# **Appendix 9A.** International public health diplomacy and the global surveillance of avian influenza

## **BERNICE RAVECHÉ**

# I. Introduction

Experts widely agree that another influenza pandemic is on the horizon. The pressing questions are when, where and in which form a strain of avian influenza, a variation of the H5N1 virus, will cause a pandemic in humans. Influenza has caused some of the most devastating epidemics in human history. The influenza pandemic between 1918 and 1919, known as the Spanish flu, claimed an estimated 40–100 million lives and was the result of a strain of avian influenza, H1N1, in the same family of viruses as H5N1.<sup>1</sup> Scientists state that an avian influenza pandemic could be a precursor to a 1918-like pandemic, which could seriously affect the world's population. According to mathematical models based on the lack of human immunity to the H5N1 virus and the current mortality rate of the virus, an avian influenza pandemic could claim more than 100 million lives.<sup>2</sup> Although vaccines can combat seasonal influenza outbreaks and more advanced disease surveillance systems exist now than in 1918, an avian influenza pandemic presents enormous potential challenges to global health and security.

The process of globalization has multiplied the quantity and types of international flows of people and goods. The recognition that globalization can have negative as well as positive effects is contributing to an evolving approach to security that emphasizes the role of governance in safeguarding the basic functions of modern societies against a variety of potential threats. These threats are not limited to deliberate and malicious acts. This approach has not been fully conceptualized, but it is described and analysed in an emerging literature under various headings such as 'functional security', 'societal security' or 'human security'. According to this approach, security policy consists of marshalling the resources available to prevent or, if prevention fails, to respond effectively to events that jeopardize the safety of people and the areas where they live. This requires many public agencies as well as private actors to cooperate in new configurations to create and maintain the safety of these areas, which need not necessarily coincide with national borders.

Globalization has already had an impact on the nature and spread of infectious diseases, as reflected in the outbreak of severe acute respiratory syndrome (SARS) in 2003.<sup>3</sup> This impact is likely to grow as more and more parts of the world are drawn into transnational cooperation networks. The SARS outbreak underlined the need for international collaboration and communication between different parts of the global

<sup>&</sup>lt;sup>1</sup> Thomas, J. K. and Noppenberger, J., 'Avian influenza: a review', *American Journal of Health-System Pharmacy*, 15 Jan. 2007, pp. 149–65.

<sup>&</sup>lt;sup>2</sup> Thomas and Noppenberger (note 1).

<sup>&</sup>lt;sup>3</sup> Njuguna, J. T., 'The SARS epidemic: the control of infectious disease and biological weapon threats', *SIPRI Yearbook 2004: Armaments, Disarmament and International Security* (Oxford University Press: Oxford, 2004), pp. 697–712.

public health community as well as the need for political cooperation. While the SARS outbreak was contained relatively quickly, the initial response of governments showed that international cooperation cannot be taken for granted.

Given the potential for globalization to cause or exacerbate public health problems in different parts of the world, the World Health Organization (WHO) is likely to play an important role in any collective effort to build societal security. The WHO's role in governing global health is changing, as evidenced by the revised International Health Regulations (IHR) that were adopted in 2005 and began to be implemented in June 2007.<sup>4</sup> The revised IHR give the organization a historically unprecedented degree of authority over member states and their disease surveillance, response and reporting systems. The new IHR have serious implications for the actions required of countries with cases of SARS and H5N1. This appendix explores the political and economic issues associated with the prevention and control strategies for avian influenza, primarily addressing the issues related to vaccine research and development. It uses Indonesia as an example of a developing country's reluctance to adhere to WHO guidelines and recommended actions.

Section II provides a brief background of the WHO and discusses its changing role in governing global health in accordance with the revised IHR. Section III briefly describes influenza, its epidemiology and the global outbreak situation since 2003. It also outlines the current primary and secondary prevention strategies to control an avian influenza outbreak in poultry, which have been gathered from a review of literature from scientific journals, the WHO, the United Nations Food and Agriculture Organization (FAO), the World Organization for Animal Health (Office International des Epizooties, OIE) and the United States Centers for Disease Control and Prevention (CDC). Section IV is a case study of Indonesia that discusses the current outbreak situation, past and present strategies implemented by the Indonesian Government to control and prevent an avian influenza outbreak in animals and humans, and the associated challenges. The case study also provides a timeline of events, from the Government of Indonesia's initial refusal to send virus samples to the WHO up to its decision in early 2008 to send avian influenza samples to a WHO laboratory. The conclusions are presented in section V.

# II. The changing role of the World Health Organization

The WHO's primary roles and responsibilities include 'providing leadership on matters critical to health ... shaping the research agenda ... setting norms and standards and promoting and monitoring their implementation, articulating ethical and evidence-based policy options; providing technical support ... and monitoring the health situation'.<sup>5</sup> Established in 1946 as a specialized UN agency, the WHO is undergoing an identity crisis because of its drastically changing role, the increased authority granted to it by the IHR and, most importantly, the increasing influence of global health trends on domestic and foreign policy. The WHO is not the only international organization that is dedicated to global health security, but it is the only such organization that is well connected with the ministries of health of almost every

<sup>&</sup>lt;sup>4</sup> World Health Organization (WHO), Fifty-eighth World Health Assembly, Resolution WHA58.3: Revision of the International Health Regulations, 23 May 2005, <a href="http://www.who.int/csr/ihr/IHRWHA58\_3-en.pdf">http://www.who.int/csr/ihr/IHRWHA58\_3-en.pdf</a>>.

