Statement by Dr. Julie L. Hall
Medical Officer
World Health Organization

5 May 2003

Before the
Subcommittee on National Security, Emerging Threats, and International Relations
Committee on Government Reform
U.S. House of Representatives

The role of global surveillance in protecting nations from the evolving infectious disease threat

This statement provides a brief overview of the dynamics of the infectious disease threat, explains the role of global surveillance as a defense strategy, and describes the systems now in place for detecting outbreaks early and mounting a strong response. The example of severe acute respiratory syndrome, or SARS, is used to illustrate the strengths and weaknesses of these systems when confronted with an especially challenging new disease. Lessons learned from the evolving SARS outbreak are then used to assess global capacity to respond to other infectious disease threats, most notably the next influenza pandemic and the possible deliberate use of biological agents to cause harm. Priority areas for urgent improvement are identified and discussed.

The dynamics of the infectious disease threat

Continual evolution is the survival mechanism of the microbial world. Infectious disease agents readily and rapidly multiply, mutate, adapt to new hosts and environments, and evolve to resist drugs. This natural propensity to change has been greatly augmented by the pressures of a crowded, closely interconnected, and highly mobile human population, which has given infectious agents unprecedented opportunities to exploit. The result has been an equally unprecedented emergence of new diseases, resurgence of older diseases, and spread of resistance to a growing number of antimicrobials over the past three decades.

As adversaries, microbial pathogens have particular advantages in terms of invisibility, mobility, adaptability, and silent incubation periods that render national borders

meaningless. Infectious agents, incubating in symptomless air travellers, can move between any two cities in the world within 36 hours and slip undetected past any border. They can also be transported over long distances by migratory birds, again rendering national borders meaningless. Disease vectors, hidden in cargoes or riding in the cabins or luggage holds of airplanes, can likewise enter new territories undetected and establish permanent residence there. Vulnerability to these threats is universal and has been amply demonstrated in practice.

Some examples A few recent examples illustrate both the geographical sweep of the infectious disease threat and the specific ways in which emerging and re-emerging diseases strain global and national capacity.

- The threat posed by drug resistance is ominous and universal. Health care in all countries is now compromised by the shrinking number of effective first-line antimicrobials and the need to resort to more costly, and often more hazardous, alternative drugs, when available. Drug resistance to common bacterial infections is now so pervasive that it raises the specter of a post-antibiotic era in which many life-saving treatments and routine surgical procedures could become too risky to perform.

- A new strain of epidemic meningitis emerged in 2002, defying emergency preparedness as conventional vaccines proved to be ineffective. The new strain struck again in early 2003, necessitating emergency arrangements with the pharmaceutical industry and funding agencies to produce sufficient quantities of an effective and affordable vaccine. Despite this effort, the supply has been inadequate to protect all at-risk populations. The result: close to 6,000 cases of a diseases that causes permanent brain damage in up to 20% of cases, and more than 800 deaths.

- The invariably fatal variant Creutzfeldt-Jakob disease, first recognized in 1996 and probably transmitted to humans through beef, has defied the best scientific efforts to develop a treatment or cure. Although the number of cases has been small, the new disease shook public confidence in the meat supply in ways that are still being felt.

- Year by year, the highly unstable influenza virus is a reminder of the ever-present threat of another lethal influenza pandemic that could stretch global capacity – in terms of manpower, hospital beds, vaccine development and production, and supplies of antiviral drugs – to its limit.

These developments have eroded past confidence that high standards of living and access to powerful medicines could insulate populations in wealthy countries from infectious disease threats abroad. They have also restored the historical significance of infectious diseases as a disruptive force – this time cast in a modern setting characterized by the close interdependence of nations, rapid international travel, and instantaneous communications. As a result, outbreaks of new and epidemic-prone diseases have consequences that extend far beyond the sphere of public health to affect economies and, in some cases, disrupt social stability. These consequences likewise extend beyond the individually affected countries to have repercussions felt around the world.

