

Regulatory and scientific frameworks for zoonosis control in Japan – contributing to International Health Regulations (2005)

H. Takahashi-Omoe^{(1)*} & K. Omoe⁽²⁾

(1) Science and Technology Foresight Center, National Institute of Science and Technology Policy, Ministry of Education, Culture, Sports, Science and Technology, 3-2-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013, Japan

(2) Laboratory of Food Safety Science, Department of Veterinary Medicine, Faculty of Agriculture, Iwate University, Ueda 3-18-8, Morioka, Iwate, 020-8550, Japan

* Corresponding author: omoe@nistep.go.jp

Submitted for publication: 21 February 2008

Accepted for publication: 22 June 2009

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the National Institute of Science and Technology Policy, the Ministry of Education, Culture, Sports, Science and Technology or Iwate University

Summary

Zoonoses have earned recognition as the source of serious problems for both public and animal health throughout the world. Emerging infectious diseases have been occurring at an unprecedented rate since the 1970s and a large proportion of these diseases are considered zoonotic. To aid in controlling zoonoses, countermeasures have been strengthened against these diseases and are maintained at both national and international levels. A typical example of this international effort can be found in the revised International Health Regulations (2005), known as the IHR (2005), which were instituted by the World Health Organization and have been implemented since 2007.

In Japan, the appropriate Ministries have established frameworks for controlling zoonoses that employ both administrative and scientific approaches to fulfill the demands of the IHR (2005). In this paper, the authors present the Japanese framework for controlling zoonoses, as a useful example for global public and animal health management in coming years.

Keywords

Basic and applied research – Emerging infectious disease – International Health Regulations 2005 – Japan – Laws and regulations – Legislation – Zoonoses.

Introduction

Zoonoses have become a major threat to human and animal health. Emerging infectious diseases have been occurring at an unprecedented rate of one or more per year, in animal and human populations, since the 1970s (6, 64), and 60.3% of emerging infectious disease events are considered to be zoonotic (49). Since it is highly likely that zoonoses and animal diseases with the potential to affect human health will continue to emerge (51), stronger countermeasures must be taken against these diseases and maintained at both national and international levels. Among such effective countermeasures are the

International Health Regulations (IHR) of 2005, instituted by the World Health Organization (WHO) (65, 66).

These IHR (2005) have been implemented since 2007 to develop an international management system for public health, by improving national surveillance and response capacities during public health emergencies of international concern (PHEIC) in WHO Member States (65, 66). These global public health emergencies encompass both infectious and non-infectious disease events, whether naturally occurring, caused accidentally, or created intentionally. Within PHEIC, zoonoses are of primary concern, as a result of the marked impact of such recent outbreaks as severe acute respiratory syndrome

(SARS), Nipah virus infection, West Nile fever and so on. Moreover, there is concern that a pandemic human influenza, caused by a new subtype of influenza virus, is a possible PHEIC. For these reasons, zoonosis control is considered to be an area of high priority.

Japan has long addressed zoonosis control through regulatory and scientific frameworks, consisting of legislation and various funding systems for both basic and applied research into zoonosis control. In addition to such frameworks, a special action plan for an influenza pandemic (20) has been developed by government bodies. Moreover, to contribute to IHR (2005) more effectively, a framework for communicating with WHO was set up in 2007 (37).

Under the regulatory framework, both preventive and emergency measures against zoonoses have been implemented in Japan. The former include surveillance of zoonoses and restrictions on importing animals that are susceptible to these diseases. The latter include the agreed initial reaction to a disease outbreak. In this paper, the authors place particular emphasis on the regulatory framework for preventing zoonoses in Japan, and give concrete examples. In addition, they outline the research framework for zoonosis control. The authors believe that the approach taken by Japan serves as a useful example for global public and animal health management, contributing to the successful implementation of IHR (2005).

An overview of the regulatory framework

In Japan, two laws play a central role in preventing and controlling zoonoses. The first is the 'Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients with Infections' (the Infectious Diseases Control Law: Law No. 114, October 1998; latest amendment: Law No. 73, June 2008) (14, 16, 19, 55). The second is the 'Domestic Animal Infectious Diseases Control Law' (Law No. 166, May 1951; latest amendment: Law No. 102, October 2005) (9). The former aims to control human infectious diseases, including zoonoses, principally under the Ministry of Health, Labour and Welfare (MHLW). The latter attempts to prevent the outbreak and spread of infectious diseases in domestic animals, including those with the potential to affect humans, under the jurisdiction of the Ministry of Agriculture, Forestry and Fisheries (MAFF). In addition, the 'Rabies Prevention Law' (Law No. 247, August 1950; latest amendment: Law No. 160, December 1999) has been implemented as a specific control on rabies, known to be a severe zoonotic viral disease (62). Since rabies is endemic in Asia and Africa, etc., despite its elimination in Japan (62, 67), susceptible

species are still managed rigorously by law. The authors examined this legislation in greater detail in a previous study (62), and describe the essential features of the Infectious Diseases Control Law and the Domestic Animal Infectious Diseases Control Law below.

Regulatory framework under the Infectious Diseases Control Law

The Infectious Diseases Control Law stipulates five categories of disease. Categories 1 to 4 comprise diseases that must be reported promptly after diagnosis (Category 1 includes the highest-risk diseases). Category 5 includes diseases that should be surveyed nationally. Unconfirmed diagnoses and new zoonoses are categorised separately; see Table I. These five categories include many zoonoses, which account for 52% (52 diseases) of the total number of designated diseases under the law (Table I) (18, 19, 36).

Of the 52 zoonoses targeted by the Infectious Diseases Control Law, enterohaemorrhagic *Escherichia coli* infection outbreaks in humans were reported to occur most frequently, during the period 2001 to 2006 (43) (Table II). For other zoonoses, the number of outbreaks has not changed markedly in either humans or animals. Consequently, the total number of outbreaks has not significantly altered.

Since June 2007, a new regulation has been implemented in Japan, restricting the handling of infectious agents, to prevent the outbreak of such diseases, whether occurring accidentally or deliberately (16, 17, 40). This regulation is based on long-standing administrative guidelines for preventing bioterrorism (8, 31), and the standards and guidelines for microbiological biosafety in laboratories, established by the appropriate organisations (61). Since the IHR (2005) cover infectious disease events that occur naturally, as well as those caused accidentally or intentionally, this Japanese regulation on handling infectious agents is also extremely pertinent to the international regulations.

This regulation ranks infectious agents into groups from one to four:

- group 1 comprises infectious agents that are banned from possession or use for research
- group 2 comprises infectious agents that may be possessed and used for research with prior permission from the MHLW
- group 3 comprises infectious agents that can be possessed and researched with notification to the MHLW (permission not needed)
- group 4 lists agents for which security standards must be observed but notification and permission are not needed.

Table I
Zoonoses listed by the Infectious Diseases Control Law

Classification ^(a)	Definitions/characteristics	Zoonoses listed in this category
Target zoonoses to be reported by physicians		
Category 1	Diseases to be reported promptly after diagnosis Diseases that have comprehensive and extremely high risks, including infectiousness and serious symptoms	Six of seven diseases in Category 1 Crimean-Congo haemorrhagic fever, Ebola haemorrhagic fever, Lassa fever, Marburg disease, plague, South American haemorrhagic fever
Category 2	Diseases to be reported promptly after diagnosis Diseases that have comprehensive high risks, including infectiousness and serious symptoms (fewer risks than Category 1)	Three of five diseases in Category 2 Severe acute respiratory syndrome (due to the SARS coronavirus), tuberculosis, avian influenza virus infection (H5N1)
Category 3	Diseases to be reported promptly after diagnosis Diseases without particularly high comprehensive risks, but which can cause major outbreaks in groups with particular jobs	Two of five diseases in Category 3 Enterohaemorrhagic <i>Escherichia coli</i> infection, shigellosis
Category 4	Diseases to be reported promptly after diagnosis Diseases whose outbreak and spread should be prevented by the government through research into their outbreak, and the provision and disclosure of necessary information, based on the results, to the public and medical professionals	Thirty-eight of forty-one diseases in Category 4 Anthrax, avian influenza infection (excluding H5N1), botulism, brucellosis, dengue fever, echinococcosis/hydatidosis, epidemic typhus, hantavirus pulmonary syndrome, haemorrhagic fever with renal syndrome, hepatitis E, herpes B virus infection, Japanese encephalitis, Japanese spotted fever, leptospirosis, Lyme disease, lyssavirus infection (excluding rabies), malaria, monkeypox, Nipah virus infection, psittacosis, Q fever, rabies, relapsing fever, Rift Valley fever, scrub typhus (Tsuksugamushi disease), tularemia, West Nile fever (including West Nile encephalitis), yellow fever, Eastern equine encephalitis, glanders, Hendra virus infection, Kyasanur Forest disease, melioidosis, Omsk haemorrhagic fever, Rocky Mountain spotted fever, tick-borne encephalitis, Venezuelan equine encephalitis, Western equine encephalitis
Category 5	Diseases to be reported by physicians promptly after diagnosis in all cases, or reported from the sentinel clinics and hospitals To be reported every week or month	Three of forty-two diseases in Category 5 Amoebiasis, cryptosporidiosis, giardiasis
Target zoonoses to be reported by veterinarians		
	Animal diseases that infect humans with the diseases in Category 1	Ebola haemorrhagic fever in monkeys, Marburg disease in monkeys, plague in prairie dogs
	Animal diseases that infect humans with the diseases in Category 2	Tuberculosis in monkeys, severe acute respiratory syndrome (due to the SARS coronavirus) in Chinese ferret badgers, raccoon dogs and masked palm civets, avian influenza H5N1 in avian species
	Animal diseases that infect humans with the diseases in Category 3	Shigellosis in monkeys
	Animal diseases that infect humans with the diseases in Category 4	West Nile fever in avian species, echinococcosis/hydatidosis in dogs