<sup>&</sup>lt;sup>5</sup> WHO, 'The role of the WHO in public health', <http://www.who.int/about/role/en/>.

country, making it a crucial stakeholder in protecting and enhancing global public health security.

The WHO was established on the principle that 'the health of all peoples is fundamental to the attainment of peace and security and is dependent upon the fullest co-operation of individuals and States'.<sup>6</sup> In its early history the WHO primarily focused on improving the health of people in developing countries in order to facilitate commerce and economic growth in both the developing and developed world. The predecessor to the IHR was created in 1903 in order to control diseases spread in ports and by ships engaged in international trade. In their earliest form the IHR only applied to cholera and the plague but in 1912 and 1926 yellow fever, typhus, relapsing fever and smallpox were added to the list of reportable diseases.<sup>7</sup> After the WHO was created, the IHR fell under the WHO's mandate, and it gained the sole right to modify and implement them. Except for the WHO's massive campaign to eradicate smallpox in the late 1960s and early 1970s, the IHR have never been fully implemented or adopted by states because of the fear of economic retribution or embargo on a country's goods and services if it reported an outbreak of smallpox or another of the deadly diseases listed in the IHR. The 2003 SARS outbreak, the HIV/ AIDS pandemic and avian influenza have prompted the WHO to revise the IHR again in the hope that states will implement them in a timely manner and abide by this legal framework in order to increase global public health security.

### The revised International Health Regulations

The revised International Health Regulations were adopted on 23 May 2005 and implemented on 15 June 2007. Because of the IHR's long history of ineffectiveness and non-compliance by a minority of member states, the WHO revised the IHR using a legal framework that gives the WHO an unprecedented legal authority over the global disease surveillance and reporting requirements of the member states. The revised IHR take an all-risks approach to diseases. States are to report all events that could result in public health emergencies of international concern, including those caused by chemical agents, contaminated food and radioactive material. The revised IHR also give the director-general of the WHO the authority to ascertain when a disease is considered a global public health threat or emergency.

Under the revised IHR, states are required to notify the WHO within 24 hours of an emerging global health threat that has not been encountered previously. This rapid notification system is intended to promote timely information sharing among member states in the event of an infectious disease outbreak. When Indonesia refused to send samples to the WHO in 2003, the revised IHR had not yet begun to be implemented, but the revised notification system was designed to protect the health of the global population by preventing states from taking similar actions. Furthermore, each state is required to 'develop, strengthen and maintain core national public health capacities', with the additional creation of a national IHR focal point, which is designed to assess, report and respond promptly to public health risks and emergencies. The revised IHR also require the WHO to share non-governmental data sources with member states and related international organizations to enable a coordinated and appropriate

<sup>&</sup>lt;sup>6</sup> WHO, Constitution of the World Health Organization, Oct. 2006, <a href="http://www.who.int/governance/eb/constitution/en/">http://www.who.int/governance/eb/constitution/en/</a>, preamble.

<sup>&</sup>lt;sup>7</sup> Zacher, M., 'The transformation in global health collaboration since the 1990s', eds F. C. Cooper, J. J. Kirton and T. Schrecker, *Governing Global Health* (Ashgate: Burlington, Vt., 2007), pp. 16–27.

response to an emerging public health risk. Utilizing non-governmental sources of data was useful to the WHO during the SARS outbreak.<sup>8</sup> Recognizing the importance of non-governmental sources of data in the revised IHR will help to promote the WHO's Global Outbreak Alert and Response Network (GOARN) and encourage international scientists and researchers to share valuable information.<sup>9</sup>

The revised IHR reflect a shifting paradigm in global health as well as the changing role of the WHO. In the WHO's *World Health Report 2007* global public health is discussed solely in terms of a securitization paradigm.<sup>10</sup> The driving motivation for the revision of the IHR was to strengthen international public health security which, according to the WHO, is contingent upon strengthening countries' disease surveillance and response systems to ensure timely management of public health risks.<sup>11</sup> In June 2007, in order to guide the implementation of the revised IHR, the WHO published a strategy for implementation and identified four strategic actions that countries must complete: action 1, to 'strengthen national disease surveillance, prevention, control and response systems'; action 2, to 'strengthen public health security in travel and transport'; action 3, to 'strengthen WHO global alert and response systems'; and action 4, to 'strengthen the management of specific risks'.<sup>12</sup>

This implementation plan for the revised IHR relies on a coordinated and established public health infrastructure that many developing countries still lack. The WHO dealt sparingly with incentives or sanctions that countries will receive if they follow the revised IHR or choose not to adhere to this action plan. More importantly, it does not address how countries are to fund the required projects. In a 2007 article, Phillipe Calain discusses the barriers to implementation of the revised IHR on the grounds that they threaten state sovereignty. He argues that international political commitment to comply with the revised IHR is negatively affected by 'perceived threats to sovereignty, blurred international health agendas, lack of internationally recognized codes of conduct for outbreak investigations and erosion of the impartiality and independence of international agencies' (mainly referring to the WHO).<sup>13</sup>

# III. Background on avian influenza

Influenza viruses are categorized into three types: A, B and C.<sup>14</sup> Only influenza A and B viruses can cause disease in humans. Influenza A is the type that causes seasonal

<sup>8</sup> Fidler, D. P. and Gostin, L. P., 'The new international health regulations: an historic development for international law and public health', *Journal of Law, Medicine & Ethics*, vol. 34, no. 1 (spring 2006), pp. 85–96.

