

Health monitoring of non-human primate colonies

Recommendations of the Federation of European Laboratory Animal Science Associations (FELASA) Working Group on Non-Human Primate Health accepted by the FELASA Board of Management, 21 November 1998

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1 Preamble

Biomedical research has a need to use non-human primates in cases where no other species offer the specific scientific information required or the necessary predictability of results for the development of medicines and vaccines. Biomedical research institutions would prefer purpose-bred animals of known history with an amount of background information necessary for an unbiased interpretation of findings from animal experiments. It is also anticipated that the microbiological status of such animals is easier to define and to control and better than that of animals from other sources.

Due to the difficulty in predicting requirements and the high investment costs of setting up colonies especially with breeders born in captivity, the breeding establishments existing at present have not yet established sufficiently large breeding colonies, especially with captive-born breeders, to fulfil the requirements of biomedical research for purpose-bred animals of all of the commonly used species. However, even animals from other sources should be delivered with a report on the health status after a quarantine period at the supplier institution. Good Laboratory Practice requires that sufficient background information is available to allow for accurate interpretation of findings from animal experiments. This means that besides

endeavouring to rid breeding colonies of unwanted agents, regular monitoring and honest reporting of the findings is imperative. Moreover, a reliable health monitoring programme at the supplier's centre usually allows clients to shorten the quarantine procedures that are prescribed by national authorities in the countries of destination. A certification of the health status of non-human primates should also accompany all primate shipments from suppliers to research institutions or between these institutions. Individual lifetime records should, besides mentioning any periods of illness, test results of individual samples and vaccinations, be accompanied by a health status certification of the colony from which it originates and other colonies in which it was kept.

At present no single recognized health control programme exists for laboratory primates. The requirements outlined in these recommendations are intended to harmonize existing protocols. They may be subject to remodelling due to the emergence of possible new pathogens as well as to developments in the use of non-human primates in biomedical research, chiefly in view of transplantation studies. Many, if not the majority, of the available purpose-bred animals of the larger non-human primate species still belong to the F₁ generation of parents captured in the wild. These are potential carriers of microbiological agents endemic in the wild population. In view of the longevity of primates,

problems with the breeding performance of animals born and reared in captivity, and the high demand for purpose-bred animals, this situation will continue for some years. According to those tests which have already been performed on request, some breeding colonies are free of certain, but usually not all of the microbiological agents potentially interfering with biomedical research data or transmissible to humans. Besides, monkeys are often susceptible to the same agents as humans and, therefore, may acquire some that are not present in their natural environment through close contact with humans. Health monitoring of the animal care staff is essential both for the protection of the staff itself, as well as to avoid introducing disease agents.

The recommendations are directed to breeders, other suppliers and users holding non-human primate colonies for prolonged periods of time. It is concerned with the most commonly used species in Europe. These are:

- Cynomolgus monkeys (*Macaca fascicularis*)
- Rhesus monkeys (*Macaca mulatta*)
- Green monkeys or vervets (*Cercopithecus aethiops*, synonym: *Chlorocebus aethiops*)
- Baboons (*Papio*, various species)
- Squirrel monkeys (*Saimiri sciureus*)
- Marmosets (generally *Callithrix jacchus*)

It was not considered necessary to include apes, since these are used in Europe only at two specialized institutes having their own specific health control requirements.

2 Certification of health status of animals by the supplier

Though it would be desirable to gradually obtain non-human primates free of pathogens, it must be realized that, unlike rodents, such animals are at present not available in sufficient numbers. The main aim of these recommendations are, however, to encourage suppliers to provide the users with all the information that is important for the interpretation of their experimental results and for working safely with the animals received.

Breeding establishments should be able to control and document the health status of their colonies and the animals supplied. This involves thorough clinical or pathological examinations of individual animals and the use of regular appropriate laboratory tests of the population maintained in the same unit. Animals from sources other than closed breeding colonies should be kept under quarantine at the supplier centre and undergo the same examinations for the presence of disease before delivery.

Single negative laboratory tests obtained shortly before shipment are only of relevance if the animals have been prevented from contact with potentially infected animals (or humans) for the incubation period of the disease. If this is not the case it would be more informative to know the incidence of positive animals within the group or unit in which the monkeys were kept. A 'unit' is defined as a self-contained microbiological entity. As a rule all individuals of a unit with seropositive animals, or animals showing other evidence of infection should be considered as potential carriers of the infectious agent if not otherwise proven.

