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DEVELOPMENT OF AN OIE INTERNATIONAL ANIMAL HEALTH CODE RECOMMENDATION ON ZOONOSES TRANSMISSIBLE FROM NON-HUMAN PRIMATES

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Summary

Status and contents of a draft recommendation on zoonoses transmissible from non-human primates, developed by an EAZWV-OIE expert group are described. The draft focusses on defining the health of non-human primates and on the practice of protective measures against the transmission of infectious diseases. The two basic elements needed for assuring public health are the process of health certification before, and the process of quarantining after international transportation, whereby the rule should apply that the less information is available on an animal, the more lengthy and stringent the quarantine procedures required must be. It is stressed, that some amount of risk for zoonotic disease transmission should always be recognised, because all risk can not be eliminated. It can only be minimised by following proper techniques and procedures.

Zusammenfassung

Der gegenwärtige Stand und Inhalt eines Entwurfs einer von einer EAZWV-OIE-Expertengruppe erarbeiteten Empfehlung betreffend von anderen Primaten auf den Menschen übertragbare Zoonosen, werden beschrieben. Der Entwurf konzentriert sich darauf, den Gesundheitszustand der Primaten und die notwendigen Schutzmassnahmen für die Vermeidung der Übertragung von Infektionskrankheiten zu definieren. Die beiden Grundelemente zum Schutz der öffentlichen Gesundheit sind die Prozesse der tierärztlichen Bescheinigung vor und der Quarantäne nach dem internationalen Transport. Dabei gilt die Regel, dass die Quarantäne um so strenger sein muss, je weniger Gesundheitsinformationen über ein Tier verfügbar sind. Es wird festgehalten, dass bei Primaten ein gewisses Zoonosenrisiko immer besteht, weil nicht alle Risiken ausgeschaltet werden können. Diese können durch geeignete Verfahren lediglich minimiert werden.

Résumé

Cet article décrit l'état actuel et le contenu du projet de recommandation élaboré par un groupe d'experts de l'EAZWV et de l'OIE, recommandation concernant les zoonoses qui se transmettent des autres primates à l'homme. Ce projet a pour objectif de définir l'état de santé des primates et les mesures de protection nécessaires pour éviter la transmission de maladies infectieuses. Les deux éléments fondamentaux pour la protection de la santé publique sont l'attestation vétérinaire, qui

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précède le transport international, et la quarantaine, qui suit ce transport. La règle qui s'applique en pareil cas est la suivante: la quarantaine sera d'autant plus stricte que les informations sanitaires sur l'animal font défaut. Il est clair qu'il existe toujours un risque de zoonose chez les primates. En effet, il n'est pas possible d'élimer tous les risques; on peut seulement les réduire par des méthodes appropriées.

Key words
Nonhuman primates, anthropozoonoses, viruses, bacteria, parasites, OIE, international trade, standards

Introduction

The development of international animal health standards is a long and cumbersome exercise, but, if successful, will result in facilitating international movements of animals without jeopardising public and animal health and safety. It is the purpose of the present paper, to inform on how EAZWV and other experts co-operated with the OIE in developing a recommendation on zoonoses transmissible from non-human primates, and on the current status of this recommendation.

At the 63rd meeting of the International Committee, May 1995, the Chairman of OIE's Code Commission presented a first draft of such a recommendation to be included in the International Animal Health Code, inviting Member States to submit comments. As only a few responses were received, the OIE asked the first author to review and revise the draft in consultation with experts from different countries. Subsequently, an EAZWV Working Group was formed, which liaised with government experts who had commented on the original draft, with EAZA, the IUCN Veterinary Specialist Group, Washington DC (USA), and the Working Group on Primate Health Control established by the Federation of European Laboratory Animal Science Association (FELASA).

On 19-22 November 1996, the OIE convened a meeting of an **Ad hoc Group on Zoonoses Transmissible from Non-Human Primates,** consisting of the authors of this paper. Other EAZWV members contributed by correspondence. Some of the literature used by the group is quoted at the end of this paper.

