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DRAFT REPORT OF THE MEETING OF THE OIE AD HOC GROUP ON AVIAN INFLUENZA

Paris, 12-14 November 2003

The OIE *ad hoc* Group on avian influenza met at the OIE Headquarters from 12 to 14 November 2003.

The members of the OIE *ad hoc* Group and other participants are listed in [Appendix I](#). The Agenda adopted is given in [Appendix II](#).

On behalf of the Director General of the OIE, Dr D. Wilson welcomed the experts and thanked them for their willingness to address the requests from Member Countries to work further on revising the chapter of the OIE *Terrestrial Animal Health Code* (hereafter referred to as the “*Terrestrial Code*”) on avian influenza (AI).

An updated document outlining the latest information on avian influenza, drawn up by several members of the *ad hoc* Group, is at [Appendix III](#).

Based on the epidemiology of the disease, avian commodities usually traded and the comments received from Member Countries, the *ad hoc* Group revised the proposals made at its previous meeting ([Appendix IV](#)).

The *ad hoc* Group discussed the definition of AI and the consequent reporting obligations of Member Countries, and revised the definition taking into account the essential link with the concept of compartmentalisation in assessing the risks associated with trade. The *ad hoc* Group noted that a geographical approach to an outbreak of AI was still permitted but that an approach based on management was an additional option for Member Countries.

In addressing different disease control strategies, the *ad hoc* Group recognised vaccination as a useful tool to support eradication and set guidelines for trade in commodities from vaccinated poultry.

The *ad hoc* Group revised the commodity articles, taking into account the biological differences between low pathogenic notifiable avian influenza (LPNAI) and highly pathogenic notifiable avian influenza (HPNAI) regarding the likelihood of transmission of virus via various commodities and the likely consequences.

The *ad hoc* Group reviewed Article 2.1.14.2, recognising the need for targeted surveillance. It considered that targeted surveillance should focus on areas of high poultry density (especially turkeys), free-range poultry and establishments lying along wild bird migration pathways. The *ad hoc* Group felt, however, that it did not have the expertise to define detailed surveillance guidelines and strongly encouraged Member Countries to propose such guidelines to the OIE for examination by appropriate experts.

Appendix XXVI (contd)

The *ad hoc* Group recognised that fresh meat and table eggs probably present a much lower likelihood of transmitting LPNAI than HPNAI viruses, but, due to incomplete scientific data, the recommendations proposed for these commodities only partly reflect this difference. The *ad hoc* Group addressed this difference through a proposed new definition for '*NAI-free establishment*' which distinguishes between the two regarding permitted distances from establishments infected with LPNAI or HPNAI.

Articles 2.1.14.5 and 2.1.14.6 were combined as the *ad hoc* Group believed that the focus in both should be on the health status of the parent flock.

Regarding destruction of the NAI virus, the *ad hoc* Group recognised that parameters for destruction were dependent on virus strain, virus concentration and commodity characteristics, and noted that sufficient up-to-date scientific data were unavailable for most virus strains and the majority of commodities.

The *ad hoc* Group considered that recent developments in knowledge of the virus necessitated the text in the *Terrestrial Manual* on virus detection / isolation being reviewed.

Measures for commodities for human consumption address both the likelihood of transmission to other birds and the public health aspects. Birds with previous or current infections are not permitted to be traded, nor are meat nor eggs from such birds. The *ad hoc* Group noted that only two episodes of H9N2 virus infection had been reported in humans (consisting of two and five cases), despite the widespread occurrence of this subtype in poultry, especially in Asia; as a result, it did not take that subtype into account in its recommendations.

.../Appendices

MEETING OF THE OIE *AD HOC* GROUP ON AVIAN INFLUENZA*Paris, 12-14 November 2003*

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MEETING OF THE OIE *AD HOC* GROUP ON AVIAN INFLUENZA

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Agenda adopted

- 1) Update on scientific and epidemiological information on avian influenza
 - 2) Examination of comments from OIE Member Countries
 - 3) Examination of revisions proposed by the Bureau of the OIE Terrestrial Animal Health Standards Commission
 - 4) Other issues
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AVIAN INFLUENZA – Brief Review

Introduction

The severe form of avian influenza [AI] termed highly pathogenic [HPAI], at one time known as "fowl plague", is throughout the world one of the two most feared diseases of poultry and other birds. This is not only because of the devastation it may cause, with flock mortality of up to 100%, but also the economic impact that may ensue due to trading restrictions and embargoes placed on infected areas. Many countries, including all those in the European Union, enforce statutory control measures in the event of outbreaks of either disease [CEC 1992] and it is recognised as an OIE list A disease.

Actiology

Influenza viruses are segmented, negative strand RNA viruses that are placed in the family Orthomyxoviridae and are divided into three types of influenza virus, A, B and C, which now have genus status. Only influenza A viruses have been reported to cause natural infections of birds. Type A influenza viruses are further divided into subtypes based on the antigenic relationships in the surface glycoproteins haemagglutinin (HA) and neuraminidase (NA). At present 15 HA subtypes (H1-H15) and nine neuraminidase subtypes (N1-N9) have been recognised. Each virus has one H and one N antigen, apparently in any combination. Although the range of subtypes and combinations occurring naturally in mammals appears to be restricted, all subtypes and the majority of possible combinations have been isolated from avian species.