3 List of pathogenic and other undesirable microbiological agents

In Tables 1 and 2 of the appendix a list of microorganisms and parasites is provided which is chiefly based on current concern, on the health risk for personnel handling the animals, and the frequency with which the agents are found in laboratories using non-human primates. Other criteria for inclusion were infections that may spread in a colony without or prior to clinical symptoms, and could cause disease in more susceptible species or immune-deficient animals. Beside those agents included in Tables 1 and 2 of the appendix, non-human primates are known to harbour a number of further microorganisms and parasites that may be pathogenic or interfere with experiments. Of those not considered in the tables *Yersinia pestis*, that is known to be endemic in the rat population in certain regions, and *Bordetella* spp., *Helicobacter pylori*, *Klebsiella*, *Pseudomonas aeruginosa* as ubiquitous microorganisms as

well as *Filaria* spp. that have occasionally been found in groups of New World primates may turn out to be important in the future.

Not much is known of the influence of inapparent infections on the experimental results, but where this is the case it is mentioned in Table 1 and the agent has been included in the tables even though an infection may have no known clinical importance for the animals themselves or humans.

Based on current concern in view of transmission to humans and frequency of findings, a reduced list of microbiological agents and parasites for which testing is considered as mandatory is presented for the primate groups from the three areas of Africa, Asia and South America. For most of the agents in the following three lists monitoring is commonly requested. However, any other agent, including those mentioned in Tables 1 and 2 should be reported in health certificates when found to be present or identified as cause of a disease outbreak.

3.1 Macaques

Herpes B (*Cercopithecine herpesvirus 1*)

Hepatitis A virus

Simian immunodeficiency virus (SIV)

Simian T-cell lymphotropic virus (STLV-1)

Simian retrovirus type D (SRV/D)

Filovirus screen with specification if positive

Mycobacteria spp.

Salmonella spp.

Shigella spp.

Leptospira spp.

In endemic areas: *Pseudomonas pseudomallei* (*Burkholderia pseudomallei*)

Entamoeba histolytica

Toxoplasma gondii

Pneumonyssus simicola (diagnosis at necropsies)

Intestinal helminths

Ectoparasites

Dermatophytosis

3.2 Baboons and vervets

Herpesvirus papio 2 (*Cercopithecine herpesvirus 12*, HPV/2) in baboons

Herpesvirus cercopithecinus (*Cercopithecine herpesvirus 2*, SA 8) in vervets

Hepatitis A virus

Simian immunodeficiency virus (SIV)

Simian T-cell lymphotropic virus (STLV-1)

Filovirus screen with specification if positive

In endemic areas: Monkeypox virus;
Yellow fever virus

Mycobacteria spp.

Salmonella spp.

Shigella spp.

Leptospira interrogans

Entamoeba histolytica

Toxoplasma gondii

Intestinal helminths

Ectoparasites

Dermatophytosis

In endemic areas: Plasmodia

3.3 *Saimiri sciureus* and *Callithrix jacchus*

Salmonella spp.

Shigella spp.

Leptospirosis interrogans

Entamoeba histolytica

Intestinal helminths

Ectoparasites

Dermatophytosis

In endemic areas: Plasmodia

It is advised that initially or after changes of the colony composition a complete microbiological profile of the non-human primate colony be established. The term 'initially' refers to the start of a new unit, commencement of a diagnostic test programme in an established unit, after a disease eradication programme or during quarantine of non-human primates intended for biomedical research. For primate colonies already committed to a health control programme, the initial more frequent testing for the declaration of absence of an infectious agent is not necessary, provided three consecutive tests at one-year intervals within the preceding two years were negative.

Once the microbiological status has been defined, the requirement for inclusion in a regular testing programme only applies to those agents for which there is a risk of introduction and spread within the colony or unit. A colony or unit may, however, only be declared free of a certain agent if it has

been tested for the corresponding agent according to Table 2. For diseases declared to be absent in the region of the non-human primate colony by a competent national authority no monitoring for that specified agent is needed. The same may apply to a colony into which no new animals are introduced provided it is housed in units for which an infection by a specific agent can be excluded due to its closed construction.