<sup>9</sup> The WHO created GOARN in Apr. 2000. It provides an international network for the technical coordination of international alert and response activities for both governmental and non-governmental data sources.

<sup>10</sup> WHO, World Health Report 2007—A Safer Future: Global Public Health Security in the 21st Century (WHO: Geneva, 2007), <a href="http://www.who.int/whr/2007/en">http://www.who.int/whr/2007/en</a>.

<sup>11</sup> WHO, *Global Collaboration to Meet Threats to Public Health Security* (WHO: Geneva, 2007), <http://www.who.int/whr/2007/overview/en/index2.html>.

<sup>12</sup> WHO, International Health Regulations (2005): Areas of Work for Implementation (WHO: Geneva, June 2007), <a href="http://www.who.int/csr/ihr/area\_of\_work/en>">http://www.who.int/csr/ihr/area\_of\_work/en></a>.

<sup>13</sup> Calain, P., 'Exploring the international arena of global public health surveillance', *Health Policy* and *Planning*, vol. 22 (2007), pp. 13–20.

<sup>14</sup> Influenza viruses belong to the orthomyxovirus family and are spherical or tubular enveloped viruses containing an 8-segmented negative sense RNA genome within a matrix  $(M_1)$  and membrane  $(M_2)$  protein shell. The RNA genome is associated with a nucleoprotein and a transcriptase protein. Influenza types A, B and C are differentiated by their  $M_1$  and  $M_2$  proteins and nucleoproteins.

Country	2003		2004		2005		2006		2007		Total	
	С	D	C	D	С	D	С	D	С	D	С	D
Azerbaijan	0	0	0	0	0	0	8	5	0	0	8	5
Cambodia	0	0	0	0	4	4	2	2	1	1	7	7
China	1	1	0	0	8	5	13	8	5	3	27	17
Djibouti	0	0	0	0	0	0	1	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	23	6	41	16
Indonesia	0	0	0	0	20	13	55	45	41	36	116	94
Iraq	0	0	0	0	0	0	3	2	0	0	3	2
Laos	0	0	0	0	0	0	0	0	2	2	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	1	1
Pakistan	0	0	0	0	0	0	0	0	1	1	1	1
Thailand	0	0	17	12	5	2	3	3	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	8	5	101	47
Total	4	4	46	32	98	43	115	79	83	55	346	213

Table 9A.1. H5N1 human cases globally, 2003-2007

C = cases; D = deaths.

*Source*: World Health Organization, 'Cumulative number of confirmed human cases of avian influenza reported to WHO', 28 Dec. 2007, <a href="http://www.who.int/csr/disease/avian\_influenza/country/cases\_table\_2007\_12\_28/en>">http://www.who.int/csr/disease/avian\_influenza/country/cases\_table\_2007\_12\_28/en></a>.

influenza, which affects approximately 10–20 per cent of the world's population each year, and can also infect other animal species.<sup>15</sup> It is divided into subtypes, based on the two surface proteins, hemagglutinin (HA) and neuraminidase (NA).<sup>16</sup> These surface proteins are responsible for the infectious capacity of the virus by direct interaction with host cell proteins. Thus, HA and NA govern the host range and specificity of the virus as well as the degree of immune evasion.<sup>17</sup> Using this classification, influenza A strains are named according to their HA subtype followed by their NA subtype, as is the case with the highly pathogenic avian influenza strain H5N1. Currently, 16 HA subtypes and 9 NA subtypes are known. The global human population has no immunity to H5N1 because this strain was previously only present in wild fowl and poultry populations. Humans are therefore susceptible to infection.

Wild fowl are the main reservoir for influenza A viruses. While wild fowl mainly carry influenza A asymptomatically, domesticated birds such as chickens, turkeys and ducks are highly susceptible to the viruses and will develop severe symptoms following infection and have a high mortality rate. The disease caused by H5N1 in humans

<sup>15</sup> WHO, 'Avian influenza: food safety issues', 27 Apr. 2007, <http://www.who.int/foodsafety/micro/avian/en/>.

<sup>16</sup> Influenza B viruses are subdivided into strains, not subtypes, on the basis of the HA and NA composition because influenza B viruses do not cause severe pandemics similar to influenza A. Furthermore, influenza B does not undergo the process of antigenic shift. However, influenza B can cause severe human disease and death. HA and NA are both glyocproteins (proteins carrying large sugar residues with sialic acids) and are anchored to the virus surface membrane.

<sup>17</sup> The term 'host range' refers to the range of species in which a pathogen can cause infections and disease. 'Immune evasion' refers to the lack of specific antibodies towards a novel antigen (i.e. from a new influenza strain carrying mutations).

is clinically more aggressive than seasonal influenza. According to the WHO, there have been 346 human cases of H5N1, of which 213 were fatal (see table 9A.1).<sup>18</sup> The overall case fatality rate thus far has been roughly 60 per cent, with the 10–19 age group suffering the most fatalities. This epidemiological pattern is consistent with the morbidity and mortality trends of the 1918 pandemic, where influenza mostly claimed the lives of young adults ranging in age from 20 to 44.<sup>19</sup> Because the case fatality rate is dependent on the number of H5N1 cases reported, and not all cases are reported, the true case fatality rate of H5N1 will never be known.