Host Range

Although influenza viruses have been isolated from a large number of species covering 12 of the 50 Orders of birds (Stallknecht, 1998), the number, variety and widespread distribution of influenza viruses has been far greater in waterfowl, Order Anseriformes, than in other birds. In the surveys listed by Stallknecht and Shane (1988) a total of 21,318 samples from all species resulted in the isolation of 2,317 (10.9%) viruses. Of these samples 14,303 were from birds of the Order Anseriformes and yielded 2,173 (15.2%) isolates. The next highest isolation rates were 2.9% and 2.2% from the Passeriformes and Charadriiformes respectively and the overall isolation rate from all birds other than ducks and geese was 2.1%. However, in shorebirds and gulls, the predominant influenza viruses are of subtypes different to those in waterfowl. Each year waterfowl congregate in huge flocks, usually on lakes, before migratory flights are undertaken. Data from the 3-year study by Hinshaw et al., (1980) on ducks congregating on lakes in Alberta, Canada prior to their southern migration showed that influenza virus isolation rates from juvenile ducks may exceed 60%. The perpetuation of influenza viruses in free-living waterfowl is probably related to the passage of virus from adult to juvenile birds on lakes where the birds congregated before migration. Considerable quantities of the virus are excreted with the faeces, estimated up to $10^{8.7}$ mean egg infectious doses per g of faeces from infected ducks (Webster et al., 1978). This contaminates lake or pond water, to the extent that virus may be isolated from untreated lake water where large numbers of waterfowl are found.

Phylogenetic studies (Rohm et al., 1995; Banks et al., 2000a,b) of AI viruses show that lineages and clades of isolates are more related to geographical and temporal parameters than the host from which they were isolated and there is no distinction between wild and domestic bird isolates.

HPAI viruses have been isolated rarely from free-living birds and, apart from tern/S.Africa/61, when they have been isolated it has usually been close to known outbreaks in poultry.

Disease

Influenza A viruses infecting poultry can be divided into two distinct groups on the basis of their ability to cause disease. The very virulent viruses HPAI in which mortality may be as high as 100%. These viruses have been restricted to subtypes H5 and H7, although not all viruses of these subtypes cause HPAI. There have been 19 reported primary isolates of such viruses from domestic poultry since 1959 (Table 1). All other viruses cause a much milder disease consisting primarily of mild respiratory disease, depression and egg production problems in laying birds. Sometimes other infections or environmental conditions may cause exacerbation of influenza infections leading to much more serious disease. For example, in outbreaks of LPAI in Italy in 1999, high mortality was often recorded in young turkeys, reaching 97% in one flock (Capua et al., 2000).

Appendix XXVI (contd)Appendix III (contd)**Molecular basis of virulence**

The haemagglutinin (HA) glycoprotein for influenza viruses has two important functions that are imperative for the infectivity of the virus. First it brings about attachment to host cell and then fusion between the host cell membrane and the virus membrane so that the viral genetic material is introduced into the host cell. This glycoprotein is produced as a precursor, HA0, which requires post translational cleavage by host proteases before it is able to induce membrane fusion and virus particles become infectious (Rott, 1992). The HA0 precursor proteins of avian influenza viruses of low virulence for poultry have a single arginine at the cleavage site and another at position -3 or -4. These viruses are limited to cleavage by host proteases such as trypsin-like enzymes and thus restricted to replication at sites in the host where such enzymes are found, i.e. the respiratory and intestinal tracts. HPAI viruses possess multiple basic amino acids [arginine and lysine] at their HA0 cleavage sites either as a result of apparent insertion or apparent substitution (Vey et al, 1992, Wood et al, 1993, Senne et al, 1996) and appear to be cleavable by a ubiquitous protease[s], probably one or more proprotein-processing subtilisin-related endoproteases of which furin is the leading candidate (Stieneke-Grober et al., 1992). These viruses are able to replicate throughout the bird, damaging vital organs and tissues which results in disease and death (Rott, 1992). For example, all H7 subtype viruses of low virulence have had the amino acid motif at the HA0 cleavage site of either -PEIPKGR*GLF- or -PENPKGR*GLF-, whereas examples of cleavage site amino acid motifs for HPAI H7 viruses are: -PEIPKKKKR*GLF-, -PETPKRKRKR*GLF-, -PEIPKKREKR*GLF-, -PETPKRRRR*GLF-, -PEIPKGSRVRR*GLF-. The last example, from the Italian 1999-2000 outbreaks had what was considered the minimum requirement of two basic amino acids at position -1 and -2 plus a basic amino acid a -4.

Although the first 18 HPAI viruses in Table 1 have multiple basic amino acid motifs as do all HPAI viruses sequenced that were isolated prior to 1959, this is not true of the viruses isolated from the HPAI outbreaks in Chile in 2002. The H7N3 viruses isolated in these outbreaks had motifs with insertion of 11 amino acids but without the apparent minimum requirement of basic amino acids, as their sequences were either PEKPKTCSPLSRCRETR*GLF (4372) or PEKPKTCSPLSRCRKR*GLF (4957).