Periodical testing is also not necessary—except for scientific or epidemiological reasons—if laboratory test results or overt clinical disease indicate that the colony harbours a certain microorganism or parasite and if no measures have been taken to eliminate it. In the latter case the presence of the agent has to be mentioned in all subsequent health reports until an attempt to eradicate it has been undertaken.

While it will reveal the efficiency of the vaccination scheme, antibody testing of vaccinated animals is also not necessary for the health monitoring report. The vaccination, however, has to be mentioned in the certificate, and is no proof of absence for that particular agent.

4 Monitoring procedures, sampling and sample sizes

The test methods mentioned in Table 2 reflect currently applied techniques used in the relevant publications and by the existing specialized diagnostic laboratories. In general the most appropriate and updated method should be used. No attempt has been made to suggest the use of a specific method, but by experience of members of the group, for some microorganisms the results may differ between the diagnostic laboratories and the test methods applied. It is, therefore, absolutely necessary to mention the applied method and the testing laboratory in the report. Improvement of the reliability of the diagnostic tests is highly desirable.

The minimal number of samples (serum, faeces) for screening colonies or units shall be 10. These samples should be gathered randomly for each 'unit' (understood as self-contained microbiological entity) from indi-

vidual animals. They should not be pooled. Theoretically this sample size will detect an infection incidence of 25–30% in the unit with a probability of 95%. Negative results in single tests only mean that those animals selected for screening had not developed antibodies or were not shedding bacteria or parasites at the time the samples were taken. Equivocal or unexpected test results should be confirmed by repeating the test with the same animal and possibly using another diagnostic method. On the other hand in periodical standard investigations different animals should be used in succeeding tests.

All samples should be taken from live animals or at least within a few hours after the death of the animals. However, the identification of any pathogenic agent in organic material at even a later stage is regarded as proof for the presence of this agent within the colony.

Serum samples for antibody testing should preferably be obtained from animals over one year in age whereas faecal samples for the detection of bacteria and parasites are often more informative when taken from juvenile animals or at weaning and on three consecutive days.

Some clients require tests to be performed on each individual animal before shipment. In the future this may also be a requirement of national veterinary offices. It is considered as good practice to inspect each outgoing animal before shipment. Taking the required number of 10 animals per unit annually into account, the results of these examinations may, of course, and should be used for the health monitoring report on the unit from which the animals for exportation were selected.

Additional or intermediate tests to those listed above may be required for the diagnosis in animals with clinical signs of disease or on request of clients for the clarification of unexpected results. It is also reasonable to perform a full necropsy of all dead animals from a unit and include the findings in the health monitoring programme and reports. Such findings as well as those obtained from routine clinical inspection (e.g. ectoparasites) may help reduce the costs for standard periodic investigations. For some parasites (e.g.

lung mites and *Filaria* spp.) necropsies are the only reliable diagnostic method.

For the shipment of serum samples to diagnostic laboratories it may be requested to inactivate the serum to reduce the risk of human infection. Methods recommended are heat inactivation (56°C for 30 min) or addition of merthiolate to the serum (1:10). All sample vials must be shipped leak- and break-proof.

Some countries require a CITES certification for the import of serum from non-human primates. Since the regulations for the import and transport of biologicals vary from one nation to the other and may occasionally be modified, it is recommended to obtain the necessary instructions from the testing laboratory well in advance of the shipment.

5 Eradication and treatment: declaration of freedom of specified agents

The eradication possibilities referred to in Table 2 should be considered as suggestions. Experience gained with attempts to obtain pathogen-free colonies are scarce at present. Methods used for other laboratory animals (Caesarean section, embryo transfer) are hardly feasible for non-human primates for obvious reasons. Even hand-rearing of newborn animals could lead to behavioural problems when they are to be used as founders of breeding colonies.

Where therapeutics are available this is indicated in Table 1. Antibiotic treatment is, however, not always reliable for complete elimination of microbes. For some diseases no effective treatment is known. In such cases separation of infected from non-infected animals and initial frequent testing of the latter (if necessary during a quarantine period in individual cages) may be the only solution for eliminating pathogenic agents from colonies or units.

Vaccination may in some cases be acceptable as protective measure for animal groups if free of the corresponding microorganism and when the risk of re-infection is otherwise unavoidable. However, the differentiation between vaccinated and naturally infected

animals could cause problems. Vaccination may also not be advisable for animals to be used in immunological studies.