The role of global surveillance

Defense against the infectious disease threat ultimately depends on early detection and rapid intervention. For emerging diseases to be contained and epidemics prevented, protective and preventative measures need to be instigated quickly. Because of the world's interdependence and high mobility, the window of opportunity to prevent international spread is often very short and an outbreak in one corner of the world can quickly become an epidemic in another.

Global surveillance provides a mechanism by which information about potential biological threats can be gathered from all parts of the world, analyzed and disseminated rapidly. It provides an early warning system for the international community and can give unaffected areas the time that would not otherwise be available to prepare and prevent further spread of the disease. The pooling of information from different countries also allows a more comprehensive picture of an emerging threat to be developed than would be available from one single national source. Such information often provides vital early clues about the nature of an emerging infection and the types of control methods that are most likely to be effective.

Ideally, national and local surveillance systems would be the strong base of this global system and give it great sensitivity and speed. However, national surveillance systems around the world, in wealthy as well as developing countries, suffer from a long history of underfunding. In many developing countries, including those where new infectious diseases most frequently emerge, surveillance is patchy outside large disease control programmes, such as those for AIDS, tuberculosis and malaria, and reporting is slow, incomplete and unreliable. As a further problem, some countries are reluctant to reveal the presence or true magnitude of an outbreak for fear of the economic consequences. In a sense, then, the practical measures being taken by WHO to institute and improve global surveillance and international response are currently having to compensate for weaknesses in many national systems while also encouraging improvements in those national systems. Action simply must be taken, however, given that we all live in a world where biological threats, including emergence of new diseases, more virulent forms of old diseases or deliberately released pathogens, are real possibilities.

Systems now in place

Since 1997, WHO has been building up an integrated operational system for strengthening global defense against the transboundary threat posed by outbreaks and epidemics. The system is centrally co-ordinated by a team at WHO headquarters in Geneva and supported by a "virtual" network architecture. This Global Alert and Response system gives priority to prompt detection and rapid containment of outbreaks, with improved surveillance as the cornerstone. Defense relies on a three-pronged approach: combating known risks, detecting and responding to unexpected events, and continually improving global and national preparedness. The system is constantly being strengthened as experience is gained, new mechanisms are developed, and new electronic

tools become available. The whole system benefits from the presence of WHO offices in 141 countries and the fact that 192 countries are member states of WHO.

Global Outbreak Alert and Response Network (GOARN) In April 2000, WHO formally launched the Global Outbreak Alert and Response Network (GOARN) as a mechanism to link together, in real time, 110 existing organizations and networks which together possess much of the data, expertise, and skills needed to keep the international community alert to outbreaks and ready to respond. By electronically linking together existing networks the World Health Organization is able quickly to learn of significant events and to mobilize verification and response activities in spite of WHO's limited resources.

From January 1998 through March 2002, the WHO has investigated 538 outbreaks of international concern in 132 countries. The most frequently reported outbreaks were of cholera, meningitis, haemorrhagic fever, anthrax, and viral encephalitis. During the past two years, WHO, working with partners from the Global Outbreak Alert and Response Network, has launched broad and effective international containment activities in Afghanistan, Bangladesh, Burkina Faso, China, Cote d'Ivoire, Republic of Congo, Egypt, Ethiopia, Gabon, Hong Kong SAR, Kosovo, India, Madagascar, Pakistan, the Philippines, Saudi Arabia, Sierra Leone, Senegal, Singapore, Sudan, Tanzania, Uganda, Viet Nam, and Yemen.

The U.S. government continues to be a valuable partner for WHO in developing global alert and response capabilities and participating in the GOARN network. Various U.S. government agencies contribute to this effort, in line with their specialized capabilities and the particular threat being addressed. Most extensive is WHO's long tradition of reliance on the practical experience, technical expertise, and staff resources of the Centers for Disease Control and Prevention (CDC) to conduct a range of fundamental activities needed to contain the international spread of infectious diseases. This collaboration has become even closer and more vital as the number of outbreaks requiring an international response continues to escalate. The recent establishment of the Global Emerging Infections Surveillance and Response System (GEIS) within the Department of Defence is another especially welcome resource for expanding the global reach of surveillance, research, training, and access to high-quality laboratory support. USAID also supports WHO surveillance activities, particularly the strengthening of national capacities.