The main concern related to human and avian influenza A viruses is their ability to quickly change and adapt their genomes, and hence widen their host ranges. This occurs in two different ways. First, the accumulation of mutations over time that facilitates the evasion of host immune responses through selection is referred to as 'antigenic drift'.<sup>20</sup> Second, genetic reassortment (antigenic shift) between human and animal influenza viruses can occur in an intermediate host.<sup>21</sup> Influenza viruses can infect a wide variety of species, including humans, fowl, swine, horses and sea mammals (e.g. seals). Such infections, in turn, provide ample subtype combinations for novel influenza strains to develop if the opportunity arises. Such a situation is common in many parts of Asia, where domestic poultry and swine may reside in close proximity and be exposed to the excrement of wild migratory birds carrying H5N1 and to human handlers carrying the human subtypes. It is believed that swine are the intermediary reservoir from which aggressive influenza strains emerge. Emerging influenza strains warrant close observation, rapid disease surveillance and reporting because such a reassortment might occur and result in a new strain with high pathogenicity in humans and the capability for rapid human-to-human transmission.

The first documented human cases of H5N1 occurred in 1997 in Hong Kong, where 18 individuals were infected.<sup>22</sup> This outbreak was caused by direct contact with infected poultry. In response to the outbreak in humans and poultry, 1.5 million birds were culled within three days in order to prevent further human infection. This drastic strategy quelled the outbreak in Hong Kong until the surge of H5N1 cases in South East Asia in 2003. The incubation period for seasonal influenza in humans is roughly 2 to 3 days. However, current data suggest that the incubation period for humans infected with H5N1 ranges from 2 to 16 days. Because H5N1 is an emerging infectious disease, there is still a paucity of data and limited evidence about its manifestation in humans and other animal species. This complicates the diagnosis of an individual with H5N1 because symptoms in past patients have ranged from high fever, diarrhoea, vomiting and influenza-like symptoms to acute encephalitis. The efficacy of antivirals like oseltamivir to reduce viral replication and improve survival is

<sup>21</sup> Reassortment in influenza viruses occurs as a result of the genomes segmented nature: the segments can combine with similar segments—even segments from influenza viruses of different origin or host species—thereby producing novel variants of varying HA and NA subtypes.

<sup>22</sup> WHO (note 10), p. 46.

<sup>&</sup>lt;sup>18</sup> These numbers are taken from the last WHO report released in 2007. WHO, 'Cumulative number of confirmed human cases of avian influenza reported to WHO', 28 Dec. 2007, <a href="http://www.who.int/csr/disease/avian\_influenza/country/cases\_table\_2007\_12\_28/en>">http://www.who.int/csr/disease/avian\_influenza/country/cases\_table\_2007\_12\_28/en></a>.

<sup>&</sup>lt;sup>19</sup> Taubenberger J. K., and Morens D. M., '1918 influenza: the mother of all pandemics', *Emerging Infectious Disease*, vol. 12, no. 1 (Jan. 2006), pp. 15–22.

<sup>&</sup>lt;sup>20</sup> Mutations are common, and random, mis-incorporations of nucleotides during the replication of genomes. They are more prevalent in viruses with RNA genomes. Selection refers to Darwinian natural selection where inefficient virus particles will be selected and removed by host immune response or through the creation of defective particles.

limited because this drug needs to be administered within 48 hours of the onset of the illness and, in most cases, the disease is detected and diagnosed in its later stages.

### Primary and secondary prevention strategies

In its 2005 Recommended Strategic Action Plan for responding to the avian influenza pandemic threat, the WHO stated that all of the necessary criteria in order for an avian influenza pandemic to occur had been met—with the exception of the ability for H5N1 to transfer efficiently from person to person.<sup>23</sup> Although there has been one known case of human-to-human transmission among a family in Indonesia, human-to-human transmission has not been sustained in the current strain of the virus. The human transmissibility of H5N1 could be increased through a reassortment event in which genetic material is exchanged between humans and birds during co-infection or through a gradual adaptive mutation process. In order to prevent human exposure to H5N1, countries should primarily focus on controlling the disease in animals and then prevent human behaviour that would expose them to the disease.

However, the main strategies to minimize human contact with birds and excrement are difficult to implement in developing countries with weak public health infrastructure and disease surveillance systems. Additionally, many of the prevention strategies designed to control the H5N1 virus call for dramatic changes in farming strategies and the culling of large numbers of domestic poultry. This has been very difficult to institute in rural South East Asian communities, where poultry is the main source of income as well as food. South East Asian governments, particularly Indonesia, have been unable to compensate farmers for culled poultry. This financial challenge is a major barrier to animal disease prevention strategies. Consequently, farmers have often been reluctant to report sick poultry to government officials. Furthermore, the H5N1 virus has been manifesting itself among domestic ducks that show no signs or symptoms of carrying the illness.

The resistance to culling poultry has, in some cases, been overcome by force, with the military and police carrying out the culling process. As a result, when villagers are aware of a local mandate to cull poultry some have hidden their chickens or quickly sold them at market to avoid loss. At the root of the problem of stopping the spread of infection is simply that many districts lack knowledge about H5N1 and how to prevent infection.

An established public health infrastructure that adheres to current bio-safety and bio-security measures to block the introduction of the virus is necessary to prevent avian influenza from affecting domestic poultry.<sup>24</sup> Primary prevention strategies encompass all levels of domestic poultry production from large, so called sector 1 corporations to smaller sector 4 backyard farms and 'wet markets' (i.e. open food markets). These strategies include routine monitoring of poultry for signs of illness, hygienic poultry butchering practices, routine cleaning of faecal matter from storage and transport facilities as well as mass education to promote bio-safety measures. Once the virus has been identified, the 'stampede method' is recommended during

<sup>&</sup>lt;sup>23</sup> WHO, *Responding to the Avian Influenza Threat: Recommended Strategic Actions* (WHO: Geneva, 2005), <a href="http://www.who.int/csr/resources/publications/influenza/WHO\_CDS\_CSR\_GIP\_2005\_8/en">http://www.who.int/csr/resources/publications/influenza/WHO\_CDS\_CSR\_GIP\_2005\_8/en</a>.

