strains.

VACCINES

Vaccines are an essential tool for the control of influenza. Unfortunately, current domestic capacity for the manufacturing of influenza vaccines can meet only a small fraction of the need projected for a pandemic response. For this reason, \$4.7 billion of the \$6.7 billion in the President's Fiscal Year (FY) 2006 supplemental appropriations request for the implementation of the *HHS Pandemic Influenza Plan* is intended to increase U.S.-based pandemic influenza vaccine-production capacity, vaccine stockpiles, and vaccine research. The goal is to have the capacity to produce sufficient pandemic influenza vaccine to protect every American within six months of an outbreak.

With regard to the development of an H5N1 vaccine, we have made rapid progress. HHS/NIH/NIAID-supported researchers at St. Jude Children's Research Hospital obtained a clinical isolate of a highly virulent H5N1 virus in Viet Nam in early 2004, and used a technique called reverse genetics to create an H5N1 vaccine reference strain from this isolate. HHS/NIH/NIAID then contracted with Sanofi-Pasteur and Chiron Corporation to manufacture pilot lots of 8,000 and 10,000 vaccine doses, respectively, of the inactivated virus vaccine, for use in clinical trials. The Sanofi Pasteur vaccine is now undergoing clinical testing in healthy adults and healthy elderly people, and will soon begin evaluation in children.

Preliminary results from these trials provide both good and sobering news.

The good news is that the vaccine is safe, and induces a vigorous immune response that augurs well for protecting people against the H5N1 virus.

The sobering news is that two *large* doses of the Sanofi product were needed to elicit an immune response likely to be protective. However, preliminary results from a Phase I clinical trial of an H9N2 influenza vaccine candidate made by Chiron indicate that addition of an adjuvant—a vaccine component that increases the immune response—can reduce the required dose substantially. Clinical trials of H5N1 candidates using adjuvants and other strategies to reduce the necessary dose are ongoing or imminent.

In addition to these inactivated virus vaccines, HHS/NIH/NIAID is collaborating with industry to pursue several other vaccine strategies. These include recombinant subunit vaccines, in which cultured cells are genetically engineered to produce influenza virus proteins that are then used in a vaccine, and DNA vaccines, in which scientists inject influenza genetic sequences directly into the vaccinee to stimulate an immune response. In addition, from the mid-1970s to the early 1990s, HHS/NIH/NIAID intramural and extramural researchers developed a cold-adapted, live attenuated influenza vaccine strain that later became the influenza vaccine marketed as FluMist®, licensed by the HHS Food and Drug Administration (FDA). Today, HHS/NIH/NIAID intramural researchers are working with colleagues from MedImmune, Inc., under a Cooperative Research and Development Agreement, to produce and test a library of similar vaccine candidates against all known influenza strains with pandemic potential.

HHS also has awarded a total of more than \$162 million in contracts to Sanofi-Pasteur and Chiron to produce bulk inactivated H5N1 vaccine for the Strategic National Stockpile to ensure the manufacturing techniques, procedures, and conditions used for large-scale production will yield a satisfactory product. Moving to large-scale production of the vaccine in parallel with clinical testing of pilot lots is an indication of the urgency we have determined is needed to address H5N1 vaccine development. We could use the doses of H5N1 vaccine we have ordered, as necessary, to vaccinate health care workers, researchers, and, if indicated, the public in affected areas.

In addition to creating a safe and effective vaccine candidate, it is imperative that we have the ability to produce large quantities of vaccine quickly in the United States. To accomplish this, HHS is pursuing a multi-faceted strategy to create domestic influenza vaccine manufacturing capacity capable of producing 300 million vaccine courses within six months of the onset of a human influenza pandemic.

The initial component of this strategy is to increase the number of domestic manufacturers of traditional egg-based influenza vaccines; only one currently exists within the United States. Doing so will allow the United States to manufacture a 20 million course pre-pandemic vaccine stockpile by 2009, without disrupting the production of annual seasonal influenza vaccine. In the event that a pandemic appears imminent—or earlier if circumstances warrant—we could use this pre-pandemic vaccine to immunize healthcare workers, front-line responders, vaccine-manufacturing personnel, and others critical to the pandemic response. With the addition of the domestic infrastructure required to produce the pre-pandemic vaccine, egg-based production capacity will be able to provide an additional 60 million courses of vaccine within six months of the emergence of a pandemic.

Egg-based production alone, however, cannot bring us to our goal of having the surge capacity in the United States to produce 300 million courses of vaccine in a six-month time frame. Instead, the best hope for acquiring a vaccine manufacturing capacity in the United States that we could ramp up rapidly on short notice lies in expanding and accelerating our investment in non-egg-based technologies, specifically cell-based influenza vaccines. Much of the investment in vaccines outlined in the HHS *Plan* goes toward this initiative. The proposed investments will allow creation of new domestic facilities that would provide the surge capacity to manufacture approximately 240 million vaccine courses within six months of a pandemic outbreak.

The HHS *Plan* also calls for upgrading existing domestic manufacturing facilities to enable the production of pandemic influenza vaccine in an emergency.

To that end, HHS will work with HHS/FDA to establish contingency arrangements with vaccine manufacturers that will allow them to quickly adapt their facilities either to produce influenza vaccines or to carry out other critical functions, such as repackaging bulk vaccine produced by other manufacturers.

It is important to note, however, that while the technology for producing influenza vaccine in cell cultures is promising, successful development of the production methods and licensure of the product are years in the future, and by no means guaranteed. Moreover, how quickly we reach our production goals will depend on the development of adjuvants and other dose-sparing techniques that could reduce the amount of vaccine needed to protect the U.S. population, and on whether required incentives for industry can be successfully implemented.

Recognizing the urgent need to create and expand vaccine-manufacturing capacity, we must remove or mitigate deterrents to participation in the vaccine enterprise by companies with substantial industrial capacity and experience. Accordingly, the Administration is proposing limited liability protections for vaccine manufacturers and providers, except in cases of willful misconduct.

We believe this proposal will reduce the liability risks that dissuade companies from producing pandemic countermeasures, while retaining appropriate access by the American public to reasonable and justified legal remedies.

Under the International Partnership on Avian and Pandemic Influenza, which the President launched in September, we also are beginning to coordinate our vaccine research with that undertaken by other nations and private companies outside the United States. The World Health Organization Secretariat recently sponsored the first of what we hope will be a series of meetings to allow us to exchange information with and learn from our colleagues in other countries who are in various stages of research on human vaccines against the H5N1 virus. HHS/NIH/NIAID and the Office of Public Health Emergency Preparedness also are providing technical assistance to the Government of Viet Nam as it proceeds with the development of a human H5N1 vaccine, including support for clinical trials.

ANTIVIRALS

Antiviral medications are an important counterpart to vaccines as a means of controlling influenza outbreaks, both to prevent illness after exposure and to treat infection after it occurs. Four drugs currently are available for the treatment of influenza, three of which HHS/FDA has also licensed for influenza prevention for certain populations. HHS/NIH/NIAID supports research to identify new anti-influenza drugs through the screening of new drug candidates in cell-culture systems and in animal models. In the past year, we have identified seven promising candidates. Efforts to design drugs that precisely target viral proteins and inhibit their functions also are under way. In addition, HHS/NIH/NIAID is developing novel, broad-spectrum therapeutics that might work against many influenza virus strains. Some of these target viral entry into human cells, while others specifically attack and degrade the viral genome.

Efforts also are under way to test and improve the existing anti-influenza drugs. Researchers have determined that currently circulating H5N1 viruses are resistant to two older drugs—rimantadine and amantadine—but are sensitive to a newer class of drugs, called neuraminidase inhibitors. This class of drugs includes oseltamivir (marketed as Tamiflu®), approved by HHS/FDA for treatment of individuals older than one year. Studies to further characterize the safety profile of oseltamivir for very young children are in the advanced planning stage. Studies are also in progress to evaluate novel drug targets, as well as long-acting next-generation neuraminidase inhibitors. In addition, development and testing in animals of combination antiviral regimens against H5N1 and other potential pandemic influenza strains are under way.

If a human influenza pandemic were to occur, a sufficient supply of stockpiled antiviral drugs to treat and care for infected individuals would be critical. Therefore, the HHS Plan requests an investment of \$1.4 billion to increase the availability of these drugs. These funds would help us achieve the President's goal of having available 81 million courses of antivirals, which would be sufficient to treat 25 percent of the U.S. population (75 million courses) while allowing for a reserve supply (6 million courses) that we could use to contain an initial U.S. outbreak. Funding would also accelerate the development of promising new antiviral drug candidates in collaboration with academia and industry since there is a possibility that none of the antivirals available today will be fully effective against whatever strain sparks a pandemic influenza among humans.

The planned strategy for the U.S. government and States to acquire up to 81 million courses of antiviral drugs will enable manufacturers to make significant expansion in U.S.-based manufacturing capacity, and thereby position the United States to meet future demands much more readily than is currently possible. HHS also will work with its State partners to encourage them to acquire antivirals for rapid use for their populations.

CONCLUSION

In closing, Mr. Chairman, I want to reiterate that the threat from pandemic influenza, whether from an H5N1 influenza virus or another influenza virus still unknown, is real and growing. I participated in the trip that Secretary Leavitt led to Southeast Asia in October, and what I saw confirmed this belief. Although we do not know when the next human influenza pandemic will occur, or how devastating it will be, we can be certain that a new influenza virus ultimately will emerge. The historical precedent of the 1918 pandemic clearly demonstrates that a newly emerging influenza virus can wreak catastrophic damage worldwide in a matter of months.

The world is obviously very different today than it was in 1918. In some ways we are more vulnerable. Travel that took weeks in 1918 only takes hours today. Our globalized economy is exquisitely sensitive to the disruptions that would inevitably occur during a pandemic. Many parts of the world have weak public health and health-care delivery systems, and poverty and overcrowding are widespread, as we witnessed in Southeast Asia. Science and medicine, though, have progressed dramatically, and we now have tools such as sophisticated viral surveillance techniques, effective vaccines, antibiotics to treat secondary bacterial infections, and antiviral drugs against influenza that should aid in our response to an emerging influenza pandemic. These tools, however, will be of little use if we cannot bring them to bear when we need them. For that to occur, we must take all possible measures now to ensure that our public health and pharmaceutical manufacturing infrastructure is equipped to respond to a pandemic.

Thank you for this opportunity to testify before you today. I would be pleased to answer any questions that you may have.

Chairman HYDE. Thank you, Dr. Fauci. We will now entertain questions. I will recognize the Members for 5 minutes, in the expectation that they will bind themselves to that constraint, because we have another panel of witnesses, one who will testify over video-conference from Switzerland. So we don't want to lose that connection.

Mr. Smith.

Mr. SMITH. Thank you very much, Mr. Chairman. Let me just ask our panel first on the Regional Emergency Disease Interven-

tion Center, or REDI Center. To the best of my knowledge, I don't think any of you mentioned that.

Is that being utilized in this effort? As you know, it is based in Singapore. Could you expound perhaps on that?

Secondly, Dr. Margaret Chan, the Assistant Director General of WHO, says in her testimony that beginning in late December 2003, outbreaks of highly pathogenic H5N1 Avian influenza in poultry were reported in nine Southeastern Asian nations, including Korea, Vietnam, Japan, Thailand, Cambodia, Laos, Indonesia, China, and Malaysia.

Of these countries, three have controlled their outbreaks and are now considered disease-free: Japan, Republic of Korea, Malaysia. Are they disease-free? And how is that determined? And can they become re-diseased?

I mentioned earlier that I was just in Vietnam. I want to ask you if you would to describe the United States assistance to Vietnam. How well is their poultry vaccination doing? Is it effective? Is it ineffective?

As we know, there is a lack of transparency with that government, and perhaps other governments. They are concerned, I think, at least I detected, what the impact might be on tourists. So you wonder whether or not all of this information is completely above-board.

And finally, on the safety to eat, WHO also suggests that is it safe to eat poultry products. Their answer is yes, provided certain precautions are followed. They do talk about the importance of raw juices and the like, but then suggest that the washing of hands with soap and hot water are sufficient for this purpose. Is that true? If you could touch on that, as well.

Dr. SCHUCHAT. I can answer a couple of the questions. In terms of the ready facility in Singapore, the emergency supplemental funds for the tsunami, part of that funding has gone there to help with some of the regional training. I think the focus is going to be on infection control issues.

And in general, the tsunami funding strategy, the idea is to use some of the regional strength in Asia to help in country, and then broader. So that there is quite a good facility in Thailand that is helping with regional training.

In terms of the question about assistance in Vietnam, others may want to add, but I think that clearly that is a critical area of need. There is quite a bit of emphasis in terms of strengthening technical capacity. HHS has identified staff to be placed in Vietnam with actually superb staff to help with the technical training to lead the effort.

Chairman HYDE. When will they be put there, Doctor?

Dr. SCHUCHAT. I think it is imminent. I can submit to you the dates, but I know that people have been identified.

In terms of the poultry issue, the cases of H5N1 Avian influenza in humans that have been identified have primarily been in people with very close contact with ill poultry. Handling of ill chickens is not a good idea without protective equipment. And of course, as my colleagues pointed out, we need the farmers to be able to come forward when they are having affected flocks.

Eating cooked chicken is safe.

Dr. FAUCI. Could I just add one thing about the ready center? It is that Dr. William Steiger of the Office of Global Health Affairs at the Department of Health and Human Services has been working very closely with the individuals in the ready center in trying to coordinate activities of the department with the ready center. So it is a very important resource. They have some very talented people there.

And we have actually even before the pandemic influenza situation really lit up, we had some very good and close interactions with them.

I just would add one thing regarding your question about disease-free. That is really a moving target. And the reason it is a moving target is because of the fact that migratory birds, some of which don't get symptomatic in their pathways, can infect and reinfect. So there are times when, if you looked at how things evolve from Vietnam, from Thailand to Cambodia to Vietnam, China and back, there were periods of time when a country would be saying that they are disease-free. And likely, they may have been disease-free, only to a couple of months later come back and get human cases, and then find out you actually have poultry that are infected. So it is really a very difficult, almost self-propagating, problem with regard to disease-free.

You might recall that China had said that they were disease-free. And then all of a sudden there were three new cases in China, and then you look and you wind up finding out that there are millions of chickens that are infected in China. It is a moving target.

Chairman HYDE. Mr. Faleomavaega.

Mr. FALEOMAVAEGA. Thank you, Mr. Chairman. I want to commend Secretary Roth for his very comprehensive and very impressive presentation in terms of our national call to attention of this very serious situation.

I come away impressed, but I want to follow up on my good friend, the gentleman from Iowa's concerns. I am impressed with the fact that we are putting all these Federal agencies, the highest levels, the President himself. But I am a little puzzled as to what are we doing with HIV/AIDS? While we may not call it a pandemic, but I believe we have been struggling with this issue so serious, as far as I am concerned more serious, because it is happening.

We are not talking about seasonal influenza, we are talking about a very serious situation that is happening, especially among third world countries, that we do not seem to, I don't seem to get that sense of commitment, not just from our country, but maybe the other countries as well.

You had indicated earlier that 88 countries were called together with this international conference. What happened to the other 103 countries that are supposed to make up our world community?

As I recall, I think there are 191 countries that make up the United Nations. And I just wanted to get a perspective, and from our other members of the panelists, we are calling, hey, you know, this is a real serious issue. But I somehow am a little puzzled, if by way of, say, are we just as committed in conducting a war against HIV/AIDS? Because I am not getting that same sense of real commitment, not only from our country, but other countries of the world, as well.

I think Secretary Rock was the one that—but I am open to any of you if you can share with me your concerns about this.

Dr. FAUCI. Let me just start off. I think because you don't see something on the front page of the newspapers this week or last week, I think it would really be an understandable mistake to think that there isn't an extraordinary commitment on the part of the Administration for HIV/AIDS.

Just to give you some examples. This past year we spent \$21 billion on HIV/AIDS. The President's emergency plan for AIDS relief, the \$15 billion program over 5 years, is now recognized by virtually everyone as being an extraordinary success, having gotten now over 400,000 people on therapy in the 15 targeted countries, 12 in South Africa and Southern Africa, two in the Caribbean, and now in Vietnam.

The goal of treating two million people preventing seven million infections, and caring for 10 million people is in fact on target.

So though you don't hear about it with the intensity now that everyone is discussing pandemic influenza, we really do have a very serious commitment, both domestically and internationally, with HIV/AIDS.

Mr. FALÉOMAVAEGA. I appreciate that, and I do stand corrected if I may have misstated my position. But I still am very concerned with all the tremendous organizational happenings now taking place, not only within our Administration, but also by other countries. But it just doesn't seem to come across that way, in my humble opinion.

Secretary Rock.

Mr. ROCK. Thank you, and thank you for referencing the International Partnership. If I just might make one additional candid comment, if I may.

It is true that we brought together 88 countries and eight international organizations for the first senior officials meeting.

I would argue that probably a third of those countries fully appreciated, maybe less than a third, fully appreciated the gravity of the issue at the time that we brought them together. Since then we have seen marked improvement.

Right now the WHO is indicating that there are about 120 countries that are putting together preparedness plans. And in that sense, what we are most concerned about is harmony and uniformity, and adequate levels of those national plans.

I think we have raised the visibility in terms of political leadership. Vietnam you reference earlier. Vietnam in fact has—

Mr. FALÉOMAVAEGA. I am sorry, Secretary Rock, I have got a couple more questions. Just a quick question to Dr. Hill. And I am getting into the numbers game again.

You mentioned that 107 countries have been eligible for AID assistance on this pandemic issue. But I give again the question, what happened to the other 84 countries.

It seems to me that we have to take this globally, and not just pick and choose who we like. At least in my understanding, if it is a pandemic, no matter what country, we are all affected by it. And I just wanted to know how come the other 84 countries are not eligible in our book.

Mr. HILL. Fortunately, the good news is that where we have the most problem, the countries that are most at risk are high on that list of countries that we can and do work with.

But you are obviously right. If there was a serious threat anywhere else, we would figure out a way to find the capacity to work with them, whether we have a mission there or not.

The good news is, is that we are trying to get people to think beyond Southeast Asia. And it is important to think about Southeast Asia. But as it moves to Eastern Europe, through Russia to Eastern Europe, eventually to Africa, et cetera, we have to be doing the planning now.

We are working, for example, with Tanzania, to help them get ready for what may come. But we have got to be ahead of this game. And whether it is on that 107-country list or not, we are even working with PAHO in terms of the Americas to help them get ready, too.

Mr. FALCOMA. I realize my time is up, Mr. Chairman. Just an observation. Dr. Hill, you mentioned about a national communications campaign. We can't even get our local fire and police departments to communicate properly as first responders if there was to be another national emergency. And I think we need to look into that a little more seriously.

Thank you, Mr. Chairman.

Chairman HYDE. Thank you, Mr. Tancredo.

Mr. TANCREDO. Thank you, Mr. Chairman. Just one quick question is all I have, and it is a relatively mundane one at that.

Could you explain to me how it is that a farmer, a poultry farmer in, well, anywhere actually, but certainly where they have an outbreak in that person's flock, would be incentivized to do something about it quickly? Is there, you know, do we purchase—somehow is there something that happens that purchases the rest of the animals so that they are not concerned and don't try to sell off everything before they are identified?

Mr. HILL. This is really an extraordinarily important question. It is one we have been giving a lot of thought to. Because the real key is to get them to come forward, and talk in time before we can do something that will make a difference. Because if it gets out past those first few days, it is very hard to stop. So you have got to have a plan in place.

One idea that has come forward that I think has a lot of potential is to replace culled chickens, for example, with vaccinated chicks. We need to work with the poultry producers, the big farms, et cetera, who vaccinate, and have the chicks and the biosecurity measures are in place. If we would work with the private sector and with these groups to come and find the money necessary to purchase them, this could provide an incentive. You could promise farmers that if they would come forward, an effort would be made to replace either birds that died or that were culled.

So we have to think creatively about this, because this is what is going to help them go ahead and report what is going on.

Mr. TANCREDO. But right now there is nothing that actually does that.

Mr. HILL. There are some countries that are providing some compensation. Whether it is full compensation or enough, those are all issues that we have got to push very hard on.

Mr. ROCK. I might add, by the way, one of our challenges, of course, is that in many cases these are backyard farms. These are not large and industrial operations.

Mr. TANCREDO. Right, but that is what made me think of it. You just go through the process in your mind about what happens in that kind of a setting, and you can easily see where somebody would go, wait a minute, I have got something happening here, and I am going to get what I can out of this while I can, and in the meantime spread the disease.

Mr. HILL. Just one additional point on that. The communications part of this is absolutely critical. Because the communication is not just about reporting when a bird or a group of birds are dying in very suspicious ways. It is telling people what the threats are if this thing gets out of hand.

Because they rely on these chickens for their livelihood, in some cases their very food. So that is going to be a very important piece of information for them, to know how this is going to affect them.

But the disease is going to affect them, too. It can kill them. It will kill their whole communities. And so if they understand the scale of this, and if there is going to be an attempt to help them, they would be more likely to come forward. But not if they don't believe it. Not if they don't understand what can be unleashed if they don't do something about these birds.

Mr. BURTON. Would the gentleman yield real quickly? Let me just say that one of the things that hasn't been mentioned, that might be considered even in third-world countries, is reimbursement for the loss. Because once they know that they are not going to lose their fannies when they have to kill their whole crop of chickens is that there will be reimbursement.

Now, I don't know how you get that message out. But in China and around the world, if we could work with them to make sure that there is no loss of revenue because they report that stuff, it might be a real help.

Thank you, gentleman, for yielding.

Mr. TANCREDO. I have no further questions. Thank you, I yield back.

Chairman HYDE. Thank you. Ms. Watson of California.

Ms. WATSON. Thank you, Mr. Chairman. I have a series of questions, and I am going to throw them out there, and you can respond if you can.

Listening very intently, what disturbs me is that I don't hear how we are trying to educate not only ourselves in this country, but other nations, too, how do we educate against this threat?

I heard several very disturbing things to me. One is that the virus has evolved in ways that increases the complexity of control, and heightens concern about the pandemic threat. How do we get a handle on this evolution? What are we doing in terms of our research?

And what are we doing for humans to avoid risky contact with sick or affected animals? And is this the only way that it can be transmitted?

I just heard someone respond that eating various animals, birds and so on, that had been cooked reduces the risk. I would like somebody to expound on that. How are we planning ahead? Since we brought attention to it, we are having this hearing, and you have stated that this virus will evolve and maybe what we are preparing as an immunization might not be effective a year or 5 years from now. Can somebody respond? And Dr. Schuchat, I see you nodding your head, so you are the one, then.