The elimination of many of the agents listed in the attached Tables 1 and 2 from monkey colonies may only be achieved in stages. Nevertheless, consideration should be given from the onset about precautions against the spread of these agents within the colonies and introduction by wild mammals, birds, insects, man and materials. Such measures may include fences or walls with electrical wiring around the compounds, entry locks with disinfectants and spacing the individual enclosures or units sufficiently far apart to avoid cross contamination. Within the compounds or units rodent and insect traps could be used to eliminate possible vectors. A plan for the disinfection of material that could be exchanged between units as well for the periodical disinfection of enclosures should be established. Attention should be paid to the construction of the waste-water system as a possible source of cross-contamination.

6 Health monitoring report

A major purpose of health monitoring of animals of breeding and other supplier establishments or in experimental units is to provide the user with data on variables that might influence the outcome of the experiment. These data are part of the experiment and have to be considered during the interpretation of the results by the investigator and by the reader of a publication. Authors of scientific articles should, therefore, be able to provide the information on the health status of their animals used on request.

For non-human primates that may harbour disease agents transmissible to man, monitoring and reporting the health status of the animals is also essential for protective measures to be taken on behalf of personnel handling the animals at the breeding site, during transport and at the research centre.

The health monitoring certificate of a non-human primate facility should include the following information:

- (1) Species, breed, and unit for which the report is valid.
- (2) Date of colony/unit establishment or restocking or re-derivation.
- (3) Microorganisms/parasites monitored and listed alphabetically in the order: viruses; bacteria, fungi, protozoa, other parasites. In general species names of microorganisms and parasites should be used. General genus designations are acceptable where group diagnosis is sufficient.
- (4) Date of latest investigation, diagnostic method used and name of the testing laboratory.
- (5) Results of latest investigation: number of positive/negative animals versus number of animals tested.
- (6) Dates, test method, testing laboratory and results of the two or three preceding investigations if results of latest investigation are negative.
- (7) Dates, test method, testing laboratory and results of intermediate ad hoc investigations (necropsies, sick animals, customer requested microorganisms) not included in the standard health monitoring programme should be added as complementary information.
- (8) If abbreviations are used for test methods or diagnostic laboratories these should be explained separately.

As an example for a health report for primate units in accordance with FELASA recommendations a specimen sample form for macaques is added as an appendix. Reports concerning other species should be adapted according to the lists in Parts 3.1 to 3.3 of this Report.

7 Final remarks

While it is clear that FELASA cannot accept responsibility for tests and their implications, breeders or users of laboratory animals who are reporting on the health status of their animals may use the wording 'in accordance with FELASA recommendations' under the following conditions:

- The microorganisms monitored correspond with those listed as mandatory in this recommendation. Additional patho-

genic microorganisms found should also be reported.

- Frequency of investigations and number of animals submitted to tests correspond with these recommendations.
- Reporting of current and historical results, treatments and vaccinations comply with these recommendations.
- The breeding colonies are under on-site veterinary supervision and standard operating procedures are available.

FELASA is aware of the fact that following these recommendations will increase the costs for supplying non-human primates. It has, therefore, been the aim of the Working Group to recommend only a minimal frequency of testing by defining the conditions under which further testing of certain microorganisms need not be performed, and allowing for the inclusion of results from other investigations (e.g. for the shipment of animals) in the standard monitoring system.

Experience shows that results obtained from different diagnostic laboratories may vary considerably depending on the methods used. Aims to standardize or correlate the methods applied by use of reference laboratories should be encouraged.

Improving the health status of non-human primate colonies will take some time. It is, therefore, at present not possible to exclude animals with potential pathogens completely from research. Nevertheless, regular control and reporting of the health status are basic requirements for the characterization of animals used in research.