Source: based on data published by the National Institute of Infectious Diseases and the Japanese government (18, 19, 36)

a) Categories which include defined zoonoses are described in this table. In addition, new categories, such as: 'Pandemic human influenza and relevant infections', 'Designated infectious disease' (a disease which is designated as needed by government ordinance), 'New infectious disease', and 'Target disease for syndrome-based surveillance' (unknown disease characterised by fever and respiratory symptoms, or unknown fever with rash or vesicles), are set by the latest amended Infectious Diseases Control Law

These groups do not completely correspond to the five disease categories listed under the Infectious Diseases Control Law, although they do partially overlap. Their ranking depends on infectivity and severity, and determines whether possessing, importing, delivering or transferring these agents is prohibited, allowed with permission or allowed with notification (17, 40) (Fig. 1). Fifty-one infectious agents which cause disease are listed and, of these, some 86% (44 disease-causing agents) can cause zoonoses (see diseases in bold type in Figure 1).

These systems have been evaluated to assess whether the law works effectively to control infectious diseases,

including zoonoses. The MHLW, as the supervising authority, is constantly evaluating the systems in council and makes modifications if needed (see 63, as an example). A specific assessment programme, which involved extensive evaluation of this legislation across all appropriate Offices and Ministries, was undertaken by the Ministry of Internal Affairs and Communications (MIC) between December 2004 and March 2005, and again between January and February 2006 (45). The MIC programme involved:

- MHLW
- MAFF

Table II
Number of reports of zoonosis outbreaks in humans and animals under the Infectious Diseases Control Law

This table covers only those diseases for which outbreaks were reported

Zoonoses	2001	2002	2003	2004	2005	2006
Zoonoses reported by physicians						
Category 1			No disease was reported			
Category 2			No disease was reported ^(a)			
Category 3						
Enterohaemorrhagic <i>Escherichia coli</i> infection	4,435	3,183	2,999	3,764	3,589	3,922
Shigellosis	844	699	473	604	553	490
Category 4						
Botulism	NS	NS	0	0	3	2
Bruceellosis	0	1	0	0	2	5
Dengue fever	50	52	32	49	74	58
Echinococcosis/hydatidosis	15	10	21	26	20	20
Hepatitis E virus infection	NS	NS	2	41	43	71
Japanese encephalitis	5	8	1	5	7	7
Japanese spotted fever	40	36	52	66	62	49
Leptospirosis	NS	NS	1	18	17	24
Lyme disease	15	15	5	5	8	13
Malaria	109	83	78	75	67	62
Psittacosis	35	54	44	40	34	22
Q fever	42	47	9	7	8	2
Rabies	0	0	0	0	0	2
Scrub typhus (Tsutsugamushi disease)	491	338	402	313	345	417
West Nile fever (inc. West Nile encephalitis)	NS	NS	0	0	1	0
Category 5						
Amoebiasis	429	465	520	610	698	752
Cryptosporidiosis	11	109	8	92	12	18
Giardiasis	137	113	103	94	86	86
Total	6,658	5,213	4,750	5,809	5,629	6,022
Zoonoses reported by veterinarians						
Shigellosis in monkeys	NS	NS	NS	0	45	45
Echinococcosis/hydatidosis in dogs	NS	NS	NS	0	5	2
Total	NS	NS	NS	0	50	47

Source: based on data published by the Japanese government (43)

NS: not surveyed because the disease was not required to be reported at that time

a) Human tuberculosis from this category is not included because the disease is currently transferred from human to human, not via animals

- the Ministry of Land, Infrastructure, Transport and Tourism
- quarantine service facilities
- local government
- those medical institutions that respond to severe infectious diseases in Categories 1 and 2, as stipulated by the Infectious Diseases Control Law, and new or unconfirmed diseases.

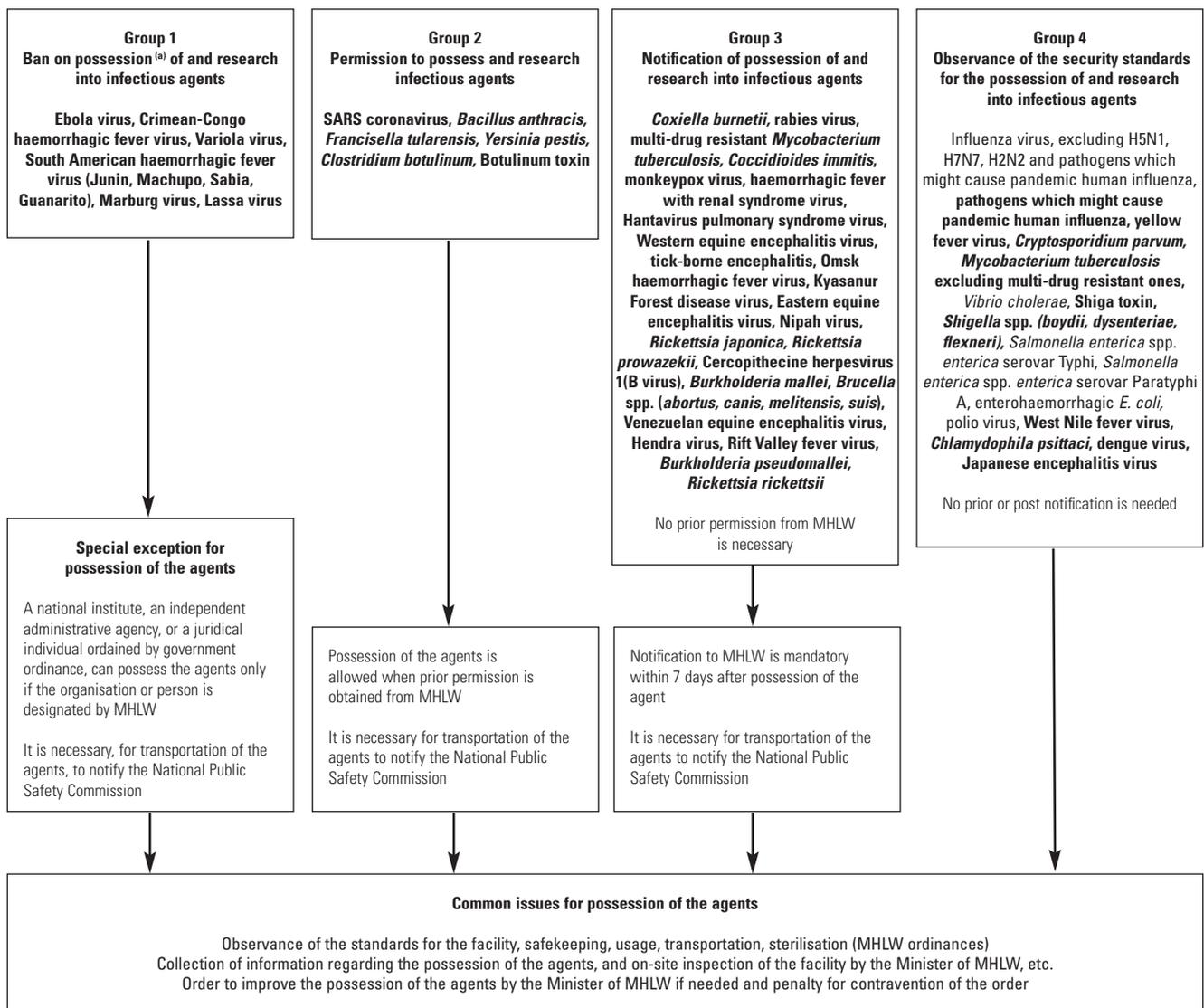
This assessment programme demonstrated that the systems for surveillance, analysis and disclosure of infectious disease outbreaks worked well. However, some manuals on quarantine measures and equipment for responding to envisaged outbreaks of Category 1 and 2 diseases and pandemic human influenza were not being managed appropriately. With guidance from MIC, these inadequacies have been resolved.