Dr. SCHUCHAT. Absolutely. I think that education and risk communication are central to emerging infectious diseases. And the pandemic influenza and the H5N1 Avian influenza concerns are really the ultimate challenge in risk communication. We need to put an emphasis on that in the U.S. as we hear reports about other countries, and also as we think about having potential confusion between the annual seasonal flu issues and the risk of the Avian flu problem.

But in the international arena, risk communication is, as my colleagues have mentioned, vital. It needs to be customized to the local populations' concerns. What are the questions about livelihood, about eating, about handling the animals that are really part of their cultures.

And so I think quite a bit of thought and care needs to go into how risk communication is done.

The CDC is very involved in this, of course, in the U.S. We are trying to help both local and state health departments, the business community, and other sectors know what they need to know about the emerging problems. Today the Secretary of HHS will be announcing checklists available for businesses of what do you need to know, what do you need to do in advance of a pandemic. What can you do now to be ready. And in the international arena, the communication and improving awareness is a key part of the strategy that is proposed.

Ms. WATSON. Let me ask Mr. Rock this, as well as what I threw out. Human-to-human transmission, would you comment on that? Would it be in our best interest not to export animals or birds from another country that we know there have been infections? Do we close our borders? Please respond.

Mr. ROCK. Thank you very much. And I wanted to also touch for a quick second on your communications issue.

In what may be a bit of an overgeneralization, there are really two types of communications that we are talking about here. One is a public awareness type of communication, so that the public understands the level of risk and adopts the appropriate behaviors. And in some cases, that is to manage rather than to heighten concern.

And the other is a more directed technical type of communication, for the actual folks that are most directly involved in dealing with poultry or dealing with the medical community as to how they should act and how they should behave and how they should work.

We are engaged on both of those levels, not only in the region, but in the State Department budget. We are requesting sufficient funds to bring some of those officials back to the United States to learn about public awareness activities and how we work through our public health organizations, as well.

Ms. WATSON. Let me just say that if you have been immunized for the flu, how then do you communicate to those who, at risk, that there is a human carrying this virus, if we do identify human? I am just trying to figure out person-to-person, human-to-human. The research side I think we are addressing, but I want to know how we reduce the risk to humans in this country.

Dr. FAUCI. Well, it depends on what risk you are referring to. Right now if you are talking about, we don't have pandemic flu among birds in this country. We don't have that now. So that also gets to the point of one of your other questions about contact with animals.

One of the things we have got to be careful of because when I testify at various forum, people have anxiety about whether they should be going near their pets. We don't have H5N1 bird flu or any animal flu in this country, that is the first thing.

With regard to human-to-human transmissibility, that was what I was referring to early on when I was talking about common sense public health measures of what we should be doing in the seasonal flu situation anyway. And that is why I think how we prepare ourselves from a public health standpoint, as well as from a vaccine and antiviral standpoint, but the seasonal flu is going to help us enormously if and when, and we hope never, we have to be confronted with a pandemic flu.

There are very simple types of public health measures of how you avoid, as best as possible. There is a situation called social distancing. So if you influenza in the community, you make a decision about whether or not you close a school. You give guidance about not sending sick children to school. If you are sick, don't go to work. If you have crowded areas like sports arenas in the middle of a flu, to avoid those. Those are the things that we need to underscore anyway, even if we never see a pandemic flu.

Chairman HYDE. Mr. Leach of Iowa.

Mr. LEACH. I would like to ask a question of Dr. Fauci and Dr. Schuchat.

One of the aspects of Tamiflu that has caught the attention of the world community is that we have a single producer, and that producer is in negotiations to allow other producers. But we have problems of patents and legal systems, and we have a lot of discourse about the United States isn't the best place to develop certain things because of legal liabilities, et cetera.

And so I would like to ask the two of you, because I think you have probably done more thinking than anybody on issues of structure of our society, do we need changes in law to allow the government to manage a more rapid production of an emergency kind of vaccination approach? And are there things that the Congress should address in this regard?

Now, there was a reference earlier that you need compensation in China for people who destroy their bird flocks. Do we need to have laws that say that the government is responsible in the event of things that go wrong? Because in all vaccinations, there is a fraction of a percentage of some nature that something will go wrong.

Are there disincentives that we have in our legal system to developing these things? And that means that, Dr. Fauci, you pointed

out a couple new approaches that your institution has largely been in charge, I understand, of developing. How do you work with the private sector to get these produced? Or do you have visualized government labs producing it? I doubt it.

But are there things the Congress can do to help you, as you visualize this? And what would you recommend?

Dr. FAUCI. Yes. An extraordinarily and important relevant question, Mr. Leach. I am glad you asked that.

Yes, we thought about this an awful lot. And sometimes one might suggest that the government should take over the vaccine production or the drug production. That just won't work.

What we need to do is partner with industry in a productive way, in which we assume shared risks with them to develop the capacity to meet the demands of public health emergencies that are not intuitively profit-making endeavors for them when they could invest their money in making a blockbuster drug.

The idea of enhancing the production capacity and partnering with companies is integral to the HHS pandemic plan, and is built into actually the rationale behind the President's budget request.

So I think the first thing that, if you are asking my opinion of what the Congress can do to help, is help us get that budget package through, the \$7.1 billion, of which \$6.7 billion is HHS, of which a considerable amount addresses the precise question you are asking me: How can we get this situation and these circumstances, so that we don't have the risk of not having a counter-measure like a vaccine or a drug. So there are things that we can do.

Mr. LEACH. Are there legal system things beyond dollar things?

Dr. FAUCI. Well, the issue of liability continues to come up. That is something that we need to address. How it is addressed and what forum, with what legislation, I think needs to be worked out by people who know a lot more about it than we do. But we need to get the issue of liability off the table.

Because although it may not be the single issue that is going to stop the show, as it were, there is a considerable reluctance on the part of industry to get involved in an already risky endeavor if there is the possibility that they are going to wind up getting a loss with a suit.

Dr. SCHUCHAT. Just to add briefly, I agree with Dr. Fauci's comments.

I think the other thing that is a struggle for the industry is the predictability of demand, which makes supply not follow. So I think one of the goals of the proposed budget is to try to really deal in the long term with enhancing supply, ensuring a stable demand for seasonal flu vaccine, that will then get us better at giving out the vaccine each year, get consumers and the public ready, more familiar with receiving the vaccine, and have the manufacturers understand that there is an annual seasonal flu market to be used.

Mr. LEACH. Thank you.

Mr. BURTON. Mr. Chairman, will you yield briefly? When it comes my turn to talk, I want to address the issue you just raised about liability exposure. I think it is extremely important, and I hope my colleagues will pay particular attention when it comes, because I think it is a very relevant issue.

Thank you.

Chairman HYDE. Ms. McCollum.

Ms. MCCOLLUM. Thank you, Mr. Chairman. I just want to go back to the issue the panel has been discussing.

We have got, as far as farmers raising chickens, we have got in Thailand, there is actual poultry producers, and they are getting up to speed, and they are getting educated, and they know what is going on.

And then we run into small farms which are easily identifiable. And I know for a fact USAID has been doing a great job in Vietnam kind of going out and identifying those folks, and having the conversations hand-in-glove with the government.

Then we get into the issue of, I took the opportunity to recently be in Bali. And the chickens, I don't know how they tell whose chicken is whose, but they are just running around, and then maybe a family is eating a chicken. But it is a big discussion about eating that chicken.

And I mean, there is compensation for the big and the small farms. But for a family, a chicken is a savings account. I mean, that is where you go to when you have not had anything to eat for several days, and you figure out some way to negotiate, probably not cash for cash, but maybe for some corn or for something for your family to eat. That is your savings account.

So people are not going to part with those generously without knowing that there is something in it for them and their families. So those discussions, we have them—I mean, I understood that. I still don't understand it in as much depth as I probably do today, had I not spent 4 days living in close proximity to a village and watching that.

When we go on codels, we might drive down a road and see it. But until you really do it, you don't understand what that really means to that family.

On the whole issue about communications. I mean, I agree, we don't communicate very well here in the United States, let alone you start taking countries that at best have maybe a weak community radio station that is going to be out talking, and then the number of people that have their radio, the people who don't hear it right the first time and are miscommunicating what is going on, and how things get spread. This is an issue we are having with HIV/AIDS. With all the dollars and resources that we have put into HIV and AIDS, there are still huge misunderstandings about prevention and what we need to do.

So I look forward to seeing a more fleshed-out plan in the future on this issue.

I am going to go back to one of my original questions. And I want to thank the Chair for enabling me to attend a conference in New York on global health issues just about a month ago.

Dr. Hill, I am concerned about NGOs. I am concerned about NGO staff. I am concerned about people who have secondary contracts that are in country performing these duties. And I am concerned about them because I have already spoken with NGOs that have told me, well, I have people that are not reupping in Asia; they want to go to Latin America, because they don't want to be in a hot zone. I have NGOs asking us if we are going to have Tamiflu available for them; are they going to be in line for inocula-

tions, what is going to happen. You have Embassy and Peace Corps staff that you have to deal with.

But in some of these countries where there is tourism and there are people available, we are going to have U.S. citizens showing up at the Embassies.

So my question is, I am not asking for anything that is classified or whatever—I can certainly see that separately—but what are we doing? What is our communication plan to our contract directors who are maybe providing HIV/AIDS in some of these countries?

Mr. MCCOTTER. Hi. Let me address this issue about who are you going to use? What NGOs? And are international NGOs going to be frightened off, and not only not do Avian influenza work, but not do HIV work or some other work? Polio work in some of these countries we are trying to eradicate it, where it has reemerged.

I think those are fears that we are going to have to address and be prepared to talk about.

Let me answer this in two parts. Number one, the best way we can communicate is not primarily through international NGOs. Now, they may have a leadership role, but we recently had some discussions in Indonesia where we set up a plan for 900,000 people to go door to door throughout the islands of Indonesia with the communication messages they need to have for interaction with their animals and their birds.

Now, obviously the huge majority of those, 99-plus percent, are not foreign at all. The first thing we have got to do is we have to activate the networks that are there, and are going to be there no matter what.

Now, we have to protect those international folks who are there, as well, as best we can, and keep them fully aware of what the dangers are. And if something starts to happen, we owe it to them to let them know. And this is the place where Secretary Rock and the State Department have to work not only with their FSNs, their foreign service nationals who work in the Embassies, and there is a plan underway to think about them and how they are affected by what happens, but also the contractors that are in country, the international NGOs that are there.

The Embassies are the lifeline to getting the right information out to them. And sometimes that is very important to us, because they are our connection to our partners who are getting things done.

But I do want to stress how important it is for us in terms of the amount of money we have, and the effectiveness of what we want to try to achieve. Most of that has got to be indigenous. We have got to activate their systems with the right messages.

And the messages are not costly messages. It has to do with, for example, keep your domestic fowl separated. Keep the different kinds separated. Put them under sheds if you can do it, so that they don't have connections or contacts with the wild birds. That means you try to provide them grants or loans or something for the sheds that allow them to follow that communication. You need to give them something tangible that they can do that will make them less at risk, and that is the point of the communication strategy.

But we have to back it up with programs that will allow them to carry it out.

Chairman HYDE. The gentlelady's time has expired. Mr. Burton.
Mr. BURTON. Mr. Chairman, I think Mr. Rohrabacher was next if he has questions. So I will wait until he has his time.

Chairman HYDE. Well, the gentleman must have a schedule that I don't have. But if you yield to Mr. Rohrabacher—

Mr. BURTON. No, I don't want to yield to him, I want my time. But he was here before I was, and I just want to make sure he gets his time.

Chairman HYDE. Well, that is very generous of you.

Mr. BURTON. I know it. I am a wonderful guy.

Chairman HYDE. I wouldn't go that far. [Laughter.]

Mr. Rohrabacher.

Mr. BURTON. Why is it I am always the straight man with you, Mr. Chairman?

Mr. ROHRABACHER. I certainly appreciate that courtesy. Thank you very much, Mr. Burton.

I just want to focus in one area. And again, I am sorry I was called out to a meeting, so I missed about a half an hour of this session, but I think it is really important what you are doing. And this issue is vitally important for us to discuss. And again, I applaud the Chairman for providing the leadership of putting this together.

The estimate you have is between 209,000 Americans and almost two million American deaths could result from this, should this develop into a pandemic, is that correct?

Dr. FAUCI. Yes. That is based on mathematical models of the two types of scenarios: A 1957/1968 scenario, which is the 200,000, and the 1918 scenario, which is the 1.9 million.

So when you project, you have to be careful with mathematical models, because they are only as good as the assumptions that you put into the model. But that is how you get that wide range. What happens if it follows the pathway of a mild pandemic versus a very severe pandemic.

Mr. ROHRABACHER. And that is just deaths that we are talking about.

Dr. FAUCI. Those are estimates, absolutely.

Mr. ROHRABACHER. No, deaths, not estimates. How many people would you be expecting to actually contract this influenza and suffer considerably?

Dr. SCHUCHAT. The models that you are talking about were based on the medium pandemic, is based on 15 to 25 percent of the population becoming ill. So we are talking about in terms of just illness, illness that could be managed at home, you know, one in four.

This is, as Dr. Fauci says, this is modeling, looking at what we know about previous pandemics. But a pandemic virus is a new thing, and we don't know exactly how it is going to behave.

Mr. ROHRABACHER. So we are facing a situation now where it would not surprise the experts if one in four Americans would contract this. And it is very painful. Maybe you could describe what someone goes through in this?

Dr. FAUCI. Well, it is not a question of being surprised. I would be surprised if that were not the case, because that is the general

attack rate that you have with influenzas. In fact, maybe even higher than that.

Mr. ROHRABACHER. And what does that mean in terms of an individual—

Dr. FAUCI. Well, there is a wide range of responsiveness and clinical manifestations. When you look at how biology goes with infections, you generally have something resembling a bell-shaped curve. You have some people who just get absolutely devastating disease quickly, die quickly. There is going to be some on the other end of the curve who get infected, and do really, really very well.

And then there is going to be a very wide range of symptoms, from getting sick and recovering, from getting sick and really being in trouble, to getting sick and dying.

Mr. ROHRABACHER. You say sick. What does sick mean?

Dr. FAUCI. Sick means, well, the symptoms are well recognized when you deal with influenza. They become more severe and lead to more complications when it is a pandemic. You wind up with fever, muscle aches, what we call prostration, literally an inability to get out of bed.

It can then go to pulmonary signs and symptoms, difficulty breathing. In its severest form, you can have an effusion of inflammatory cells into the lungs which, in its worst form, can actually lead to a pulmonary death. That was one of the major modus of exit of people during the 1918 flu who had pneumonia, some of which were secondary bacterial pneumonias, but a lot of which were primary pulmonary problems related to very intensive inflammatory response that pour into the lungs.

Mr. ROHRABACHER. So this is an intense suffering of those people who are involved with this.

Dr. FAUCI. It is a bad disease.

Mr. ROHRABACHER. It is a bad disease.

Dr. FAUCI. Yes.

Mr. ROHRABACHER. So one, it is possible that we could have a couple hundred thousand people affected; it is possible it could go up to one in four being infected, and possibly up to two million dying from this. Is it children, babies, and older people who are most likely to die, is that correct?

Dr. FAUCI. In regular influenza, seasonal influenza, you are concerned about elderly, greater than 65, particularly those who have one or more conditions that are debilitating, particularly lung or heart disease, and then children from six to 23 months.

When you are dealing with a pandemic, history has told us that all bets are off with regard to ages. Young individuals get as sick as some of the older, and vice-versa.

Mr. ROHRABACHER. What are the chances now, and I am sorry if I missed this because I was called off to that meeting in the outer office there. Maybe you can go to the panel. If you had to tell us what you think the chances are of a pandemic actually breaking out, and I understand if a pandemic happens, it will, within a year, reach the entire planet, and correct me if I am wrong on that.

What are the chances of that type of pandemic actually happening? Just tell me how you are scoring this.

Mr. ROCK. Beginning with me, let me say that I don't think I could begin to predict what those chances are. But I will put one

small data point into the mix. And that is that we are hearing from all the experts is that in the absence of transparency and immediate reporting, if you don't catch it within 3 weeks, it is going to be beyond your ability to control and contain. So the probability is going up dramatically.

Chairman HYDE. The gentleman's time has expired. Mr. Engel.

Mr. ENGEL. Thank you, Mr. Chairman. I have just gotten back from Geneva, where I and six of my colleagues have had meetings with the World Health Organization with regard to the pandemic flu.

And one of the things that they stressed in our meetings is that they believe it is important to delay the onset of the flu; that even if we could delay it for a few weeks or a month or so, it would be very beneficial in our trying to contain it.

I am wondering if any of you would care to elaborate on that. Because that was something that many of us had not been aware of, and that we were all very interested in hearing about.

Dr. SCHUCHAT. Yes, I can begin with that. I think that ideally, we would have very excellent surveillance all over the world, and know exactly when a spark is lit that is the beginning of a pandemic, and be able to snuff it out right there. That is a pretty daunting order.

And so the approach that is aggressively being pursued is for local containment, to at least be able to contain what you can, and slow the spread from one place reaching others.

In the world that we live in, with such globalization, international travel, and such inter-dependency, an outbreak anywhere is really a pandemic risk everywhere. So what you gain by trying to delay the spread is time to get the counter-measures out.

So we have this long-term strategy to improve the vaccine production capability and the antiviral capability, but you actually have to be able to probably make a new vaccine to whatever the strain is that is causing the pandemic. That is not a matter that can be carried out overnight. So delay gives us more time for vaccine production and delivery.

Mr. HILL. There are three issues I would mention. The reason WHO correctly stated that they would love to see a delay is because there are three fronts that we are fighting on simultaneously.

Obviously, the research front. Anything that happens with vaccines and antivirals will help us down the road.

The animal husbandry practices that need to change to make a population less vulnerable to this are not fixable overnight. They take weeks, months, in some cases years. So we fight for every day, every month we can get, because that will help us, but we know that can't be done overnight.

And then thirdly, there are some steps that we are taking, can be taken within a few weeks or months, which have to do with surveillance and containment. And again, we need all the time we can get to put those in place.

So even if it is a couple of years before something really hits, we will use every minute of that time profitably.

Mr. ENGEL. Thank you. What would you say are the key strengths and weaknesses of the coordinated response by the World

Health Organization in tandem with the Food and Agricultural Organization and the World Organization for Animal Health? Are there global actors that could provide more direct assistance in the coordinated response? And if so, which ones? And what are the ways that we, in the Congress, could provide further help?

Mr. ROCK. If I may, just to start that response. I noted that in our most recent meetings in Geneva, all three of the organizations that you referred to are busily working on identifying what we would call the standards or the criteria for operations in each of their areas. What are the standards, the expected rules that should be in place in any preparedness plan.

The next step in that process is coordination among those three major international organizations. And we urged them to come together and do that. The establishment within the UN system of a special coordinator on Avian and pandemic influenza, that is Dr. David Navarro working directly for the Secretary General, is designed to help bring that uniformity to the organization's process. They anticipate that they will be the leads, the co-leads in an international response. And we would agree with that. But they are a technical lead, and they will require enormous assistance and cooperation from other organizations. That is why we are working to pull together rapid response teams that would be able to help them, and I know CDC is very active in that regard.

Mr. HILL. Three quick points. We don't need to be theoretical here at all, because the track record of the United States working closely with these groups is extremely strong.

Let me give you a very practical example. When the \$10 million came to USAID from the Congress here a few months ago, we immediately decided that \$6 million of that would go to FAO. And we worked with them, had worked out a strategy. They have gotten the money, they are using it, they are great with animal situations. And we gave several million more to WHO.

There is quite a bit of money in the amount that the President proposed recently on November 1 that will go to FAO and WHO through USAID.

Secretary Leavitt showed, at the highest level, the commitment of the United States to show to the world that this is an international team, and not a U.S. team. When he brought with him on the delegation with us not just somebody from the Secretary of State's Office of State and from USAID and USDA, he brought the head of the World Health Organization. He brought a senior person from FAO. He brought somebody from OIE, the Animal Health Organization that is so critical. Every time we appeared before a group of political leaders in Vietnam or Cambodia or Laos or Thailand, it was always a joint front saying this is a global problem, we have agreement about what needs to be done.

And I think it is one of the things that the United States should be most proud of, is that they are already intimately engaged in the partnership that Bud Roth was talking about earlier, is another example of the U.S. playing very, very closely with the international partners to have a coherent policy and strategy.

Chairman HYDE. Mr. Burton of Indiana.

Mr. BURTON. Well, first of all let me congratulate our health agencies on their hard work in getting out in front on this. I think

it is fantastic, and I think that ultimately you are going to save a lot of lives.

There is one thing that really bothers me, though, and that is the Vaccine Injury Compensation Fund. It has not been user-friendly in the past. Many people who have legitimate claims have gone 10, 12 years without getting compensation, because the Congress I think did not get all the things squared away when they passed that.

And one of the things that bothers me is that in legislation that will come before the House dealing with the Avian flu, there may be, and probably will be, some kind of liability protection for the pharmaceutical industry regarding this vaccine.

Now, I am for that. I want to give the pharmaceutical industries the liability protection that they want. But in exchange for that, it is imperative, in my opinion, that we beef up the funds that are in the Vaccine Injury Compensation, there is about \$3 billion in there right now. And we may need to figure out a way to get more in there, because there may be a lot of people damaged not from the flu, but from problems created by getting the vaccination.

Now, we have had kids that have gotten numerous vaccinations that contain mercury. It is a preservative, thimerosal, and you know all about that, Dr. Fauci, we have talked about this before. And as a result, a lot of these people, there is thousands of families in this country that have been damaged, and they get nothing. The kids are going to grow up to be 60, 70 years old, they are going to be burden on society, and there has been nothing done to help those families deal with this problem because they have been damaged by the vaccination. I know there is arguments about that, but mercury is toxic, and it is in there.

Now, the same thing could occur with the flu vaccine. So I would urge you, as leaders in the health agencies, to tell the legislators who are going to be sponsoring this legislation that we have to revise the Vaccine Injury Compensation Fund, number one, to be more user-friendly. Number two, to make sure there is adequate money in there to deal with the problem, if there are side effects from these vaccinations. And if we need additional funds in there, we can add a small amount to each vaccination to build up the fund until we get over this hump.

And the third thing is, if they do that, if they do that, I will be very anxious and supportive of leading the fight to give them liability protection, because I think they need to have that. Because we are going to need them in the future for not only this pandemic possibility, but for other things that are going to come down the pike.

But we need to make sure that people who are damaged by vaccinations don't have to fight and fight and fight and fight, and not get anything for the damage that has been caused by these vaccinations. And that has been one of the major problems that I have seen in the past.

And so, you know, as leaders, I would like to hear what you have to say about this, because I have already been told that there is going to be liability protection in any Avian flu vaccination legislation. And to not deal with these other two problems—adequate funding for people who have been damaged, and making sure that

the Vaccine Injury Compensation Fund is more user-friendly—if we don't have those two things in there, I will tell you, I will take a point of personal privilege for 1 hour during the time that this legislation comes forward, and I will go into this in minute detail, pointing out that we are not doing anything to protect the population, not against the vaccination, not against the flu, but against the vaccination itself.