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This document was compiled using the expertise of the members of the Working Group and their personal literature resources. For further reading we refer to the following documents:

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Table 1 Microorganisms and parasites of current concern in non-human primates, disease, transmission, zoonotic potential and treatment possibilities

Agent	Carrier species	Clinical symptoms in primates	Transmission	Zoonotic potential: symptoms in man (risk category according to EU)	Special remarks
(1) Viruses					
B virus, <i>Herpesvirus simiae</i> , Cercopithecine herpesvirus 1	Macaques	Mostly asymptomatic, occasionally lesions in mouth	Saliva and body fluids in bites and scratches, mucosal contamination	Neurological/lethal (3)*	
<i>Herpesvirus cercopithecus</i> , (SA 8), Cercopithecine herpesvirus 2	Vervets, (baboons)	Mostly asymptomatic, recurrent herpetic lesions	Saliva	Zoonotic potential not recorded	
<i>Herpesvirus papio 2</i> (HVP/2), Cercopithecine herpesvirus 12	Baboons	Mostly asymptomatic	Saliva, venereal	Zoonotic potential not recorded	
<i>Herpes T</i> , <i>Herpesvirus platyrrhinae</i> , Saimiriine herpesvirus 1	South American species	Mostly asymptomatic in Saimiris, but severe lip ulcerations and mortality in <i>callithricidae</i> and owl monkeys	Saliva and excreta are infective	Zoonotic potential not recorded	<i>Callithrix</i> species may also become asymptomatic carriers
<i>Herpesvirus saimiri</i> , Saimiriine herpesvirus 2	<i>Saimiri sciureus</i>	Mostly asymptomatic, occasionally lesions in mouth, but malignant lymphoma in marmosets	Experimental inoculation; natural route of infection unknown	None (not classified)	
Hepatitis A virus	All species	Asymptomatic, hepatitis rare	Contact with excreta	Hepatitis (2)	Vaccine available
Hepatitis B virus	Gibbons and great apes	Occasionally antibodies identified in macaques and vervets, but no proven disease	Blood contact, skin lesions	Hepatitis (3)	Antibodies found in macaques (ELISA) not confirmed in serum neutralization tests
SV 40	Macaques, transmissible to other species	Asymptomatic	Contact with secretions and urine, infected vaccines	Presumed cancerogenic potential (2 for Papovavirus)	Interference with cancer research and vaccine production
Simian haemorrhagic fever virus	Patas and possibly other African species, macaques probably only terminal infection	In macaques haemorrhagic disease with high mortality, no symptoms in patas, occasionally pathogenic in vervets	Contact with excreta, secretions and blood (needles)	Not proven (not classified)	High antibody incidence in newly imported patas. Occasional seropositive baboons reported. Outbreaks in macaques ascribed to accidental contacts (transport, vials)

Marburg virus	Vervets	Exanthema, haemorrhagic diarrhoea reported in macaques	Contact with blood and tissue from infected animals	Haemorrhagic diarrhoea, lethal (4)
Ebola-Reston virus	<i>Macaca fascicularis</i>	Asymptomatic or up to severe haemorrhagic disease	Contact with excreta, aerogenic not excluded	No known pathogenicity in humans, however, (3) for other Ebola
Simian immunodeficiency virus (SIV)	Old World monkeys, species-specific, as source. Secondary transmission to Asian species	Mostly asymptomatic in African species. AIDS-like disease in Asian species	Blood contact, skin lesions	No human cases known, but seroconversion reported (3 for HIV)
Simian T-cell lymphotropic virus-1 (STLV-1)	Old World species	Asymptomatic but occasionally associated with lymphoproliferation	Possibly bites and scratches	Resembles HTLV-1 which may cause leukaemia (3 for HTLV-1)
Simian retrovirus, type D (SRV/D)	Asian species	Simian AIDS	Possibly bites and scratches contaminated with saliva	Antibodies found in humans but no known pathogenicity
Foamy virus	Old and New World species	Usually asymptomatic	Possibly contact with excreta	Antibodies found in humans but no known pathogenicity
Monkeypox virus	Various species in Central Africa/Zaire	Mostly asymptomatic; fever, exanthema in susceptible species	Contact with excreta, aerogenic	Pox lesions (3)
Lyssa virus (rabies)	Various species	Rabies	Saliva in wounds	Rabies (3)
Yellow fever virus	African and New World species	Varying from inapparent to lethal in South American species	Mosquitoes	Yellow fever (3)
(2) Bacteria <i>Campylobacter jejuni</i> • fetus	Various species including primates	Mostly asymptomatic; diarrhoea, abortion possible	Direct contact with excreta	Gastrointestinal (2)

Antibiotic treatment possible

(continued)

Table 1 (continued)