Current theories suggest that AI subtype H5 and H7 viruses of high virulence emerge from viruses of low virulence by mutation (Garcia et al, 1996, Perdue et al., 1998) although there must be more than one mechanism by which this occurs. This is supported by phylogenetic studies of H7 subtype viruses, which indicate that HPAI viruses do not constitute a separate phylogenetic lineage or lineages, but appear to arise from non-pathogenic strains (Rohm et al., 1995; Banks et al., 2000a) and the *in vitro* selection of mutants virulent for chickens from an avirulent H7 virus (Li et al., 1990). It appears that such mutations occur only after the viruses have moved from their natural host to poultry.

Spread

Spread of AI viruses is related chiefly to the excretion of high concentrations of virus in the faeces of infected birds. All the indications for HPAI are that the viruses of H5 or H7 subtype are introduced initially from feral birds as viruses of low virulence and then they subsequently mutate to virulence. It follows that important control measures that can be taken are to prevent the introduction of LPAI viruses, prevent their spread and, if mutation to HPAI does take place, to prevent the spread of HPAI viruses.

Primary Introduction

All available evidence suggests that primary introduction of AI viruses into an area is by wild birds, usually waterfowl, but gulls and shorebirds have also been implicated. This may not necessarily involve direct contact as infected waterfowl may take the viruses to an area and these may then be introduced to poultry by a variety of mechanisms that may transfer the virus mechanically in infective faeces and respiratory secretions. Surface water used for drinking water may also be contaminated with influenza viruses and a source of infection. The occurrence of AI outbreaks in poultry is consistent with this: (1) there is a higher prevalence of infection of poultry on migratory waterfowl routes, e.g. Minnesota in USA, Norfolk in England; (2) there is a higher prevalence of infection of poultry kept in exposed conditions, e.g. turkeys on range, ducks on fattening fields; (3) surveillance studies in areas such as Minnesota have shown the same variation in virus subtypes in sampled waterfowl and turkey outbreaks; (4) influenza outbreaks show a seasonal occurrence in high-risk areas, which coincides with migratory activity; (5) in most documented specific outbreaks evidence has been obtained of probable waterfowl contact at the initial site.

Appendix XXVI (contd)Appendix III (contd)

Although waterfowl and other wild birds appear to be responsible, albeit indirectly, for most influenza introductions to domestic poultry, other possibilities should not be ruled out. For example, it seems highly likely that H1N1 viruses may pass readily between pigs, humans and turkeys and the introduction of viruses of this subtype to turkey flocks from infected pigs has been well documented.

Since wild birds are a source for primary introduction of AI viruses, it is preferable to design farm practices to minimise direct or indirect contact with wild birds. Since one of the major reservoirs of influenza viruses is in migratory waterfowl, ideally commercial farms should be located away from migratory routes. However, in many countries, particularly USA, Italy and other European countries at least part of the poultry industry has evolved, possibly from hunting origins, so that the greatest concentrations correspond precisely to these flyways. Similarly, poultry may be less likely to become infected with AI viruses if kept indoors (Lang, 1982), but there are strong pressures to rear them on range and for some species, e.g. ostriches, this is a necessity. Rearing of several species on the same farm, especially with one or more reared outdoors, is also a practice likely to attract infected wild birds and result in transfer of infective faeces inside. Use of surface drinking water and the presence of lakes that attracted waterfowl close to the farms were associated with the HPAI outbreaks in Australia (Westbury, 1998). On what was the index farm in the catastrophic outbreaks in Pennsylvania in 1983/4 the farmer had created an artificial pond to keep ducks and attract wild waterfowl (Webster and Kawaoka, 1988).

Secondary spread

Secondary spread of AI viruses is mainly by mechanical transfer of infective faeces, in which virus may be present at high concentrations and may survive for considerable periods (Utterback, 1984). Birds or other animals that are not themselves susceptible to infection may become contaminated and spread the virus. Shared water or food may also become contaminated. However, for domestic poultry the main source of secondary spread is man. In several specific accounts of HPAI infections strong evidence has implicated the movements of caretakers, farm owners and staff, trucks and drivers moving birds or delivering food, and artificial inseminators in the spread of virus both on to and through a farm (Wells 1963; Homme et al., 1970; Halvorson et al., 1980; Alexander and Spackman, 1981; Glass et al., 1981).

Vaccination

In some countries, vaccines designed to contain or prevent HPAI are specifically banned or discouraged by government agencies because they may interfere with stamping out control policies. However, most HPAI control regulations reserve the right to use vaccines in emergencies.

There is little doubt, both in experiments and in the field, that if birds are sufficiently well immunised against the HA subtype corresponding to that of the challenge virus they will be protected from the worst effects of HPAI and the clinical disease and mortalities associated with LPAI. There is therefore economic pressure to invest in vaccination to insure against a potential short term but significant economic loss whenever there is a perceived threat from AI. However, conversely the high cost of vaccination, since it is necessary to inject inactivated avian influenza virus or live recombinant fowlpox-avian influenza vaccines, means there is economic pressure to stop once the threat has lessened.