Regulatory framework under the Domestic Animal Infectious Diseases Control Law

The Domestic Animal Infectious Diseases Control Law (9) stipulates two categories of disease, according to:

- economic loss
- difficulty of preventing an epidemic
- impact on humans.

Category 1 comprises 'Official diseases', those that could have a significant impact and require the enforcement of stringent regulations and must be officially reported when they occur. Twenty-six infectious diseases are included in this category, ten of which are zoonoses. The other



MHLW: Ministry of Health, Labour and Welfare
 SARS: Severe acute respiratory syndrome
 a) possession, importation and delivery of infectious agents

Fig. 1
Regulatory framework for managing the handling of infectious agents in Japan
 Agents that cause zoonoses are in bold type. Source: based on government data (17, 40)

category is ‘Report-requested diseases’, which are considered to have fewer significant effects than ‘Official diseases’. Seventy-one diseases are listed in this category, of which 12 are zoonoses. These zoonoses are listed in Table III, alongside those designated by the Infectious Diseases Control Law (15, 17, 18, 56).

When a listed disease is suspected or confirmed in livestock, the diagnosing veterinarian or animal owner is required to report the case immediately to a prefectural or city governor through the director of the nearest animal public health centre. It is also a legal requirement that the animal is isolated, and euthanased if necessary.

Table IV shows the outbreak status of these listed zoonoses in Japan (24, 25, 26, 28, 29). The total number of outbreaks decreased remarkably in 2003; however, subsequently, the number showed little change. The number of outbreaks of Newcastle disease in 2007 was about one-tenth that of 2001. Additionally, as of October 2009, rabies in livestock has not been reported since 1957, and Rift Valley fever and glanders have not been reported at all (2008 and 2009 data are not shown in Table IV). The 2004 outbreaks of highly pathogenic avian influenza were the first reported in Japan for 79 years. Subsequently, the number of infected animals has decreased each year.

Table III
Zoonoses listed by the Animal Infectious Diseases Control Law and/or by the Infectious Diseases Control Law

Zoonoses listed in the Animal Infectious Diseases Control Law	Infectious agents causing the zoonoses listed in the Animal Infectious Diseases Control Law	Target animals in the Animal Infectious Diseases Control Law	Classification of diseases in the Infectious Diseases Control Law	Classification for handling infectious agents under the Infectious Diseases Control Law
Official diseases (legally designated animal infectious diseases)				
Enzootic encephalitis	Japanese encephalitis virus; West Nile virus; Eastern equine encephalitis virus; Western equine encephalitis virus; Venezuelan equine encephalitis virus, etc.	Cattle, buffalo, deer, horses, sheep, goats, swine, wild boar	Category 4 (Japanese encephalitis; West Nile encephalitis; Eastern equine encephalitis; Venezuelan equine encephalitis) Acute encephalitis, excluding the above diseases, Rift Valley fever and tick-borne encephalitis, belongs in Category 5	Group 3 (Eastern equine encephalitis virus; Western equine encephalitis virus; Venezuelan equine encephalitis virus) Group 4 (Japanese encephalitis virus; West Nile encephalitis)
Rabies	Rabies virus and other lyssaviruses	Cattle, buffalo, deer, horses, sheep, goats, swine, wild boar	Category 4 (rabies, lyssavirus infection)	Group 3 (rabies virus; rabies virus fixed strain)
Rift Valley fever	Rift Valley fever virus	Cattle, buffalo, deer, sheep, goats	Category 5 (Rift Valley fever)	Group 3 (Rift Valley fever virus)
Anthrax	<i>Bacillus anthracis</i>	Cattle, buffalo, deer, horses, sheep, goats, swine, wild boar	Category 4 (anthrax)	Group 2 (<i>B. anthracis</i>)
Brucellosis	<i>Brucella abortus</i> ; <i>B. melitensis</i> ; <i>B. suis</i> ; <i>B. ovis</i>	Cattle, buffalo, deer, sheep, goats, swine, wild boar	Category 4 (diseases caused by <i>B. abortus</i> ; <i>B. melitensis</i> ; <i>B. suis</i> ; <i>B. canis</i>)	Group 3 (<i>B. abortus</i> ; <i>B. melitensis</i> ; <i>B. suis</i> ; <i>B. canis</i>)
Tuberculosis	<i>Mycobacterium bovis</i> ; <i>M. tuberculosis</i>	Cattle, buffalo, deer, goats	Category 2 (tuberculosis)	Group 3 (multi-drug resistant <i>M. tuberculosis</i> that is resistant to at least isoniazid and rifampicin)
Transmissible spongiform encephalopathy	Abnormal prion protein (PrP ^{sc})	Cattle, buffalo, deer, sheep, goats	Category 5 (Creutzfeldt-Jakob disease)	Not listed
Glanders	<i>Burkholderia mallei</i>	Horses	Category 4 (glanders)	Group 3 (<i>B. mallei</i>)
Highly pathogenic avian influenza	Influenza A virus of H5 and H7 subtypes	Chickens, ducks, turkeys, quail	Designated disease (influenza H5N1)	Group 4 (influenza A virus of H5N1 and H7N7)
Newcastle disease	Newcastle disease virus	Chickens, ducks, turkeys, quail	Not listed	Not listed
Report-requested diseases				
Melioidosis	<i>Burkholderia pseudomallei</i>	Cattle, buffalo, deer, horses, sheep, goats, swine, wild boar	Category 4 (melioidosis)	Group 3 (<i>B. pseudomallei</i>)
Tetanus	<i>Clostridium tetani</i>	Cattle, buffalo, deer, horses	Category 5 (tetanus)	Not listed
Leptospirosis	<i>Leptospira interrogans</i> serovar Pomona, Canicola, Icterohaemorrhagiae, Grippityphosa, Hardjo, Autumnalis, Australis (7 serovars)	Cattle, buffalo, deer, swine, wild boar, dogs	Category 4 (leptospirosis)	Not listed
Salmonellosis	<i>Salmonella</i> serovar Dublin, Enteritidis, Typhimurium, Choleraesuis (4 serovars)	Cattle, buffalo, deer, swine, wild boar, chickens, ducks, turkeys, quail	Category 3 (typhoid fever caused by <i>S. enterica</i> subsp. <i>enterica</i> serovar Typhi; Paratyphoid fever caused by <i>S. enterica</i> subsp. <i>enterica</i> serovar Paratyphi)	Group 4 (<i>S. enterica</i> subsp. <i>enterica</i> serovar Typhi; <i>S. enterica</i> subsp. <i>enterica</i> serovar Paratyphi)
Trypanosomiasis	<i>Trypanosoma brucei</i> ; <i>T. congolense</i> ; <i>T. vivax</i> ; <i>T. evansi</i> ; <i>T. theileri</i> ; <i>T. equiperdum</i>	Cattle, buffalo, horses	Not listed	Not listed
Nipah virus infection	Nipah virus	Horses, swine, wild boar	Category 4 (Nipah virus infection)	Group 3 (Nipah virus)
Equine morbillivirus pneumonia	Hendra virus	Horses	Category 4 (Hendra virus infection)	Group 3 (Hendra virus)
Tularemia	<i>Francisella tularensis</i> subsp. <i>tularensis</i> , subsp. <i>holarctica</i> , subsp. <i>mediasiatica</i> , subsp. <i>Novicida</i>	Horses, sheep, swine, wild boar, rabbits	Category 4 (tularemia)	Group 2 (<i>F. tularensis</i> subsp. <i>tularensis</i> , subsp. <i>holarctica</i>)
Toxoplasmosis	<i>Toxoplasma gondii</i>	Sheep, goats, swine, wild boar	Not listed	Not listed
Swine erysipelas	<i>Erysipelothrix rhusiopathiae</i>	Swine, wild boar	Not listed	Not listed
Nairobi sheep disease	Nairobi sheep disease virus	Sheep, goats	Not listed	Not listed
Contagious ecthyma	Orf virus	Deer, sheep, goats	Not listed	Not listed

Source: based on data published by the Japanese government (15, 17, 18, 56)

Regulatory framework for the border control of zoonoses

Restricting the importation of certain animals, through a ban on imports, quarantine measures and the submission of health certificates, has been systematically implemented under the Infectious Diseases Control Law, the Domestic Animal Infectious Diseases Control Law and the Rabies Prevention Law (Fig. 2) (2, 39). Several species are banned from importation because they may transmit severe zoonoses to humans, e.g.:

- prairie dogs (*Cynomys ludovicianus*) may carry plague
- Chinese ferret badgers (*Melogale moschata*) and masked palm civets (*Paguma larvata*) may transmit SARS
- bats may carry Nipah virus infection and lyssavirus infection
- multimammate mice (*Mastomys natalensis*) may be infected with Lassa fever

– monkeys may carry Ebola haemorrhagic fever and Marburg disease.