Such practical assistance can be invaluable. For example, when an outbreak is caused by a previously unknown or highly pathogenic organism, certain activities, such as sampling and analysis for definitive identification of the agent, must be carried out by experienced specialists and frequently require the security of biosafety level III or IV laboratories. In this regard, the WHO global network of more than 270 collaborating institutes and laboratories with expertise in infectious diseases, including 40 housed in CDC, provides a vital resource. Moreover, the sharing of such resources is a far more cost-effective option than attempting to build highly specialized capacity in an enlarged number of countries.

Real-time disease intelligence One of the most powerful new tools for gathering epidemic intelligence is a customized search engine that continuously scans world Internet communications for rumors and reports of suspicious disease events. This is the Global Public Health Intelligence Network (GPHIN), a computer application developed by Health Canada and used by WHO since 1997. GPHIN operates as a sensitive real-time early warning system by systematically searching for key words in over 950 news feeds and electronic discussion groups around the world. Human review and computerized text mining are used to filter, organize and classify the more than 18,000 items it picks up every day, of which around 200 merit further analysis by WHO.

In outbreak alert and response, every hour counts, as the window of opportunity for preventing deaths and further spread closes quickly. GPHIN has brought tremendous gains in timeliness over traditional systems in which an alert is sounded only after case reports at the local level progressively filter to the national level before being formally notified to WHO. GPHIN currently picks up – in real time – the first hints of about 40% of the roughly 200 to 250 outbreaks subsequently investigated and verified by WHO each year. While the early alert to outbreaks of genuine concern is most important, GPHIN also allows WHO to step in quickly to refute unsubstantiated rumors before they have a chance to cause social and economic disruption.

During outbreak response, WHO uses a custom-made geographical mapping technology to assist in the location of cases and rapid analysis of the epidemic's dynamics. This epidemiological mapping technology is also used to predict environmental and climatic conditions conducive for outbreaks. An event management system, introduced in 2001, is now used to gather and communicate data throughout the course of outbreak investigation and response. The system generates a dynamic picture of operations, aids organization of logistics, and provides a systematic way to prepare better, respond faster, and manage resources more effectively.

Preparedness mechanisms: stockpiling of supplies For outbreaks of some diseases, control depends on the rapid immunization of populations that can number in the millions and has, in the past, completely exhausted vaccine reserves and created international crises. For epidemic meningitis, WHO established in 1997 a coordinating mechanism, engaging research institutes and manufacturers, that maintains an emergency stockpile of vaccines and other supplies, oversees their distribution, and also works to forecast epidemics and reduce the price of vaccines. To date, 9.8 million doses of meningococcal vaccine have been distributed through this mechanism. In 2001, a similar mechanism for yellow fever vaccine facilitated the emergency management of a large urban outbreak, averting an estimated 30,000 deaths. Most recently, WHO, assisted by industry and the Bill and Melinda Gates Foundation, has made a new meningitis vaccine available to African countries just months (instead of the usual years) after detection of an emerging epidemic caused by a new strain of the pathogen.

Privileged access to countries WHO staff, consultants, and expert advisers have privileged access to all 192 member states. This privilege allows WHO, in the interest of safeguarding international health, to transcend the prevailing political reality in which access to critical expertise might be denied because of one country's political relationship

with others. On many occasions, the Organization's ability to secure UN laissez-passer status has proved decisive in getting CDC and other U.S. experts quickly and smoothly into countries where, for diplomatic reasons, entrance might otherwise be delayed or denied. This ability to obtain privileged visa status can be extended to all security-cleared partners who become members of a WHO response team.

WHO also has unique and permanently positioned geographical resources. These include six regional offices and an additional 141 country offices, located within or in close proximity to ministries of health. Although the size of these offices varies according to the disease situation in the country concerned, all offices are staffed with medical experts and often with epidemiologists, and all have the essential logistic equipment, including vehicles and local communications, needed for the prompt on-the-scene investigation of a suspected outbreak. In the event of an outbreak of urgent international concern, WHO country offices facilitate the arrival of international assistance by arranging flights, customs and immigration clearance, and accommodation. All offices are now electronically linked to WHO and thus to its global network of institutional resources and collaborators.