The existence of a large number of virus subtypes together with the known variation of different strains within a subtype pose serious problems when selecting strains to produce influenza vaccines. In addition, some isolates do not grow to a sufficiently high titre to produce adequately potent vaccines without costly prior concentration. The vaccines produced have either been autogenous, i.e. prepared from isolates specifically involved in an epizootic, or have been prepared from viruses possessing the same haemagglutinin subtype that yield high concentrations of antigen. In the USA, some standardisation of the latter has been carried out in that the National Veterinary Services Laboratories have propagated and hold influenza viruses of each subtype for use as seed virus in the preparation of inactivated vaccines (Bankowski, 1985). The vaccines used extensively in the USA (Halvorson, 1998) and in Italy (D'Aprile, 1986) against viruses of low pathogenicity, and against HPAI in Mexico (Garcia et al., 1998) and Pakistan (Naeem, 1998) have been prepared from infective allantoic fluid inactivated by betapropiolactone or formalin and emulsified with mineral oil.

Recently vaccines have been developed employing new technologies such as baculovirus derived H5 and H7 haemagglutinins (Crawford et al., 1999) and fowl poxvirus recombinants expressing H7 haemagglutinin (Boyle et al., 2000).

Appendix XXVI (contd)Appendix III (contd)

In the USA since the 1970s there has been widespread use of inactivated vaccines produced under special licence on a commercial basis (Halvorson, 1998; McCapes & Bankowski, 1987; Price, 1982). These vaccines have been used primarily in turkeys against viruses that are not highly pathogenic but which may cause serious problems, especially in exacerbating circumstances. Significant quantities of vaccine have been used in Minnesota to protect turkeys against LPAI (Halvorson, 1998) This involves prediction and/or early detection of the subtype likely to cause problems each year for incorporation into the vaccine. Vaccine uptake has varied considerably and generally reflected the number of outbreaks of LPAI or the cost of LPAI to the industry. The 178 outbreaks of LPAI caused primarily by virus of H9N2 subtype occurring in turkeys in Minnesota 1995 resulted in the highest loss recorded of over US\$ 6,000,000 (Halvorson et al., 1998).

Since July 1995, the use of vaccines of H5 or H7 subtype had been restricted in the USA, but they have been used within a control programme under federal, state and industry control (Myers & Morgan, 1998). Inactivated vaccine was prepared from the LPAI virus of H7N3 responsible for a series of outbreaks in turkeys in Utah in 1995 and used, with other measures, to bring the outbreaks under control (Halvorson et al., 1998).

Outside the USA, vaccination against AI has not been used widely or consistently. Zanella et al., (1981) described the production and testing of inactivated vaccines intended to combat the respiratory problems seen in turkeys in NE Italy and associated with LPAI influenza infections. Papparella et al., (1995,1996) reported that while vaccination against AI was only allowed officially in Italy in certain specific circumstances (i.e. as a ring vaccine), inactivated vaccines against H6N2 and H9N2, strains considered enzootic in Italian turkeys, were in common use in breeder birds. Werner (1999) reported use in turkeys of an inactivated vaccine to protect against H9N2 virus.

An inactivated H5N2 vaccine was used in Mexico as a result of the widespread HPAI outbreaks caused by H5N2 virus that began in December 1994 (Villareal & Flores 1997). Between the beginning of 1995 and May 1997 847 million doses of vaccine were licensed for use. Beginning in 1998, recombinant fowlpox vectored vaccine with avian influenza H5 gene insert has been used in Mexico, El Salvador and Guatemala. Inactivated H7N3 vaccine was also used extensively in Pakistan following the widespread HPAI outbreaks in 1995 (Naeem, 1998).

Recently in Italy an inactivated vaccine containing an H7N3 virus was used to vaccinate against a LPAI virus of H7N1 subtype. This enabled infected birds to be distinguished from vaccinated birds using a test to detect antibodies to N1 (Capua et al, 2002).

Zoonotic potential

Influenza is a highly contagious, acute illness in humans for which there are recognisable accounts of epidemics dating back to ancient times. In the 20th century the sudden emergence of antigenically different strains in humans, termed *antigenic shift*, occurred on 4 occasions, 1918 (H1N1), 1957 (H2N2), 1968 (H3N2) and 1977 (H1N1), resulting in pandemics. Frequent epidemics have occurred between the pandemics as a result of accumulated point mutations in the prevalent virus leading to gradual antigenic change, termed *antigenic drift*, which in turn results in infections in a proportion of the population that has become immunologically susceptible. The intra-pandemic influenza epidemics may have a considerable impact on a given population as a result of significant mortality, especially amongst the elderly and other vulnerable groups, and the severe economic cost associated with debilitating illness in a large portion of the population. However, the true influenza pandemics are unmistakable and by far the worst influenza pandemic was the one beginning in 1918. It has been estimated that during the pandemic between 20 to 40 million people died.