I mean, we cannot give millions of vaccinations knowing that there is going to be side effects, and leave these people high and dry if they are damaged. And we can do it, but we need to do it at the same time that we are passing the flu legislation.

So I am for giving them liability protection, but there has to be adequate funds in the Vaccine Injury Compensation Fund. And we have to make it more user-friendly. If we can do that, everybody is going to be happy, including the pharmaceutical companies. If not, there is going to be a war on the Floor and in the Senate. I have already contacted my colleagues in the Senate telling them, you know, when we put in Homeland Security, the liability protection for the kids who have been damaged by mercury in my opinion, we were able to get that out of Homeland Security. And that fight will be magnified if this isn't incorporated into legislation dealing with the flu vaccine.

So I just want to tell you that in advance, because I love you guys. You know that, Dr. Fauci, I love you. But this has got to be in there. And if you have a comment, I would like to hear it.

Dr. FAUCI. Well, thank you. I love you, too, Mr. Burton.

I want to say that, you know, we have discussed this many times in the past, and we appreciate your leadership in this in trying to strike that right balance.

Mr. BURTON. Is that what you call it?

Dr. FAUCI. No, actually it is, in striking the right balance between liability and compensation. Because that is something that I know is very important, and that we have discussed many times. And I agree with you, we have to have a right balance there.

Chairman HYDE. Thank you very much. This panel has reached completion. And I want to compliment each of you for being very instructive and very helpful, very knowledgeable. It is reassuring to know, no matter how daunting the problem is, we have people such as yourselves who are combatting this scourge, and I congratulate all of you. Thank you so much.

The next panel. Dr. Margaret Chan joins us today via video-conference from Geneva. Dr. Chan, who is from the People's Republic of China, joined the Hong Kong Department of Health in 1978, and became Director of Health in 1994. During her 9-year tenure as Director, she effectively managed outbreaks of Avian flu, and of SARS.

In 2003 she joined the World Health Organization as Representative of the Director General of Pandemic Influenza. In this role, Dr. Chan is regarded as one of the world's foremost experts, and the Committee is truly fortunate to have her speak with us today.

Our next witness will be introduced by Ms. McCollum. Ms. McCollum, will you introduce the next witness?

Ms. MCCOLLUM. Thank you, Mr. Chair. I am very pleased to have the opportunity to introduce Dr. Michael Osterholm. Dr.

Osterholm is the Director of the Center for Infectious Disease, Research, and Policy at the University of Minnesota, and the Associate Director of the Department of Homeland Security National Center for Food Protection and Defense.

He is also a professor at the University of Minnesota, and has recently been appointed by Secretary Leavitt to the National Science Advisory Board on Biosecurity. He has served as the consultant to then-HHS Secretary Thompson on bioterrorism, and was appointed to the Secretary's Advisory on the Council of Public Health Preparedness. He is a member of the Institute of Medicine and National Academy of Sciences, as well as a frequent consultant to the World Health Organization Food and Drug Administration, and the Centers for Disease Control.

Dr. Osterholm has previously served as Minnesota's Department of Health for 24 years. The last 15 years he was our State Epidemiologist, where I had an opportunity to work with him on many issues. During that time he led us through many investigations into outbreaks, including food-borne illnesses, lyme disease, HIV infection in hospital workers. He is the author of over 300 papers and abstracts, and a reviewer for 24 journals, and the recipient of awards too numerous to mention in the limited time that I have.

Dr. Osterholm is one of the world's foremost experts on the Avian flu, and has published several papers. And you will see him appearing in many news reports discussing the potential for the pandemic.

He graciously came to Capitol Hill to brief the Members on this important issue for the first meeting of the Congressional Global Health Conference. And many, many staff, as well as Members, appreciated his input, and now I know are emailing him on a regular basis.

Dr. Osterholm is a valuable resource not only on health care, but on the well being of this planet. He is a powerful speaker, and I am proud to call him a friend of Minnesota, the United States, the world, and mine. Thank you very much for taking time to join us.

And Mr. Chair, thank you for extending me the courtesy to introduce him not only as a special person on this issue, but a friend of mine, as well.

Chairman HYDE. Thank you, Ms. McCollum. And first we will turn to Dr. Chan, who is with us via satellite.

Good morning to you, and thanks for taking the time to be with us, Doctor.

**STATEMENT OF MARGARET CHAN, M.D., REPRESENTATIVE OF
THE DIRECTOR-GENERAL FOR PANDEMIC INFLUENZA,
WORLD HEALTH ORGANIZATION**

Dr. CHAN. Good morning, Chairman, Members of the Committee. I would like to thank you very much for this opportunity to address such a distinguished Committee.

On behalf of the World Health Organization's Director-General, I would like to thank the United States for giving us a state-of-the-art operations room for outbreak response. And I am sitting in this room now, sir.

This will be the nerve center of our efforts to coordinate the global response to a pandemic. I will give you an overview of the

present situation with H5N1 Avian influenza, and an assessment of the pandemic risk. In so doing, I will be drawing on first-hand information from WHO country officers, as well as the conclusions reached during a high-level meeting on the subject held at WHO last month.

Participants of that meeting gave us a very frank assessment of what we, as an international community, are up against. Several countries affected by the outbreak admitted that they have no capacity whatsoever to deal with a disease of this nature. The stakes are high. The costs to agriculture in Asia alone have surpassed \$10 billion U.S. dollars.

Today, more than 160 million birds have died or been destroyed. The livelihoods of about 300 million farmers have been severely affected, and no one can say when this will end.

At present, Avian influenza is primarily a disease of birds. The virus does not easily cross from birds to infect humans, but when it does, it causes very severe disease, affecting multiple organs and systems. The clinical deterioration of patients is very dramatic, and exceptionally rapid.

To date, five Asian countries have reported about 140 human cases. More than half of these were fatal.

Conditions favoring the start of a pandemic are certain to exist because the virus has become endemic in large parts of several Asian countries. The risk of more human cases will persist, and every single human case gives the virus a chance to undergo the changes it needs to ignite a pandemic.

Our present level of concern is definitely higher than a year ago. Looking at the situation in affected countries and recent research findings about the virus, we believe we have moved, over the past several months, steadily and surely ever closer to a pandemic.

Monitoring of the virus, which is being conducted by laboratories in the surveillance network, of which the U.S. HHS CDC is a very important partner, has revealed some mutations since the year 2004. The research conducted by U.S. scientists and published in October of this year has identified some similarities between these mutations and the genes in the reconstructed virus which is responsible for the pandemic of 1918.

We also know that the 1918 virus, like the H5N1 virus, was purely Avian in all its genes. No one can know at this point in time whether the H5N1 virus will retain its present exceptional virulence when it acquires the ability to spread easily among humans.

In the event of a pandemic, all populations will be susceptible. All countries will be at lethal risk.

But we are not without defenses if we act collectively right now. During the November meeting in Geneva here, we introduced a five-pronged strategic action plan, which builds on previous technical guidance for countries. The plan aims to achieve two objectives.

First, to ensure full exploitation of all opportunities to prevent the H5N1 virus from developing the ability to ignite a pandemic. And should this effort fail, two, to ensure that measures are in place to reduce the morbidity and mortality, and the social and economic disruption that can be expected during the next pandemic.

Opportunities to intervene preemptively are reflected in our strategic actions. Reduce human exposure to the virus, strengthen early warning systems, and intensify rapid containment operations.

Essential to all these three actions is a very much, we need a much better capacity to detect, to confirm, and to report human cases in affected countries. And preparedness activities are covered in the remaining two actions.

Build capacity to cope with the pandemic, and coordinate global scientific research, particularly concerning the development of a pandemic vaccine.

Chairman and Members, more details about this strategy are contained in my prepared statement, which I have respectfully submitted to this Committee.

Thank you very much.

[The prepared statement of Dr. Chan follows:]

Statement by
Dr Margaret Chan
Assistant Director-General
Communicable Diseases
World Health Organization

**Avian influenza and the pandemic
threat:
Global situation assessment**

Committee on International Relations,
House of Representatives

Hearing on *Avian Flu: Addressing the Global
Threat*

7 December 2005

Introduction

The World Health Organization would like to thank Chairman Hyde and the Committee for the invitation to provide a statement in the context of its timely hearing on "Avian Flu: Addressing the Global Threat." Just one month ago, on 7-9 November 2005, WHO co-hosted, with FAO, OIE, and the World Bank, a meeting in Geneva on avian and pandemic influenza. The meeting, which was attended by more than 600 experts from over 100 countries, marked the largest gathering held to date to assess the multiple threats arising from outbreaks of highly pathogenic avian influenza, caused by the H5N1 virus, that have been ongoing in parts of the world since mid-2003.

The meeting was considered unique in the number of participants, the high level of government representation, and the co-sponsorship of the four international agencies. For the first time, international and regional financial institutions were included to address economic issues and advise on mechanisms for funding priority interventions. The World Bank gave its estimate of the economic consequences of an influenza pandemic. Under the unique conditions of the 21st century, a pandemic could easily cost the world economy US\$ 800 billion within a year. Developing countries and aid agencies gave their assessment of how a pandemic would affect ongoing development projects: they would be ruined.

Discussions took place with a sense of urgency sharpened by the recent appearance of the virus in new countries, projections that further spread is almost certain, and an increase in reports of sporadic human cases. The meeting was followed a week later by confirmation of the first human cases of H5N1 infection in China.

Apart from taking stock of the current situation and related threats to human and animal health, the meeting aimed to make an inventory of precise needs, establish priorities, and map out ways to meet them. Mechanisms for matching these needs with rapid, adequate, and flexible funding were also explored. Discussions benefited from first-hand accounts from a diversity of countries either directly affected by outbreaks in birds and humans or considered at high risk. Expressions of need were open and candid. Several front-line countries frankly admitted their inability to deal with a disease of this nature on their own, despite full awareness of what failure would mean for the international community. These presentations helped give the shared sense of urgency a focus by defining specific needs and challenges. They also moved the discussion forward by suggesting concrete lines of action.

Deep concern about the consequences of a pandemic steered discussion, on human health matters, towards consideration of two main sets of actions. These were aimed at (1) preventing the emergence of a pandemic virus or, should this prove impossible, delaying the initial international spread of a pandemic, and (2) preparing all countries to cope with a pandemic in ways that mitigate morbidity and mortality and also reduce economic and social disruption. Participants agreed that the threat of a pandemic was of shared and significant concern for all countries, and that actions to prevent a pandemic or mitigate its consequences were likewise a shared responsibility of countries.

Given the high level of concern and sense of solidarity, it is understandable that participants readily agreed on ten main conclusions and a 12-point set of actions. These are reproduced in Annex 1. Following the meeting, WHO prepared a five-pronged strategic action plan, which sets out strategies for acting pre-emptively now and, should these actions fail, for mitigating the consequences of a pandemic. This plan is summarized in Annex 2. As stated by the WHO Director-General at the close of the meeting, implementation of the recommended actions will begin immediately. A follow-up meeting, to decide on funding priorities and mechanisms, will be held in Beijing in early January 2006.

As requested, this statement provides a global overview of the epidemiological situation, stressing features that fuel concerns that a pandemic may be imminent. A summary of the situation in South-East Asia, Russia, and Europe is provided, together with an explanation of the roles and responsibilities of WHO in responding to the crisis. The status of pandemic vaccines and antiviral drugs – the two medical interventions for reducing morbidity and mortality during a pandemic – is assessed in terms of prospects for their availability, soon enough and in sufficient quantities. As guidance for the international response, some relevant lessons from the SARS experience are briefly described.

Reasons for concern about the H5N1 influenza virus

- *The virus causes extremely severe disease in humans. It has considerable pandemic potential. The source of human exposure is not easily removed.*
- *The virus is evolving in ominous ways.*
- *The world may be on the brink of another pandemic.*

Severe human disease. Of all influenza viruses that circulate in birds, the highly pathogenic H5N1 virus, currently becoming widespread in animals, is of greatest concern for human health for several reasons. First, though avian influenza viruses rarely cross the species barrier to infect humans, H5N1 has done so on three occasions since 1997. This virus has also caused by far the greatest number of human cases of very severe disease and the greatest number of deaths. Unlike normal seasonal influenza, where infection causes only mild respiratory symptoms in most people, the disease caused by H5N1 follows an unusually aggressive clinical course, with rapid deterioration and high fatality. Primary viral pneumonia (which does not respond to antibiotics) and multi-organ failure are common. For unknown reasons, most cases have occurred in previously healthy children and young adults.

Pandemic potential. The H5N1 virus has considerable potential to spark another influenza pandemic. At present, all conditions for the start of a pandemic have been met save one: the establishment of efficient and sustained human-to-human transmission. Each additional human case gives the virus an opportunity to combine with other viruses or adapt in ways that allow it to spread easily among humans. The risk of human cases persists as long as the virus continues to circulate in birds; the virus will not be eliminated from birds for some years to come.

A tenacious virus in poultry. The current outbreaks in poultry are historically unprecedented in their scale and geographical scope. Never before have so many birds been affected in such a large number of countries. Despite intense control efforts, the virus has become firmly entrenched in large parts of Asia. On numerous occasions, countries thought close to control have experienced setbacks as outbreaks recurred and then spread rapidly. Timeframes for controlling the disease are now being measured in years. Recent evidence that wild waterfowl are now carrying the virus in its highly pathogenic form is particularly worrisome, as all experts agree that elimination of the virus from wild birds is impossible.

An ominous evolution. Like all influenza viruses, H5N1 is notoriously unstable and unpredictable. In an historically unprecedented situation involving a constantly changing virus, unusual developments can be expected, and these have occurred. During the past 18 months, the virus has evolved in ways that increase the complexity of control and heighten concern about the pandemic threat.

Domestic ducks can now excrete lethal virus without showing signs of illness, thus acting as a "silent" reservoir of the virus, perpetuating transmission to other birds. This adds yet another layer of complexity to control efforts and removes the warning signal for humans to avoid risky contact with sick or affected animals. Second, the relationship between the virus and its natural

animal reservoir, wild waterfowl, appears to have changed, possibly for the first time in centuries. The spring 2005 die-off of more than 6,000 migratory birds at a nature reserve in central China, caused by highly pathogenic H5N1 virus, was highly unusual and probably unprecedented. Scientists are increasingly certain that at least some wild waterfowl are now harbouring and excreting highly pathogenic H5N1 virus and carrying this virus with them along their migratory flyways. The recent spread of the virus to Russia and parts of Europe is thought to have occurred via this wild-bird vector; spread to additional areas is considered inevitable.

When compared with H5N1 viruses from 1997 and early 2004, viruses now circulating are more lethal to experimentally infected mammals and survive longer in the environment. Mammalian species previously considered resistant to infection have developed disease and can spread it to others within their species. Expansion of the mammalian host range of the virus is of concern as it gives this purely avian virus more opportunities to adapt to a form that spreads more easily among mammals, including humans.

Perhaps most significantly, recent research on both human and animal viruses circulating in Asia in 2005 has detected several mutations, some of which may affect transmissibility in humans. Research following recent reconstruction of the highly lethal 1918 pandemic virus determined that this virus was entirely avian and may have evolved along an evolutionary pathway similar to that being seen with the H5N1 virus.

On the brink of a pandemic. For all these reasons, WHO and international experts believe that the world is now closer to another influenza pandemic than at any time since 1968, when the last of the previous century's three pandemics began.

A pandemic is caused by a new influenza virus that has either never circulated in humans or has not done so for a number of years. Because humans will have little if any immunity to this "foreign" virus, susceptibility is virtually universal. This lack of immunity also results in more severe disease than seen during seasonal epidemics of normal influenza. The result is a worldwide epidemic (pandemic) that sweeps through susceptible populations, rapidly encircles the globe, and causes excess morbidity and mortality, usually far above that seen during seasonal epidemics. Whereas seasonal influenza usually has its most severe effects on a limited number of risk groups (the very young and the elderly, persons with underlying chronic disease or compromised immune systems), pandemics can cause severe illness and deaths in all age groups, including the young and healthy. The newness of the virus also means that existing vaccines will not confer protection.

With the H5N1 virus now considered endemic in large areas, and spreading to new ones, the probability that a human pandemic will occur has increased. As no virus of the H5 subtype has ever circulated widely in human populations, human vulnerability to infection with this virus will be universal. On the positive side, experts anticipate that the virus will lose some of its virulence (the present case fatality rate is higher than 50%) when it improves its transmissibility; this is not, however, known with certainty. Historically, pandemics have encircled the globe in 6 to 9 months, even at times when international travel was mainly by ship. Today, experts believe that the first pandemic of the 21st century will reach all parts of the world within 3 months.

Status of H5N1 outbreaks in South-east Asia

The recent history of avian influenza in Asia begins in 1996, when a highly pathogenic H5N1 virus was isolated from a farmed goose in Guangdong Province, China. The following year, Hong Kong experienced poultry outbreaks, caused by this virus, on farms and in wet markets. Coincident with these outbreaks, the first instances of human infections with the H5N1 virus were recorded in Hong Kong. Altogether, 18 cases, of which 6 were fatal, were identified in

that outbreak. This event changed scientific thinking about how pandemic viruses might emerge, raising – for the first time – the possibility that an entirely avian virus, capable of causing severe human disease, could be the origin of the next pandemic if given enough opportunities to infect humans and adapt to them. The destruction of Hong Kong's entire poultry population of around 1.5 million birds within 3 days is thought by some experts to have averted an influenza pandemic at that time. Human cases were again detected in Hong Kong in February 2003 in members of a family with a recent travel history to Fujian Province, China.

After a period of quiescence, the virus resurfaced at some time during mid-2003, and quickly erupted into the largest outbreaks of this disease seen in history. Beginning in late December 2003, outbreaks of highly pathogenic H5N1 avian influenza in poultry were reported in nine South-east Asian nations (listed in order of reporting): Republic of Korea, Vietnam, Japan, Thailand, Cambodia, Lao People's Democratic Republic, Indonesia, China, and Malaysia. Of these countries, three have controlled their outbreaks and are now considered disease-free: Japan, Republic of Korea, and Malaysia. Elsewhere, experience shows how firmly entrenched this virus has become and how difficult its complete elimination will be. Despite the death or destruction of around 160 million birds, at a cost to agriculture of an estimated US\$ 10 billion, the virus is now considered endemic in Indonesia and Viet Nam and in some parts of Cambodia, China, Thailand, and possibly also Lao PDR.

In late December 2003, human infections were identified in people exposed to infected poultry in Vietnam. Since then, just under 140 human cases have been laboratory confirmed in five Asian countries (Cambodia, China, Indonesia, Thailand, and Viet Nam), and more than half of these people have died. At present, however, the species barrier is significant. The number of human cases is small in comparison with the huge number of birds affected, over large geographical areas, for two years, and under circumstances offering abundant opportunities for human exposure to occur.

Control of the disease in animals faces several serious challenges, and opportunities for further human infections to occur will persist. In some affected countries, up to 80% of poultry production takes place in small backyard flocks, where surveillance is weak, reporting is poor, and control measures are difficult to implement. These are the areas of greatest concern for human health: to date, the majority of human cases have been linked to exposure to infected household poultry in rural and periurban areas. In these areas, poultry usually roam freely scavenging for food, often entering homes or sharing outdoor areas where children play. Populations traditionally sell or consume birds when signs of illness appear in a flock. This practice has proved hard to change, especially when poultry are a principal source of income and food and cannot be wasted. Behaviours thought to carry a high risk of infection include the home slaughtering, butchering, defeathering, and preparation for consumption of diseased birds.

Most affected countries cannot adequately compensate farmers for culled poultry, thus discouraging the reporting of outbreaks in the rural areas where the vast majority of human cases have occurred. Veterinary services frequently fail to reach these areas. Detection of human cases is impeded by patchy surveillance. Moreover, the initial symptoms of H5N1 infection mimic those of many other diseases commonly seen in affected countries, further increasing the risk that cases are being missed. Diagnosis of human cases is impeded by weak laboratory support and the complexity and high costs of testing. Few affected countries have the staff and resources needed to thoroughly investigate human cases and, most importantly, to detect and investigate clusters of cases – an essential warning signal that the virus may be improving its transmissibility among humans. Because of this inadequacy of the surveillance system, the possibility that human cases are occurring – undetected and unreported – cannot be ruled out. Such lapses are of critical importance to the international community, as timely case reporting constitutes the backbone of the early warning system for detecting the emergence of a pandemic virus. Unless the situation improves, early warning signals that the virus has increased its transmissibility among humans will be missed, and the world will once again be taken by surprise when international spread of a pandemic begins, at which time opportunities

for pre-emptive action will be lost. Once a fully transmissible virus emerges, pandemics are considered unstoppable.

The role of WHO in field-level operations

WHO staff at country offices work closely with ministries of health, assist in the diagnostic confirmation and field investigation of cases, and provide the interface between these ministries and the international community. Diagnostic confirmation of human cases is technically challenging; work with the virus can be safely performed only in laboratories with a high level of biosecurity, and such laboratories are rarely available in affected countries. For these reasons, WHO provides diagnostic support through its coordination of the global network of influenza laboratories specialized in work on the H5 virus subtype. In the US, this network includes the US Centers for Disease Control and Prevention (CDC) of the Department of Health and Human Services and a second laboratory, for animal influenza viruses, at St Jude Children's Research Hospital in Memphis. The US Naval Medical Research Unit 2 (NAMRU 2), located in Jakarta, Indonesia, has been another source of rapid diagnostic support, particularly for cases in Indonesia that have been occurring since mid-September 2005. All of these laboratories are equipped to handle H5N1 viruses at the highest level of biosecurity. WHO country staff arrange for patient samples to be shipped safely to these laboratories for diagnostic confirmation. These laboratories also conduct molecular studies of viruses to look for genetic changes that might signal improved transmissibility and to ensure that work on a pandemic vaccine (which must closely match circulating virus strains) remains on track.

While molecular studies of the virus are one important part of the early warning system, rapid detection and investigation of human cases are even more important, particularly when clusters of cases, closely related in time and place, are detected. Investigations of possible human-to-human transmission are complex. In many areas, the virus is now so pervasive that it is difficult to determine, when clusters occur, whether people acquired the virus from some shared environmental source or each other. At the request of governments, WHO regularly sends international teams of experts, drawn from institutions in its Global Outbreak Alert and Response Network (GOARN), to conduct on-site investigations when unusual disease events of potential international public health importance – such as H5N1 cases in humans – occur. Such teams also assist in the development of national surveillance and diagnostic capacity. Experts from the CDC are usually part of these teams. WHO also procures essential supplies to support laboratory work and the clinical management of cases. Video conferences and teleconferences are regularly held with international experts to gather consensus on the evolution of the threat and to assist WHO in its overall assessments of the situation.