<sup>&</sup>lt;sup>24</sup> See Kuhlau, F., *Countering Bio-threats: EU Instruments for Managing Biological Materials, Technology and Knowledge*, SIPRI Policy Paper no. 19 (SIPRI: Stockholm, Aug. 2007), <http://books.sipri. org/>. Bio-safety is safety while working with pathogens. Bio-security is security at facilities containing pathogens and other sensitive materials.

the early stages of infection among domestic poultry. This method includes creating three zones surrounding the infected poultry and culling all poultry in zones 1 and 2 (those closest to the detection site). In order to be effective, the stampede method must be complemented by a compensation package for owners of the culled poultry. These established best practice guidelines to prevent and control avian influenza outbreaks are applicable to developed countries but are not necessarily appropriate for developing countries.

However, according to the updated *Global Strategy for Prevention and Control of H5N1 Highly Pathogenic Avian Influenza* developed by the FAO and the OIE, in countries where H5N1 is endemic, experience indicates that eliminating infected flocks only provides short-term mitigation.<sup>25</sup> Appropriate changes need to be made in disease management practices on farms and in high-risk marketing practices to regulate the uncontrolled movement of poultry through live bird markets.

Vaccination is an alternative secondary prevention strategy to control the number of poultry that are infected with H5N1, but there have been recent debates over the efficacy of this strategy. On 22 March 2007 in Verona, Italy, 400 experts from the OIE, the FAO and the Istituto Zooprofilattico Sperimentale delle Venezie (IZSVe) with the support of the European Commission attended a conference to review the current vaccination programmes of various countries in order to provide best practice guidelines. The conference recommended that poultry should be vaccinated against avian influenza in Egypt, Indonesia and Nigeria, where the disease has become endemic. The OIE stated that a 'successful vaccination campaign depends mainly on the use of high quality vaccines complying with OIE standards, appropriate infrastructure to ensure the rapid and safe delivery of vaccines (cold chain), monitoring of vaccinated flocks, movement control of poultry, and adequate financial resources'.<sup>26</sup> In addition to the enormous economic costs of a mass vaccination programme for infected or possibly infected animals, a successful vaccination programme requires a strong public health infrastructure and veterinary personnel, elements which are not present in Indonesia and other countries to which avian influenza is endemic.

Regardless of the lack of data verifying its efficiency, vaccinating poultry is highly recommended by developed countries because it produces more numerical evaluation data. In addition, it is a more tangible proactive strategy than emphasizing long-term behaviour change that does not produce quantifiable results. Avian influenza cannot be controlled or prevented by relying solely on the 'quick fix' that vaccines provide. If vaccination programmes are not implemented properly with the most up-to-date quality of vaccine and are not aggressively monitored, they can actually accelerate the mutation of the virus. According to the WHO's Manila spokesman, Peter Cordingley, 'vaccination can sometimes cause silent transmission of infection from asymptomatic birds. Mass vaccination programmes entail people tramping around the countryside from farm to farm and they can spread the disease with them. The first response must be culling.<sup>27</sup> Furthermore, such programmes can complicate the current veterinary monitoring systems of healthy and sick poultry by masking symptoms

<sup>27</sup> Parry, J., 'Vaccinating poultry against avian flu is contributing to spread', *British Medical Journal*, vol. 331 (26 Nov. 2005), p. 1223.

<sup>&</sup>lt;sup>25</sup> UN Food and Agriculture Organization (FAO) and World Organization for Animal Health (OIE), *Global Strategy for Prevention and Control of H5N1 Highly Pathogenic Avian Influenza* (FAO: Rome, Mar. 2007), <a href="http://www.fao.org/avianflu/en/">http://www.fao.org/avianflu/en/</a>>.

<sup>&</sup>lt;sup>26</sup> Zampaglipone, M., 'Combining poultry vaccination with other disease control measures to combat H5N1: international conference in Verona reviews vaccination methods', World Organization for Animal Health, Press release, Verona, 22 Mar. 2007, <a href="http://www.oie.int/eng/press/en\_070322.htm">http://www.oie.int/eng/press/en\_070322.htm</a>.

in infected animals. Because vaccination does not completely eradicate the virus from a flock and therefore a region or country, some countries have even banned vaccination because it interferes with the stampede method of totally eliminating the disease from an infected region.<sup>28</sup>

# IV. Case study: Indonesia

Indonesia is currently the 'hot zone' of the H5N1 outbreak in both humans and poultry. As of December 2007, Indonesia has had the most human cases of H5N1 and the highest case fatality rate, approximately 81 per cent, of any country with human cases of H5N1.<sup>29</sup> International scientists and epidemiologists are still trying to determine why the case fatality rate is so high in Indonesia compared to other countries like China, where it is 63 per cent, Thailand, where it is 68 per cent, and Viet Nam, where it is only 47 per cent. More puzzling than the high fatality rate is that several cases of family clusters of H5N1 have been reported. On 18 May 2006 the WHO documented the largest family cluster of H5N1 cases—an Indonesian family where seven people were infected, spanning four households-suggesting evidence of human-to-human transmission. It is believed that the first victim became infected through contact with infected poultry and then proceeded to infect six other family members.<sup>30</sup> The WHO and the international community have been very concerned about the situation in Indonesia because of these scientific anomalies and the hypothesis that, if the virus were to mutate, Indonesia is likely to be the location for a reassortment event. In addition to being the epicentre of the avian influenza global epidemic, Indonesia was selected as a case study for this appendix because of its government's vocal disapproval of the WHO's current virus sharing programme due to perceived unequal access to influenza vaccines between developed and developing countries.