In the case of quarantine, animal quarantine officers conduct on-site inspections of imported animals in vessels and aeroplanes and transfer the animals to designated MAFF quarantine facilities for clinical, serological, microbiological, biochemical and pathological inspection. The quarantine procedure differs, according to animal species and exporters (Table V). The Yokohama Head Office is a hub for animal quarantine services, and, as of June 2009, there were six branch and 17 sub-branch animal quarantine facilities across Japan. Approximately half of the 356 quarantine officers who work for the Head Office and animal quarantine facilities are veterinarians, and the remaining half are specialists in animal husbandry, etc.

As Table VI shows, during the period from 2003 to 2007, the number of quarantined animals decreased (in spite of an increase in the number of imported monkeys) (3).

Table IV
Number of reports of zoonosis outbreaks in animals under the Domestic Animal Infectious Diseases Control Law

Disease category	2001	2002	2003	2004	2005	2006	2007
Official diseases							
Enzootic encephalitis	4	6	1	3	11	11	3
Rabies	0	0	0	0	0	0	0
Rift Valley fever	0	0	0	0	0	0	0
Anthrax	0	0	0	0	0	0	0
Brucellosis	1	1	0	0	0	0	1
Tuberculosis	1	1	1	0	1	1	0
Transmissible spongiform encephalopathy	4	2	7	5	8	10	3
Glanders	0	0	0	0	0	0	0
Highly pathogenic avian influenza	0	0	0	24	188	6	4
Newcastle disease	21,201	24,656	0	2,822	564	500	250
Report-requested diseases							
Melioidosis	0	0	0	0	0	0	0
Tetanus	80	56	65	71	85	100	85
Leptospirosis	102	184	144	167	71	40	50
Salmonellosis	3,475	1,074	603	995	988	1,701	1,487
Trypanosomiasis	0	1	1	1	0	0	0
Nipah virus infection	NS	NS	NS	NS	0	0	0
Equine morbillivirus pneumonia	0	0	0	0	0	0	0
Tularemia	0	0	0	0	0	0	0
Toxoplasmosis	36	38	32	46	19	46	51
Swine erysipelas	1,781	1,600	1,755	1,555	1,667	1,597	1,479
Nairobi sheep disease	0	0	0	0	0	0	0
Contagious ecthyma	3	1	1	0	0	0	15
Total	26,688	27,620	2,610	5,689	3,602	4,012	3,428

Source: based on animal hygiene statistics published by the Ministry of Agriculture, Forestry and Fisheries (24, 25, 26, 28, 29)
NS: not surveyed because the disease was not required to be reported at that time

Restriction on import of animals			Tighter
	Notification of health certificate	Quarantine	Ban on import
<i>Law Concerning the Prevention of Infectious Diseases and Patients with Infectious Diseases</i>		Monkeys used for research and exhibition, under specified conditions only	Chinese ferret badgers, bats, raccoon dogs, masked palm civets, prairie dogs, <i>Mastomys natalensis</i> , monkeys, except those to be used for research or exhibition (specified condition)
<i>Notification System for the Importation of Animals</i>	Live terrestrial mammals, live birds and carcasses of rodents, etc. ^(a)		
<i>Domestic Animal Infectious Diseases Control Law</i>		Cattle, buffalo, deer, horses, sheep, goats, swine, wild boar, chickens, ducks, turkeys, quail, rabbits	
		Dogs	
<i>Rabies Prevention Law</i>		Cats, raccoons, foxes, skunks	

a) Animals, except for Artiodactyla, Perissodactyla, Lagomorpha, poultry, dogs, cats, raccoons, foxes, skunks, and monkeys under specified conditions, which have already been quarantined, or whose importation is banned by the Law Concerning the Prevention of Infectious Diseases and Patients with Infectious Diseases, Domestic Animal Infectious Diseases Control Law and/or Rabies Prevention Law

Fig. 2

Regulatory system of restricting importations of animals into Japan

Source: based on government data (2, 39)

Among these quarantined animals, 45 were detected as being infected or suspected of infection, as follows:

- six cattle were confirmed infected with brucellosis
- there were 38 suspected cases of brucellosis (all in cattle except for one case in swine)
- there was one suspected case of leptospirosis (in cattle).

No dogs, cats, raccoons or foxes were found to be infected with rabies and no monkeys were infected with Ebola haemorrhagic fever or Marburg disease during this period (information from the Yokohama Head Office of the Animal Quarantine Service). All of the infected or suspected animals were generally euthanased, except for some cases, which were later confirmed to be uninfected, or which recovered from the disease and were sent back to the exporting country.

The system for submitting health certificates, which is regulated by the Notification System for the Importation of Animals (enforced since September 2005), under the Infectious Diseases Control Law, is considered to play a complementary role in quarantine, because the system targets live terrestrial mammals, live birds and the carcasses of rodents, etc. The exceptions are animals that have already been quarantined under the Domestic Animal Infectious Diseases Control Law or the Rabies Prevention

Law, or whose importation is banned by the Infectious Diseases Control Law (Fig. 2) (39).

In this system, imported animals must be accompanied by health certificates issued by the government authorities of the exporting country, declaring the animals to be free of diseases, such as rabies in all species of mammals, plague and tularemia in rodents, and West Nile fever and highly pathogenic avian influenza in birds.

The diseases and animals covered by this system were decided by risk assessment on the basis of:

- the pathogenicity of the disease in humans
- the possibility of medical treatment for the human illness
- the epidemic situation throughout the world
- the number of imported animals which might be vectors or reservoirs of the disease, and so on (32, 42).

Under this system, the following numbers of animals were reported as being imported:

- from September to December 2005: 837,376
- from January to December 2006: 2,906,274
- from January to December 2007: 2,890,524.

Table V
Requirements for the quarantine of imported animals

Animal species	Target diseases	Allowed exporters	Prior notification	Detention period for quarantine
Monkeys	Ebola haemorrhagic fever, Marburg disease	United States of America, People's Republic of China, Indonesia, Philippines, Vietnam, Surinam, Guyana and Cambodia	Must be submitted to the Animal Quarantine Service 70-40 days before arrival in Japan	30 days or longer
Cattle, buffalo, deer, sheep, goats, swine, wild boar (cloven-hoofed animals), chickens, ducks, turkeys, quail (domestic fowl), horses, rabbits	Official and report-requested diseases listed in the Domestic Infectious Diseases Control Law	In the case of cloven-hoofed animals, permitted exporters are designated ^(a)	Must be submitted to the Animal Quarantine Service before arrival in Japan; 120-90 days before (for cloven-hoofed animals and horses) and 70-40 days before (for domestic fowl), no need for prior notification (rabbits)	15 days for cloven-hoofed animals, 10 days for domestic fowl and horses, 1 day for rabbits
Dogs, cats, raccoons, foxes, skunks	Rabies (dogs, cats, raccoons, foxes, skunks) and leptospirosis (dogs)	Taipei China, Iceland, Sweden, Norway, the United Kingdom (only Great Britain and Northern Ireland), Australia, New Zealand, the Fiji Islands, Hawaii and Guam are designated as rabies-free regions (designated regions) ^(b)	Must be submitted to the Animal Quarantine Service at least 40 days before arrival in Japan	From 12 hours to 180 days, depending on animal species and exporters (either from designated regions or others)

Source: based on documents published by the Japanese Animal Quarantine Service (2)

a) Korea, Finland, Sweden, Norway, Hungary, Germany, Denmark, Poland, Italy (except the island of Sardinia), Switzerland, Netherlands, Belgium, France, Liechtenstein, Austria, Spain, Ireland, Iceland, United Kingdom (Great Britain and Northern Ireland), Canada, United States of America (the mainland, Hawaii and Guam), Mexico, Belize, Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica, Panama, Dominican Republic, Chile, Northern Mariana Islands, New Zealand, Vanuatu, New Caledonia, Australia, Singapore, Romania, Slovenia, Croatia and Bosnia-Herzegovina. All regions were designated in May 2008 b) All regions were designated on 7 June 2005

To give further details, and as an example: in 2007, 447,404 mammals, 96,329 birds and 2,346,791 carcasses were reported (38).

Framework corresponding to the International Health Regulations (2005)

The IHR (2005) require WHO Member States to develop and maintain their capacity to detect, assess and report public health events at local, intermediate and national levels (65, 66).

In Japan, which is a WHO Member State, MHLW has established a 'National Focal Point', which is responsible for communicating with the 'WHO IHR (2005) Contact Points'. Moreover, the Ministry has reorganised the network for managing information on PHEIC. The organisational framework, in accord with IHR

(2005) requirements, is summarised in Fig. 3 (37). Since setting up the domestic network for IHR (2005), and as of September 2008, no events of suspected PHEIC due to a zoonosis outbreak have been reported in Japan (57).