The outbreaks in Russia and Europe

Beginning in late July 2005, highly pathogenic H5N1 was detected in wild and domestic birds in Siberia (Russia) and in adjacent parts of Kazakhstan. Almost simultaneously, Mongolia reported H5N1 in a large number of dead migratory birds. In Russia, poultry outbreaks have since spread westward towards Europe. In October 2005, Turkey and Romania confirmed H5N1 outbreaks in poultry, and Croatia detected the virus in dead migratory birds. In December 2005, Ukraine detected outbreaks in domestic birds. All newly affected areas are located along the flight paths of migratory birds. Deaths of wild and domestic birds in several other areas, including parts of Africa that lie on migratory routes, are under investigation.

Throughout Europe, vigilance for the appearance of outbreaks in wild and domestic birds and for the occurrence of associated human cases is high. Outbreaks in animals have been detected and reported quickly, and extensive control measures have followed immediately. WHO epidemiologists and virologists have assisted in investigations, when requested. Diagnostic

reagents have been sent to national laboratories, and WHO has provided training in H5N1 diagnostic techniques. Viruses have been shared internationally and are undergoing analysis at WHO reference laboratories. These laboratories have also helped to rule out, authoritatively, the many false rumours of human cases. To date, no human cases have been associated with any of these newer animal outbreaks outside Asia.

Several high-level meetings of European ministries of health and agriculture have been held to discuss the avian influenza threat and consider the best preventive and control measures. These meetings have led to the development or refinement, with WHO assistance, of pandemic response plans in the vast majority of European countries.

Europe has areas with dense poultry populations and has experienced outbreaks of highly pathogenic avian influenza in recent years, though caused by influenza viruses other than H5N1. While the further evolution of poultry outbreaks caused by H5N1 in Europe cannot be predicted, prompt detection of outbreaks and the rapid introduction of control measures will hopefully prevent the virus from establishing endemicity outside its present epicentre in South-east Asia. Differences in farming systems between western Europe and Asia, and the greater availability of resources in Europe, should give established control measures a greater chance of success. Many European countries do, however, have rural areas where poultry flocks are kept in close contact with households, and these areas could pose a heightened risk of human cases should outbreaks in poultry become established. Of particular concern are continuing reports of fresh outbreaks in Romania. As the H5N1 virus can persist in the environment for long periods at cold temperatures, authorities in Russia are concerned that fresh outbreaks could occur spontaneously in the spring. Moreover, bird migrations are recurring events: the risk of fresh outbreaks associated with this vector will persist.

Vaccines and antiviral drugs

Vaccines and antiviral drugs are the most important medical interventions for reducing morbidity and mortality during a pandemic. Vaccines are the most important intervention for conferring population-wide protection, but vaccine effectiveness requires a close match with the actual pandemic strain of the virus. Because a pandemic strain, capable of efficient and sustained human-to-human transmission, does not yet exist, the specific pandemic vaccine does not yet exist either. As no country will have adequate vaccines at the start of a pandemic, antiviral drugs assume particular importance as the only possible medical intervention for protecting priority groups pending the arrival of vaccines. Antiviral drugs might also be used to contain or delay the spread of a pandemic at its source. For both vaccines and antiviral drugs, present constraints – which are considerable – mean that most developing countries will have no or very limited access to either throughout the course of a pandemic.

Vaccines. Vaccines are considered the first line of defence during a pandemic. For several reasons, no country will have adequate supplies of vaccine at the start of a pandemic and for many months thereafter. Large-scale commercial vaccine production of a pandemic vaccine is not expected to commence until about three to six months following the emergence and characterization of a pandemic virus.

Manufacturing capacity for influenza vaccines is overwhelmingly concentrated in Europe and North America. Current maximum production capacity – estimated at around 420 million doses of trivalent seasonal vaccine per year – falls far below the demand that will arise during a pandemic.

WHO, through its network of specialized influenza laboratories, has constantly monitored the evolution of seasonal viruses and also of the H5N1 virus since its initial infection of humans in 1997. These laboratories prepare the prototype virus strain that is being provided to industry as the “seed” for vaccine development. Constant molecular analyses of viruses, conducted by

these laboratories, help ensure that this “seed” strain continues to closely match the genetic characteristics of currently circulating viruses. This activity is particularly important in view of mutations in the H5N1 virus detected during 2005.

During the November 2005 meeting on pandemic influenza, the availability of pandemic vaccines, shortly after the start of a pandemic and in sufficient quantities, was identified as the greatest challenge facing the international community. If this challenge is not met, access to vaccines will almost certainly be confined to populations in countries having domestic vaccine manufacturing capacity. At present, around 80% of vaccine manufacturing capacity is concentrated in Europe and North America. Just under 20 countries have domestic manufacturers producing influenza vaccines for the seasonal influenza viruses; several of the largest of these companies are presently working on the development of a pandemic vaccine. Some of these development projects have reached the stage of clinical trials; clinical trials of other candidate vaccines are expected to begin shortly. In early November 2005, WHO convened a meeting of influenza vaccine manufacturers to assess progress in the development of a pandemic vaccine and to conduct an inventory of global manufacturing capacity, particularly in developing countries. While overall capacity looks somewhat more encouraging than one year ago, if a pandemic were to begin within the next few months, no company would be ready to move immediately into commercial production of a pandemic vaccine. Several companies have plans to expand production capacity, but these plans will not be realized for at least another 2 to 3 years.

Finite capacity to produce antigen – the component of the vaccine that elicits the immune response – is a critical limiting factor. Strategies for producing vaccines that are effective, yet use less antigen, could profoundly increase current manufacturing capacity. At present, little knowledge exists to guide formulation of an influenza vaccine that is both effective and economizes on the use of antigen. Clinical trials are under way to test different formulations, and these trials will provide some answers. WHO has encouraged companies to test vaccine formulations that include an adjuvant. This substance boosts the immune response, and theoretically could allow adequate protection at lower quantities of antigen. Work on this approach is also under way.

As a pandemic vaccine needs to be a close match to the actual pandemic virus, commercial production cannot begin prior to emergence and characterization of the pandemic virus. WHO has, however, encouraged industry and regulatory authorities to develop fast-track procedures for licensing and marketing authorization of a pandemic vaccine, and this has been done.

WHO is using international meetings to urge the international community to find ways to increase manufacturing capacity and ensure that developing countries have access to an effective vaccine at an affordable price. As another strategy, WHO has provided direct assistance to some developing countries engaged in work on a pandemic vaccine. On current trends, however, most developing countries will have no access to a vaccine during the first wave of a pandemic and perhaps throughout its duration.

Antiviral drugs. Pending the availability of vaccines, several antiviral drugs are expected to be useful for prophylaxis (prevention of illness) or treatment purposes. Two drugs (in the neuraminidase inhibitors class), oseltamivir (commercially known as Tamiflu) and zanamivir (commercially known as Relenza), have been shown, in laboratory studies, to reduce the severity and duration of illness caused by seasonal influenza. The efficacy of the neuraminidase inhibitors depends on their administration within 48 hours after symptom onset. For cases of human infection with H5N1, the drugs may reduce the severity of disease and improve prospects of survival, if administered early, but clinical data are limited. The H5N1 virus is expected to be susceptible to the neuraminidase inhibitors.

Another class of antiviral drugs, the M2 inhibitors amantadine and rimantadine, could potentially be used against pandemic influenza, but resistance to these drugs may develop

rapidly and this could significantly limit their effectiveness. Some currently circulating avian H5N1 strains are fully resistant to the M2 inhibitors, while others remain fully susceptible.

For the neuraminidase inhibitors, the main constraints – which are substantial – involve limited production capacity and a price that is prohibitively high for many countries. Because of the complex and time-consuming manufacturing process, the sole manufacturer of oseltamivir is unable fully to meet demand and faces a backlog of orders. At present manufacturing capacity, which has recently quadrupled, it will take a decade to produce enough oseltamivir to treat 20% of the world's population. The complex manufacturing process also makes it difficult to transfer production technology to other facilities. Nonetheless, strategies for doing so are being explored as a matter of urgency, and particular attention is being given to the option of manufacturing oseltamivir in developing countries.

Since supplies are severely constrained, countries now stockpiling antiviral drugs need to decide in advance on priority groups for administration, particularly for prophylactic purposes. Frontline health care workers would be an obvious first choice, but such decisions are the responsibility of governments. While antiviral drugs can confer some measure of protection pending the availability of vaccines, these drugs should not be used to perform the same public health function as vaccines – even if supplies would permit. The mass administration, for prophylactic purposes, of antiviral drugs to large numbers of healthy people for extended periods is not recommended, as this could accelerate the development of drug resistance.

Following a donation by industry, WHO will have a dedicated stockpile of antiviral drugs (oseltamivir), sufficient for 3 million treatment courses, by early 2006. These drugs are strictly reserved for use in the first areas affected by an emerging pandemic virus. Recent studies, based on mathematical modelling, suggest that these drugs could be used prophylactically near the start of sustained human-to-human transmission to reduce the risk that a fully transmissible pandemic virus will emerge or at least to delay its international spread, thus gaining time to augment vaccine supplies. The drugs will be stored centrally; WHO has considerable experience in the rapid dispatch of medical supplies during emergencies.

The success of this strategy, which has never been tested, depends on several assumptions about the early behaviour of a pandemic virus, which cannot be known in advance. Success also depends on excellent surveillance and logistics capacity in the initially affected areas, combined with an ability to enforce movement restrictions in and out of the affected area. To increase the likelihood that early intervention using the WHO rapid-intervention stockpile of antiviral drugs will be successful, surveillance in affected countries needs to improve, particularly concerning the capacity to detect clusters of cases closely related in time and place.

Should the virus behave in ways that preclude rapid intervention to contain a pandemic or delay its spread, drugs in the stockpile will be used to provide treatment in the initially affected countries.

Urgent activities in an emergency situation

The seriousness of the present threat to international public health calls for emergency actions calculated to provide the greatest level of protection as quickly as possible. The most reliable and predictable way immediately to improve the world's defences is to build on existing structures and mechanisms that have worked well in similar emergencies.

No health emergency on the scale of a severe influenza pandemic has confronted the international community for several decades. At the same time, however, WHO and its international partners have acquired considerable experience in responding to outbreaks of new and epidemic-prone diseases that have occurred, in unprecedented numbers, in recent years.

Each outbreak presents a unique set of problems that have to be solved, innovatively and quickly, under emergency conditions. Each outbreak response has left WHO and its partners with more experience and more technical innovations to draw on when crafting a response plan for the next unique event. These experiences, and the existing mechanisms that sustain them, can be immediately adapted to provide a strengthened response near the start of a pandemic. WHO now has a flexible fund of operational options to draw on, and these are backed by standardized protocols for outbreak investigation and standard operating procedures as well as by considerable experience under a variety of country settings.

The type of support that can be provided by WHO and its institutional partners in the Global Outbreak Alert and Response Network (GOARN) will probably be most decisive in the first countries experiencing evidence of efficient human-to-human transmission.

For almost two years, several Asian nations have undertaken resource-intensive activities in the interest of protecting the international community from an unpredictable, yet potentially catastrophic event. These activities have been undertaken despite low national budgets for health care and the presence of many other high-priority diseases. Many of these activities, specific to the control of avian influenza and prevention of another pandemic, must now be given full international support. Only through such support will the international community receive the data needed for a reliable risk assessment which, in turn, guides many interventions to be undertaken according to the various WHO phases of pandemic alert. If this support is not provided, triggers for scaling up activities will be missed and the world may, once again, be taken by surprise when a pandemic virus emerges.

Lessons from SARS

The international outbreak of severe acute respiratory syndrome (SARS) was a watershed event. It revealed how much the world has changed in terms of the impact that outbreaks of a severe new disease can have in a highly mobile and closely interconnected world. During a fortunately brief stay in its new human host, the SARS virus travelled rapidly along the routes of international air travel to infect more than 8,000 people in about 30 countries. Of these people, SARS killed just under 800.

The SARS experience was remarkable in several ways. It caused enormous economic damage and social disruption in areas far beyond the outbreak sites. The previous estimates of the economic costs of that outbreak, US\$ 30 billion, are now considered conservative. The SARS experience showed that decisive national and international action, taking full advantage of modern communication tools, could prevent a new disease from establishing endemicity. It raised the profile of public health and appreciation of the importance of international cooperation in health to new heights.

SARS primed politicians to understand both the far-reaching consequences of outbreaks and the need to make rapid containment a high priority. SARS also stimulated efforts to find ways to make the impact of the next international outbreak less dramatic.

Many – but not all – of these lessons are useful as the world braces itself against the prospect of another human influenza pandemic. The unprecedented scientific and medical collaboration that characterized the SARS outbreak, with leading experts openly sharing their latest findings, can also be expected to help the world understand a new pandemic virus quickly and translate this new knowledge rapidly into practical advice for control. The threat posed by the H5N1 virus has already attracted political attention at the highest levels, including the launch of the US-initiated International Partnership for Avian and Pandemic Influenza. This is valuable to advance necessary prevention and preparedness activities worldwide at national, regional, and global levels.

Unlike SARS, however, pandemic influenza is considered unstoppable once international spread is fully under way. The classic public health interventions – screening, early detection of cases, and tracing and follow-up of contacts – that proved decisive in containing SARS will not be sufficient to interrupt the transmission of a pandemic influenza virus. Because influenza virus can be transmitted prior to the onset of symptoms, programmes to screen for symptoms will not detect all carriers. The very short incubation period leaves too little time to conduct contact tracing. Each influenza patient can be expected to transmit the virus to another person within 2 days; the number of cases will grow exponentially. Moreover, influenza spreads easily through the air via coughing or sneezing; SARS transmission required close face-to-face contact with a patient.

One important lesson from SARS is paramount: the importance of real-time monitoring of the evolving situation, supported by advice from the world's best experts, and immediate communication of information. The effectiveness of non-pharmaceutical measures for control will depend on the characteristics of the pandemic virus (attack rate, virulence, principal age groups affected, patterns of spread within and between countries), and these cannot be known in advance. After a pandemic is declared, WHO will monitor its evolution in real time and issue updated advice accordingly. Recommendations about the most effective control measures will therefore become more precise as the epidemiological potential of the virus unfolds. Virtual networks of experts will advise WHO on such issues as projected patterns of spread, modes of transmission, laboratory diagnosis, and clinical management of patients, and this information will be communicated immediately. All experts hope that use of good risk communications practices at every level and an informed public will facilitate the smooth implementation of control measures, while also reducing some of the social and economic disruption that make pandemics such dreaded events.

WHO will continue to work with its 192 Member States and other international organizations on an ongoing basis to assess the threat of pandemic influenza and to help improve preparedness and response to mitigate the consequences of a pandemic.

Annex 1: International recommendations for responding to the pandemic threat

Over the last several years WHO has issued a number of documents to assist countries, at various levels of development, in preparing their strategies and detailed responses to pandemic influenza. These technical and strategic documents are available on the WHO Website (www.who.int). Last month, WHO launched a new website (http://www.who.int/csr/disease/avian_influenza/pandemic/en/index.html) devoted to assessment of the influenza pandemic threat.

During the 7-9 November 2005 international meeting on avian and pandemic influenza, participants agreed on ten main conclusions and twelve recommendations for integrated and immediate action.

Conclusions

1. Minimizing the threat at source to both animal and human populations through rapid reduction of the viral burden of H5N1 is essential. This entails timely notification of outbreaks in birds, poultry culling and vaccination as indicated, including "backyard" flocks, and provision of appropriate compensation for farmers.
2. "Early warning" and surveillance systems for animal and human influenza are critical to effective response. The current window of opportunity to intervene is measured in days. Transparent and immediate reporting is essential.
3. The introduction of avian infection with H5N1 to other countries is predicted, following the patterns of migratory birds, and as a result of production systems and market practices. Other strains of avian flu are also an ongoing and emerging threat and must be monitored. Strengthened veterinary services are a crucial aspect of detection and response. Open sharing of virus samples is essential. Quality assured animal vaccines produced to international standards should be used in healthy poultry when appropriate.
4. At present many governments are not ready to cope with outbreaks, still less a pandemic. Preparedness is vital in every country, in every region. Integrated country plans will build on and strengthen existing systems and mechanisms. They will be comprehensive, costed, and evaluated. Response mechanisms should be rehearsed through simulation exercises. These plans will include protection of vulnerable groups such as children, refugees and displaced populations.
5. Resources needed to slow down or contain the emergence of a pandemic are insufficient. Supplies of antiviral drugs currently do not meet potential demand. Issues remain of equitable access to medicines and deployment of stockpiles.
6. A universal non-specific pandemic vaccine may be the ultimate protective solution for human influenza. "Smart" solutions are being investigated. Issues of technology transfer, resolution of licensing and regulatory obstacles, sustained use of good manufacturing practices and pre-qualification are under discussion. Predictable, increased orders for seasonal flu vaccine will support greater manufacturing capacity, including in developing countries.
7. Communications. The recent series of high-level meetings on avian influenza and human pandemic influenza have successfully created a shared agenda. The public needs clear, regular, reliable information. Civil society, nongovernmental organizations and other community groups must be involved.
8. A rich array of resources is potentially available to support government and institutional efforts. Countries that have successfully controlled outbreaks of avian influenza are prepared to help others.

9. Mechanisms for donor support are in place. There is broad commitment to minimize transaction costs of international support through alignment and harmonization. International support to country plans should supplement national resources, as well as existing donor resources, and should target resource-poor countries.
10. Investments are urgently needed at national level – potentially reaching 1 billion dollars over the next three years. An additional 35 million dollars is needed immediately to support high priority actions by technical agencies at the global level over the next six months.

Recommended actions

1. Support the development of integrated national plans for avian influenza control and human pandemic influenza preparedness and response.
2. Assist countries in aggressive control of avian influenza in birds, and deepen the understanding of the role of wild birds in virus transmission.
3. Nominate "rapid response" teams of experts to support epidemiological field investigations.
4. Strengthen country and regional capacity in surveillance, laboratory diagnosis, and alert and response systems.
5. Expand the network of influenza laboratories, with regional collaborative systems for access to reference laboratories.
6. Establish and integrate multi-country networks for the control or prevention of animal trans-boundary diseases, and regional support units as established in the Global Framework for the Progressive Control of Trans-boundary Animal Diseases.
7. Expand the global antiviral stockpile, and prepare standard operating practices for its rapid deployment to achieve early containment.
8. Assess the needs and strengthen veterinary infrastructure in line with OIE standards.
9. Map out a global strategy and work plan for coordinating antiviral and influenza vaccine research and development, and for increasing production capacity and equitable access.
10. Put forward proposals to the WHO Executive Board at its 117th (January 2006) meeting for immediate voluntary compliance with relevant articles of the International Health Regulations 2005.
11. Finalize detailed costing of country plans and the regional and global requirements to support them, in preparation for the January 2006 pledging meeting to be hosted by the Government of China.
12. Finalize a coordination framework building on existing mechanisms at the country level, and at the global level, building on international best practices.

Annex 2: WHO strategic action plan

Concerning human health matters, four main opportunities to act were identified during the 7-9 November 2005 meeting: reduce high-risk behaviors associated with human infections; improve the detection, investigation, and reporting of human cases and, in so doing, strengthen the early warning system; contain an emerging pandemic virus; and increase pandemic preparedness. A fifth item – considered by many participants to be the most pressing need for adequate preparedness – concerned world capacity to manufacture sufficient quantities of pandemic vaccines and antiviral drugs, at sufficient speed, and to make these interventions broadly accessible to all countries.

These five actions formed the basis of the five-pronged strategic plan developed by WHO immediately after the meeting. The plan aims to achieve two over-arching objectives:

1. to ensure full exploitation of all opportunities to prevent the H5N1 virus from developing the ability to ignite a pandemic and, should this effort fail,
2. to ensure that measures are in place to mitigate the high levels of morbidity and mortality and social and economic disruption that can be expected during the next pandemic.

Each strategic action has a goal that contributes to these larger objectives.

Strategic action	Goal
1 Reduce human exposure to the H6N1 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

The plan sets out expected results over the next two years and gives indicators for measuring progress. It also identifies seven institutional capacities that will be strengthened by the proposed strategic actions. Apart from preparing the world to cope with the present emergency situation, the strengthening of these capacities will improve the world's ability collectively to defend itself against many other emerging and epidemic-prone diseases.

Chairman HYDE. Thank you very much, Dr. Chan. And now, Dr. Osterholm.

**STATEMENT OF MICHAEL T. OSTERHOLM, M.D., DIRECTOR,
CENTER FOR INFECTIOUS DISEASE RESEARCH AND POLICY**

Dr. OSTERHOLM. Thank you, Mr. Chairman. I would also like to thank Representative McCollum for your very kind words, and also acknowledge that I feel very honored to be on the same panel with Dr. Chan, who we all hold in great esteem for her work, not only on behalf of her native homeland of Hong Kong, but also at the WHO.

First of all, I would like to summarize my comments in four areas. One, I want to clarify a point that has come up several times here today about the eventuality of a pandemic. We must never forget that influenza pandemics are like earthquakes, hurricanes, and tsunamis; they occur. We will have another pandemic again, just as we will have more hurricanes. There have been 10 pandemics in the last 300 years, and as you noted in your opening comments, these have varied in their severity.

As Dr. Chan has just outlined, there are real reasons to believe that an H5N1 pandemic, should it emerge, very much has the makings to be a 1918-like pandemic because of the biology, not because we just hope that it is going to be that bad.

Second of all, I firmly believe that based on our experiences with outbreaks such as SARS, and even the post-9/11 anthrax attacks, that if an influenza pandemic would begin today, borders will close. The global economy will literally shut down. Pharmaceutical supplies, including drugs and very important childhood vaccines not intended for influenza, but for everyday lives, will be in extreme short supply, if available at all. Health care systems will be overwhelmed, and frankly, panic will reign.

Access to pandemic influenza vaccines and effective antiviral drug treatments will be limited for the entire world for years to come because of our lack of modern technology vaccines, and a gross inadequate worldwide production capability.

Today we have talked about the need and the ability to deliver vaccines to the United States. Even if we could wave a magic wand across this country and prevent the impact of a pandemic here, the rest of the world will experience a pandemic when they don't have vaccine. The economic and global implications of that are still going to result in dramatic collateral damage to our country.

In addition, we can no longer assume that business continuity plans for both our multi-national companies and small businesses, largely based on the concept of a regional event of a limited duration, will approximate the actual impact and consequence of an influenza pandemic. Rather, I believe an influenza pandemic will be like a 12- to 18-month global blizzard that will ultimately change the world as we know it. This will occur even if we experience a mild worldwide pandemic of millions of deaths, rather than many millions of deaths.