The RNA of influenza A viruses consists of 8 distinct segments that code for 10 proteins. Because the viral RNA is segmented, genetic reassortment can occur in mixed infections with different strains of influenza A viruses. This means that when two viruses infect the same cell, progeny viruses may inherit sets of RNA segments made up of combinations of segments identical to those of either of the parent viruses. This gives a theoretical possible number of 2⁸ (=256) different combinations that can form a complete set of RNA segments from a dual infection, although in practice only a few progeny virions possess the correct gene constellation required for viability. Demonstration that the H3N2 1968 pandemic virus differed from the 1957-1968 H2N2 virus in the substitution of two genes, PB1 and the important surface glycoprotein HA gene, with genes almost certainly from an influenza virus of avian origin, led to the suggestion that antigenic shift occurred as a result of reassortment of genes in dual infections with viruses of human and avian origin (Fang et al., 1981; Kawaoka et

Appendix XXVI (contd)Appendix III (contd)

al., 1989). However, although volunteer experiments had shown that transitory infections resulted when humans were infected with viruses of avian origin (Beare & Webster, 1991), no natural infections of humans with avian viruses had been reported. It was clear that there was some barrier to the establishment of avian influenza viruses in the human population that was related to one or more of the genome segments. Both human and avian viruses are known to infect pigs readily. It was, therefore, suggested that pigs acted as “mixing vessels” in which reassortment between human and avian influenza viruses could take place with the emergence of viruses with the necessary genome segments(s) from the virus of human origin to allow replication and spread in the human population, but with a different haemagglutinin surface glycoprotein, so that the human population could be regarded as immunologically naïve (Scholtissek, et al., 1985). This theory was also thought to account for the apparent emergence of pandemics in the 20th century in the Far East where agricultural practices mean high concentrations of people, pigs and waterfowl live closely together (Shortridge & Stuart-Harris, 1982).

However, in the last 6 years avian influenza virus infections of humans have been detected on four occasions, with three different subtypes.

In 1996 an H7N7 virus was isolated in England from the eye of a woman with conjunctivitis who kept ducks. This virus was shown to be genetically closest in all 8 genes to viruses of avian origin and to have >98% nucleotide homology in the HA gene with a virus of H7N7 subtype isolated from turkeys in Ireland in 1995 (Banks et al., 1998).

In May 1997 a virus of H5N1 subtype was isolated from a young child who died in Hong Kong and by December 1997 the same virus was confirmed by isolation to have infected 18 people, six of whom died (Shortridge et al., 2000). There was evidence of very limited human to human spread of this virus (Buxton Bridges et al., 2000), but clearly the efficiency of transmission must have been extremely low. There have been no new cases since December 1997. The viruses isolated from the human cases appeared to be identical to viruses first isolated from chickens in Hong Kong in March 1997 following an outbreak of highly pathogenic disease. Both human and avian isolates possess multiple basic amino acids at the HA0 cleavage site (Suarez et al., 1998).

In recent years outbreaks in poultry due to viruses of H9 subtype, usually H9N2, have been widespread. During the second half of the 1990s outbreaks, due to H9N2 subtype have been reported in Germany, Italy, Ireland, South Africa, USA, Korea, China, the Middle East, Iran and Pakistan (Banks et al., 2000b). These have often been associated with widespread and serious disease problems in commercial chickens. In March 1999 two independent isolations of influenza virus subtype H9N2 were made from girls aged one and 4 who recovered from flu-like illnesses in Hong Kong (Peiris et al., 1999a; 1999b). Subsequently, 5 isolations of H9N2 virus from humans on mainland China in August 1998 were reported.

The obvious inference is that the very high mortality, 6/18, amongst the people infected with the H5N1 virus in Hong Kong was because the virus was capable of systemic infection due to the presence of multiple basic amino acids at the HA0 cleavage site. This would allow cleavage to be mediated by a furin-like protease(s) and the virus to spread systemically. However, evidence that this was the case is lacking. Generally, the 18 patients presented with severe respiratory symptoms. For those that died, several of whom were vulnerable due to complicating medical conditions present prior to infection, pneumonia appeared to be the main cause as it often is in deaths occurring as a result of infections with influenza viruses “normally” in the human population. A serological survey after the outbreak identified 17% seroprevalence in poultry workers in Hong Kong but without any known occurrence of clinical disease.

The isolation of the H7 virus from the woman with conjunctivitis was fortuitous, the first isolation of H5N1 in Hong Kong as a result of the death of the patient and all other isolates of avian viruses from humans resulted from enhanced awareness and surveillance exercises. In all these cases there was no evidence of human to human spread except with the H5N1 infections where there was evidence of very limited spread. This is in keeping with the finding that all these viruses possessed all eight genes of avian origin. It may well be that infection of humans with avian influenza viruses occurs much more frequently than originally assumed, but due to their limited effect go unrecognised. For the human population as a whole the main danger appears to be if people infected with an “avian” virus are infected simultaneously with a “human” influenza virus. In such circumstances reassortment could occur with the potential emergence of a virus fully capable of spread in the human population, but with an HA for which the human population was immunologically naïve. Presumably this represents a very rare coincidence, but one which could result in a true influenza pandemic.

Appendix XXVI (contd)Appendix III (contd)**References**

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Table 1: Primary HPAI virus isolates from poultry* since 1959

1.	A/chicken/Scotland/59 (H5N1)
2.	A/turkey/England/63 (H7N3)
3.	A/turkey/Ontario/7732/66 (H5N9)
4.	A/chicken/Victoria/76 (H7N7)
5.	A/chicken/Germany/79 (H7N7)
6.	A/turkey/England/199/79 (H7N7)
7.	A/chicken/Pennsylvania/1370/83 (H5N2)
8.	A/turkey/Ireland/1378/83 (H5N8)
9.	A/chicken/Victoria/85 (H7N7)
10.	A/turkey/England/50-92/91 (H5N1)
11.	A/chicken/Victoria/1/92 (H7N3)
12.	A/chicken/Queensland/667-6/94 (H7N3)
13.	A/chicken/Mexico/8623-607/94 (H5N2)
14.	A/chicken/Pakistan/447/94 (H7N3)
15.	A/chicken/NSW/97 (H7N4)
16.	A/chicken/Hong Kong/97 (H5N1)
17.	A/chicken/Italy/330/97 (H5N2)
18.	A/turkey/Italy/99 (H7N1)
19.	A/chicken/Chile/2002 (H7N3)
20.	A/chicken/The Netherlands/2003 (H7N7)

* Where outbreaks were widespread and affecting more than one species, the isolate from the first outbreak identified is listed.