Scientific framework for zoonosis control

In addition to the domestic and international regulatory frameworks described above, the Japanese government has established projects to promote research into the control of infectious diseases, including zoonoses. These projects are being led by the MHLW, the Ministry of Education, Culture, Sports, Science and Technology (MEXT), MAFF and the Ministry of the Environment (MOE) (21). Long-standing and regular research funds organised by these Ministries include health science and labour research grants from MHLW and grants-in-aid for academic research by MEXT (58). In addition, the Ministries have

Table VI
Number of imported quarantined animals

Animal species ^(a)	2003	2004	2005	2006	2007
Cattle	23,168	21,059	25,505	25,719	25,100
Swine	158	180	241	223	126
Sheep	2	35	62	233	0
Goats	0	6	13	0	0
Other cloven-hoofed animals	36	2	0	0	17
Horses	4,200	5,478	5,492	6,423	5,987
Rabbits	10,662	29,901	14,086	13,619	12,827
Domestic fowl, including poultry	101,7931	1,193,387	1,023,069	718,882	531,103
Dogs	16,892	14,376	8,309	8,099	7,281
Cats	2,457	2,611	1,635	1,655	1,600
Raccoons	0	0	0	0	0
Foxes	36	46	2	13	0
Skunks	0	16	0	0	0
Monkeys	3,821	6,590	5,915	7,198	7,464
Others	245,933	102,150	110,110	0	0
Total	1,325,296	1,375,837	1,194,439	782,064	591,505

Source: based on statistics from the Japanese Animal Quarantine Service (3)

a) Cattle, swine, sheep, goats, other cloven-hoofed animals, horses, rabbits and domestic fowl were quarantined under the Domestic Animal Infectious Diseases Control Law. Dogs, cats, foxes, raccoons and skunks were quarantined under the Rabies Prevention Law and monkeys under the Infectious Diseases Control Law

organised special research projects if needed. For example, during the fiscal year of 2007:

– MHLW spent approximately 5,900,000,000 yen on a project called: Research Enterprise for Emerging and Reemerging Infectious Diseases (21, 41)

– MAFF spent about 860,000,000 yen on Technology Development for the Control of Bovine Spongiform Encephalopathy and Zoonoses (27)

– MEXT spent approximately 2,800,000,000 yen on a Formation Programme of Research Centres for Emerging and Reemerging Infectious Diseases (21, 30).

Each Ministry supports research from the standpoint of the activities under its control. The MHLW oversees the promotion of applied research for the control of both human infectious diseases and zoonoses, to improve public health; MAFF is involved in developing technology to reduce the risk of zoonoses and promote a safe and stable food supply; MEXT promotes the development of basic research on infectious diseases in general, and MOE supports epidemiological studies in animals for their more humane treatment and management, enabling significant improvements in animal welfare.

In addition to the work of these Ministries, described above, independent administrative funding agencies and foundations, such as the Japan Society for the Promotion of Science (www.jsps.go.jp/english/index.html), the Japan

Science and Technology Agency (www.jst.go.jp/EN/index.html), the Bio-oriented Technology Research Advancement Institution (<http://brain.naro.affrc.go.jp/index-e.html>), and the Japan Health Sciences Foundation (www.jhsf.or.jp/English/index_e.html), etc. have all supported various studies for zoonosis control.

Research supported by the above Ministries and organisations has also been conducted by various other organisations in Japan, such as the National Institute of Infectious Diseases (www.nih.go.jp/niid/index-e.html), the National Institute of Animal Health (<http://niah.naro.affrc.go.jp/index.html>), universities, research institutes and so on. Such research is extremely diverse, for example:

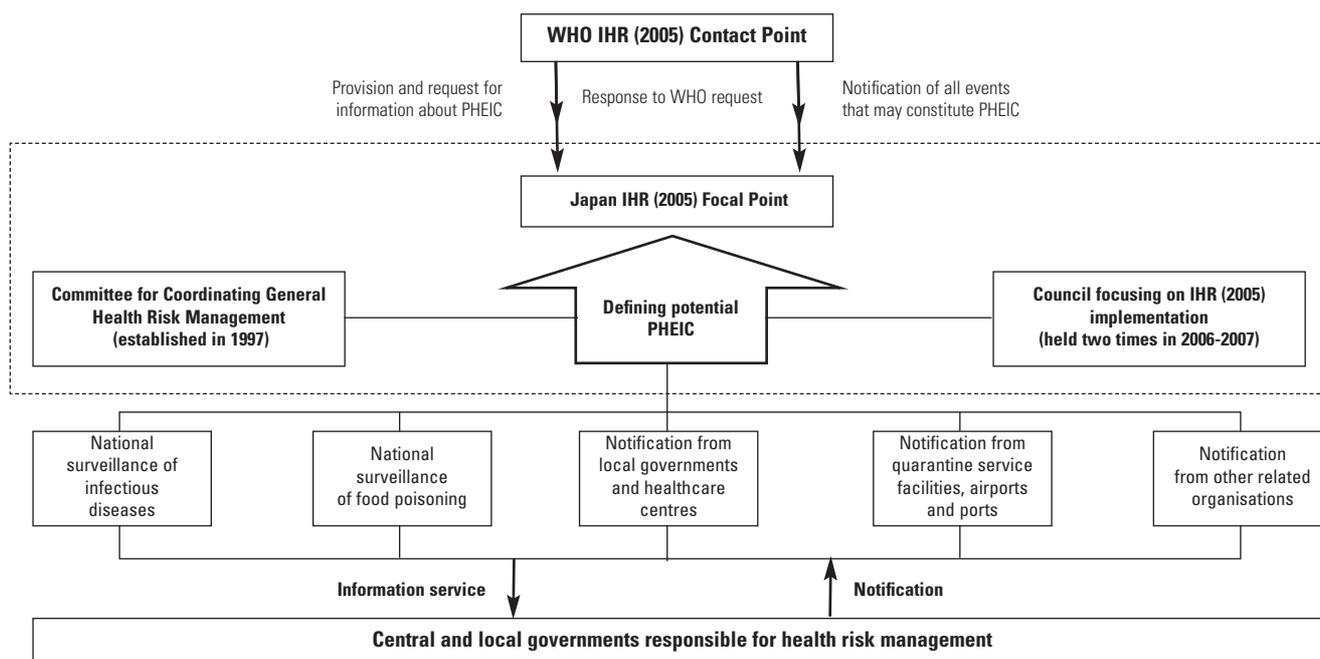
– basic studies on the pathogenesis of zoonoses such as Hantavirus and Ebola virus (58)

– applied research leading directly, it is hoped, to the prevention, diagnosis and treatment of such diseases as pandemic influenza (59), malaria (33) and bovine spongiform encephalopathy (27)

– a clinical study on pre-pandemic vaccines (44)

– epidemiological studies on *Echinococcus multilocularis* (33), highly pathogenic H5N1 influenza (48), and rabies and lyssaviruses (59)

– a survey of bird migration routes and virus transmission (22)



WHO: World Health Organization
 IHR (2005): International Health Regulations (2005)
 MHLW: Ministry of Health, Labour and Welfare
 PHEIC: Public health emergency of international concern

Fig. 3

Domestic network for implementing the International Health Regulations (2005) in Japan

Source: based on government data (37)

- risk analyses of zoonosis outbreaks (59)
- database development and modelling studies on influenza (1, 11, 60)
- development of a web-based text mining system for infectious disease surveillance (4)
- surveys on formulating guidelines for the hygienic management of pets (34)
- approaches to developing research infrastructures for Japanese facilities at biosafety level 4 (BSL-4) (23) and joint research centres between Japanese and foreign laboratories (30).

Moreover, since 2007, MHLW has launched research projects on health crisis management, including countermeasures against epidemic infectious diseases, which have the potential to establish regulatory systems that are closely geared to IHR (2005) (35). The projects are wide-ranging, and include:

- the development of systems for predicting damage and assessing public health support in the event of bioterrorism
- the establishment of a health crisis management system through the Global Health Security Initiative (an international partnership to strengthen global health preparedness and response to threats of terrorism and pandemic influenza) (12).

Discussion and conclusions

The risk of a zoonosis outbreak exists throughout the world, and is causally related to multiple factors, such as: the international movement of people and animals, ecological and environmental changes and degradation, changes in human behaviour, and so on (6, 52, 53). Japan is no exception and has characteristic risk factors as a result of its social structure. In Japan, the number of only children, families of two, those living alone and solitary elderly people has gradually increased, because of the falling birth rate and the fastest-aging society in the world. Such family structures have led to an increased demand for companion animals as family members, increasing the risk of zoonotic infection (47, 68). In fact, in the year 2000, the numbers of domestic dogs and cats in Japan were 10,054,000 and 7,718,000, respectively, and these totals have increased each year at the rate of about 5% (47).