The H5N1 outbreak in Indonesia started in mid-2003, originally in the provinces of Banten and Kava. The disease spread rapidly to all provinces of Java and the Ministry of Agriculture internationally declared the H5N1 outbreak in January 2004. Although the WHO, the OIE and the FAO recommend that culling be the first response to an outbreak, that method was not an option for the Indonesian Government because Java (containing 60 per cent of the country's birds) is the centre of the Indonesian poultry production and farmers could not be compensated for their economic losses. The Indonesian Government therefore initiated a mass vaccination programme in early 2004 for all sector 4 farms as an attempt to control the disease. However, this programme failed because of the limited amount of vaccine available, the lack of appropriate equipment, facilities and personnel to transport and administer the vaccine, and the low operating budget. It is possible that this rushed vaccination programme further exacerbated the outbreak, which is now endemic in 30 of Indonesia's 33 provinces.<sup>31</sup>

<sup>29</sup> The data in this section are based on table 9A.1.

<sup>&</sup>lt;sup>28</sup> Saad, M. Z., 'Opinion: doing the thing to do away with bird flu', *New Straits Times*, 9 July 2007.

<sup>&</sup>lt;sup>30</sup> WHO, 'H5N1 avian influenza: timeline of major events', 28 Jan. 2008, <a href="http://www.who.int/csr/disease/avian\_influenza/timeline2008\_01\_30.pdf">http://www.who.int/csr/disease/avian\_influenza/timeline2008\_01\_30.pdf</a>>.

<sup>&</sup>lt;sup>31</sup> FAO, 'Tapping local knowledge in Indonesia to battle avian influenza', 26 July 2007, <http://www.fao.org/newsroom/en/news/2007/1000631>.

Indonesia is an archipelago consisting of over 6000 inhabited islands with a population of 220 million people,<sup>32</sup> over half of whom reside in Java, which was hardest hit by H5N1. The Indonesian poultry sector employs roughly 10 million people who care for over 1.3 billion chickens that are spread throughout 30 million backyard farms and are sold or traded in 13 000 daily wet markets.<sup>33</sup> This extensive poultry production and trading system provides a perfect breeding ground for H5N1. The health care sector, both human and animal, is highly decentralized with little national control. Over 400 local districts independently address health and agricultural needs. After the Asian financial crisis in 1997-98, the national veterinary services were drastically downsized, leaving some islands and provinces without any trained government veterinarians. The decentralization of the public health infrastructure in Indonesia has severely affected the national disease surveillance and reporting systems and has serious implications for the health of Indonesians. Many local districts lack the capacity and capability for disease reporting and surveillance, and the current epidemiological detection systems are costly to implement. Peter Roeder, a field consultant for the UN in Indonesia, has stated that there is no on-the-ground systematic programme in Indonesia and the situation is 'a bloody mess'.<sup>34</sup> Furthermore, case detection is often imprecise because of the high prevalence of other respiratory illnesses in areas endemic for H5N1 that present similar initial symptoms to avian influenza.

On 7 March 2006 the Indonesian National Committee for Avian Influenza Control and Pandemic Influenza Preparedness education campaign was instituted in order to provide massive public health education about avian influenza. This educational campaign stressed the effective steps that individuals can take to reduce the risk of contracting the H5N1 virus through limiting their contact with infected species, practicing hygienic and appropriate slaughtering practices as well as routine cleaning of storage and market facilities. There has been no formal evaluation of this education campaign, but there is limited anecdotal evidence of a persistent lack of knowledge among the Indonesian public about H5N1 and how to prevent human infection.<sup>35</sup>

Since mid-2006 there has been progress in utilizing local knowledge and community capacity to compensate for the lack of national and local veterinary services available as a result of decentralization. Participatory epidemiology and participatory surveillance are two methods developed by FAO epidemiologists that enlist local farmers to help in disease tracking and surveillance. Formally known as participatory disease surveillance and response (PDS/R), this method was successful in the FAO's Global Rinderpest Eradication programme in Africa in the early 1990s, where there was also an underdeveloped veterinary system. Including community members in disease surveillance methods helps build local sustainable capacity and knowledge about H5N1 and ways to control the virus in poultry. Veterinarians in Indonesia welcome this programme because there are too many backyard farms and districts to

<sup>&</sup>lt;sup>32</sup> UN Population Fund (UNFPA), 'Indonesia', <http://www.unfpa.org/profile/indonesia.cfm>.

<sup>&</sup>lt;sup>33</sup> Butler, D., 'Indonesia struggles to control bid flu outbreak', *Nature*, 13 Oct. 2007, p. 937.

<sup>&</sup>lt;sup>34</sup> Butler, D., 'Disease surveillance needs a revolution', *Nature*, 2 Mar. 2006, pp. 6–7.