CHAPTER 2.1.14.
AVIAN INFLUENZA

Article 2.1.14.1.

For the purposes of this *Code*, avian influenza (AI) is defined as ‘an infection of poultry caused either by any influenza A virus which has an IVPI in 6-week-old chickens greater than 1.2 or by an influenza A virus of H5 or H7 subtype’.

For the purposes of this *Terrestrial Code*, notifiable avian influenza (NAI) is defined as an infection of poultry caused by any influenza A virus of the H5 or H7 subtypes or by any AI virus with an intravenous pathogenicity index (IVPI) greater than 1.2 (or as an alternative at least 75% mortality) as described below. NAI viruses can be divided into highly pathogenic notifiable avian influenza (HPNAI) and low pathogenicity notifiable avian influenza (LPNAI):

- 1) HPNAI viruses have an IVPI in 6-week-old chickens greater than 1.2 or, as an alternative, cause at least 75% mortality in 4 to 8 week-old chickens infected intravenously. H5 and H7 viruses which do not have an IVPI of greater than 1.2 or cause less than 75% mortality in an intravenous lethality test should be sequenced to determine whether multiple basic amino acids are present at the cleavage site of the haemagglutinin molecule (HA0); if the amino acid motif is similar to that observed for other HPNAI isolates, the isolate being tested should be considered as HPNAI.
- 2) LPNAI are all Influenza A viruses of H5 and H7 subtype that are not HPNAI viruses.

Poultry is defined as ‘all birds reared or kept in captivity for the production of meat or eggs for consumption, for the production of other commercial products, for restocking supplies of game, or for breeding these categories of birds’.

For the purpose of *international trade*, this chapter deals not only with the occurrence of clinical signs caused by NAI virus, but also with the presence of infection with NAI virus in the absence of clinical signs. Articles dealing with trade in *commodities* recommend different sanitary measures, depending on the presence or absence of clinical signs.

The following defines the occurrence of AI virus infection:

- 1) ~~AI virus has been isolated and identified as such from poultry or a product derived from poultry, or~~
- 2) ~~viral antigen or viral RNA specific to H5 or H7 subtype of AI virus has been identified in samples from poultry or a product derived from poultry, or~~
- 3) ~~antibodies to H5 or H7 subtype of AI virus that are not a consequence of vaccination have been detected in poultry.~~

The following defines the occurrence of NAI virus infection:

- 1) HPNAI virus has been isolated and identified as such or specific viral RNA has been detected in poultry or a product derived from poultry, or
- 2) LPNAI virus has been isolated and identified as such or specific viral RNA has been detected in poultry or a product derived from poultry, or

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- 3) antibodies to H5 or H7 subtype of NAI virus that are not a consequence of vaccination, nor indicative of a non-specific reaction, have been detected in poultry; in such cases, virus isolation should be attempted to establish whether the serological positivity is due to LPNAI or HPNAI; if appropriate samples are not available or if results are negative, this should be regarded as LPNAI.

NAI free establishment means an establishment in which there has been no clinical sign of NAI for the past 21 days; and which is not situated within 3 kilometres of an establishment infected with HPNAI and within one kilometre of an establishment infected with LPNAI.

For the purposes of this *Terrestrial Code*, the *incubation period* for NAI shall be ~~28~~ 21 days.

Standards for diagnostic tests are described in the *Terrestrial Manual*.

Any vaccine used should comply with the standards described in the *Terrestrial Manual*.

Article 2.1.14.1.bis

The NAI status of a country or compartment can be determined on the basis of the following criteria:

- 1) the outcome of a risk assessment identifying all potential factors for NAI occurrence and their historic perspective;
- 2) NAI is notifiable in the whole country, an on-going NAI awareness programme is in place, and all notified suspect occurrences of NAI are subjected to field and, where applicable, laboratory investigations;
- 3) appropriate surveillance is in place to demonstrate the presence of infection in the absence of clinical signs in poultry, and the risk posed by birds other than poultry; this may be achieved through an NAI surveillance programme in accordance with this chapter and Chapter 1.3.6.

Article 2.1.14.2.

NAI free country or compartment

A country or compartment may be considered free from NAI when it has been shown that NAI infection has not been present for the past 12 months. If ~~a stamping-out policy is applied~~ infected poultry are slaughtered, this period shall be ~~6~~ 3 months after the slaughter of the last infected poultry.

The NAI status should be determined by an ongoing surveillance and monitoring programme (carried out in conformity with the provisions of Chapter 1.3.6.) based on virus isolation, virus detection or serology. The programme may need to be adapted to target parts of the country or compartment at a higher risk due to historical or geographical factors, population data, or proximity to recent outbreaks.