Moreover, since the population density in Japan is relatively high (343 people per km² in 2005, ranking fifth among countries with a population of 10 million or more) (46), there is a significant risk of accelerating the transmission of infectious diseases through human society. The diversification of companion animal species, from dogs, cats, and birds to reptiles and amphibians, etc. is also a concern for the increase of zoonosis outbreaks (7, 68). For example, human salmonellosis associated with reptiles

(13, 54) has been reported in Japan, as well as in other countries (10). Generally speaking, Japanese nationals are now making contact with an increased number and much larger variety of animals, and are consequently exposed to greater risk of zoonotic infection.

Despite the introduction of systematic regulation under the Infectious Disease Control Law and Animal Infectious Diseases Control Law, the total number of outbreaks of zoonoses changed little between 2001 and 2006 in humans, and between 2003 and 2007 in animals (Tables II and IV). The MIC programme, which reviews the enforcement of the Infectious Diseases Control Law (45), has pointed out several management inadequacies in zoonosis control in quarantine stations and hospitals. Further development and assessment of management systems is essential for Japan in the future. This MIC programme (45) was ground-breaking, because it was the first to evaluate Offices and Ministries in the field of infectious disease control. As a result of this programme, the front lines of zoonosis control, such as quarantine services, have been strengthened. However, the programme is of limited duration and has not pursued the latest systems for zoonosis control. To respond effectively and on a continuing basis to the various zoonoses detected, administrative disease control systems should be periodically reviewed and revised as needed. In this light, regular evaluation systems which are effective, reasonable and involve regular and effective communication and co-operation between Ministries and other stakeholders should be established in Japan.

In accord with the increased global demand for multidirectional studies on zoonoses (50, 53) and a gradual increase in the overall publication of articles on infectious disease research (5), Japan has promoted research into zoonosis control from many perspectives. In particular, studies funded by the MHLW and MAFF take a needs-oriented approach to achieve practical results, being

directly integrated into the national framework for zoonosis control. On the other hand, many basic studies to detect the host factors determining tropism and pathogenesis, etc. are supported mainly by MEXT. The outcomes of such basic studies may not yet be clear and are not directly linked to political measures to control zoonoses. However, they have the potential to provide useful tools and technology for the prevention, detection, diagnosis and treatment of these diseases and occupy an important place in prospective policies for disease control in Japan. Japanese Ministries should therefore follow a scientific approach, achieving the best possible balance between basic and applied research and taking global research trends into consideration. Seen in this light, the establishment of regulatory and scientific frameworks in response to zoonoses is crucial for disease control in Japan, as is contributing to the global management of public and animal health, and the successful implementation of IHR (2005).

Since the end of the survey conducted by the author, patients in Japan have been reported as being infected with the pandemic H1N1 2009 virus since May 2009. This paper does not cover countermeasures against the disease outbreak.

Acknowledgements

The authors thank Dr Kazuya Yamanouchi, a scientific advisor to the World Organisation for Animal Health (OIE) *Scientific and Technical Review* for his reading of the manuscript. In addition, they are grateful to the officials working in the Food Safety and Consumer Bureau and the Yokohama Head Office of the Animal Quarantine Service, Ministry of Agriculture, Forestry and Fisheries, for providing statistical data on animal hygiene. ■

Cadre réglementaire et scientifique pour le contrôle des zoonoses au Japon en vue d'une participation au Règlement sanitaire international (2005)

H. Takahashi-Omoe & K. Omoe

Résumé

Les zoonoses sont une source reconnue de problèmes pour la santé publique et la santé animale à travers le monde ; en effet, depuis les années 1970 les maladies infectieuses émergentes apparaissent à un rythme sans précédent et une très grande proportion de ces maladies est de nature zoonotique. Afin de

contrôler les zoonoses, des mesures de lutte contre les maladies ont été renforcées et maintenues à l'échelle nationale et internationale. Exemple typique de l'effort international, le Règlement sanitaire international (RSI 2005 révisé) a été préparé par l'Organisation mondiale de la santé et mis en œuvre dès 2007.

Au Japon, les ministères compétents ont mis en place un cadre pour contrôler les zoonoses à partir d'approches administratives et scientifiques qui remplissent les exigences du RSI 2005. Les auteurs décrivent le cadre mis en place au Japon, qui peut utilement servir d'exemple de gestion de la santé publique et de la santé animale pour les années à venir.

Mots-clés

Législation – Lois et règlements – Maladie infectieuse émergente – Recherche fondamentale et appliquée – Règlement sanitaire international 2005 – Zoonose.



Marco reglamentario y científico para el control de las zoonosis en Japón encaminado a contribuir al cumplimiento del Reglamento Sanitario Internacional (2005)

H. Takahashi-Omoe & K. Omoe

Resumen

Las zoonosis son una fuente reconocida de problemas graves para la salud pública y animal a nivel mundial; desde los años 1970 están apareciendo enfermedades infecciosas emergentes a un ritmo sin precedentes de las cuales una gran parte se consideran zoonóticas. Con el fin de controlar las zoonosis, las medidas contra estas enfermedades se han intensificado y mantenido a nivel nacional e internacional. Un ejemplo típico del esfuerzo internacional lo constituye el Reglamento Sanitario Internacional organizado por la Organización Mundial de la Salud, conocido como RSI (2005), que se ha venido implementando desde 2007.

En Japón los Ministerios correspondientes han establecido marcos para controlar las zoonosis desde un enfoque tanto administrativo como científico que cumplen los requisitos del RSI (2005). Los autores presentan el marco de control de zoonosis implementado en Japón como ejemplo útil de un sistema de gestión global de la salud pública y animal para los próximos años.

Palabras clave

Enfermedad infecciosa emergente – Investigación básica y aplicada – Legislación – Leyes y reglamentos – Reglamento Sanitario Internacional 2005 – Zoonosis.



References

- Aihara K., Ohkusa Y. & Maeda H. (2006). – The world's first development of a large-scale analysis system for pandemic influenza in consideration of crowded commuter trains [in Japanese]. *In* 57th Regular news conference of the Institute of Industrial Science, University of Tokyo, 11 January 2006. Available at: www.iis.u-tokyo.ac.jp/topics/2006/060111.pdf (accessed on 6 January 2010).
- Animal Quarantine Service, Japanese Ministry of Agriculture, Forestry and Fisheries (2008). – Bring animals into Japan. Available at: www.maff.go.jp/aqs/english/animal/im_index.html (accessed on 6 January 2010).
- Animal Quarantine Service, Japanese Ministry of Agriculture, Forestry and Fisheries (2008). – Statistics on animal quarantine [in Japanese]. Available at: www.maff.go.jp/aqs/tokei/toukei.html (accessed on 6 January 2010).
- BioCaster Global Health Monitor (2009). – Communicable disease surveillance from internet news. Available at: <http://biocaster.nii.ac.jp/index.php?lang=en> (accessed on 6 January 2010).
- Bliziotis I.A., Paraschakis K., Vergidis P.I., Karavasiou A.I. & Falagas M.E. (2005). – Worldwide trends in quantity and quality of published articles in the field of infectious diseases. *BMC infect. Dis.*, **5** (1), 16. Available at: www.biomedcentral.com/1471-2334/5/16 (accessed on 6 January 2010).
- Brown C. (2004). – Emerging zoonoses and pathogens of public health significance – an overview. *In* Emerging zoonoses and pathogens of public health concern (L.J. King, ed.). *Rev. sci. tech. Off. int. Epiz.*, **23** (2), 435-442. Available at: www.oie.int/boutique/extrait/435442brown.pdf (accessed on 6 January 2010).
- Cabinet Office of Japan (2003). – Public opinion survey of humane treatment of animals in 2003 [in Japanese]. Available at: www8.cao.go.jp/survey/h15/h15-doubutu/ (accessed on 6 January 2010).
- Cabinet Secretariat of Japan (2001). – Concerning the countermeasures against bio- and chemical terrorisms [in Japanese]. *In* Official announcement of the Cabinet Secretary, 19 December 2001. Available at: www.kantei.go.jp/jp/kakugikettei/2001/1219nbctaisyo.html (accessed on 6 January 2010).
- Cabinet Secretariat of Japan (2008). – Act on Domestic Animal Infectious Diseases Control. *In* Translations of laws and regulations (in compliance with standard bilingual dictionary). Available at: www.cas.go.jp/jp/seisaku/hourei/data/adaidc.pdf (accessed on 6 January 2010).
- De Jong B., Andersson Y. & Ekdahl K. (2005). – Effect of regulation and education on reptile-associated salmonellosis. *Emerg. infect. Dis.*, **11** (3), 398-403. Available at: www.cdc.gov/ncidod/EID/vol11no03/04-0694.htm (accessed on 6 January 2010).
- Deguchi H. (2006). – Analysis of the program and project for prevention of pandemic influenza using social simulation [in Japanese]. *In* 1st Workshop organized by the Center for Agent-Based Social Systems Sciences, 19 April, Tokyo Institute of Technology. Tokyo Institute of Technology, Kanagawa. Available at: www.absss.titech.ac.jp/cabsss/podcast/anti_pandemic_simulation_001.pdf (accessed on 6 January 2010).
- Global Health Security Initiative (2008). – Introducing the global health security initiative. Available at: www.ghsi.ca/english/index.asp (accessed on 6 January 2010).
- Hayashitani H., Iwata T. & Nakadai A. (2008). – Salmonella in reptiles [in Japanese]. *Modern Media*, **54** (6), 165-170.
- Infectious Disease Surveillance Center, National Institute of Infectious Diseases (1999). – National epidemiological surveillance of infectious diseases in compliance with the enforcement of the new Infectious Diseases Control Law. *Infect. Agents Surveill. Rep.*, **20** (4), 230. Available at: <http://idsc.nih.go.jp/iasr/20/230/de2309.html> (accessed on 6 January 2010).
- Infectious Disease Surveillance Center, National Institute of Infectious Diseases (2004). – Table I. Official diseases and report-requested diseases [in Japanese]. *In* Countermeasures to control highly pathogenic avian influenza among poultry populations in Japan – Ministry of Agriculture, Forestry and Fisheries (MAFF). *Infect. Agents Surveill. Rep.*, **25** (11), 297-299. Available at: <http://idsc.nih.go.jp/iasr/25/297/graph/dt29791.gif> (accessed on 6 January 2010).
- Infectious Disease Surveillance Center, National Institute of Infectious Diseases (2007). – Amendment of the Infectious Diseases Control Law, Japan, as of June 2007. *Infect. Agents Surveill. Rep.*, **28** (7). Available at: <http://idsc.nih.go.jp/iasr/28/329/tpc329.html> (accessed on 6 January 2010).
- Infectious Disease Surveillance Center, National Institute of Infectious Diseases (2007). – Infectious agents and toxins corresponding to target diseases of the Infectious Diseases Control Law, revised on 1 June 2007. *In* Amendment of the Infectious Diseases Control Law, as of June 2007. *Infect. Agents Surveill. Rep.*, **28** (7), 185-188. Available at: <http://idsc.nih.go.jp/iasr/28/329/graph/t3291.pdf> (accessed on 6 January 2010).
- Infectious Disease Surveillance Center, National Institute of Infectious Diseases (2007). – Target diseases of the Infectious Diseases Control Law, revised on 1 April 2007. *In* Amendment of the Infectious Diseases Control Law, as of June 2007. *Infect. Agents Surveill. Rep.*, **28** (7), 185-188. Available at: <http://idsc.nih.go.jp/iasr/28/329/graph/t3292.pdf> (accessed on 6 January 2010).