The Ad hoc Group defined its overall objective as the promotion of public health and safety by providing guidance to all parties, national veterinary services administrations, importers and exporters, in the safe international transfer of non-human primates. It was also hoped that the guidance provided would help facilitate the processes of international shipment in order to promote the maximisation of animal health and well-being.

The draft developed by the expert group was presented to the 65th meeting of the International Committee, May 1997, calling for comments from the Member states. A few comments were received, which have to be evaluated by the Code Commission. This means that the recommendation will be adopted not earlier than in May 1998, i.e. four years after work on the first draft was initiated.

Basic Format of the Recommendation

Unlike in other chapters of the OIE Code, the recommendation was developed in recognition of the particular and unique nature of the subject animals, non-human primates. Therefore, primary emphasis was not given to the steps necessary for the control of any specific zoonotic agent, but rather the need to address the zoonotic disease potential of the entire group of animals was stressed. The recommendation focusses on defining the health and infectious disease status of non-human primates and on the practice of protective measures against the transmission of infectious diseases. Prudence dictates the assumption that a non-human primate harbours a transmissible disease dangerous to humans until proven otherwise. For purposes of public health, this assumption must transcend the specific activities of the transportation process and be applied to all activities where close contact occurs between humans and non-human primates.

The two basic elements needed for assuring public health and humane animal care are the process of health certification before, and the process of quarantining after international transportation. Both fall under the jurisdiction of national veterinary service administrations, for which the recommendation should serve as guidance for developing and implementing their non-human primate international transportation policies and regulations.

Based on the unique zoonotic disease implications of non-human primates, and the need to assume that non-human primates harbour zoonotic diseases unless specifically proven otherwise, the outline of the recommendation follows a division centred on the level of certainty realistically obtainable about an animal's zoonotic disease status in the health certification process. The main discriminator is the existence and level of certainty obtainable about the animal's history of disease exposure and status. A distinction is made between wild-caught animals for which no previous disease history was available, and animals captive born and reared in captivity, i.e. in a controlled environment, and for which there has been a permanent veterinary and animal care presence and for which very accurate and full disease histories are available.

It must be understood, that some amount of risk for zoonotic disease transmission should always be recognised. All risk can not be eliminated. It can only be minimised by following proper techniques and procedures.

Species Coverage

On the issue of the species to be covered, the Group agreed that all non-human primates, from prosimians to great apes, should be addressed, and not only the principle species used in biomedical research. There was consensus that tree shrews (Tupaiidae) should not be included since they are not currently considered non-human primates (6). The Group recognised, that different species of non-human primates may require different practices to accommodate particular species needs and characteristics, and this was reflected in the articles of the chapter.

The Group felt that it was not practical to exclude from international transportation all animals harbouring infectious agents. Such an exclusion was not considered a practical solution to the problem of the potential for disease transmission. Rather, zoonotically infected animals can and are being transported currently with minimum risk as long as safety precautions are practised.

Health Certification

The Group felt that it was essential to develop guidelines that would support and complement existing international agreements on animal transportation and usage, in particular the Convention on International Trade in Endangered Species of Wild Fauna and Flora. The linking of the requirement for CITES documentation with the health certification process was thought to be a practical method of assuring adherence to CITES provisions, and help assist those veterinary services administrations that are responsible for implementing CITES.

In analogy to the International Animal Health Code’s recommendations on domestic livestock, the responsibility for health certification for non-human primates was placed with the veterinary services of the exporting country. The health certification process should be viewed as producing the best attainable assessment of the animal's health before exportation, but it should never be equated to a guarantee of a disease-free health status.

As part of the documentation needed for health certification, a description of the veterinary and animal health monitoring programme implemented at the site from which the animal is coming is needed. This information will serve to help both the veterinary services of the importing country and the persons receiving the animals make appropriate decisions on the quarantine procedures required for the animals.

A link between the health certification process and the individual identification of animals was considered essential to the success of zoonotic disease control measures. Different methods of identification (tattoo or other physical marker, microchip etc.) were considered acceptable so long as the end result was the permanent unmistakable identification of an individual animal.