Freedom of infection in a country or zone can be demonstrated with random and/or targeted serological surveillance at a minimum interval of 6 months designed to provide at least a 95% level of confidence of detecting a prevalence of NAI infected enterprises of 1%. Freedom of infection in an enterprise can be demonstrated with an ongoing surveillance programme designed to provide at least a 95% level of confidence of detecting a prevalence of NAI infection of 10%. Each establishment should be sampled to provide a 95% level of confidence of detecting a prevalence of NAI of 20%. For commercial ducks the surveillance programme should be based on virus isolation or detection in the absence of validated serological methods.

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In the case of a country or zone in which vaccination is being conducted, the ongoing surveillance and monitoring programme (carried out in conformity with the provisions of Chapter 1.3.6.) based on virus isolation, virus detection or serology should be carried out on all vaccinated flocks at a minimum interval of 6 months. In each vaccinated flock, the number of birds to be tested should provide at least a 95% level of confidence of detecting a prevalence of NAI infection of 20%. In the case of an enterprise in which vaccination is being conducted, the ongoing surveillance and monitoring programme (carried out in conformity with the provisions of Chapter 1.3.6.) based on virus isolation, virus detection or serology should be carried out to provide at least a 95% level of confidence of detecting a prevalence of NAI infection of 10%. If a serological test is used, it should be able to distinguish vaccinated birds from infected birds. Additional security should be provided by the use of relevant serological tests in identifiable sentinel birds which can be tested to help identify field infections in vaccinated flocks.

Article 2.1.14.3.

When importing from an NAI free country or compartment, *Veterinary Administrations* should require:
for live poultry (other than day-old poultry)

the presentation of an *international veterinary certificate* attesting that the poultry:

- 1) showed no clinical sign of NAI on the day of shipment;
- 2) were kept in an NAI free country or compartment since they were hatched or for the past ~~28~~ 21 days;
- 3) either have not been vaccinated against NAI, or have been vaccinated and the date of vaccination and the details of the vaccine are stated.

[Note: If the poultry were vaccinated against NAI, the nature of the vaccine used and the date of vaccination should be stated in the certificate.]

Article 2.1.14.4.

Regardless of the NAI status of the country of origin, *Veterinary Administrations* should require:
for the importation of live birds other than poultry

the presentation of an *international veterinary certificate* attesting that the birds:

- 1) showed no clinical sign of NAI on the day of shipment;
- 2) were kept in isolation approved by the Veterinary Services ~~a quarantine station~~ since they were hatched or for the ~~28~~ 21 days prior to shipment and showed no clinical sign of NAI during the ~~isolation~~ quarantine period;
- 3) were subjected to a diagnostic test 7 to 14 days prior to shipment to demonstrate freedom from NAI.

Article 2.1.14.5.

When importing from an NAI free country or compartment, *Veterinary Administrations* should require:
for day-old live poultry

the presentation of an *international veterinary certificate* attesting that the poultry:

- ~~1) showed no clinical sign of NAI on the day of shipment;~~
- 2) were kept in an NAI free country or compartment since they were hatched;

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- 3) were derived from parent flocks which had been kept in an NAI free country or compartment for 21 days prior to the collection of the eggs;
- 4) and/or the parent flock had/had not been vaccinated.

(Note: If the day-old poultry or the parents of the poultry were vaccinated against NAI, the details of the vaccine and the date of vaccination should be provided.)

Article 2.1.14.5.bis.

When importing from an NAI free country or compartment, *Veterinary Administrations* should require:
for *hatching eggs*

the presentation of an *international veterinary certificate* attesting that the eggs:

- 1) came from an NAI free country or compartment;
- 2) were derived from parent flocks which had been kept in an NAI free country or compartment for 21 days prior to the collection of the eggs;
- 3) were derived from parent flocks which had not been vaccinated against NAI, or had been vaccinated against NAI and the date of vaccination and the details of the vaccine are stated.

Article 2.1.14.6.

When importing from an NAI free country or compartment, *Veterinary Administrations* should require:
for ~~*hatching eggs*~~ or *eggs for consumption*

the presentation of an *international veterinary certificate* attesting that the eggs come from an NAI free country or compartment.

Article 2.1.14.6.bis.

When importing from a country or compartment not considered free from NAI, *Veterinary Administrations* should require:

for *eggs for consumption*

the presentation of an *international veterinary certificate* attesting that the entire consignment of eggs comes from birds:

- 1) which have been kept in an NAI free establishment;
- 2) which have been tested serologically or by virus detection to give a 95% probability of detecting a 5% prevalence of NAI infection, every 21 days, with negative results.

Article 2.1.14.7.

When importing from an NAI free country or compartment, *Veterinary Administrations* should require:
for *egg products*

the presentation of an *international veterinary certificate* attesting that the egg products come from, and were processed in, an NAI free country or compartment.

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Article 2.1.14.8.

When importing from an NAI free country or compartment, *Veterinary Administrations* should require:
for poultry semen

the presentation of an *international veterinary certificate* attesting that the donor birds:

- 1) showed no clinical sign of NAI on the day of semen collection;
- 2) were kept in an NAI free country or compartment for the ~~28~~ 21 days prior to semen collection.

Article 2.1.14.9.