SARS: an especially demanding test of global capacity

SARS demonstrates dramatically the global havoc that can be wreaked by a newly emerging infectious disease. It has also been an extremely demanding test of the effectiveness of WHO and its partners in GOARN to mount an adequate response, get teams and supplies into countries, and ensure adequate monitoring and reporting. The urgency of SARS has further challenged WHO to set in motion high-level international scientific and medical collaboration in which natural competition for publication and prestige is set aside in order to identify the SARS causative agent with unprecedented speed and to develop diagnostic tests and effective treatment protocols.

At this moment, public health authorities, doctors, nurses, scientists, and laboratory staff around the world are struggling to cope with SARS at a time when some hope remains that the disease might still be contained. Economists and market analysts are simultaneously struggling to calculate the present and future costs, initially estimated at $30 billion in the Far East alone. Public panic is widespread, some government officials have lost their jobs, and social stability has been jeopardized in some of the hardest hit areas. Hospitals, schools, and borders have been closed, and several governments have advised their citizens not to travel to hard-hit areas. "Hot zones" of particular concern have included Toronto, Hong Kong, Singapore, Taiwan, Beijing and, increasingly, much of the rest of China. With the exception of Taiwan, all of these areas belonged to the first wave of outbreaks, prior to the WHO global alert issued on 15 March. Viet Nam, another country in the initial wave of outbreaks, became the first country to control its SARS outbreak on 28 April.

SARS is the first severe and easily transmissible new disease to emerge in the 21st century. Though much about the disease remains poorly understood and frankly puzzling, SARS has shown a clear capacity for rapid spread along the routes of international air

travel. WHO regards every country with an international airport, or bordering an affected area, as at potential risk of an outbreak.

On 21 February, SARS was carried out of Guangdong Province, China by an infected medical doctor who had treated patients in his home town. He brought the virus to the ninth floor of a four-star hotel in Hong Kong. Days later, guests and visitors to the hotel's ninth floor had seeded outbreaks of cases in the hospital systems of Hong Kong, Viet Nam, and Singapore. Simultaneously, the disease began spreading around the world along international air travel routes as visitors at the hotel travelled home to Toronto and elsewhere, and as other medical doctors who had treated the earliest cases in Viet Nam and Singapore travelled internationally for medical or other reasons.

The number of probable SARS cases passed the 6000 mark on Friday 2 May, with 27 countries reporting cases from five continents. More than 400 deaths have occurred. China is reporting a cumulative total of probable cases that is approaching 4000 as each day's nationwide reporting adds at least 100 new cases. Although outbreaks in Hong Kong, Singapore, and Toronto show signs of having peaked, new cases and deaths continue to be reported. Taiwan, with a rapidly growing number of cases and deaths, is a worrisome new development.

A particularly serious threat SARS needs to be regarded as a particularly serious threat for several reasons. The disease has no vaccine and no treatment, forcing health authorities to resort to control tools dating back to the earliest days of empirical microbiology: isolation and quarantine. The virus comes from a family notorious for its frequent mutations, raising important questions about the future evolution of outbreaks and prospects for vaccine development. Epidemiology and pathogenesis are poorly understood. All available diagnostic tests have important limitations. If tests are poorly conducted or results wrongly applied, patients excreting virus and thus capable of infecting others can slip through the safety net of isolation and infection control. The disease continues to show a disturbing concentration in hospital staff – the human resource vital to control. A significant proportion of patients require intensive care, thus adding to the considerable strain on hospital and health care systems. Evidence is mounting that certain source cases make a special contribution to rapid spread of infection. SARS has an incubation period that allows rapid spread along international air-travel routes.