Third, one part of the pandemic preparedness planning that must receive immediate attention is the implementation of the concept that I have called critical product continuity. Critical product continuity is the termination of those products and services that

our country routinely enjoys that must be available during a pandemic in order to minimize potentially catastrophic collateral health and security consequences, and the subsequent comprehensive actions that must be taken by both government and the private sector to ensure their availability.

There are many essential products today that we count on to maintain the quality of life that we think of. For example, in the health care delivery system, regardless of where routine and influenza-related patients' care takes place, we will need even more of our routine drugs and vaccines, not those just for the influenza, but for all aspects of our life. We will need masks, gloves, IV bags, syringes, routine diagnostic materials, needles, laboratory and diagnostic tests. Most of these products today have supply chains in production locations that are primarily outside of the United States. Remember the closed borders that we talked about earlier that will likely result with the beginning of the pandemic.

Other critical product categories include both domestic and foreign suppliers, are our food supply, and for essential parts for the maintenance of our critical infrastructure such as our water supplies, electricity, and vital communications. If one were to do a very detailed analysis of our electrical grid system today and understand how critical many of the off-shore produced component pieces are of that system, one could understand the implications of just that one infrastructure.

Let me give you one final example. Today when we think of the shortage of vaccine and flu drugs, it is an obvious jump to the issue of a flu pandemic potential. But today millions of Americans count on routine prescription drugs and over-the-counter pharmaceutical supplies to treat a variety of life-threatening, chronic, or routine illnesses. But as part of the global, just-in-time economy world that we live in, the pharmaceutical industry has responded to investor demand for greater efficiency and higher investment return. In order to achieve these great productivities, the industry, both through inventory management or just-in-time delivery, and identifying cheaper production environments and limited supply chains mostly overseas, have resulted in extremely vulnerable pharmaceutical industry environment for sustaining ongoing production during such events as a pandemic.

For example, more than 80 percent of the raw materials used in the production of the pharmaceuticals that we routinely enjoy in this country come from outside the United States. The American Society of Health System Pharmacists have determined that 49 drugs or vaccine products in the United States are currently unavailable, in short supply, or at risk of short supply due to manufacturing, inventory, or supply chain issues.

This is just one example of what we are not prepared for in terms of the collateral damage associated with the pandemic. Again, I remind you there are many other very essential services.

In conclusion, I would like to suggest that this area of activity has been largely unaddressed by any area of the Federal Government, and to a very real degree by the private sector. It is one that unless we start planning now, literally with the same resources, commitment, and vision that we have of influenza vaccine and

drug-related activities, we will pay a large price with collateral damage that is at this time very difficult to even begin to imagine.

So it is my hope that this Committee will recognize this important international and resultant domestic issue, and help provide the leadership in Congress to begin to readily address it.

Thank you, Mr. Chairman.

[The prepared statement of Dr. Osterholm follows:]

PREPARED STATEMENT OF MICHAEL T. OSTERHOLM, M.D., DIRECTOR, CENTER FOR INFECTIOUS DISEASE RESEARCH AND POLICY

Chairman Hyde, Congressman Lantos and other distinguished members of the Committee on International Relations, I'm honored to appear before you this morning to discuss the critical threat of pandemic influenza and the implications of the global, just-in-time economy on our nation's ability to respond to and during a pandemic.

First, while there has been wide-spread attention paid to the possibility that the H5N1 influenza virus (or avian influenza) may be the cause of the next pandemic, I believe that there is confusion with regard to the likelihood that an H5N1 pandemic will occur. Congress has heard over recent months from a number of informed witnesses that we must be much better prepared to respond to the threat of an H5N1 pandemic.

I want to clarify one point with regard to the eventuality of such a pandemic. We must never forget that influenza pandemics are like earthquakes, hurricanes and tsunamis; they occur. Dating back to antiquity, influenza pandemics have posed the greatest threat of a world-wide calamity caused by infectious disease. Over the past 300 years, ten influenza pandemics have occurred among humans. The most recent came in 1957–58 and 1968–69 and although several tens of thousands of Americans died in each one, these were considered mild compared to others. The 1918–19 pandemic was not. According to a recent analysis it killed 50–100 million people globally. Today with a population of 6.5 billion, more than three times that of 1918, even a mild pandemic could kill many millions of people.

A number of recent events and factors have heightened our concern that a specific near-term pandemic may be imminent. It could be caused by the H5N1 strain currently circulating in Asia and parts of Europe. At this juncture, we as scientists cannot be certain. Unfortunately there are many ominous signs that make this risk something that only a fool would dismiss. We cannot know exactly when a pandemic will hit or whether it will rival the experience of 1918–19 or be more muted like 1957–58 and 1968–69. The reality of a coming pandemic however, cannot be avoided, only its impact can be lessened. Some important preparatory efforts are underway, but much more needs to be done by institutions at many levels of society throughout the world.

I firmly believe that based on our past experiences with outbreaks such as SARS and even the post-9/11 anthrax attack, that if an influenza pandemic began today, borders will close, the global economy will shut down, pharmaceutical supplies, including drugs and very important childhood vaccines will be in extreme short supply, healthcare systems will be overwhelmed and panic will reign. Access to pandemic influenza vaccines and effective antiviral drug treatments will be limited for the entire world for years to come because of our lack of modern technology vaccines and a grossly inadequate worldwide production capability. To minimize the fallout of a pandemic during this time, the industrialized world must create a detailed response strategy far beyond just enhancing influenza vaccines and treatment drugs, and one that involves both the public and private sectors. In addition, we can no longer assume that business continuity plans for both our multinational companies and small businesses, largely based on a concept of a regional event of a limited duration, will approximate the actual impact and consequence of an influenza pandemic. Rather, I believe an influenza pandemic will be like a 12 to 18 month global blizzard that will ultimately change the world as we know it today. This will occur even if we experience a milder worldwide pandemic of millions of deaths rather than many millions of deaths.

I have detailed the basic steps necessary for preparing for the next pandemic whether it begins tonight, next year, or even ten years from now in an article in the July–August issue of *Foreign Affairs*. That article has been provided to you for reference. I will attempt not to repeat the points covered in that article, but rather reflect on a single critical area that I believe continues to be largely neglected by

governments throughout the world and by many of our leading private-sector companies.

The arrival of an influenza pandemic will trigger a reaction that will change the world overnight. Foreign trade and travel will be reduced or even ended in an attempt to stop the virus from entering new countries—even though such efforts will probably fail given the infectiousness of influenza and the volume of illegal crossings that occur at most borders. It is likely that transportation will also be significantly curtailed domestically, as states and communities seek to keep the disease contained. Our modern world has come to rely on the speedy, “overnight” distribution and delivery of many products including medical supplies, our food and replacement parts for essential infrastructure-related equipment. With an influenza pandemic, global, regional, and national economies will come to an abrupt halt—something that has never happened due to HIV, malaria, or TB despite their dramatic impact on the developing world.

One part of pandemic preparedness planning that must receive immediate attention is the implementation of a concept that I have called “critical product continuity” (CPC). “Critical product continuity is the determination of those products and services that our country routinely enjoys that must be available during a pandemic in order to minimize potentially catastrophic collateral health and security consequences and the subsequent comprehensive actions that must be taken by both governments and the private sector to ensure their availability.” For example, in the health care delivery system, regardless of where routine and influenza-related patient care takes place, we will need even more of our routine drugs and vaccines, medical devices and other products such as needles, syringes, IV bags, gloves, masks and routine diagnostic materials such as standard laboratory and diagnostic tests. Most of these products have supply chains and production locations that are primarily outside of the United States. Other critical product categories include both domestic and foreign suppliers of our food supply and for essential parts for the maintenance of critical infrastructures such as our water supplies, electricity and vital communications. We must also ensure a source of heating during the winter months for our northern climates; gasoline for critical domestic and international transportation; routine waste management and sanitation; and even corpse management. It is difficult to imagine how discretionary items such as non-vital electronics, jewelry, automobiles and entertainment will be needed during this time to ensure our health and safety. While any negative impact to our economy will be unfortunate, we must make difficult strategic decisions about which products and services our government, together with selected private sector companies, must maintain through critical supply chain support, the maintenance of adequate workforces and necessary transportation assurance whether domestic or abroad.

Let me provide you with one example of a critical product continuity that if not addressed now will result in dramatic collateral damage to our country during the 12 to 18 months of an influenza pandemic. Today, millions of Americans count on routine prescription drugs and over-the-counter pharmaceutical supplies to treat a variety of life-threatening, chronic or routine illnesses. As part of the global just-in-time economy world that we live in, the pharmaceutical industry has responded to investor demands for greater efficiency and thus higher investment return. In order to achieve greater productivity within this industry, both inventory management or just-in-time delivery, and identifying cheaper production environments with limited supply chain costs, have resulted in an extremely vulnerable pharmaceutical industry environment for sustaining ongoing production during events such as a pandemic. For example, more than 80 percent of the raw materials used in the production of pharmaceutical products available in this country come from outside the United States. Any interruption of trade and transportation of multiple regions of the world will result in numerous pharmaceutical products not being available in this country or at the minimum; they will be in very short supply. In addition, inventory management often contributes to potential drug shortages. Common business practice today dictates a “just-in-time” inventory system. Manufacturers generally stock a 30-day supply of raw materials and products, distributors will often have a 30–45 day supply in hand and most pharmacies average 10–16 inventory turnovers per year. While this practice makes inventory control sense, a small glitch in supply or production can become a major supply problem resulting in drug shortages. Today, even with a pharmaceutical production system absent of any major international calamities that disrupt production and transportation, the American Society of Health-System Pharmacists has determined that 49 drugs or vaccine products in the United States are currently unavailable, in short supply or at risk of short supply due to manufacturing, inventory or supply chain issues. These products include routinely used antibiotics, cancer and cardiac drugs and a variety of other standard treatments. Unfortunately, even consumers with health insurance or

government-supported pharmaceutical drug benefits can not anticipate a potential pandemic by stockpiling a several month supply of essential drugs because most benefit requirements do not allow the purchase of more than one month supply of drug. Imagine this country during a pandemic, when most of the routine pharmaceutical products that we count on every day are likely no longer available. Add that to the dramatic impact of pandemic influenza and an already terrible situation becomes even worse. Given the very large proportion of raw materials used in pharmaceutical products that come from outside the United States, this issue should be a major concern of this Committee and others involved with our international relations and trade considerations. We must understand the implications and plan for the shutdown of our global economy and supply chains now; not during a pandemic.

While I have chosen to highlight the issue of critical product continuity and the pharmaceutical industry, it is important that the committee remember that there are many other product areas as noted above that must be considered as we plan for getting through "the next 12 to 18 month pandemic". I am unaware of any government or private sector effort to identify and respond in a comprehensive manner to this critical product continuity issue. I have been fortunate in recent weeks to work with former Health and Human Services Secretary Tommy G. Thompson, now part of the Akin, Gump, Strauss Hauer and Feld law firm here in Washington, DC, to identify ways to empower and assist the private sector in responding to this critical product continuity issue. However, in the first instance our federal government must understand that it will take an effort with the similar commitment of resources, vision and management as we are putting forward for influenza vaccine and drug research, procurement and distribution if we are to minimize the serious collateral damage that will occur to our society as a result of critical product and services shortages during the next pandemic. It is my hope that this Committee will recognize this important international and domestic issue and provide the leadership in Congress to rapidly address it.

Thank you.

Chairman HYDE. Thank you, Doctor, for a very important statement. Mr. Leach.

Mr. LEACH. Dr. Chan, if I could ask you a question about China. In one sense it is very impressive that China has inaugurated a massive vaccination plan. In another sense, it has been suggested that it may be counter-productive; that is, vaccinating in given types of ways may make it more difficult to develop human vaccines.

Is that true or not? And is it wise to vaccinate, or unwise? Or is it something that we ought to be congratulating China for its efforts?

Dr. CHAN. Thank you very much for that very important question. Clearly, China has recently announced that it is going to vaccinate its 14 billion poultry in China.

Now, if we look at the strategic recommendation from the Food and Agricultural Organization and the World Organization for Animal Health, vaccination is one of the measures that is being recommended.

But, I mean, there is a caveat to that. It has to be done properly in terms of the vaccine quality, in terms of implementation. And we were receiving media reports that there may be counterfeit vaccine. Now, if that is the case, we don't know whether this is the case, but as rumor goes, if indeed we are talking about poor-quality vaccine, poor implementation plan, that gives rise to reasons for concern.

But the good thing is China has become more and more engaging now, and China is working closely with WHO, through the Ministry of Health, and is also working with the FAO in the Beijing office. And with this kind of high engagement and high political commitment, the technical agencies would be happy to work along-

side with China. And really I hope the vaccination implementation strategy that they are going to promulgate will be done in the best practice.

Mr. LEACH. I thank you. And just as a Member of Congress, I think we ought to welcome the seriousness with which the Chinese Government is taking this issue at this time. And there have been so many criticisms of China, I think it is important that when they take steps that are serious, that that ought to be recognized.

Secondly, I want to turn to Dr. Osterholm in this, because there is this issue that we are looking at these things emerging in Asia from a bird population. But have we applied as much concern for possible vaccinations in our country if it comes to our country? Are we prepared to vaccinate the bird population, as well as the human population?

Dr. OSTERHOLM. Mr. Representative, one of the issues that has, I think, not been well understood is the sequence of events, and the risk of who is likely to infect who as a potential pandemic begins to emerge.

Right now the concern we obviously have is what I call this genetic roulette table of Asia, where, with a large concentration of humans and domestic birds, provides this unlimited opportunity for the virus to continue to mutate, and to potentially expose humans.

But once that virus makes the jump to humans and goes human to human, the risk from animals to human almost becomes irrelevant. Now it is humans transmitting to the animals. And in fact, in 1918 in this country, hogs didn't start dying in hog farms until sick farmers took the virus back to the hogs.

And so in a sense, the ongoing issue about protecting the animals becomes irrelevant, because humans are now the primary disseminators of this virus around the world. And the birds, like us, will eventually get over, get through it, as we obviously know the vast majority of the world will still survive.

So I don't know if there will even be an effort to vaccinate birds here in this country once a pandemic begins, other than to protect the bird flocks themselves so that we might sustain a food supply.

Mr. LEACH. That is a very thoughtful response. But let me just say, what about the possibility that our bird flocks become infected before there is human-to-human transmission? Is vaccination appropriate or inappropriate? And are we prepared?

Dr. OSTERHOLM. The role of vaccination I think is, at best, controversial. Obviously I am not a veterinarian, although I have worked with this issue a great deal.

I believe that the poultry flocks in this country will be largely protected against this virus, not from vaccine, but from the biosecurity containment that we grow them in. While farmers today often take criticism for growing birds in-house—i.e., under a roof, not out on the free range—that provides a very, very high level of biosecurity, and a protection from the wild bird potential transmission.

So I think in those areas, that is what will be sufficient, and will be not only sufficient in the sense of preventing this, but it will be a better way to go than using vaccine.

Ironically, the birds that we may likely have a problem with in this country are going to be what some health food people think are a better bird, the free-range birds; those who are allowed to grow

outside, where they may have contact, should this virus enter through wild birds. There I cannot tell you what the veterinary world is looking at, but I think you have already heard concerns that vaccine in birds is not the panacea. In some cases, if not a high-quality vaccine, if not continued, it may actually facilitate the transmission of the virus, as opposed to actually stopping it.

Chairman HYDE. Ms. McCollum.

Ms. MCCOLLUM. Thank you, Mr. Chairman. Dr. Chan, the focus has been on Asia, but I serve on the African Subcommittee here on the International Relations Committee. And my concern, as you know, there is a large migratory path through Tanzania and the countries surrounding the Great Lakes Region. Many of those countries are nations at peace; some have conflict. Their health care system is already overstressed. And I will give an example; in Malawi, they have a total of 13 veterinarians for the entire country.

What are we doing internationally to gear up? The focus needs to be in Asia; we know it is in Asia. But what are we doing to gear up in Africa? And what do you need? What does the world community need in order to not cut back on the health care infrastructure in Asia, and at the same time not cut back on HIV health care infrastructure in Africa? And then I have a question for Dr. Osterholm.

Dr. CHAN. Thank you very much for that question. Clearly, if we go by the estimation of our animal experts, the next port of call of the migratory birds would be in Africa. And it is correct to be concerned with the situation, because precisely for what you have mentioned, the frail health care system.

Already we have many people suffering from HIV/AIDS, malaria, and poor nutrition, anemia, and so on and so forth. If indeed Avian influenza hits Africa, this is the last thing we want to see. And precisely for that high level of concern and high sense of urgency, our effort in the regional office, the Regional Director has been working hand-in-glove with us on different fronts, really to prepare the continent, Africa as a whole, to deal with this urgent issue.

First thing is, you know, we have worked with them to enhance the awareness, and also the political commitment of ministries of health and other political leaders. The second point is, we are trying to help these countries to design, develop, and test pandemic preparedness plans.

For your information, not so many countries in this region has a pandemic preparedness plan.

The third thing is, our concern is with the small backyard farmers who have very little understanding of the issue. And the earlier comment in your first panel, I was listening in to that panel, many important points were made.

What are some of the communication messages we can get to the villagers, and be culturally sensitive in the kind of language they understand, and practical action points that, in that setting, that can be implemented. So these are the things that we are working on.

As we are speaking now, there is a big group of communicators from several countries, from Africa, attending a pandemic communications consultation workshop here in Geneva. And these were

the kind of messages we were receiving from our countries in Africa, as well as the communicators. Precisely the points that was made by other representatives in the first session. So those are the actions that we will take forward.

Thank you.

Ms. MCCOLLUM. Dr. Osterholm, if you would give, you gave, in your limited amount of time you had a lot to cover. But if you could maybe follow the path that you did when you addressed our Congressional group a month ago, of either respirators or any of the other supply chain for even taking care of people with the flu, let alone all the supply chain that goes with everyday life that we are so dependent upon. I really think if you would take this time to be a little more detailed, it would be helpful to anybody listening.

Dr. OSTERHOLM. Let me just give you a very quick example of supply chain concern that would obviously impact on the patient, and then a very brief one on terms of the worker.

Today in this country we have 105,000 mechanical ventilators in our hospitals. That is it. On any one given day 80,000 are in use, and during the regular flu season we get right up to 105,000. We have never thought of taking somebody off a ventilator because somebody else needs it more; we have never had that particular situation.

We do not have the ability to supply ventilators, as we have been learning for the last 5 years, because the manufacturing is very long, complicated, and we can't buy them. So we will quickly move out of intensive care medicine into standard medicine without a ventilator.

Second of all, today, when you look at many of the drugs that I just talked about, look at the issue of Tamiflu itself. Primarily made from a precursor chemical from China, which has been very difficult to synthesize, is made in Basel, Switzerland, with a very long, complicated supply chain. That could be rewritten for many of our drugs today that anywhere in a shutdown of global trade or travel, you will basically shut down the production and the movement of that product from location A to location B.

Even looking at our surge capacity for things like IVs, and where those are made off-shore, most of them are. You begin to realize that we will have a crashing health care system at a time when the surge capacity has never been greater.

Frankly, I can't envision any other kind of care for flu except lots of cots lined up in big community centers, which if you were to take a picture of that wouldn't look much different than it did in 1918.

Even to the extent to protect our workers today, when we talk about the masks that a worker might need, or the gloves, most of these products are made by one, two, or three multi-national companies that have very large market shares, which most of the production is off-shore. Most of it has long complicated supply chains, for which there is little to no surge capacity, as I pointed out. Even for respirator masks, the kind we talked about during SARS, the two primary manufacturers of those literally ran out at the end of SARS. And had it gone on longer or had it even been extended beyond the very limited part of the world where it was, we would have not had those masks.

Now, who today in health care is going to go to work taking care of patients with a life-threatening infectious agent when you don't have a vaccine to protect the worker, you don't have adequate drugs, and you don't even have a mask? That is the kind of thing that we are confronting that is far beyond just the issue of when can we get vaccine and when can we get drugs. If we are not prepared for that, we will have, I think, a situation magnified many times beyond what anyone saw with SARS, where we had health care workers in Canada that wouldn't go to work because of their concern. That, I think, will be a tipping point at a time when we already are going to need a much, much greater surge capacity, not less.

Chairman HYDE. I am reluctant to bring this to a close, but it is time. And Doctor, you and Dr. Chan also have made enormous contributions to this subject, which is overwhelmingly complicated and overwhelmingly urgent and important. And we will study carefully your full statements, and hopefully take some significant action.

But we thank you profoundly for your contribution, both of you. Thank you, Dr. Chan. Thank you, Dr. Osterholm.

Dr. CHAN. Thank you, Chairman.

Dr. OSTERHOLM. Thank you, Mr. Chairman.

Chairman HYDE. The Committee stands adjourned.

[Whereupon, at 12:56 p.m., the Committee was adjourned.]

APPENDIX



FOREIGN AFFAIRS

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Preparing for the Next Pandemic

By Michael T. Osterholm

From *Foreign Affairs*, July/August 2005

Summary: If an influenza pandemic struck today, borders would close, the global economy would shut down, international vaccine supplies and health-care systems would be overwhelmed, and panic would reign. To limit the fallout, the industrialized world must create a detailed response strategy involving the public and private sectors.

Michael T. Osterholm is Director of the Center for Infectious Disease Research and Policy, Associate Director of the Department of Homeland Security's National Center for Food Protection and Defense, and Professor at the University of Minnesota's School of Public Health.

FEAR ITSELF

Dating back to antiquity, influenza pandemics have posed the greatest threat of a worldwide calamity caused by infectious disease. Over the past 300 years, ten influenza pandemics have occurred among humans. The most recent came in 1957-58 and 1968-69, and although several tens of thousands of Americans died in each one, these were considered mild compared to others. The 1918-19 pandemic was not. According to recent analysis, it killed 50 to 100 million people globally. Today, with a population of 6.5 billion, more than three times that of 1918, even a "mild" pandemic could kill many millions of people.

A number of recent events and factors have significantly heightened concern that a specific near-term pandemic may be imminent. It could be caused by H5N1, the avian influenza strain currently circulating in Asia. At this juncture scientists cannot be certain. Nor can they know exactly when a pandemic will hit, or whether it will rival the experience of 1918-19 or be more muted like 1957-58 and 1968-69. The reality of a coming pandemic, however, cannot be avoided. Only its impact can be lessened. Some important preparatory efforts are under way, but much more needs to be done by institutions at many levels of society.

THE BACKDROP

Of the three types of influenza virus, influenza type A infects and kills the greatest number of people each year and is the only type that causes pandemics. It originates in

wild aquatic birds. The virus does not cause illness in these birds, and although it is widely transmitted among them, it does not undergo any significant genetic change.