Regardless of the NAI status of the country of origin, *Veterinary Administrations* should require:
for the importation of semen of birds other than poultry

the presentation of an *international veterinary certificate* attesting that the donor birds:

- 1) were kept in isolation approved by the Veterinary Services quarantine for the ~~28~~ 21 days prior to semen collection;
- 2) showed no clinical sign of NAI during the isolation quarantine period;
- 3) were tested between 7 and 14 days prior to semen collection and shown to be free of NAI.

Article 2.1.14.10.

When importing from NAI free country or compartment, *Veterinary Administrations* should require:
for fresh meat and processed meat of poultry, and poultry viscera

the presentation of an *international veterinary certificate* attesting that the entire consignment of meat comes from birds:

- 1) which have been kept in an NAI free country or compartment since they were hatched or for the past ~~28~~ 21 days;
- 2) which have been slaughtered in an *approved abattoir* and have been subjected to ante-mortem and post-mortem inspections for NAI with favourable results.

Article 2.1.14.11.

~~When importing from NAI free country or compartment, *Veterinary Administrations* should require:
for poultry viscera~~

~~the presentation of an *international veterinary certificate* attesting that the entire consignment of meat comes from birds:~~

- ~~1) which have been kept in an NAI free country or compartment since they were hatched or for the past 28 days;~~
- ~~2) which have been slaughtered in an *approved abattoir* and have been subjected to ante-mortem and post-mortem inspections for NAI with favourable results.~~

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Article 2.1.14.12.

When importing from a country or compartment not considered free from NAI, *Veterinary Administrations* should require:

for fresh meat and viscera of poultry

the presentation of an *international veterinary certificate* attesting that the entire consignment of meat comes from birds:

- 1) which have been kept in a *free establishment* ~~for at least 28 days~~ and regularly inspected by the official veterinarian;
- 2) which have been tested to give a 95% probability of detecting a 5% prevalence of NAI infection not more than 7 days prior to slaughter using virus detection or virus isolation tests, and serological tests, with negative results in all cases;
- 3) which have been slaughtered in an *approved abattoir* which has not processed poultry infected with NAI since last cleaned and disinfected, and have been subjected to ante-mortem and post-mortem inspections for NAI with favourable results.

Article 2.1.14.12 bis

~~When importing from a country or compartment free from clinical signs of NAI but not considered free from NAI infection, *Veterinary Administrations* should require:~~

~~for fresh meat of poultry~~

~~the presentation of an *international veterinary certificate* attesting that the entire consignment of meat comes from birds:~~

- ~~1) which have been kept in an country or compartment free from clinical signs of NAI but not considered free from NAI infection since they were hatched or for the past 28 days;~~
- ~~2) which have been slaughtered in an *approved abattoir* and have been subjected to ante-mortem and post-mortem inspections for NAI with favourable results.~~

Article 2.1.14.13.

When importing from country or compartment not considered free from NAI, *Veterinary Administrations* should require:

for processed meat, viscera and egg products of poultry

the presentation of an *international veterinary certificate* attesting that:

- 1) the commodity is derived from fresh meat and/or viscera which meets the requirements of Article 2.1.14.12.; or
- 2) the commodity is derived from eggs for consumption which meet the requirements of Article 2.1.14.6.bis; or
- 3) the commodity has been processed to ensure the destruction of the NAI virus, and the necessary precautions were taken after processing to avoid contact of the commodity with any source of NAI virus.

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Article 2.1.14.14.

When importing from NAI free country or compartment, *Veterinary Administrations* should require: for products of animal origin (from poultry) intended for use in animal feeding, or for agricultural or industrial use the presentation of an *international veterinary certificate* attesting that these products come from birds which have been kept in an NAI free country or compartment since they were hatched or for the past ~~28~~ 21 days.

Article 2.1.14.15.

When importing from a country or compartment not considered free from NAI, *Veterinary Administrations* should require:

for meal containing meat and/or feathers and/or bones (from poultry)

the presentation of an *international veterinary certificate* attesting that:

- 1) the commodity has been processed to ensure the destruction of the NAI virus;
- 2) the necessary precautions were taken after processing to avoid contact of the commodity with any source of NAI virus.

Article 2.1.14.16.

When importing from an NAI free country or compartment, *Veterinary Administrations* should require:

for feathers and down (from poultry)

the presentation of an *international veterinary certificate* attesting that the entire consignment of feathers or down comes from birds which have been kept in an NAI free country or compartment since they were hatched or for the past ~~21~~ 28 days.

Article 2.1.14.17.

When importing from a country or compartment not considered free from NAI, *Veterinary Administrations* should require:

for feathers and down (from poultry)

the presentation of an *international veterinary certificate* attesting that that:

- 1) the commodity has been processed to ensure the destruction of the NAI virus;
- 2) the necessary precautions were taken after processing to avoid contact of the commodity with any source of NAI virus.

Article 2.1.14.18.

Regardless of the NAI status of the country of origin, *Veterinary Administrations* should require for the importation of meat or other products from birds other than poultry

the presentation of an *international veterinary certificate* attesting that:

- 1) the commodity has been processed to ensure the destruction of the NAI virus;
- 2) the necessary precautions were taken after processing to avoid contact of the commodity with any source of NAI virus.

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