With the notable exception of AIDS, most new diseases that emerged during the last two decades of the previous century or have become established in new geographical areas have features that limit their capacity to pose a major threat to international public health. Many (avian influenza, Nipah virus, Hendra virus, Hanta virus) failed to establish efficient human-to-human transmission. Others (*Escherichia coli* O157:H7, variant Creutzfeldt-Jakob disease) depend on food as a vehicle of transmission. Diseases such as West Nile fever and Rift Valley fever that have spread to new geographical areas require a vector as part of the transmission cycle. Still others (*Neisseria meningitidis* W135, and the Ebola, Marburg, and Crimean-Congo haemorrhagic fevers) have strong geographical foci. Although outbreaks of Ebola haemorrhagic fever have been associated with a case-

fatality rate in the range of 53% (Uganda) to 88% (Democratic Republic of the Congo), person-to-person transmission requires close physical exposure to infected blood and other bodily fluids. Moreover, patients suffering from Ebola during the period of high infectivity are visibly very ill and too unwell to travel.

The SARS response To date, the global response, coordinated by WHO and strongly supported by CDC, has been designed to rapidly seal off opportunities for SARS to establish itself as a common disease. The initial emergency plan, mapped out in mid-March, called for an attack on the ground and in the "air". On the ground, WHO sent teams of experts and specialized protective equipment for infection control in hard-hit hospitals to countries requesting such assistance. In the "air", WHO used the model of its electronically interconnected global influenza network to quickly establish a similar "virtual" network of 11 leading laboratories, connected by a shared secure website and daily teleconferences, to work around the clock on identification of the SARS causative agent and development of a robust and reliable diagnostic test. This network, in turn, served as a model for similar electronically linked groups set up to pool clinical knowledge and compare epidemiological data. WHO also decided to issue daily updates on its website to keep the general and travelling publics informed and, to the extent possible, counter rumors with reliable information.

On 15 March, based on information from WHO country offices and GOARN partners, followed by risk analysis by the WHO headquarters operational team, WHO issued a rare emergency travel advisory designed to alert national authorities, medical personnel, and travelers to an emerging threat that was quickly taking on international dimensions. Global vigilance was immediately heightened, with the result that most countries subsequently reporting cases have managed, through prompt detection, isolation and good infection control, to prevent the scale of transmission experienced in the SARS "hot zones". On 2 April and again on 19 April, WHO issued the toughest travel advisories in its 55-year history when it recommended postponement of all but essential travel to designated high-risk areas.

WHO teams continue to provide operational support and specialized expertise in the most seriously affected areas. Requests for additional country assistance continue to be received, most notably from authorities in China. Abundant additional support is available to all through information posted at the WHO website (www.who.int/csr/sars). Guidance ranges in nature from forms for collecting and reporting data, through guidelines for clinical management and infection control in hospitals, to the materials for local production of diagnostic tests. The evolution of the outbreak is constantly and closely monitored and daily updates are posted on the website. On 17 April, exactly a month after its establishment, the laboratory network announced conclusive identification of the SARS causative agent: a new coronavirus unlike any other known human or animal virus in its family. The laboratory reagents needed to calibrate, standardize and assure the quality of laboratory tests are being made available by WHO, at no cost, to laboratories designated by ministries of health.

Learning from SARS: how to prepare for other emergencies caused by infectious diseases

When the first suspected SARS cases began appearing in the U.S., many hospital staff cited the WHO advisory, and their subsequent high-level of awareness, as one reason why cases were quickly detected and isolated, with the result that further transmission was either avoided entirely or kept to a very small number of cases. A second explanation offered for the comparatively mild and well-contained SARS situation in the U.S. is the high level of nationwide planning and preparedness that followed the deliberate distribution of anthrax-tainted mail in the US postal system in October 2001.

The International Health Regulations provide the legal framework for global surveillance and reporting of infectious diseases and a mechanism by which measures to prevent international spread can be enforced. The regulations, which are currently undergoing a substantial revision, will be discussed by Ministers of Health at the World Health Assembly later this month. The SARS outbreak provides firm evidence of the need for such regulations and concrete examples of the areas in which revision and updating are urgently needed.

The novel nature of the SARS virus created an extra step in the containment response: scientific identification and characterization of the causative agent to allow development of a diagnostic test, treatment protocols, and a scientifically sound basis for recommending control measures. Experience with SARS has shown that, with strong global leadership by WHO, scientific expertise from around the world can work in a very effective collaborative manner to identify novel pathogens. This function would be invaluable in the event of the deliberate release of a biological agent or during future emergence of a novel or poorly understood pathogen.