Quarantine

A quarantine procedure at the time of animal receipt into a country is an essential element, if not the critical element for predictable and controlled animal health assessments. During the quarantine, activities are directed at protecting personnel and other animals against communicable agents. Its basic components include isolation of imported animals, veterinary health observations, necropsies of dead animals, diagnostic testing, and personnel health protection.

Quarantine facilities must be premises with a distinct and fully limiting barrier between the inside and the outside for the purpose of holding animals in isolation from other animals and non-essential personnel. They must provide for the complete isolation of the animals being contained, and comprises both a physical structure, and an established and implemented programme for maintaining animals in isolation. The programme includes: established criteria for animal admission, procedures for the isolation or elimination of diseased animals, a description of the animal disease monitoring programme, procedures for the health screening and surveillance of humans entering the facility, facility cleaning arrangements, the disposal of used feed, water, supplies and animal wastes, measures to exclude pests, and dead animals disposition. Entry and exit of animals, animal care staff and other humans must be controlled to minimise environmental exposures to animals and inadvertent exposure to transmissible infectious agents.

The quarantine programme must reflect the zoonotic potential of non-human primates in general, and depend on the information available on individual animals undergoing the quarantine procedures. The life history of the animal concerned, and the presented documentation on the animal's zoonotic disease potential, should influence the length and extensiveness of the quarantine process. The less information available on an animal, the more lengthy and stringent the quarantine procedures required.

It should be noted that, nowadays, most non-human primates imported by zoological gardens are born and raised in controlled environments, in the case of non-human primates destined for biomedical research, only three species are bred in larger quantities in captivity or under semi-captive conditions: cynomolgus monkeys (Philippines, other South East Asian countries, Mauritius), rhesus monkeys (China, USA and to a lesser extent in Europe), and marmosets (USA, Europe).

Who should provide quarantine services should be decided by the national veterinary services administrations. Zoos or other private but nationally recognised establishments should not be eliminated from consideration as long as they can meet the required standards.

Following discussions at the 65th meeting of the OIE International Committee, May 1997, the Working Group was mandated to elaborate recommendations for quarantine requirements. At the time of writing, these are under development. They will be assessed by the relevant OIE bodies during 1998.

The periods of time chosen for quarantine represent those which are sufficient for animals incubating diseases, before or during international transportation, to become clinically ill during quarantine and to resolve their infections before release from quarantine. For some latent infections harboured for the life of the animals, such as herpes B virus, no amount of time in quarantine will make the animal non-infectious. For these diseases it must be assumed that target animals are universally infected and infective, and that public health protection should not be placed on eliminating infectious animals, but by protecting persons coming in contact with these animals by of personnel protection practices.

Zoonotic Disease Agents Addressed

No all inclusive list of non-human primate zoonotic diseases was given, but the list of zoonotic disease agents was limited to those agents which should be actively addressed by all quarantine programmes. The agents listed were those for which reliable testing is readily available, and effective interventions can and should occur to correct the disease condition before the end of the quarantine period: Hepatitis B (gibbons and great apes only), *Mycobacterium hominis* and *M. bovis*, *Salmonella* spp., *Shigella* spp., *Yersinia* spp., Endo- and ectoparasites. The absence from the list of other zoonotic agents should not be interpreted as meaning they have no significance to public health. On the contrary, because of the difficulties in accurately defining the presence of these agents in non-human primates, these agents should be assumed present in relevant species, and animals should be handled accordingly at all times. The need to address these agents may depend on the ultimate use of the animals and on the importer's willingness to accept potentially infected animals.

A good example is herpes B virus in macaques. Many experts consider it impossible to certify these animals free of virus even after negative diagnostic testing. Although the probability of attracting a herpes B virus infection is extremely small, the possible fatal implications for humans coming into contact with latently infected and intermittently infective animals, requires that the disease potential is not ignored. Mandatory testing for B virus in quarantined animals, however, is not an effective means of identifying problem animals. A better approach is to consider all macaques infected and handle them accordingly.