<sup>&</sup>lt;sup>35</sup> Thieme, O., Background paper presented at the Technical Meeting on Highly Pathogenic Avian Influenza and Human H5N1 Infection, Rome, 27–29 June 2007. Basic public education about H5N1 should be the first and main focus of the Indonesian Government, yet on 14 June 2007 the Indonesian national committee for avian influenza announced that it recommended a more robust vaccination programme be implemented to control the H5N1 outbreak. Indonesian National Committee for Avian Influenza Control and Pandemic Influenza Preparedness, Press release, 14 June 2007, <a href="http://www.komnasfbpi.go.id/news\_june14\_07.html">http://www.komnasfbpi.go.id/news\_june14\_07.html</a>.

### 466 NON-PROLIFERATION, ARMS CONTROL, DISARMAMENT, 2007

monitor given the limited personnel. It is impossible for any highly technologically advanced disease surveillance system to work efficiently without a developed fundamental public health infrastructure. Indonesia is a prime example of the difficulty that scientists face in accessing the more than 6000 inhabited islands to monitor over 1.3 billion chickens, retrieving accurate data and reporting. Once appropriately evaluated, the PDR/S technique should be a valuable tool for both developed and developing countries, enabling them to improve their disease surveillance systems by collaborating with their citizens.

The US Agency for International Development (USAID), the Australian Agency for International Development (AusAID) and the Government of Japan have contributed over \$10 million to support the PDS/R initiative in Indonesia.<sup>36</sup> However, a large portion of international funding has been allocated to modern disease surveillance technology and high-level laboratories in developing countries. The US Department of Defense has proposed setting up high-tech labs modelled on the US network of infectious disease laboratories. The motivation behind such laboratories is to improve the US early-warning system. Mark Savey, the head epidemiologist directing France's food safety agency, cautions against relying on modern disease surveillance technology to track and control infectious diseases: 'You don't need satellites, PCR and geographic information systems to fight outbreaks. The lab's top priority should be building large teams of local staff, who are familiar with the region and its practice. If you do not have that, then surveillance will stay in the Middle Ages.'37 International aid comes coupled with considerable pressure on the receiving country to cooperate with outside agendas that might not correspond with the receiving country's priorities.

### The avian influenza virus sharing debate

In December 2006 the Indonesian Government withheld samples from the WHO because of uneven distribution of influenza vaccines, especially those made from virus samples collected in Indonesia. For more than 50 years the Global Influenza Surveillance Network has collected virus samples that enable international scientists to monitor the evolution of the virus and determine the risk of a pandemic. The Indonesian Government has demanded that prior approval be obtained for the development of a vaccine from a virus found in the country and that a discount price for such a vaccine be negotiated for countries where the H5N1 virus is endemic. The Indonesian Government referred to the 1992 Convention on Biological Diversity, which stipulates that a country has to share the benefits if others make use of its genetic resources.<sup>38</sup> To provide an incentive for Indonesia to resume sharing samples with it, the WHO has facilitated several proposals to improve access to vaccines and has awarded six countries (Brazil, India, Indonesia, Mexico, Thailand and Viet Nam) grants donated by Japan and the USA for a total of \$18 million to develop their own vaccine manufacturing capacities; this, in turn, promotes the development of domes-

<sup>&</sup>lt;sup>36</sup> FAO (note 31).

<sup>&</sup>lt;sup>37</sup> Butler (note 34).

<sup>&</sup>lt;sup>38</sup> Enserink, M., 'Indonesia earns flu accord at World Health Assembly', *Science*, 25 May 2007, p. 1108. The Convention on Biological Diversity was signed on 5 June 1992 and entered into force on 29 Dec. 1993. On the convention see <a href="http://www.cbd.int/convention">http://www.cbd.int/convention</a>.

tic capacity.<sup>39</sup> Pharmaceutical companies are not the only parties to recognize the possibility of making a large profit from vaccine development. Researchers and governments worldwide are also well aware of this lucrative possibility, which is an incentive to demanding ready access to virus genome sharing from all countries affected by H5N1. Professor Sangokt Marzuki of the Indonesian Academy of Sciences has stated that the academy had considered the potential financial benefits of developing vaccines and drugs while not sharing their data and accruing royalties from intellectual rights but that it ultimately gave in to international pressure and 'for the sake of basic human interests'.<sup>40</sup>

After a two-day meeting with top WHO officials about international protocols for virus sample sharing programmes, the Indonesian Minister of Health, Siti Fadillah Supari, agreed to resume sharing virus samples with the WHO on 26 March 2007.<sup>41</sup> In her closing remarks at the 60th annual meeting of the World Health Assembly, on 15 May 2007, the WHO Director-General, Dr Margaret Chan, acknowledged her increased role in protecting international health security as a result of the revised IHR and reminded member states of their obligations under the adopted resolution on sharing influenza viruses.<sup>42</sup> The Indonesian influenza virus sharing stalemate prompted the 'Global pandemic influenza action plan to increase vaccine supply' document on the sharing of influenza vaccines and a plan to guarantee the equitable and affordable sharing of the vaccine in the event of a pandemic.<sup>43</sup> However, this draft proposal is vague and lacks a definitive action plan to enable the WHO to meet its stated aims. As a result of this ambiguity and the lack of measurable objectives, in August 2007 Indonesian officials announced that they would again withhold virus samples unless a formal system is established that guarantees equitable access to vaccines developed from shared samples. David Heymann, the assistant WHO Director-General, stated on 6 August 2007 that 'Indonesia is putting the public health security of the whole world at risk because they're not sharing viruses'.<sup>44</sup> After an unsuccessful meeting on 23 November, WHO and Indonesian officials had still not come to an agreement over an acceptable avian influenza virus sharing programme.<sup>45</sup> However, in early 2008, after 'receiving assurances its rights to any vaccines produced from them would be recognized'. Indonesia sent 12 avian influenza samples to the WHO.46

Although there are major differences between AIDS and H5N1, both diseases have initiated heated debates concerning ethical issues related to vaccine research and development. AIDS has forced the WHO to address public health, diseases and vaccines using the legal framework of intellectual property rights and trade, more for-

<sup>39</sup> WHO, 'WHO facilitates influenza vaccine technology transfer to developing countries', 24 Apr. 2007, <a href="http://www.who.int/mediacentre/news/notes/2007/np18/en>">http://www.who.int/mediacentre/news/notes/2007/np18/en></a>.