WHO is continuing its aggressive containment activities aimed at preventing SARS from becoming a widely established threat. The immediate scientific priorities include developing a robust and reliable diagnostic test, improving our understanding of the modes of transmission and identifying effective treatment regimes. If, in spite of best efforts, the disease does become endemic, WHO and its international partners will have to settle in for a long and difficult fight. In this case, existing mechanisms developed for other public health emergencies, such as the Medicines for Malaria Venture, the Global Alliance for Vaccines and Immunization, the Global TB Drug Facility, and the International Coordinating Group for meningitis and yellow fever, would have to be looked to as possible models for ensuring the rapid development of SARS drugs and vaccines and equitable access in all at-risk countries. Use of the influenza network as a model for the SARS laboratory network suggests that such an approach brings great speed as well as efficiency.

Lessons for the future

Just as the SARS response has been guided by lessons learned during preparedness planning for the next influenza pandemic and for a possible bioterrorist attack, both of these types of potential public health emergencies will benefit from lessons learned as the international response to SARS continues.

The response to SARS has already brought to light a number of positive lessons as well as highlighted a number of challenges for future preparedness planning. The SARS experience has shown the capacity of global alerts, widely supported by a responsible press and amplified by electronic communications, to improve global vigilance and awareness at all levels, from health professionals and national authorities, to politicians and the travelling public. The quick detection and reporting of the first cases in South Africa and India are indicative of the high level of global awareness and the vigilance of the world's health systems. The present climate of high alert also helps explain the speed with which developing countries – from Namibia to Mozambique – have readied their health services with preparedness plans and launched SARS campaigns, often with WHO support, to guard against imported cases.

The SARS experience in Viet Nam has shown that immediate political commitment at the highest level can be decisive. Viet Nam demonstrated to the world how even a very poor country, hit by an especially large and severe outbreak, can triumph over a disease when reporting is prompt and open and when WHO assistance is quickly requested and fully supported.

And finally, stimulation of very rapid, high-level research has been seen clearly to be a key component of an effective response.

The key challenges to be addressed in future planning are those of surge capacity and transparency. Inadequate surge capacity in hospitals and public health systems has clearly been a major problem, especially when health care workers have themselves been victims of the disease and are the frontline troops at risk. The shortage of expert staff to co-ordinate national and global responses to a rapidly evolving public health emergency is also an issue needing investment and attention.

SARS is now known to have begun in mid-November in a southern province of China. Cases during the earliest phase of the SARS outbreak there were not openly reported, thus allowing a severe disease to become silently established in ways that made further international spread almost inevitable. This is the most important lesson for all nations: in a globalized, electronically connected world, attempts to conceal cases of an infectious disease, for fear of social and economic consequences, must be recognized as a short-term stop-gap measure that carries a very high price – loss of credibility in the eyes of the international community, escalating negative domestic economic impact, damage to the health and economies of neighboring countries, and a very real risk that outbreaks within the country's own territory can spiral out of control.

The SARS experience also has some lessons about the importance of international collaboration and strong but politically neutral global leadership. Though exceptional in terms of its impact, severity, rapid international spread, and many puzzling features, SARS is only one of around 50 internationally important outbreaks to which WHO and its partners respond in any given year. The high level of medical, scientific, political, and public attention focused on SARS is helping the world to understand the severity of the infectious disease threat and the importance of international solidarity in the face of this threat. It is also helping the world to understand the importance of global leadership and of politically neutral and privileged access to all affected countries. Finally, the response to the SARS outbreak is helping the public to understand that WHO's activities of global coordination, capacity development, communications, and mobilizing expertise enable rapid response and actually save lives. To date, in the vast majority of countries, these activities have helped health authorities confronted with imported cases prevent a SARS outbreak and thus avoid the devastating consequences seen elsewhere.

Improving infectious disease surveillance and response is indeed a matter of "national security, emerging threats and international relations" as this Subcommittee's name implies. Global public health security will continue to require effective leadership and action at a global level by WHO and its partners.