Direct transmission from the birds to humans has not been demonstrated, but when a virus is transmitted from wild birds to domesticated birds such as chickens, it undergoes changes that allow it to infect humans, pigs, and potentially other mammals. Once in the lung cells of a mammalian host, the virus can "reassort," or mix genes, with human influenza viruses that are also present. This process can lead to an entirely new viral strain, capable of sustained human-to-human transmission. If such a virus has not circulated in humans before, the entire population will be susceptible. If the virus has not circulated in the human population for a number of years, most people will lack residual immunity from previous infection.

Once the novel strain better adapts to humans and is easily transmitted from person to person, it is capable of causing a new pandemic. As the virus passes repeatedly from one human to the next, it eventually becomes less virulent and joins the other influenza viruses that circulate the globe each year. This cycle continues until another new influenza virus emerges from wild birds and the process begins again.

Some pandemics result in much higher rates of infection and death than others. Scientists now understand that this variation is a result of the genetic makeup of each specific virus and the presence of certain virulence factors. That is why the 1918-19 pandemic killed many more people than either the 1957-58 or the 1968-69 pandemic.

A CRITICAL DIFFERENCE

Infectious diseases remain the number one killer of humans worldwide. Currently, more than 39 million people live with HIV, and last year about 2.9 million people died of AIDS, bringing the cumulative total of deaths from AIDS to approximately 25 million. Tuberculosis (TB) and malaria also remain major causes of death. In 2003, about 8.8 million people became infected with TB, and the disease killed more than 2 million. Each year, malaria causes more than 1 million deaths and close to 5 billion episodes of clinical illness. In addition, newly emerging infections, diarrheal and other vector-borne diseases, and agents resistant to antibiotics pose a serious and growing public health concern.

Given so many other significant infectious diseases, why does another influenza pandemic merit unique and urgent attention? First, of the more than 1,500 microbes known to cause disease in humans, influenza continues to be the king in terms of overall mortality. Even in a year when only the garden-variety strains circulate, an estimated 1-1.5 million people worldwide die from influenza infections or related complications. In a pandemic lasting 12 to 36 months, the number of cases and deaths would rise dramatically.

Recent clinical, epidemiological, and laboratory evidence suggests that the impact of a pandemic caused by the current H5N1 strain would be similar to that of the 1918-19 pandemic. More than half of the people killed in that pandemic were 18 to 40 years old

and largely healthy. If 1918-19 mortality data are extrapolated to the current U.S. population, 1.7 million people could die, half of them between the ages of 18 and 40. Globally, those same estimates yield 180-360 million deaths, more than five times the cumulative number of documented AIDS deaths. In 1918-19, most deaths were caused by a virus-induced response of the victim's immune system -- a cytokine storm -- which led to acute respiratory distress syndrome (ARDS). In other words, in the process of fighting the disease, a person's immune system severely damaged the lungs, resulting in death. Victims of H5N1 have also suffered from cytokine storms, and the world is not much better prepared to treat millions of cases of ARDS today than it was 85 years ago. In the 1957-58 and 1968-69 pandemics, the primary cause of death was secondary bacterial pneumonias that infected lungs weakened by influenza. Although such bacterial infections can often be treated by antibiotics, these drugs would be either unavailable or in short supply for much of the global population during a pandemic.

The arrival of a pandemic influenza would trigger a reaction that would change the world overnight. A vaccine would not be available for a number of months after the pandemic started, and there are very limited stockpiles of antiviral drugs. Plus, only a few privileged areas of the world have access to vaccine-production facilities. Foreign trade and travel would be reduced or even ended in an attempt to stop the virus from entering new countries -- even though such efforts would probably fail given the infectiousness of influenza and the volume of illegal crossings that occur at most borders. It is likely that transportation would also be significantly curtailed domestically, as smaller communities sought to keep the disease contained. The world relies on the speedy distribution of products such as food and replacement parts for equipment. Global, regional, and national economies would come to an abrupt halt -- something that has never happened due to HIV, malaria, or TB despite their dramatic impact on the developing world.

The closest the world has come to this scenario in modern times was the SARS (severe acute respiratory syndrome) crisis of 2003. Over a period of five months, about 8,000 people were infected by a novel human coronavirus. About ten percent of them died. The virus apparently spread to humans when infected animals were sold and slaughtered in unsanitary and crowded markets in China's Guangdong Province. Although the transmission rate of SARS paled in comparison to that of influenza, it demonstrated how quickly such an infectious agent can circle the globe, given the ease and frequency of international travel. Once SARS emerged in rural China, it spread to five countries within 24 hours and to 30 countries on six continents within several months.

The SARS experience teaches a critical lesson about the potential global response to a pandemic influenza. Even with the relatively low number of deaths it caused compared to other infectious diseases, SARS had a powerful negative psychological impact on the populations of many countries. In a recent analysis of the epidemic, the National Academy of Science's Institute of Medicine concluded: "The relatively high case-fatality rate, the identification of super-spreaders, the newness of the disease, the speed of its global spread, and public uncertainty about the ability to control its spread may have contributed to the public's alarm. This alarm, in turn, may have led to the behavior that

exacerbated the economic blows to the travel and tourism industries of the countries with the highest number of cases."

SARS provided a taste of the impact a killer influenza pandemic would have on the global economy. Jong-Wha Lee, of Korea University, and Warwick McKibbin, of the Australian National University, estimated the economic impact of the six-month SARS epidemic on the Asia-Pacific region at about \$40 billion. In Canada, 438 people were infected and 43 died after an infected person traveled from Hong Kong to Toronto, and the Canadian Tourism Commission estimated that the epidemic cost the nation's economy \$419 million. The Ontario health minister estimated that SARS cost the province's health-care system about \$763 million, money that was spent, in part, on special SARS clinics and supplies to protect health-care workers. The SARS outbreak also had a substantial impact on the global airline industry. After the disease hit in 2003, flights in the Asia-Pacific area decreased by 45 percent from the year before. During the outbreak, the number of flights between Hong Kong and the United States fell 69 percent. And this impact would pale in comparison to that of a 12- to 36-month worldwide influenza pandemic.

The SARS epidemic also raises questions about how prepared governments are to address a prolonged infectious-disease crisis – particularly governments that are already unstable. Seton Hall University's Yanzhong Huang concluded that the SARS epidemic created the most severe social or political crisis encountered by China's leadership since the 1989 Tiananmen crackdown. China's problems probably resulted less from SARS' public health impact than from the government's failed effort to allay panic by withholding information about the disease from the Chinese people. The effort backfired. During the crisis, Chinese Premier Wen Jiabao pointed out in a cabinet meeting on the epidemic that "the health and security of the people, overall state of reform, development, and stability, and China's national interest and image are at stake." But Huang believes that "a fatal period of hesitation regarding information-sharing and action spawned anxiety, panic, and rumor-mongering across the country and undermined the government's efforts to create a milder image of itself in the international arena."

Widespread infection and economic collapse can destabilize a government; blame for failing to deal effectively with a pandemic can cripple a government. This holds even more for an influenza pandemic. In the event of a pandemic influenza, the level of panic witnessed during the SARS crisis could spiral out of control as illnesses and deaths continued to mount over months and months. Unfortunately, the public is often indifferent to initial warnings about impending infectious-disease crises – as with HIV, for example. Indifference becomes fear only after the catastrophe hits, when it is already too late to implement preventive or control measures.

READY FOR THE WORST

What should the industrialized world be doing to prepare for the next pandemic? The simple answer: far more. So far, the World Health Organization and several countries have finalized or drafted useful but overly general plans. The U.S. Department of Health

and Human Services has increased research on influenza-vaccine production and availability. These efforts are commendable, but what is needed is a detailed operational blueprint for how to get a population through one to three years of a pandemic. Such a plan must involve all the key components of society. In the private sector, the plan must coordinate the responses of the medical community, medical suppliers, food providers, and the transportation system. In the government sector, the plan should take into account officials from public health, law enforcement, and emergency management at the international, federal, state, and local levels.

At the same time, it must be acknowledged that such master blueprints may have their drawbacks, too. Berkeley's Aaron Wildavsky persuasively argued that resilience is the real key to crisis management -- overly rigid plans can do more harm than good. Still, planning is enormously useful. It gives government officials, private-sector partners, and the community the opportunity to meet, think through potential dilemmas, purchase necessary equipment, and set up organizational structures for a 12- to 36-month response. A blueprint forces leaders to rehearse their response to a crisis, preparing emotionally and intellectually so that when disaster strikes the community can face it.

Influenza-vaccine production deserves special attention. An initiative to provide vaccine for the entire world must be developed, with a well-defined schedule to ensure progress. It is laudable that countries such as the United States and Vietnam are pursuing programs with long-term goals to develop and produce H5N1 vaccine for their respective populations. But if the rest of the world lacks supplies, even the vaccinated will be devastated when the global economy comes to an abrupt halt. Pandemic-influenza preparedness is by nature an international issue. No one can truly be isolated from a pandemic.

The pandemic-related collapse of worldwide trade and its ripple effect throughout industrialized and developing countries would represent the first real test of the resiliency of the modern global delivery system. Given the extent to which modern commerce relies on the precise and readily available international trade of goods and services, a shutdown of the global economic system would dramatically harm the world's ability to meet the surging demand for essential commodities such as food and medicine during a crisis. The business community can no longer afford to play a minor role in planning the response to a pandemic. For the world to have critical goods and services during a pandemic, industry heads must stockpile raw materials for production and preplan distribution and transportation support. Every company's senior managers need to be ready to respond rapidly to changes in the availability, production, distribution, and inventory management of their products. There is no model for how to revive the current global economy were it to be devastated.

To truly be complete, all planning on international, regional, national, and local levels must consider three different scenarios: What if the pandemic begins tonight? What if it starts one year from now? What if the world is so fortunate as to have an entire decade to prepare? All are possible, but none is certain.

STARTING TONIGHT

What would happen today in the office of every nation's leader if several cities in Vietnam suffered from major outbreaks of H5N1 infection, with a five percent mortality rate? First, there would be an immediate effort to try to sort out disparate disease-surveillance data from a variety of government and public health sources to determine which countries might have pandemic-related cases. Then, the decision would likely be made to close most international and even some state or provincial borders -- without any predetermined criteria for how or when those borders might be reopened. Border security would be made a priority, especially to protect potential supplies of pandemic-specific vaccines from nearby desperate countries. Military leaders would have to develop strategies to defend the country and also protect against domestic insurgency with armed forces that would likely be compromised by the disease. Even in unaffected countries, fear, panic, and chaos would spread as international media reported the daily advance of the disease around the world.

In short order, the global economy would shut down. The commodities and services countries would need to "survive" the next 12 to 36 months would have to be identified. Currently, most businesses' continuity plans account for only a localized disruption -- a single plant closure, for instance -- and have not planned for extensive, long-term outages. The private and public sectors would have to develop emergency plans to sustain critical domestic supply chains and manufacturing and agricultural production and distribution. The labor force would be severely affected when it was most needed. Over the course of the year, up to 50 percent of affected populations could become ill; as many as five percent could die. The disease would hit senior management as hard as the rest of the work force. There would be major shortages in all countries of a wide range of commodities, including food, soap, paper, light bulbs, gasoline, parts for repairing military equipment and municipal water pumps, and medicines, including vaccines unrelated to the pandemic. Many industries not critical to survival -- electronics, automobile, and clothing, for example -- would suffer or even close. Activities that require close human contact -- school, seeing movies in theaters, or eating at restaurants -- would be avoided, maybe even banned.

Vaccine would have no impact on the course of the virus in the first months and would likely play an extremely limited role worldwide during the following 12 to 18 months of the pandemic. Despite major innovations in the production of most other vaccines, international production of influenza vaccine is based on a fragile and limited system that utilizes technology from the 1950s. Currently, annual production of influenza vaccine is limited to about 300 million trivalent doses -- which protect against three different influenza strains in one dose -- or less than one billion monovalent doses. To counter a new strain of pandemic influenza that has never circulated throughout the population, each person would likely need two doses for adequate protection. With today's limited production capacity, that means that less than 500 million people -- about 14 percent of the world's population -- would be vaccinated within a year of the pandemic. In addition, because the structure of the virus changes so rapidly, vaccine development could only start once the pandemic began, as manufacturers would have to

obtain the new pandemic strain. It would then be at least another six months before mass production of the vaccine.

Even if the system functions to the best of its ability, influenza vaccine is produced commercially in just nine countries: Australia, Canada, France, Germany, Italy, Japan, the Netherlands, the United Kingdom, and the United States. These countries contain only 12 percent of the world's population. In the event of an influenza pandemic, they would probably nationalize their domestic production facilities, as occurred in 1976, when the United States, anticipating a pandemic of swine influenza (H1N1), refused to share its vaccine.

If a pandemic struck the world today, there would be another possible weapon against influenza: antiviral medicine. When taken daily during the time of exposure to influenza, antivirals have prevented individuals from becoming ill. They have also reduced the severity of illness and subsequent complications when taken within 48 hours of onset. Although there is no data for H5N1, it is assumed antivirals would also prevent H5N1 infection if taken before exposure. There is no evidence, however, that current antiviral influenza drugs would help if the patient developed the kind of cytokine storm that has characterized recent H5N1 infections. But barring this complication, H5N1 should be treatable with Tamiflu (oseltamivir phosphate), which is manufactured by the Roche pharmaceuticals company in a single plant in Switzerland.

In responding to a pandemic, Tamiflu could have a measurable impact in the limited number of countries with sizable stockpiles, but for most of the world it would not be available. Although the company plans on opening another facility in the United States this year, annual production would still cover only a small percentage of the world's population. To date, at least 14 countries have ordered Tamiflu, but the amount of these orders is enough to treat only 40 million people. The orders take considerable time to be processed and delivered -- manufacturing can take up to a year -- and in an emergency the company's ability to produce more would be limited. As with vaccines, countries would probably nationalize their antiviral supplies during a pandemic. Even if the medicine were available, most countries could not afford to buy it. Critical antibiotics, for treatment of secondary bacterial infections, would also be in short supply during a pandemic. Even now, supplies of eight different anti-infective agents are limited in the United States due to manufacturing problems.

Aside from medication, many countries would not have the ability to meet the surge in the demand for health-care supplies and services that are normally taken for granted. In the United States, for example, there are 105,000 mechanical ventilators, 75,000 to 80,000 of which are in use at any given time for everyday medical care. During a routine influenza season, the number of ventilators being used shoots up to 100,000. In an influenza pandemic, the United States may need as many as several hundred thousand additional ventilators.

A similar situation exists in all developed countries. Virtually every piece of medical equipment or protective gear would be in short supply within days of the recognition of a pandemic. Throughout the crisis, many of these necessities would simply be

unavailable for most health-care institutions. Currently, two U.S.-based companies supply most of the respiratory protection masks for health-care workers around the world. Neither company would be able to meet the jump in demand, in part because the component parts for the masks come from multiple suppliers in multiple countries. With travel and transportation restricted, masks may not even be produced at all.

Health-care providers and managed-care organizations are also unprepared for an outbreak of pandemic influenza today. There would be a tremendous demand for skilled health professionals. New "hospitals" in high school gymnasiums and community centers would have to be staffed for one to three years. Health-care workers would probably get sick and die at the same rate as the general public -- perhaps at an even higher rate, particularly if they lack access to protective equipment. If they lack such fundamental supplies, it is unclear how many professionals would continue to place themselves in high-risk situations by caring for the infected. Volunteers who are naturally immune as a result of having survived influenza infection would thus have to be found and employed. That means that the medical community's strong resistance to using lay volunteers, which is grounded in both liability concerns and professional hubris, would need to be addressed.

Other unpleasant issues would also need to be tackled. Who would have priority access to the extremely limited antiviral supplies? The public would consider any ad hoc prioritization unfair, creating further dissent and disruption during a pandemic. In addition, there would not even be detailed plans for handling the massive number of dead bodies that would soon outstrip the ability to process them. Clearly, an influenza pandemic that struck today would demand an unprecedented medical and nonmedical response. This requires planning well beyond anything devised thus far by any of the world's countries and organizations.

A YEAR FROM NOW

Even if an H5N1 pandemic is a year away, the world must plan for the same problems with the same fervor. Major campaigns must be initiated to prepare the nonmedical and medical sectors. Pandemic planning must be on the agenda of every school board, manufacturing plant, investment firm, mortuary, state legislature, and food distributor in the United States and beyond. There is an urgent need to reassess the vulnerability of the global economy to ensure that surges in demand can be met. Critical health-care and consumer products and commodities must be stockpiled. Health professionals must learn how to better communicate risk and must be able to both provide the facts and acknowledge the unknowns to a frightened or panicked population.

If there is a year of lead-time before an H5N1 pandemic, vaccine could play a more central role in the global response. Although the world would still have a limited capacity to manufacture influenza vaccine, techniques that could allow scientists to get multiple doses from a current single dose may increase the supply. In addition to further research on this issue, efforts are needed to ensure the availability of syringes and equipment for delivering vaccine. There must also be an international plan for how the vaccine would be allocated. It is far better to struggle with the ethical issues involved in

determining such priorities now, in a public forum, rather than to wait until the crisis occurs.

Prevention must also be improved. Priority should be placed on early intervention and risk assessment. And an aggressive and comprehensive research agenda must be launched immediately to study the ecology and biology of the influenza virus and the epidemiologic role of various animal and bird species.

TEN YEARS LATER

If developed countries begin to transform radically the current system of influenza-vaccine production, an influenza pandemic ten years from now could have a much less devastating outcome. The industrialized world must initiate an international project to develop the ability to produce a vaccine for the entire global population within several months of the start of a pandemic. The initiative must be a top priority of the group of seven industrialized nations plus Russia (G-8), because almost nothing could inflict more death and disruption than a pandemic influenza.

The current BioShield law and additional legislation recently submitted to Congress will act to enhance the availability of vaccines in the United States. This aim is laudable, but it does little to address international needs. The ultimate goal must be to develop a new cell-culture vaccine or comparable vaccine technology that works on all influenza subtypes and that can be made available on short notice to all the people of the world.

WHAT COURSE TO TAKE?

The world must form a better understanding of the potential for the emergence of a pandemic influenza strain. A pandemic is coming. It could be caused by H5N1 or by another novel strain. It could happen tonight, next year, or even ten years from now.

The signs are alarming: the number of human and animal H5N1 infections has been increasing; small clusters of cases have been documented, suggesting that the virus may have come close to sustained human-to-human transmission; and H5N1 continues to evolve in the virtual genetic reassortment laboratory provided by the unprecedented number of people, pigs, and poultry in Asia. The population explosion in China and other Asian countries has created an incredible mixing vessel for the virus. Consider this sobering information: the most recent influenza pandemic, of 1968-69, emerged in China, when its population was 790 million; today it is 1.3 billion. In 1968, the number of pigs in China was 5.2 million; today it is 508 million. The number of poultry in China in 1968 was 12.3 million; today it is 13 billion. Changes in other Asian countries are similar. Given these developments, as well as the exponential growth in foreign travel over the past 50 years, an influenza pandemic could be more devastating than ever before.

Can disaster be avoided? The answer is a qualified yes. Although a coming pandemic cannot be avoided, its impact can be considerably lessened. It depends on how the leaders of the world -- from the heads of the G-8 to local officials -- decide to respond.

They must recognize the economic, security, and health threat that the next influenza pandemic poses and invest accordingly. Each leader must realize that even if a country has enough vaccine to protect its citizens, the economic impact of a worldwide pandemic will inflict substantial pain on everyone. The resources required to prepare adequately will be extensive. But they must be considered in light of the cost of failing to invest: a global world economy that remains in a shambles for several years.

This is a critical point in history. Time is running out to prepare for the next pandemic. We must act now with decisiveness and purpose. Someday, after the next pandemic has come and gone, a commission much like the 9/11 Commission will be charged with determining how well government, business, and public health leaders prepared the world for the catastrophe when they had clear warning. What will be the verdict?

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Avian influenza frequently asked questions

revised 5 December 2005

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What is avian influenza?

Avian influenza, or "bird flu", is a contagious disease of animals caused by viruses that normally infect only birds and, less commonly, pigs. Avian influenza viruses are highly species-specific, but have, on rare occasions, crossed the species barrier to infect humans.

In domestic poultry, infection with avian influenza viruses causes two main forms of disease, distinguished by low and high extremes of virulence. The so-called "low pathogenic" form commonly causes only mild symptoms (ruffled feathers, a drop in egg production) and may

easily go undetected. The highly pathogenic form is far more dramatic. It spreads very rapidly through poultry flocks, causes disease affecting multiple internal organs, and has a mortality that can approach 100%, often within 48 hours.

Which viruses cause highly pathogenic disease?

Influenza A viruses¹ have 16 H subtypes and 9 N subtypes². Only viruses of the H5 and H7 subtypes are known to cause the highly pathogenic form of the disease. However, not all viruses of the H5 and H7 subtypes are highly pathogenic and not all will cause severe disease in poultry.

On present understanding, H5 and H7 viruses are introduced to poultry flocks in their low pathogenic form. When allowed to circulate in poultry populations, the viruses can mutate, usually within a few months, into the highly pathogenic form. This is why the presence of an H5 or H7 virus in poultry is always cause for concern, even when the initial signs of infection are mild.

Do migratory birds spread highly pathogenic avian influenza viruses?

The role of migratory birds in the spread of highly pathogenic avian influenza is not fully understood. Wild waterfowl are considered the natural reservoir of all influenza A viruses. They have probably carried influenza viruses, with no apparent harm, for centuries. They are known to carry viruses of the H5 and H7 subtypes, but usually in the low pathogenic form. Considerable circumstantial evidence suggests that migratory birds can introduce low pathogenic H5 and H7 viruses to poultry flocks, which then mutate to the highly pathogenic form.

In the past, highly pathogenic viruses have been isolated from migratory birds on very rare occasions involving a few birds, usually found dead within the flight range of a poultry outbreak. This finding long suggested that wild waterfowl are not agents for the onward transmission of these viruses.

Recent events make it likely that some migratory birds are now directly spreading the H5N1 virus in its highly pathogenic form. Further spread to new areas is expected.

What is special about the current outbreaks in poultry?

The current outbreaks of highly pathogenic avian influenza, which began in South-east Asia in mid-2003, are the largest and most severe on record. Never before in the history of this disease have so many countries been simultaneously affected, resulting in the loss of so many birds.

The causative agent, the H5N1 virus, has proved to be especially tenacious. Despite the death or destruction of an estimated 150 million birds, the virus is now considered endemic in many parts of Indonesia and Viet Nam and in some parts of Cambodia, China, Thailand, and possibly also the Lao People's Democratic Republic. Control of the disease in poultry is expected to take several years.

The H5N1 virus is also of particular concern for human health, as explained below.

Which countries have been affected by outbreaks in poultry?