To supplement the table given, a second listing of agents possessing zoonotic potential was added to alert persons to the existence of these agents, for which mandatory testing was not considered practical. These agents include hepatitis A virus, hepatitis B virus, herpes B virus, filoviruses, poxviruses, retroviruses, and rabies, etc. It was also considered unnecessary to mandate testing for agents which, if present, would become clinically apparent during the quarantine period; for example: Monkeypox.

Discussion on specific agents

Tuberculosis

Since it takes a minimum of 3 weeks for a healthy but infected animal to develop delayed hypersensitivity to tuberculosis testing, a series of tests is recommended during the quarantine period to increase the likelihood of detecting positive animals. Careful interpretation of test results is essential during. False negative tests can result from improper testing techniques, very recent infection, (no sensitivity developed yet), anergy, masking by concomitant viral infections such as measles, immunosuppression, other severe illnesses, immunisations, and species specific conditions (orang utans are notorious for false negatives).

So far, there is no universally accepted method for tuberculosis testing of non-human primates. A recommended method of testing is the intradermal injection of 0.1 ml of tuberculin at the edge of the upper eye lid. Eye lid swelling and erythema at 24, 48 or 72 hours is considered a positive test result. The eyelid is the preferred site for testing, because it is easily observed without actually restraining the animal. Subsequent tests are generally alternated between eyelids. Alternatively, an intradermal test may be done on a marked, non-haired area of abdominal skin. This site is recommended for small species such as marmosets, tamarins, bushbabies or mouse lemurs. It allows for physical palpation and/or measurement for induration, and it is often used for re-testing an animal with a questionable eyelid test or as part of the baseline testing in quarantine. In the United States of America, mammalian tuberculin, which is less purified but has more tuberculin units (TU) than PPD is used on nonhuman primates because PPD may not elicit a strong enough response to facilitate the identification of infected animals. The minimum dosage is 0.1 ml of undiluted USDA veterinary tuberculin (which is equivalent to 15,000 TU based on TCA precipitated protein content). Practices are different in Europe, where, according to a 1996 EAZWV survey carried out in Belgium, Denmark, France, Germany, Italy, the Netherlands, and Switzerland, most zoos use bovine and avian PPD for routine tuberculosis testing. The results of this survey are compiled in Table 1.

For the Cebidae, Cercopithecidae, Hylobatidae and Pongidae species it is recommended that a series of a minimum of three tests at 3 to 4 week intervals during the quarantine period be conducted. These species should not be desensitised by this schedule if correctly performed. For the Callithrichidae and Callimiconidae, fewer tests are thought necessary because of the lower probability of infection in these species. Prosimians should be tested as other Old World species.

The performance of pre-export tuberculosis testing on animals coming from controlled and well documented environments is desirable since this testing can be done aseptically, in a controlled manner under veterinary supervision. This testing is proposed to help shorten the testing requirements during the post-importation quarantine. It should help strengthen the health status documentation available for the health certification process as well.

Table 1 - Survey on Tuberculosis Testing in European Zoos, December 1996

Zoo	PPD			Kochs Old Tuberculin			Location			Additional tests
	bovine	human	avian	bovine	human	avian	palpeb.	Abdom.	Other	
Anvers (BE)	0.1 ml = 2000 TU	-	0.1 ml = 2000 TU	-	-	-	yes	no	no	Serology, X-ray (new arrivals)
Zurich (CH	0.1 ml	0.1 ml	-	-	-	-	yes	no	no	simultaneously
Frankfurt (DE)	0.1 ml = 5000 TU	-	0.1 ml = 2500 TU	-	-	-	yes	no	no	
Rostock (DE)	0.1 ml = 5000 TU	-	-	-	-	-	yes	no	no	
München (DE)	0.05-1.0 ml = 2500-5000 TU	-	-	-	-	-	yes	no	no	serology and X-ray are not carried out on a routinely basis
Zoo Berlin (DE)	0.1 ml	-	-	-	-	-	yes	no	no	ELISA (in Lelystad (NL)
TP Berlin (DE)	0.1 ml =	-	0.1 ml =	-	-	-	yes	no	no	X-rays regularly, CFT,