19. Infectious Disease Surveillance Center, National Institute of Infectious Diseases (2008). – Amending the Infectious Diseases Control Law and the Quarantine Law and strengthening measles control in Japan as of May 2008. *Infect. Agents Surveill. Rep.*, **29** (7), 179-181. Available at: <http://idsc.nih.go.jp/iasr/29/341/tpc341.html> (accessed on 6 January 2010).
20. Inter-Ministerial Avian Influenza Committee (2007). – Pandemic Influenza Preparedness Action Plan of the Japanese Government, revised October 2007. Available at: www.mhlw.go.jp/english/topics/influenza/dl/pandemic02.pdf (accessed on 6 January 2010).
21. Japanese Council for Science and Technology Policy (2007). – Approach by the Ministry of Education, Culture, Sports, Science and Technology, the Ministry of Health, Labour and Welfare and the Ministry of Agriculture, Forestry and Fisheries [in Japanese]. *In* Explanatory materials No. 4 – No. 7 of the Life Science Project Team, Tokyo. Available at: www8.cao.go.jp/cstp/project/bunyabetu2006/life/2kai/haihu2.html (accessed on 6 January 2010).
22. Japanese Council for Science and Technology Policy (2008). – Study on the dynamics and genome analysis of viruses which derive from wild birds [in Japanese]. *In* Explanatory materials No. 3-1 – No. 3-2 of the Life Science Project Team, Tokyo. Available at: www8.cao.go.jp/cstp/project/bunyabetu2006/life/10kai/haihu10.html (accessed on 6 January 2010).
23. Japanese Council for Science and Technology Policy (2008). – Study on the effective control of emerging infectious diseases which are needed for biosafety level 4 facilities [in Japanese]. *In* Explanatory materials No. 2-1 – No. 2-2 of the Life Science Project Team, Tokyo. Available at: www8.cao.go.jp/cstp/project/bunyabetu2006/life/9kai/haihu9.html (accessed on 6 January 2010).
24. Japanese Ministry of Agriculture, Forestry and Fisheries (MAFF) (2005). – Annual statistics of animal infectious diseases. *In* Statistics on animal hygiene 2005. MAFF, Tokyo.
25. Japanese Ministry of Agriculture, Forestry and Fisheries (MAFF) (2007). – Monthly report about the outbreaks of official diseases and report-requested diseases in December 2006 [in Japanese]. *Anim. Hyg. Weekly*, **2950**, 118.
26. Japanese Ministry of Agriculture, Forestry and Fisheries (MAFF) (2007). – Monthly report about the outbreaks of official diseases and report-requested diseases in December 2006 [in Japanese]. *Anim. Hyg. Weekly*, **2953**, 238-240.
27. Japanese Ministry of Agriculture, Forestry and Fisheries (MAFF) (2007). – Technology development for the control of bovine spongiform encephalopathy and zoonoses [in Japanese]. Available at: www.s.affrc.go.jp/docs/project/2007/outline/2007_project_2_1.pdf (accessed on 6 January 2010).
28. Japanese Ministry of Agriculture, Forestry and Fisheries (MAFF) (2008). – Monthly report about the outbreaks of official diseases and report-requested diseases in December 2007 [in Japanese]. *Anim. Hyg. Weekly*, **3003**, 153-155.
29. Japanese Ministry of Agriculture, Forestry and Fisheries (MAFF) (2008). – Monthly report about the outbreaks of official diseases and report-requested diseases in December 2007 [in Japanese]. *Anim. Hyg. Weekly*, **3006**, 179.
30. Japanese Ministry of Education, Culture, Sports, Science and Technology (2005). – LifeScience Portalsite. Research aimed at producing visible results. Formation Program of Research Centers for Emerging & Reemerging Infectious Diseases. Available at: www.lifescience.mext.go.jp/english/projects/b07_2005.html# (accessed on 6 January 2010).
31. Japanese Ministry of Health, Labour and Welfare (MHLW) (2003). – Concerning the domestic counter-terrorism measures [in Japanese]. *In* Notification No. 1215001 and No. 1215002 in the joint names of the related departments of MHLW, 15 December. MHLW, Tokyo. Available at: www.mhlw.go.jp/kinkyu/j-terr/2003/1215-1b.html (accessed on 6 January 2010).
32. Japanese Ministry of Health, Labour and Welfare (2003). – Risk analysis of imported zoonoses [in Japanese]. *In* Proc. Working Group for Zoonosis Control, Tokyo. Available at: www.mhlw.go.jp/shingi/2003/02/dl/s0204-2c.pdf (accessed on 6 January 2010).
33. Japanese Ministry of Health, Labour and Welfare (MHLW) (2006). – Assessment of MHLW research enterprise in 2007 fiscal year (assessment before budget request). Research enterprise for AIDS, hepatitis, and emerging and reemerging infectious diseases [in Japanese]. Background materials No. 3. Council of Health Sciences, Tokyo. Available at: www.mhlw.go.jp/shingi/2006/10/dl/s1012-5k.pdf (accessed on 6 January 2010).
34. Japanese Ministry of Health, Labour and Welfare (MHLW) (2006). – 2006 guidelines on all-out hygiene control of pets [in Japanese]. MHLW, Tokyo. Available at: www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/pdf/02-10-04.pdf (accessed on 6 January 2010).
35. Japanese Ministry of Health, Labour and Welfare (MHLW) (2007). – Brief summary of studies on the health crisis management and the establishment of counter-terrorism measures in 2007 fiscal year [in Japanese]. *In* Proc. 2nd Health Crisis Management Committee, 5 June. MHLW, Tokyo. Available at: www.mhlw.go.jp/shingi/2007/06/dl/s0605-3c.pdf (accessed on 8 April 2009).
36. Japanese Ministry of Health, Labour and Welfare (MHLW) (2007). – Concerning notifications by physicians and veterinarians [in Japanese]. MHLW, Tokyo. Available at: www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/01.html (accessed on 6 January 2010).
37. Japanese Ministry of Health, Labour and Welfare (2007). – General picture of the information flow according to the International Health Regulations [in Japanese]. *In* Proc. 2nd Health Crisis Management Committee, Tokyo. Available at: www.mhlw.go.jp/shingi/2007/06/dl/s0605-3f.pdf (accessed on 6 January 2010).