From mid-December 2003 through early February 2004, poultry outbreaks caused by the H5N1 virus were reported in eight Asian nations (listed in order of reporting): the Republic of Korea, Viet Nam, Japan, Thailand, Cambodia, Lao People's Democratic Republic, Indonesia, and China. Most of these countries had never before experienced an outbreak of highly pathogenic avian influenza in their histories.

In early August 2004, Malaysia reported its first outbreak of H5N1 in poultry, becoming the ninth Asian nation affected. Russia reported its first H5N1 outbreak in poultry in late July 2005, followed by reports of disease in adjacent parts of Kazakhstan in early August. Deaths of wild birds from highly pathogenic H5N1 were reported in both countries. Almost simultaneously, Mongolia reported the detection of H5N1 in dead migratory birds. In October 2005, H5N1 was confirmed in poultry in Turkey and Romania. Outbreaks in wild and domestic birds are under investigation elsewhere.

Japan, the Republic of Korea, and Malaysia have announced control of their poultry outbreaks and are now considered free of the disease. In the other affected areas, outbreaks are continuing with varying degrees of severity.

What are the implications for human health?

The widespread persistence of H5N1 in poultry populations poses two main risks for human health.

The first is the risk of direct infection when the virus passes from poultry to humans, resulting in very severe disease. Of the few avian influenza viruses that have crossed the species barrier to infect humans, H5N1 has caused the largest number of cases of severe disease and death in humans. Unlike normal seasonal influenza, where infection causes only mild respiratory symptoms in most people, the disease caused by H5N1 follows an unusually aggressive clinical course, with rapid deterioration and high fatality. Primary viral pneumonia and multi-organ failure are common. In the present outbreak, more than half of those infected with the virus have died. Most cases have occurred in previously healthy children and young adults.

A second risk, of even greater concern, is that the virus – if given enough opportunities – will change into a form that is highly infectious for humans and spreads easily from person to person. Such a change could mark the start of a global outbreak (a pandemic).

Where have human cases occurred?

In the current outbreak, laboratory-confirmed human cases have been reported in four countries: Cambodia, Indonesia, Thailand, and Vietnam.

Hong Kong has experienced two outbreaks in the past. In 1997, in the first recorded instance of human infection with H5N1, the virus infected 18 people and killed 6 of them. In early 2003, the

virus caused two infections, with one death, in a Hong Kong family with a recent travel history to southern China.

How do people become infected?

Direct contact with infected poultry, or surfaces and objects contaminated by their faeces, is presently considered the main route of human infection. To date, most human cases have occurred in rural or periurban areas where many households keep small poultry flocks, which often roam freely, sometimes entering homes or sharing outdoor areas where children play. As infected birds shed large quantities of virus in their faeces, opportunities for exposure to infected droppings or to environments contaminated by the virus are abundant under such conditions. Moreover, because many households in Asia depend on poultry for income and food, many families sell or slaughter and consume birds when signs of illness appear in a flock, and this practice has proved difficult to change. Exposure is considered most likely during slaughter, defeathering, butchering, and preparation of poultry for cooking.

Is it safe to eat poultry and poultry products?

Yes, though certain precautions should be followed in countries currently experiencing outbreaks. In areas free of the disease, poultry and poultry products can be prepared and consumed as usual (following good hygienic practices and proper cooking), with no fear of acquiring infection with the H5N1 virus.

In areas experiencing outbreaks, poultry and poultry products can also be safely consumed provided these items are properly cooked and properly handled during food preparation. The H5N1 virus is sensitive to heat. Normal temperatures used for cooking (70°C in all parts of the food) will kill the virus. Consumers need to be sure that all parts of the poultry are fully cooked (no “pink” parts) and that eggs, too, are properly cooked (no “runny” yolks).

Consumers should also be aware of the risk of cross-contamination. Juices from raw poultry and poultry products should never be allowed, during food preparation, to touch or mix with items eaten raw. When handling raw poultry or raw poultry products, persons involved in food preparation should wash their hands thoroughly and clean and disinfect surfaces in contact with the poultry products. Soap and hot water are sufficient for this purpose.

In areas experiencing outbreaks in poultry, raw eggs should not be used in foods that will not be further heat-treated as, for example by cooking or baking.

Avian influenza is not transmitted through cooked food. To date, no evidence indicates that anyone has become infected following the consumption of properly cooked poultry or poultry products, even when these foods were contaminated with the H5N1 virus.

Does the virus spread easily from birds to humans?

No. Though more than 100 human cases have occurred in the current outbreak, this is a small number compared with the huge number of birds affected and the numerous associated

opportunities for human exposure, especially in areas where backyard flocks are common. It is not presently understood why some people, and not others, become infected following similar exposures.

What about the pandemic risk?

A pandemic can start when three conditions have been met: a new influenza virus subtype emerges; it infects humans, causing serious illness; and it spreads easily and sustainably among humans. The H5N1 virus amply meets the first two conditions: it is a new virus for humans (H5N1 viruses have never circulated widely among people), and it has infected more than 100 humans, killing over half of them. No one will have immunity should an H5N1-like pandemic virus emerge.

All prerequisites for the start of a pandemic have therefore been met save one: the establishment of efficient and sustained human-to-human transmission of the virus. The risk that the H5N1 virus will acquire this ability will persist as long as opportunities for human infections occur. These opportunities, in turn, will persist as long as the virus continues to circulate in birds, and this situation could endure for some years to come.

What changes are needed for H5N1 to become a pandemic virus?

The virus can improve its transmissibility among humans via two principal mechanisms. The first is a “reassortment” event, in which genetic material is exchanged between human and avian viruses during co-infection of a human or pig. Reassortment could result in a fully transmissible pandemic virus, announced by a sudden surge of cases with explosive spread.

The second mechanism is a more gradual process of adaptive mutation, whereby the capability of the virus to bind to human cells increases during subsequent infections of humans. Adaptive mutation, expressed initially as small clusters of human cases with some evidence of human-to-human transmission, would probably give the world some time to take defensive action.

What is the significance of limited human-to-human transmission?

Though rare, instances of limited human-to-human transmission of H5N1 and other avian influenza viruses have occurred in association with outbreaks in poultry and should not be a cause for alarm. In no instance has the virus spread beyond a first generation of close contacts or caused illness in the general community. Data from these incidents suggest that transmission requires very close contact with an ill person. Such incidents must be thoroughly investigated but – provided the investigation indicates that transmission from person to person is very limited – such incidents will not change the WHO overall assessment of the pandemic risk. There have been a number of instances of avian influenza infection occurring among close family members. It is often impossible to determine if human-to-human transmission has occurred since the family members are exposed to the same animal and environmental sources as well as to one another.

How serious is the current pandemic risk?

The risk of pandemic influenza is serious. With the H5N1 virus now firmly entrenched in large parts of Asia, the risk that more human cases will occur will persist. Each additional human case gives the virus an opportunity to improve its transmissibility in humans, and thus develop into a pandemic strain. The recent spread of the virus to poultry and wild birds in new areas further broadens opportunities for human cases to occur. While neither the timing nor the severity of the next pandemic can be predicted, the probability that a pandemic will occur has increased.

Are there any other causes for concern?

Yes. Several.

- Domestic ducks can now excrete large quantities of highly pathogenic virus without showing signs of illness, and are now acting as a “silent” reservoir of the virus, perpetuating transmission to other birds. This adds yet another layer of complexity to control efforts and removes the warning signal for humans to avoid risky behaviours.
- When compared with H5N1 viruses from 1997 and early 2004, H5N1 viruses now circulating are more lethal to experimentally infected mice and to ferrets (a mammalian model) and survive longer in the environment.
- H5N1 appears to have expanded its host range, infecting and killing mammalian species previously considered resistant to infection with avian influenza viruses.
- The behaviour of the virus in its natural reservoir, wild waterfowl, may be changing. The spring 2005 die-off of upwards of 6,000 migratory birds at a nature reserve in central China, caused by highly pathogenic H5N1, was highly unusual and probably unprecedented. In the past, only two large die-offs in migratory birds, caused by highly pathogenic viruses, are known to have occurred: in South Africa in 1961 (H5N3) and in Hong Kong in the winter of 2002–2003 (H5N1).

Why are pandemics such dreaded events?

Influenza pandemics are remarkable events that can rapidly infect virtually all countries. Once international spread begins, pandemics are considered unstoppable, caused as they are by a virus that spreads very rapidly by coughing or sneezing. The fact that infected people can shed virus before symptoms appear adds to the risk of international spread via asymptomatic air travellers.

The severity of disease and the number of deaths caused by a pandemic virus vary greatly, and cannot be known prior to the emergence of the virus. During past pandemics, attack rates reached 25–35% of the total population. Under the best circumstances, assuming that the new virus causes mild disease, the world could still experience an estimated 2 million to 7.4 million deaths (projected from data obtained during the 1957 pandemic). Projections for a more virulent virus are much higher. The 1918 pandemic, which was exceptional, killed at least 40 million people. In the USA, the mortality rate during that pandemic was around 2.5%.

Pandemics can cause large surges in the numbers of people requiring or seeking medical or hospital treatment, temporarily overwhelming health services. High rates of worker absenteeism can also interrupt other essential services, such as law enforcement, transportation, and communications. Because populations will be fully susceptible to an H5N1-like virus, rates of illness could peak fairly rapidly within a given community. This means that local social and economic disruptions may be temporary. They may, however, be amplified in today's closely interrelated and interdependent systems of trade and commerce. Based on past experience, a second wave of global spread should be anticipated within a year.

As all countries are likely to experience emergency conditions during a pandemic, opportunities for inter-country assistance, as seen during natural disasters or localized disease outbreaks, may be curtailed once international spread has begun and governments focus on protecting domestic populations.

What are the most important warning signals that a pandemic is about to start?

The most important warning signal comes when clusters of patients with clinical symptoms of influenza, closely related in time and place, are detected, as this suggests human-to-human transmission is taking place. For similar reasons, the detection of cases in health workers caring for H5N1 patients would suggest human-to-human transmission. Detection of such events should be followed by immediate field investigation of every possible case to confirm the diagnosis, identify the source, and determine whether human-to-human transmission is occurring.

Studies of viruses, conducted by specialized WHO reference laboratories, can corroborate field investigations by spotting genetic and other changes in the virus indicative of an improved ability to infect humans. This is why WHO repeatedly asks affected countries to share viruses with the international research community.

What is the status of vaccine development and production?

Vaccines effective against a pandemic virus are not yet available. Vaccines are produced each year for seasonal influenza but will not protect against pandemic influenza. Although a vaccine against the H5N1 virus is under development in several countries, no vaccine is ready for commercial production and no vaccines are expected to be widely available until several months after the start of a pandemic.

Some clinical trials are now under way to test whether experimental vaccines will be fully protective and to determine whether different formulations can economize on the amount of antigen required, thus boosting production capacity. Because the vaccine needs to closely match the pandemic virus, large-scale commercial production will not start until the new virus has emerged and a pandemic has been declared. Current global production capacity falls far short of the demand expected during a pandemic.

What drugs are available for treatment?

Two drugs (in the neuraminidase inhibitors class), oseltamivir (commercially known as Tamiflu) and zanamivir (commercially known as Relenza) can reduce the severity and duration of illness caused by seasonal influenza. The efficacy of the neuraminidase inhibitors depends, among others, on their early administration (within 48 hours after symptom onset). For cases of human infection with H5N1, the drugs may improve prospects of survival, if administered early, but clinical data are limited. The H5N1 virus is expected to be susceptible to the neuraminidase inhibitors. Antiviral resistance to neuraminidase inhibitors has been clinically negligible so far but is likely to be detected during widespread use during a pandemic.

An older class of antiviral drugs, the M2 inhibitors amantadine and rimantadine, could potentially be used against pandemic influenza, but resistance to these drugs can develop rapidly and this could significantly limit their effectiveness against pandemic influenza. Some currently circulating H5N1 strains are fully resistant to these the M2 inhibitors. However, should a new virus emerge through reassortment, the M2 inhibitors might be effective.

For the neuraminidase inhibitors, the main constraints – which are substantial – involve limited production capacity and a price that is prohibitively high for many countries. At present manufacturing capacity, which has recently quadrupled, it will take a decade to produce enough oseltamivir to treat 20% of the world's population. The manufacturing process for oseltamivir is complex and time-consuming, and is not easily transferred to other facilities.

So far, most fatal pneumonia seen in cases of H5N1 infection has resulted from the effects of the virus, and cannot be treated with antibiotics. Nonetheless, since influenza is often complicated by secondary bacterial infection of the lungs, antibiotics could be life-saving in the case of late-onset pneumonia. WHO regards it as prudent for countries to ensure adequate supplies of antibiotics in advance.

Can a pandemic be prevented?

No one knows with certainty. The best way to prevent a pandemic would be to eliminate the virus from birds, but it has become increasingly doubtful if this can be achieved within the near future.

Following a donation by industry, WHO will have a stockpile of antiviral medications, sufficient for 3 million treatment courses, by early 2006. Recent studies, based on mathematical modelling, suggest that these drugs could be used prophylactically near the start of a pandemic to reduce the risk that a fully transmissible virus will emerge or at least to delay its international spread, thus gaining time to augment vaccine supplies.

The success of this strategy, which has never been tested, depends on several assumptions about the early behaviour of a pandemic virus, which cannot be known in advance. Success also depends on excellent surveillance and logistics capacity in the initially affected areas, combined with an ability to enforce movement restrictions in and out of the affected area. To increase the likelihood that early intervention using the WHO rapid-intervention stockpile of antiviral drugs will be successful, surveillance in affected countries needs to improve, particularly concerning the capacity to detect clusters of cases closely related in time and place.

What strategic actions are recommended by WHO?

In August 2005, WHO sent all countries a document outlining recommended strategic actions for responding to the avian influenza pandemic threat. Recommended actions aim to strengthen national preparedness, reduce opportunities for a pandemic virus to emerge, improve the early warning system, delay initial international spread, and accelerate vaccine development.

Is the world adequately prepared?

No. Despite an advance warning that has lasted almost two years, the world is ill-prepared to defend itself during a pandemic. WHO has urged all countries to develop preparedness plans, but only around 40 have done so. WHO has further urged countries with adequate resources to stockpile antiviral drugs nationally for use at the start of a pandemic. Around 30 countries are purchasing large quantities of these drugs, but the manufacturer has no capacity to fill these orders immediately. On present trends, most developing countries will have no access to vaccines and antiviral drugs throughout the duration of a pandemic.

¹ Influenza viruses are grouped into three types, designated A, B, and C. Influenza A and B viruses are of concern for human health. Only influenza A viruses can cause pandemics.

² The H subtypes are epidemiologically most important, as they govern the ability of the virus to bind to and enter cells, where multiplication of the virus then occurs. The N subtypes govern the release of newly formed virus from the cells.

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Avian Flu: Global health and American security

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Abstract

As a leader in a global defense against the avian flu, the United States should generously fund a forward defense strategy, focused on education, surveillance, and a rapid response capacity in high risk countries. At best, however, that strategy can only delay a severe influenza pandemic, for which countries everywhere are ill-prepared. A killer flu could devastate poor countries already overwhelmed by public health crises, and leave more failed states in its wake. With all appropriate speed, the world needs to greatly expand production capacity for antiviral medicines and vaccines, develop better vaccine technology, and build health care and related infrastructure especially in poor countries. This will be a wise investment in American security.

I. Avian Flu as a Central Foreign Policy Concern

The threat of avian flu became daily news in the United States between Hurricane Katrina and the Pakistan earthquake, in a year that began with a calamity of biblical proportions in the Indian Ocean. While we tend to think of security threats in terms of enemies plotting against us, we still face equally or more catastrophic threats from forces which need no human connivance.

Terrorists armed with weapons of mass destruction, should they choose to exploit such weapons for maximum political effect, could put Western governments in a terrible predicament. As unprecedented and nightmarish as that would be, however, the human and economic toll would not compare with some of the possible consequences of global warming, or the evolution of an avian flu virus to a form easily passed between humans.

Risk communication specialists distinguish between sheer risk and risk compounded by outrage. Terrorist attacks, whatever their human and economic impact, carry a high outrage factor. That factor explains high government expenditures to thwart

such attacks. In contrast, mutating viruses pose greater risks, but have not inspired commensurate levels of government spending.

Health experts agree that the H5N1 virus, or a similar one, will in time successfully mutate to produce an influenza pandemic. At best, the international community might be able to delay this event, through vigilant surveillance, education of poultry farmers as to safer methods, vaccinations and culling of birds, and a rapid-response capacity to outbreaks in poultry flocks and human infections.

It might be a year, three years, or ten years before an avian flu virus outwits a global forward defense. But outwit us it will. Despite China's determination to vaccinate 14 billion birds, that task is daunting, and vaccinators themselves could spread the disease. Beyond China, another country, perhaps Cambodia, Laos, India, Bangladesh, or one in Africa with less infrastructure than China but with similar human and poultry living patterns, may provide the critical opportunity for the virus. When the breakout event occurs, the resulting pandemic could easily overburden the health systems of every country, and devastate the poorest countries already losing ground to existing health crises. More failed states may be the result.

If we ponder what a severe pandemic might mean for our own society, taking its largest toll among children, youth and young adults, we have an inkling of the sort of insecurity hundreds of millions of people face routinely. Daily, thousands perish for want of a passable road, a functioning vehicle, safe water, a trained health worker, medicine, or an adequate harvest. Security often comes down to basic infrastructure, the same infrastructure poor countries will need to have a fighting chance against a killer flu.

The essential certainty of a pandemic and the current state of global health care make the avian flu a very relevant concern of American foreign policy. If a pandemic arrives soon, or if we are perceived as having failed to help the world prepare, the consequences will only add to what Zbigniew Brzezinski terms "global restlessness"—an awakening that is "socially massive and politically radicalizing." It is a growing resentment toward the status quo, principally among youth, which age group will likely incur a high death toll in a pandemic.

Thus, the build-up of health care and related infrastructure in the poorest countries is as critical to American interests as is a forward defense to delay a pandemic, the expansion of antiviral production, and the development of better vaccine technology. The first item, adequately funded, will mean a substantial increase in foreign aid, on the order of that to which President Bush has at least twice committed the United States in his endorsement of the Millennium Development Goals. (The increase would amount to approximately 50 cents per American per day.) This might sound implausible, given the federal deficit. That deficit is a problem, but the global health deficit is a bigger problem, and indirectly a greater threat to American security.

II. Can a Forward Defense Buy the World Some Time?

An influenza pandemic will likely include successive waves, probably of increasing severity, possibly over a few years. (1) According to the World Health Organization (WHO), an influenza pandemic “is certain to be unpredictable, complex, rapidly evolving and accompanied by considerable public alarm.” (2)

Laurie Garrett, Senior Fellow for Global Health at the Council on Foreign Relations, wrote this past summer:

“The 1918 [flu] strain, which killed 50 to 100 million people, only killed about two to three percent of the people it infected. The H5N1 strain now in circulation kills 100 percent of the birds [chickens] it infects and has killed more than 50 percent of the people known to be infected so far. If it manages to mutate into a human-to-human form, and retains even half its current virulence, the death toll would be in the hundreds of millions...[A]n H5N1 pandemic with virulence above five percent would be the most catastrophic outbreak in human history...” (3)

Michael Osterholm, Associate Director of the Department of Homeland Security’s National Center for Food Protection and Defense, has written of the avian flu threat: “The signs are alarming: the number of human and animal H5N1 infections has been increasing; small clusters of cases have been documented, suggesting that the virus may have come close to sustained human-to-human transmission; and H5N1 continues to evolve in the virtual reassortment laboratory provided by the unprecedented number of people, pigs and poultry in Asia.” (4)

In March of 2004, following massive outbreaks of the bird flu among poultry in several Asian countries, which led to human infections and deaths as well, the WHO brought together more than 100 experts from 33 countries, to advise on how to best prepare a global defense. The report of that consultation noted that during the chaos of a pandemic, “health authorities would almost certainly need to make decisions, often with major social and economic consequences, in an atmosphere of considerable scientific uncertainty.” The group advised that countries with means to do so begin stockpiling antiviral drugs, and address the difficult question of what groups should have priority access to them. (5)

The participants also recommended a concerted international effort of surveillance and rapid response to “events with pandemic potential.” This would include the targeted use of antivirals to protect the immediate populations when clusters of human infections occur. These, among other measures including quarantine and isolation, could possibly delay a pandemic and allow more time for preparation. “This strategy of ‘buying time’ was linked to assumptions, partially based on modeling, that the first chains of human-to-human transmission might not reach the efficiency needed to initiate and sustain pandemic spread. In such a scenario, the first evidence of limited human-to-human transmission, most likely expressed in clusters of cases, would be the

epidemiological trigger for intense international efforts aimed at interrupting further transmission ...” (6)

In September of 2005, in a document titled “Responding to the avian influenza pandemic threat: recommended strategic actions,” the WHO stated: “the early warning system is weak.” Specifically, the document stated:

“As the evolution of the threat cannot be predicted, a sensitive early warning system is needed to detect the first sign of changes in the behavior of the virus. In risk-prone countries, disease information systems and health, veterinary, and laboratory capacities are weak. Most affected countries cannot adequately compensate farmers for culled poultry, thus discouraging the reporting of outbreaks in the rural areas where the vast majority of human cases have occurred. Veterinary extension services frequently fail to reach these areas. Rural poverty perpetuates high-risk behaviours, including the traditional home-slaughter and consumption of diseased birds. Detection of human cases is impeded by patchy surveillance in these areas. Diagnosis of human cases is impeded by weak laboratory support and the complexity and high costs of testing. Few affected countries have the staff and resources needed to thoroughly investigate human cases and, most importantly, to detect and investigate clusters of cases—an essential warning signal. In virtually all affected countries, antiviral drugs are in very short supply.”

And further:

“The dilemma of preparing for a potentially catastrophic but unpredictable event is great for all countries, but most especially for the countries affected by H5N1 outbreaks in animals and humans. These countries, in which rural subsistence farming is a backbone of economic life, have experienced direct and enormous agricultural losses, presently estimated at more than US\$ 10 billion. They are being asked to sustain—if not intensify—resource-intensive activities needed to safeguard international public health while struggling to cope with many other competing health and infectious disease priorities.” (www.who.int)

On October 15, 2005, concluding a fact-finding trip to Southeast Asia, US Health and Human Services Secretary Mike Leavitt concluded that containing an outbreak of the avian flu virus among humans is unlikely. “Can we create the network of surveillance sufficient enough to find the spark when it happens, to get there fast enough?” Leavitt asked. The chances of that happening are not good.” (*Associated Press*, October 16, 2005)

At an international conference in November of 2005, the World Bank estimated that at least \$1.5 billion over three years will be needed to control the disease among

poultry in Southeast Asia, buy antiviral drugs for poor countries and to help develop a human vaccine. The Bank noted that this estimate did not include individual spending by countries on their own preparations, or all of the costs of antivirals and vaccines, or full compensation to farmers for culled birds. And that still leaves India, Bangladesh and African countries. “The minute there are more regions or countries with animal outbreaks or human-to-human transmission, the funding needs will increase hugely,” said James Adams, head of the World Bank’s Avian Flu Task Force.