	5000 TU		2500 TU							ELISA (Lelystad (NL) if necessary
Hamburg (DE)	0.1 ml = 5000 IU	-	-	-	-	-	yes	no	no	
Karlsruhe (DE)	0.1 ml = 5000 IU	-	0.1 ml = 5000 IU	-	-	-	yes	no	no	Serology at Lelystad (NL) or Braunschweig (DE)
Leipzig (DE)	-	0.1 ml	-	-	-	-	yes	no	no	
Osnabrück (DE)	-	-	-	-	0.04-0.06 ml = 125 TU	0.04-0.06 ml = 125 TU	yes	no	no	
København (DK)	-	0.1 ml = 1 TU	-	0.1 ml = 1.0 mg= 25000 iu	-	-	yes	no	no	
Mulhouse (FR)	0.1 ml = 2000 TU	-	0.1 ml = 2500 TU	-	-	-	yes	yes*	no	*marmosets and tamarins
Paris Ménagerie (FR)	-	0.1 ml = 10 IU	-	-	-	-	yes	no	yes*	*orang utan
Peaugres (FR)	-	0.1 ml = 10 IU	-	-	-	-	yes	no	no	
La Palmyre (FR)	-	0.1 ml = 10 IU	-	-	-	-	yes*	-	-	*apes
Port St.-Père (FR)	0.1 ml = 2000 IU	-	-	-	-	-	yes	no	no	
Pistoia (IT)	-	-	-	-	-	-	no	no	no	in case of suspicion: X-ray
Castelnuovo (IT)	-	-	-	-	-	-	no	no	no	in case of suspicion: X-ray plus bact. culture of the sputum
Amsterdam (NL)	0.1 ml = 5000 TU	-	0.1 ml = 2000 TU	-	-	-	yes	no	no	ELISA, if pos. repeated X-rays
Beekse Bergen (NL)	0.1 ml = 5000 TU	-	0.1 ml = 2000 TU	-	-	-	yes	no	no	ELISA, if pos. Repeated X-rays
Rhenen (NL)									chest	concerns orangs, X-ray, faeces
Rotterdam (NL)	0.1 ml = 5000 TU	-	0.1 ml = 2000 TU	-	-	-	yes	no	no	ELISA, if pos. Repeated X-rays

Bacterial Agents

Enteric bacteria pose the highest risk potential to public health during the quarantine period. Since these agents can cause chronic infections with intermittent shedding from apparently healthy animals, testing during the first 5 days of quarantine was suggested to take advantage of the heightened probability of detecting positive animals during this period of probable stress. The detection of these agents should not necessarily lead to positive animals not being allowed out of quarantine, but should lead to decisions on the future introduction of these animals into environments known to be free of these agents or into situations where animals will come into close contact with humans not practising personnel protection methods. The prophylactic treatment of non-human primates with antibiotics should be discouraged as it will handicap the diagnosis of infected animals and will probably facilitate the development of antibiotic resistant strains of bacterial pathogens.

Parasitic Agents

Parasitic agents were included in the list because of their zoonotic potential and because of the ease and effectiveness of treatments during the quarantine period. No detailed information on treatments for these agents was given, however, because treatment should be tailored to the specific parasite detected, and the species of animals concerned.

Personnel Health Protection Measures

Given the nature and implications of zoonotic diseases in non-human primates, recommended personnel protection methods were described to be used for persons coming into contact with primates during the quarantine period. Generally, occupational safety procedures should include immunisations of personnel against high risk diseases such as hepatitis A, hepatitis B, tetanus, rabies, polio and measles, etc.; provisions for TB and enteric parasite monitoring; protocols for treating bites, scratches and other injuries; and observance of good personnel hygiene practices, including the wearing of protective clothing, no eating, smoking or drinking in animals areas or other animal use areas. Quarantine programmes may wish to also incorporate measures aimed at protecting workers

from agents endemic in the country of origin of the quarantined animals, i.e. yellow fever, or to consider making provisions for any future epidemiologic investigations by establishing documentation and detection systems for disease occurrence and spread, i.e. the establishment of serum banks on personnel and/or animals, or the establishment of systems for notifying medical authorities of the potential for zoonotic diseases in patients with histories of non-human primate exposure.

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