38. Japanese Ministry of Health, Labour and Welfare (MHLW) (2007). – Import statistics of animals 2007. MHLW, Tokyo. Available at: www.mhlw.go.jp/english/topics/importanimal/dl/05.pdf (accessed on 6 January 2010).
39. Japanese Ministry of Health, Labour and Welfare (MHLW) (2007). – New notification system for the importation of animals. In Official announcement of the MHLW in November 2004 (revised in February 2009). MHLW, Tokyo. Available at: www.mhlw.go.jp/english/topics/importanimal/index.html (accessed on 6 January 2010).
40. Japanese Ministry of Health, Labour and Welfare (MHLW) (2007). – Outline of the comprehensive package of measures to control infectious diseases, including the suitable management of infectious agents [in Japanese]. MHLW, Tokyo. Available at: www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou17/pdf/03-01.pdf (accessed on 6 January 2010).
41. Japanese Ministry of Health, Labour and Welfare (MHLW) (2007). – Summary of grants for health science in 2007 fiscal year [in Japanese]. MHLW, Tokyo. Available at: www.mhlw.go.jp/bunya/kenkyuu/jigyuu/hojokin-gaiyo07/index.html (accessed on 6 January 2010).
42. Japanese Ministry of Health, Labour and Welfare (MHLW) (2008). – How were the designated diseases selected? Question No. 37. In Questions and answers about the notification system for the importation of animals [in Japanese]. MHLW, Tokyo. Available at: www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou12/16.html (accessed on 6 January 2010).
43. Japanese Ministry of Health, Labour and Welfare (MHLW) (2008). – Number of reports about infectious disease outbreaks [in Japanese]. MHLW, Tokyo. Available at: www.bm.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou15/02-01.html (accessed on 6 January 2010).
44. Japanese Ministry of Health, Labour and Welfare (MHLW) (2008). – Summary of clinical study on pre-pandemic vaccines [in Japanese]. In Explanatory materials No. 6 of the 8th Ad hoc Meeting of pandemic influenza, Tokyo. MHLW, Tokyo. Available at: www.mhlw.go.jp/shingi/2008/07/dl/s0730-13i.pdf (accessed on 6 January 2010).
45. Japanese Ministry of Internal Affairs and Communication (MIC) (2006). – Result of administrative assessment regarding the countermeasures against infectious diseases [in Japanese]. MIC, Tokyo. Available at: www.soumu.go.jp/kanku/kanto/kanagawa/pdf/060809_1.pdf (accessed on 6 January 2010).
46. Japanese Ministry of Internal Affairs and Communication (MIC) (2008). – Figure 2.2. Population density by country (2005). In Statistical handbook of Japan 2008. MIC, Tokyo. Available at: www.stat.go.jp/english/data/handbook/c02cont.htm (accessed on 6 January 2010).
47. Japanese Ministry of the Environment (MOE) (2001). – Change of social background regarding the care and management of animals, and consciousness and request for care [in Japanese]. In Explanatory materials No. 3 of the 2nd Committee for the Humane Treatment of Animals. MOE, Tokyo. Available at: www.env.go.jp/council/14animal/y140-02/mat03.pdf (accessed on 6 January 2010).
48. Japanese Ministry of the Environment (MOE) (2008). – Information about highly pathogenic avian influenza [in Japanese]. MOE, Tokyo. Available at: www.env.go.jp/nature/dobutsu/bird_flu/index.html (accessed on 6 January 2010).
49. Jones K.E., Patel N.G., Levy M.A., Storeygard A., Balk D., Gittleman J.L. & Daszak P. (2008). – Global trends in emerging infectious diseases. *Nature*, **451** (7181), 990-994.
50. Marano N. & Pappaioanou M. (2004). – Historical, new, and reemerging links between human and animal health. *Emerg. infect. Dis.*, **10** (12), 2065-2066. Available at: www.cdc.gov/ncidod/EID/vol10no12/04-1037.htm (accessed on 6 January 2010).
51. Merianos A. (2007). – Surveillance and response to disease emergence. *Curr. Top. Microbiol. Immunol.*, **315**, 477-509.
52. Morse S.S. (2004). – Factors and determinants of disease emergence. In Emerging zoonoses and pathogens of public health concern (L.J. King, ed.). *Rev. sci. tech. Off. int. Epiz.*, **23** (2), 443-451. Available at: www.oie.int/boutique/extrait/443452morse.pdf (accessed on 6 January 2010).
53. Murphy F.A. (1998). – Emerging zoonoses. *Emerg. infect. Dis.*, **4** (3), 429-435. Available at: www.cdc.gov/ncidod/eid/vol4no3/murphy.htm (accessed on 6 January 2010).
54. Nakadai A., Kuroki T., Kato Y., Suzuki R., Yamai S., Yaginuma C., Shiotani R., Yamanouchi A. & Hayashidani H. (2005). – Prevalence of salmonella spp. in pet reptiles in Japan. *J. vet. med. Sci.*, **67** (1), 97-101. Available at: www.jstage.jst.go.jp/article/jvms/67/1/97/_pdf (accessed on 6 January 2010).
55. Nakajima K. (2005). – Enhanced zoonotic disease control measures subsequent to the revision of the Infectious Diseases Control Law. *Infect. Agents Surveill. Rep.*, **26** (8). Available at: <http://idsc.nih.gov.jp/iasr/26/306/de3062.pdf> (accessed on 6 January 2010).
56. National Institute of Animal Health (2008). – Infectious diseases designated by the Domestic Animal Infectious Diseases Control Law [in Japanese]. Available at: <http://niah.naro.affrc.go.jp/disease/fact/kansi.html> (accessed on 6 January 2010).
57. National Institute of Infectious Diseases (NIID) (2008). – Progress of IHR 2005 implementation at home and abroad [in Japanese]. In Training workshop for health crisis management in the 2008 fiscal year. NIID, Tokyo. Available at: http://idsc.nih.gov.jp/training/20kanri/pdf/Sep.19_3.pdf (accessed on 6 January 2010).

58. National Institute of Informatics (2010). – Database of research projects funded by the grant-in-aid for scientific research. Available at: <http://kaken.nii.ac.jp/en> (accessed on 6 January 2010).
59. National Institute of Public Health (NIPH) (2008). – Database of study supported by grants for health science from the Ministry of Health, Labour and Welfare [in Japanese]. NIPH, Tokyo. Available at: <http://mhlw-grants.niph.go.jp/> (accessed on 6 January 2010).
60. Riken Genome Sciences Center (2006). – Database of the predicted three-dimensional structures of neuraminidase, a target protein for the development of anti-influenza drugs. Available at: http://protein.gsc.riken.jp/Research/index_na.html (accessed on 6 January 2010).
61. Takahashi-Omoe H. & Omoe K. (2007). – Animal experimentation in Japan: regulatory processes and application for microbiological studies. *Comp. Immunol. Microbiol. infect. Dis.*, **30** (4), 225-246.
62. Takahashi-Omoe H., Omoe K. & Okabe N. (2008). – Regulatory systems for prevention and control of rabies, Japan. *Emerg. infect. Dis.*, **14** (9), 1368-1374. Available at: www.cdc.gov/eid/content/14/9/1368.htm (accessed on 6 January 2010).
63. Welfare and Medical Service Agency (2006). – Nationwide meetings for infectious disease control between central and local governments [in Japanese]. Available at: www.wam.go.jp/wamappl/bb14GS50.nsf/aCategoryList?OpenAgent&CT=40&MT=040&ST=160 (accessed on 6 January 2010).
64. Woodworth B.L., Atkinson C.T., LaPointe D.A., Hart P.J., Spiegel C.S., Tweed E.J., Henneman C., LeBrun J. *et al.* (2005). – Host population persistence in the face of introduced vector-borne diseases: Hawaii amakihi and avian malaria. *Proc. natl Acad. Sci. USA*, **102** (5), 1531-1536. Available at: www.pnas.org/content/102/5/1531.long (accessed on 6 January 2010).
65. World Health Organization (WHO) (2007). – A safer future: global public health security in the 21st century. In *World Health Report 2007*. WHO, Geneva. Available at: www.who.int/whr/2007/whr07_en.pdf (accessed on 6 January 2010).
66. World Health Organization (WHO) (2008). – International Health Regulations. WHO, Geneva. Available at: www.who.int/csr/ihr/en/ (accessed on 6 January 2010).
67. World Health Organization (WHO) (2008). – Rabies. *Epidemiology*. WHO, Geneva. Available at: www.who.int/rabies/epidemiology/en/ (accessed on 6 January 2010).
68. Yoshikawa Y. (2006). – Control and measure of zoonoses [in Japanese]. *Kansenshogaku zasshi*, **80** (2), 64-69. Available at: <http://journal.kansensho.or.jp/Disp?pdf=0800020064.pdf> (accessed on 6 January 2010).
-