<sup>40</sup> Rukmantara, A., 'Bird flu data now open to all', Jakarta Post, 13 July 2007.

<sup>41</sup> 'Bird flu sample row ends with agreement', Jakarta Post, 28 Mar. 2007.

<sup>42</sup> WHO, 'Closing remarks to the 60th World Health Assembly', 23 May 2007, <a href="http://www.who.int/dg/speeches/2007/230507\_closing/en/">http://www.who.int/dg/speeches/2007/230507\_closing/en/</a>.

<sup>43</sup> Centre for Infectious Disease Research and Policy, 'Indonesia to keep withholding virus samples for now', 9 Aug 2007, <<u>http://www.cidrap.umn.edu/cidrap/content/influenza/panflu/news/aug0907indonesia.html</u>>.

<sup>44</sup> Centre for Infectious Disease Research and Policy (note 43).

<sup>45</sup> Centre for Infectious Disease Research and Policy, 'Virus-sharing pact eludes WHO group, but work will continue', 26 Nov. 2007, <a href="http://www.cidrap.umn.edu/cidrap/content/influenza/avianflu/news/nov2607pact.html">http://www.cidrap.umn.edu/cidrap/content/influenza/avianflu/news/nov2607pact.html</a>.

<sup>46</sup> 'Indonesia resumes bird flu samples to WHO: official', Agence France-Presse, 23 Feb. 2008.

mally governed by the World Trade Organization. Indonesia's rejection of the normative system of influenza virus sharing has further forced the WHO to address the intellectual property rights issue, which is a very uncomfortable position for it and further blurs its primary mission of ensuring the highest level of health for all people.

Pharmaceutical companies and independent scientists are very interested and willing to invest in Indonesia in order to gain access to the most current version of the virus. In order for a vaccine to successfully produce immunity in a given human population, it must be developed using the most current strain of the influenza virus. Baxter Healthcare SA, a Swiss-based subsidiary of the US pharmaceutical company Baxter Healthcare International Inc., began clinical trials in Singapore and Hong Kong in July 2007 of a vaccine that was created with strains from Indonesia. These clinical trials are part of an agreement reached in February 2007 between Baxter Healthcare and the Indonesian Government according to which Baxter Healthcare will provide technical equipment and assistance to develop the vaccine in exchange for up-to-date virus specimens from infected poultry and humans within Indonesia's borders.<sup>47</sup> Siti stated that the agreement was made with Baxter Healthcare because it was the 'only company offering to produce human vaccines for the specific Indonesian bird flu strain'.<sup>48</sup> This agreement between Baxter Healthcare and the Indonesian Government is controversial and further increased tensions between the WHO, manufacturers, government and researchers over preserving intellectual property rights.

# V. Conclusions

The public health sector and the WHO are continually influenced by the growing national and international interest and investment in enhancing bio-security and biosafety. Global public health has been increasingly discussed using security rhetoric, and infectious diseases, such as avian influenza and SARS, were labelled a 'threat to global health security' by the UN Security Council in 2004. Public health and national security have a reciprocal relationship because public health can be improved through increased security, and security can likewise be improved by incorporating public health concerns. Globalization has changed the structure of global health governance by introducing new actors and interested parties due to the rise of health as a foreign policy concern. This has drastic implications for the WHO, which was the original governing body of global health and was created as a specialized agency associated with the United Nations. The WHO has felt increased pressure from governments and international organizations to securitize global public health by increasing early-warning systems and disease surveillance systems to protect the world's population from feared infectious disease outbreaks like SARS and the looming threat of avian influenza.

Countries cannot rely solely on stamping out, culling or vaccinating poultry; there must be a comprehensive H5N1 prevention plan that includes evidence-based prevention strategies to address the problem. Improving bio-safety measures is less expensive than a mass vaccination programme, although it requires changing human behaviour, which is much more time consuming, and does not provide immediate or easily measurable results for evaluation.

<sup>&</sup>lt;sup>47</sup> 'Baxter to develop bird flu vaccine for Indonesia', Jakarta Post, 8 Feb. 2007.

<sup>&</sup>lt;sup>48</sup> 'Baxter to develop bird flu vaccine for Indonesia' (note 47).

However, it must be asked whether this securitization paradigm is the best way to conceptualize global public health because countries have differing opinions on security priorities, as exemplified by the influenza virus sharing debate between Indonesia and the WHO. The revised IHR mandate member states to drastically increase their disease surveillance systems, and they thus reflect the securitization of global public health. The WHO has not addressed or given any formal guidance to countries on how they should prioritize their public health funding between current health threats while simultaneously strengthening technical disease surveillance capacities for potential pandemics like avian influenza. The future will show if the WHO can maintain impartiality and neutrality throughout the implementation of the revised IHR. If the WHO cannot prove its credibility to both developing and developed countries, it will lose its place as the leading international global health organization and global public health will further be dictated by individual countries' foreign policy.