Wealthy nations should ensure that the funds for an adequate forward defense are available, be it in Southeast Asia, South Asia, Africa or anywhere else. This should include full compensation to farmers for culled birds. This is, of course, a monumental task, but a failure to do all we can will be terribly short-sighted.

“Should that [forward defense] effort fail,” the March, 2004 WHO report noted, “inequalities in capacity and the distribution of resources mean that the consequences of a pandemic would almost certainly be most severe in the developing world. The participants stressed the importance of addressing those inequalities now—before a pandemic makes the ethical implications of failing to do so both blatantly apparent and irrevocable.”

Since many underdeveloped countries regularly face public health crises, the WHO report noted that preparations for the next pandemic “will provide benefits now, as improvements in infrastructure can have immediate and lasting benefits, and can also mitigate the effect of other epidemics or infectious disease threats.” (7)

According to Dr. Margaret F.C. Chan, chief of pandemic influenza for the WHO, many government officials have told her that their budgets for AIDS, children’s health, women’s health and other on-going problems are inadequate and thus they are hesitant to direct scarce resources to prepare for an influenza pandemic. Despite the indicators that a flu pandemic is bound to occur, it may seem theoretical compared to current crises. (8)

World progress in combating HIV/AIDS is a good indication of how ill-prepared is the world for an influenza pandemic. AIDS principally kills the most productive members of a society—“human capital” that is critical to the infrastructure. It is estimated that 6.5 million of the 40 million people infected by HIV/AIDS are within two years of death and need anti-retroviral medications immediately. Yet, in the spring of 2005, the WHO announced that it would fall short of its goal of providing anti-retroviral therapy to three million poor sufferers of HIV/AIDS by the end of the year. Reasons cited included problems in the drug supply chain and shortages of health workers. As of December 1, World AIDS Day, approximately 1 million HIV/AIDS sufferers in poor countries were receiving anti-retroviral therapy.

Even apart from an influenza pandemic, Africa alone needs an additional one million health workers, according to the Joint Learning Initiative, a research group of global health scholars and practitioners. (9)

Suppose the odds are with us, and no opportunity for the virus to successfully mutate occurs for several more years. What could the world do with extra time for preparation? Michael Osterholm proposes a “worldwide influenza Manhattan Project.” (10) He writes: “The industrialized world must initiate an international project to develop the ability to produce a vaccine for the entire global population within several months of the start of a pandemic....The ultimate goal must be to develop a new cell-culture vaccine or comparable vaccine technology that works on all influenza subtypes and that can be made available on short notice to all people of the world.” (11) New medical production facilities could be located in Asia, which is likely to be an epicenter of influenza for decades, as well as other poor regions.

In the meantime, the international community must determine how best to maximize production of antiviral medicines, even with the qualification that overuse of a drug could allow the virus to develop resistance to it. Roche Holding AG, manufacturer of the leading antiviral, Tamiflu (brand name for oseltamivir) has donated millions of courses of the medicine to the WHO as well as some individual countries, and after some initial hesitancy, has been more receptive to other manufacturers producing generic versions of the drug. Mindful of the complicating factor of overuse and resistance, Congress should make clear that it is prepared to fund fair compensation to the patent holder of any effective medication against the avian flu virus in exchange for suspension of those patent rights. Congress should make clear that it is willing as well to resort to compulsory licensing if necessary. It is hard to imagine a more compelling public interest.

In addition to developing better vaccines and greatly expanding production capacity for vaccines, antivirals and antibiotics (to treat secondary infections), worldwide we need to expand national health care and related infrastructure. Specifically, we need to construct clinics, schools and roads; train millions more health workers, disaster psychologists, teachers and security personnel; expand anti-retroviral AIDS therapy; improve sanitation and access to clean water; rebuild soils, raise agricultural productivity and increase grain reserves; and produce and stockpile critical medical supplies, transport fuels and food.

New health clinics can treat patients not only for influenza but also for a range of killer diseases already widespread in poor countries. Medical professionals who have left those countries in search of better paying jobs might be induced, with promise of sufficient pay and resources, to return home to run the new clinics and train new health workers. (12)

Laurie Garrett notes that “the greatest weakness that each nation must individually address is the inability of their hospitals to cope with a sudden surge of new patients.” Michael Osterholm notes that the United States alone would need several hundred thousand additional mechanical ventilators in a pandemic. Throughout the developed countries (not to mention the rest of the world), “Virtually every piece of medical equipment or protective gear would be in short supply within days of the

recognition of a pandemic.” Two U.S.-based companies supply most of the respiratory protection masks for health-care workers around the world, yet “Neither company would be able to meet the jump in demand, in part because the component parts of the masks come from multiple suppliers in multiple countries. With travel and transportation restricted, masks may not even be produced at all.” Without adequate supplies and protection, Osterholm writes, “it is unclear how many professionals would continue to place themselves in high-risk situations by caring for the infected.” (13)

III. Helping the Least Developed Countries

As for the poorest countries, building health care and related infrastructure is inseparable from global poverty alleviation. In the last few years, a great deal of experience and expertise has been devoted to a United Nations plan for a comprehensive attack on poverty. In addition to debt relief and trade reform, the plan includes investments in multiple sectors of the economies of poor countries. The objective is to help these countries build up their infrastructure and human capital to the point at which they can grow without such assistance.

Columbia University economist Jeffrey D. Sachs, who headed the United Nations Millennium Project that developed the plan, and author of *The End of Poverty*, argues that “success in any single area, whether in health, or education, or farm productivity, depends on investments across the board.” (14) Multiple interventions build on each other, such that the whole is greater than the sum of the parts. (See: Appendix at fluready.blogspot.com)

Critics have called the UN plan overly ambitious, citing corruption among many governments as well as low “absorptive capacity” of extremely poor countries to utilize larger amounts of aid. Economist William Easterly of New York University, and formerly of the World Bank, argues that the plan includes too many interventions, and no adequate mechanism to ensure accountability. “[U]topian-driven aid packages have so many different goals that it weakens the accountability and probability of meeting any one goal... Instead of setting utopian goals such as ending world poverty, global leaders should simply concentrate on finding particular interventions that work.” Easterly has called instead for a more “piecemeal” approach, in which fewer programs can be better evaluated. (15)

Jeffrey Sachs responds: “Basically, I don’t think that we should be choosing between whether a young girl has immunizations or water, or between whether her mother and father are alive, because they have access to treatment for AIDS, or whether she has a meal at school, or whether her father and mother, who are farmers, are able to grow enough food to feed their family and earn some income. Those all strike me as quite doable and practical things that can be done at once.” (16)

Sachs and his colleagues at the Columbia Earth Institute, with the help of other development experts, have begun implementing their strategy of multiple and

coordinated interventions in a number of poor villages. The first two targeted villages are Sauri, Kenya and Koraro, Ethiopia, both of which are receiving \$250,000 annually over five years to improve agriculture, health and education. Through a new organization titled Millennium Promise, the strategy will be extended to 100 African villages. (17)

Other development specialists, including supporters of the UN plan, note that trade, more than aid, “has the potential to increase the share of the world’s poorest countries and people in global prosperity,” in the words of the 2005 UN Human Development Report. “To help developing countries help themselves,” write Nancy Birdsall, Dani Rodrik and Arvind Subramanian, “wealthy nations must begin to lift the burdens they impose on the poor,” including many barriers to trade. (18) Those barriers can more than undo the benefits of aid. (19) Noting as well that the costs of global climate change will disproportionately burden developing countries, Birdsall, Rodrik and Subramanian argue that under a market-based system of tradable emissions rights, poor nations would be allotted enough emissions to ensure future growth—“the same right that the industrial countries have enjoyed for centuries.”

Nancy Birdsall echoes concerns about the capacity of even competent poor governments “to manage simultaneously multiple new investments and social delivery programs as well as better auditing, introducing the rule of law, undertaking judicial reform and so on.” Among other recommendations, she proposes “the creation of a completely independent evaluation system for assessing and reporting publicly on the effectiveness of aid-funded programs in Africa.” (20) To better measure the results of aid programs, Amir Attaran of the University of Ottawa proposes that dozens of demographic surveillance sites be established in the poorest countries to document births, deaths, illnesses and social services. (21)

These are important considerations that several organizations and individual governments are working to address. And while the UN plan gives priority to well-governed poor countries, Jeffrey Sachs argues that the focus on institutional reform as a prerequisite to increased aid can be overdone. “For too long,” Sachs writes, “too much economic thinking has been directed at the wrong question—how to make the poor countries into textbook models of good governance or efficient market economies. Too little has been done to identify the specific, proven, low-cost interventions that can make a difference in living standards and economic growth. When we get practical, and speak of investments in specific areas—roads, power, transport, soils, water and sanitation, disease control—the task is suddenly a lot less daunting.” (22)

Without dismissing concerns about the UN plan, the gathering influenza storm puts a premium on comprehensive, prompt action, rather than a more gradual approach dependent on institutional reform and which tries to guarantee that every dollar is optimally spent. Foreign aid to boost government investments (and in some cases bypassing governments) is not the only way to help poor countries lift themselves out of the poverty trap. But given the state of infrastructure in the poorest countries, the potential of a pandemic to essentially halt international trade, and the unknown progress of the H5N1 virus, direct foreign aid is indispensable to building a global defense.

Taking a pandemic fully into account, adjustments to the UN plan will be necessary. Even assuming that the plan is adopted without further delay, and the donor countries increase foreign aid significantly, in all likelihood, a pandemic will intervene and seriously disrupt economic development. For instance, the possible collapse of global trade has large implications for agriculture, not to mention the wealth of the donor countries. Cash crops that ordinarily might bring higher incomes than crops grown for local consumption, but which rely on long distance trade, might prove useless. Still, a great number of the interventions contemplated in the UN plan are all the more needed with a global health crisis developing.

The coming pandemic makes poverty alleviation and economic development at once more complicated and more urgent. The economic and social disruption a pandemic will cause must be weighed against the consequences of the wealthy countries failing to apply their tremendous resources to do all that they can, as late as the hour may be. Jeffrey Sachs and his colleagues are to be commended for targeting specific villages to demonstrate what is possible, but we should not take this as a reason not to commit to substantial increases in aid now. Political leaders in rich and developing countries alike should be asking which interventions contemplated in the plan especially ought to be expanded and accelerated.

Economic development is essential to stabilizing world population, for the education level of a woman is the most critical indicator of the number of children she will have. Ensuring that development happens in an equitable and sustainable manner will challenge the world's best minds, but failure to check poverty and stabilize population will produce repeated disasters. Because we cannot know the breakout date of the next pandemic, the UN plan--adjusted as necessary--must be made a top global priority.

IV Conclusion

In a "call to action," the editors of *Foreign Affairs* published an unusual issue for July/August 2005, featuring four articles on the avian flu threat. While that issue was still hot off the press, a new wave of H5N1 outbreaks among poultry appeared in Tibet, Kazakhstan and Russia, working its way toward Europe, carried by infected migratory birds from Southeast Asia. The bird flu was due for top news when Hurricane Katrina intervened. The latter event demonstrated how ill-prepared is the United States for calamities at home. While the forces of nature on their own inspire little outrage, the administration learned how an inadequate response by government can spark more than enough of it.

Lest the lesson be repeated at the global level, Congress should give the avian flu its due as a foreign policy priority. As Laurie Garrett wrote in the above-mentioned issue of *Foreign Affairs*:

In a world where most of the wealth is concentrated in less than a dozen nations representing a distinct minority of the total population, the capacity to respond to global threats is ...severely imbalanced. The majority of the world's governments not only lack sufficient funds to respond to a superflu; they also have no health infrastructure to handle the burdens of disease, social disruption, and panic. The international community would look to the United States, Canada, Japan, and Europe for answers, vaccines, cures, cash, and hope. How these wealthy governments responded, and how radically the death rates differed along worldwide fault lines of poverty, would resonate for years thereafter.(23)

Surely we do not need this threat at this time. Yet, we do need some new ideas for engaging a world that is growing increasingly suspicious of our intentions. Democracy means something to us, but evidently carries other connotations abroad. Perceptions matter, and we can ignore Brzezinski's "global political awakening" only at our peril. We may yet have several years in which to help all countries better prepare for a pandemic that is sure to come. If we do this, and make the hard choices today to free the resources necessary for that task, it may prove to be a very wise investment in our own security.

NOTES

1. "WHO guidelines on the use of vaccines and antivirals during influenza pandemics," 8/2004, (www.who.int)
 "Pandemics are different from seasonal outbreaks or 'epidemics' of influenza. Seasonal outbreaks are caused by subtypes of influenza viruses that are already in existence among people, whereas pandemic outbreaks are caused by new subtypes or by subtypes that have never circulated among people or that have not circulated among people for a long time. Past influenza pandemics have led to high levels of illness, death, social disruption, and economic loss." ("Information About Influenza Pandemics," Center for Disease Control and Prevention, www.cdc.gov)
2. "WHO consultation on priority public health interventions before and during an influenza pandemic, Executive Summary" (www.who.int)
3. "Q&A with Laurie Garrett," May 25, 2005, www.foreignaffairs.org.
4. *Foreign Affairs*, July/August, 2005.
 "A pandemic virus capable of efficient human-to-human transmission could arise via two mechanisms: virus reassortment (the swapping of genetic material between viruses) when humans or pigs are co-infected with H5N1 and a human influenza virus, and adaptive mutation during human infection. The risk that either event will occur remains so long as H5N1 is present in an animal reservoir, thus allowing continuing opportunities for human exposure and infection. The level of risk is determined most directly by the prevalence of the virus in poultry and the frequency of its transmission to humans. The risk also depends on the co-circulation of human and avian influenza viruses and the inherent propensity of these viruses to reassort." (WHO consultation on priority public health interventions before and during an influenza pandemic, Executive Summary, www.who.int)
 The Center for Disease Control and Prevention states:

"New Research suggests that currently circulating strains of H5 viruses are becoming more capable of causing disease (pathogenic) for mammals than earlier H5 viruses and are becoming more widespread in birds in the [Asian] region. One study found that ducks infected with H5N1 are now shedding more virus for longer periods of time without showing any symptoms of illness. This has implications for the role of ducks in transmitting disease to other birds and possibly to humans as well. Additionally, other findings have documented H5 infections among pigs in China and H5 infection in felines (experimental injection in housecats in the Netherlands and isolation of H5N1 viruses from infected tigers and leopards in Thailand), suggesting that cats could host or transmit the infection. *These findings are particularly worrisome in light of the fact that reassortment of avian influenza genomes is more likely to occur when these viruses demonstrate a capacity to infect multiple species, as is now the case in Asia.* (Emphasis added.) ("Recent Avian Influenza Outbreaks in Asia," August 5, 2005, www.cdc.gov)

On July 25, 2005, Maggie Fox of *Reuters* reported: "Strains of the influenza virus are constantly swapping genes among themselves and giving rise to new, dangerous strains at a rate faster than previously believed," according to David Lipman and colleagues at the National Institutes of Health.

"Influenza viruses are notorious for trading genes back and forth and mutating. Scientists previously believed that the gene swapping occurred gradually but the new study shows that several genes can be exchanged at once, causing sudden changes in important characteristics of the virus."

5. "WHO consultation on priority public health interventions before and during an influenza pandemic, Executive Summary"

6. *ibid.* A WHO press release of 8/25/2005 states:

"If the first signs of improved transmissibility are picked up quickly, there is a chance that rapid intervention, involving mass prophylactic administration of antiviral drugs, might contain the pandemic at its source or at least delay international spread, gaining time to intensify preparedness. An international stockpile of antiviral drugs is needed for this purpose. The prospect of halting a pandemic at its source or delaying its international spread is attractive, but untested, as no attempt has ever been made to alter the natural course of a pandemic. Successful intervention requires that at least 5 conditions be met:

- The first viruses that show an ability to sustain transmission among humans will not yet be highly contagious.
- The emergence of such viruses will be limited to a small geographical area.
- The first clusters of human cases caused by the virus will be rapidly detected and reported.
- Antiviral drugs will be rapidly mobilized from the stockpile, made available to the affected population, and administered to sufficiently large numbers of people.
- Movement of people in and out of the area will be effectively restricted.

Given the unpredictable nature of influenza viruses, it is impossible to know in advance if the first two conditions will be borne out in reality when a pandemic virus emerges. The remaining conditions require excellent surveillance and logistics capacity in the initially affected area, combined with an ability to enforce movement restrictions."

On August 3, 2005, the BBC reported that UK and US teams used computer models to explore the prospects of targeting an outbreak among humans of the H5N1 virus. They concluded that good surveillance plus antivirals could possibly halt it. In one scenario, the UK team found that two key conditions would need to be met in order to limit the spread of the disease to fewer than 200 people. First, the virus would have to be identified while confined to about 30 people. Second, antiviral drugs would have to be distributed rapidly to the 20,000 individuals nearest those infected. The group estimated that an international stockpile of 3 million courses (30 million capsules) of antivirals would suffice to contain an outbreak. But that would include the ability to deliver the drugs anywhere in the world at short notice. Professor Neil Ferguson of Imperial College London, who led the study said: "It's an enormous undertaking and will require cooperation among governments on a large scale."

"Another team from Emory University in Atlanta, Georgia, led by Dr. Ira Longini, simulated an outbreak in a population of 500,000 in rural Thailand, with people mixed in a variety of settings, including households, schools, workplaces and a hospital. Provided targeted use of antiviral drugs was adopted within 21 days, it would be possible to contain an outbreak, they found, as long as each infected person was not likely to infect more than an average of 1.6 people. If there was more infectivity than this, household quarantines would also be necessary, they said. Co-researcher Elizabeth Halloran said: 'Our findings

indicate that we have reason to be somewhat hopeful. If—or, more likely, when—an outbreak occurs in humans, there is a chance of containing it and preventing a pandemic.” (www.promedmail.org)

7. WHO, “Pandemic preparedness” (www.who.int)
8. *New York Times*, August 9, 2005 (Section D)
9. Laurie Garrett and Scott Rosenstein, *Harvard International Review*, May, 2005.
10. *New England Journal of Medicine*, May 5, 2005 (www.nejm.org)
11. *Foreign Affairs*, July/August. 2005.
12. Inadequate current funding and health infrastructure have resulted in “human resource shortfalls that have nearly crippled the capabilities of institutions endeavoring to create sustainable programs that can be administered with local participation and ownership,” write Laurie Garrett and Scott Rosenstein. A “talent drain” is depleting developing countries of health professionals, who leave in search of better-paying jobs in wealthier countries. (*Harvard International Review*, Spring, 2005)
13. *Foreign Affairs*, July/August, 2005.
14. Jeffrey Sachs, *The End of Poverty*, (New York: Penguin Press, 2005), p.256.
15. William Easterly, “The Utopian Nightmare,” *Foreign Policy*, September/October, 2005. Despite Easterly’s sweeping criticisms of the plan, he notes a number of aid programs which have passed rigorous evaluation, including several pertaining to health: “subsidies to families for education and health costs for their children ...deworming drugs and nutritional supplements, vaccination, HIV prevention, indoor spraying for malaria, [anti-malaria] bednets, fertilizer and clean water.”
16. “The End of Poverty: An Interview with Jeffrey Sachs,” *Mother Jones*, May 6, 2005 (www.motherjones.com)
17. “U.N. vs Poverty: Seeking a Focus, Quarreling Over Vision.” *New York Times*, September 14, 2005.
 At the outset of the program in Sauri, Kenya, many of the villagers ate one meal per day. In exchange for free seeds and fertilizers, farmers in Sauri agreed to give 10 percent of their yields to local schools, to provide a daily meal to students. This has been demonstrated elsewhere to increase school attendance. A truck, supplied by the project, will double as an ambulance and a means to transport produce to market. Villagers built a health clinic, with local materials and some supplied by the project. The government will provide the drugs. With the help of a soil scientist from Columbia University, a Kenyan soil expert, and agricultural extension workers, farmers have planted leguminous trees and plants to supply natural fertilizer. (*New York Times*, news article, April 4, 2005; editorial, May 5, 2005.)
 Sachs reports that in one growing season farm output in Sauri tripled. “With a scaled response, Africans could enjoy a 21st-century Green Revolution, tripling the continent’s food yields and escaping the chronic cycle of hunger, poverty and disease.” (“Four Easy Pieces,” op-ed, *New York Times*, June 25, 2005)
 Koraro in Ethiopia is home to 5,000 people. Half of the 1,500 children are underweight and malnourished. Few households have access to clean water. “The rest,” writes Helene Cooper, “walk four miles round-trip to haul buckets of dirty water, and the water-borne illnesses they carry, into their homes for drinking, cooking and washing up. There is no electricity, no doctor, no industry, no market ...” But there are four village committees to help implement the poverty reduction plan. These are committees for health, a school, energy and water. On the day Cooper visited the village, most able-bodied adults and teenagers were extracting rocks to use as building material for a health clinic. The government will provide technical assistance, including help to build a road. (“In Ethiopian Hills, Five Years to Create Something Out of Nothing,” Editorial Observer, *New York Times*, April 28, 2005).
 In Koraro, the assistance will provide these services: a medical doctor, a nurse, the expansion of a clinic, emergency obstetrical care, malaria control, essential medicines, a village vehicle, cell-phone and Internet connectivity, a diesel generator, a solar panel for the clinic, rainwater harvesting, bore wells for

drinking water, drip irrigation for orchards, rock terraces and trees to rehabilitate degraded landscape, soil nutrient replenishment, organic and inorganic fertilizers, improved crop and tree varieties, school meals from locally produced food, and the necessary training. ("Saving Lives in Africa," letter to the Editor, *New York Times*, May 5, 2005.

18. Nancy Birdsall, Dani Rodrik and Arvind Subramanian, "How to Help Poor Countries," *Foreign Affairs*, July/August, 2005.

19. As one concrete example, *Foreign Policy* reports: "Last year, the United States Treasury raised \$1.87 billion in revenue from tariffs imposed on imports from the four major tsunami-affected countries—India, Indonesia, Sri Lanka, and Thailand. That is twice the \$908 million in aid the U.S. Congress approved in May. In effect, the U.S. will recoup its entire aid package to tsunami victims within six months." ("Ranking the Rich," the third annual CGP/FP Commitment to Development Index, *Foreign Policy*, September/October, 2005.

20. "Reflections on 'Our Common Interest,' The Report of the Commission on Africa," Testimony before the Senate Committee on Foreign Relations, May 17, 2005.

21. "Necessary Measures," op-ed, *New York Times*, September 13, 2005.

22. Sachs, p. 289.

23. *Foreign Affairs*, July/August, 2005.