Agent	Carrier species	Clinical symptoms in primates	Transmission	Zoonotic potential: symptoms in man (risk category according to EU)	Special remarks
<i>Leptospira interrogans</i>	Rodents, various primate species	Mostly asymptomatic, occasionally fever, abortions	Food and water contaminated with urine; ingestion of mice	Fever, gastrointestinal, icterus; neuromeningal complications (2)	Antibiotic treatment possible. Vaccination for humans
• Various serovars					
<i>Mycobacterium africanum</i>	Cattle, various other species, Old World primates, humans	Progressive, generalized and lethal TB. New World species less susceptible	Excreta, enteral or through skin lesions, aerogenic	Generally respiratory (3)	Tuberculostatics not recommended because no cure possible. BCG vaccination has only transient efficacy
• <i>bovis</i>					
• <i>tuberculosis</i>					
<i>Salmonella typhimurium</i>	Various species including non-human primates	In adults mostly asymptomatic; in juveniles gastrointestinal symptoms	Ingestion of excreta	Gastrointestinal (2 or 3, depending on type)	Antibiotic treatment possible
• <i>enteritidis</i>					
<i>Shigella flexneri</i>	Various species including non-human primates	Often without symptoms except young animals	Ingestion of excreta	Gastrointestinal (2)	Antibiotic treatment possible
<i>Yersinia pseudotuberculosis</i>	Rodents, birds, transmission to non-human primates	Primates: acute lethal or chronic with diarrhoea or simply weight loss	Ingestion with contaminated food	Often subclinical or unspecific symptoms (2)	Antibiotic treatment possible
<i>Pseudomonas pseudomallei</i> (<i>Burkholderia pseudomallei</i>)	Chiefly species in Southeast Asia	Mostly without clinical symptoms, occasionally broncho-pneumonia, enteritis often occult, clinically multiple abscesses	Oral, mucosal or aerogenic	Stress-induced pulmonary affections, abscesses, often long after infection (3)	Antibiotic treatment possible but not recommended
(3) Parasites					
<i>Entamoeba histolytica</i>	All primate species	Normally asymptomatic. Arboreal species may be more susceptible for diarrhoea	Ingestion after contact with faeces	Generally non-pathogenic types (2, if pathogenic)	No successful treatment for permanent eradication. Typing for human pathogenic strains recommended

<i>Toxoplasma gondii</i>	Various species. Cats are only species considered to excrete transmissible oocysts	Usually no apparent clinical symptoms	Ingestion after contact with faeces or of contaminated rodents	Rarely fever and apathy, occasionally abortion or congenital abnormalities (2)	Contamination of humans by primates normally unlikely. Interference with research on transplantation and immunodeficiency
<i>Giardia</i> spp.	Old World monkeys	Macaques: sometimes intermittent mucoid diarrhoea	Ingestion after contact with faeces	Gastrointestinal troubles in children (2)	Available treatment not effective for permanent eradication
<i>Plasmodia</i> species	Seen in macaques, in saimiris, ateles transmitted from humans	Often asymptomatic, fever, anaemia occasionally lethal	Mosquitoes	Evidence for transmission is lacking (2 or 3 for human types)	Interference with haematology testing when indicated by origin of animals. Treatment possible
<i>Strongyloides stercoralis</i>	All primate species	Normally asymptomatic	Contact with faeces; larvae can penetrate skin	Gastrointestinal problems possible (2)	Treatment possible
<i>Trichuris</i>	All primate species, humans may be host	Usually asymptomatic, diarrhoea (heavy infestation)	Ingestion after contact with faeces	Diarrhoea (2)	Treatment possible
<i>Prosthenoorchis elegans</i>	South American species	Usually asymptomatic, occasionally anaemia	Cockroaches	Not known in humans	Treatment possible, but not reliable
<i>Pneumonyssus simicola</i>	Macaques, baboons	Usually asymptomatic	Not clear, possibly contact with sputum	Disputed	Interference with research on respiratory system. Treatment (repeated) possible
Ectoparasites	Old and New World species (occasional)	Pruritus, skin lesions	Direct contact or with contaminated material	Dermatitis	Treatment possible
• Mites					
• Lice					
(4) Dermatomycosis	Seen in macaques	Localized alopecia	Direct contact or through contaminated utensils	Localized alopecia (2)	Treatment possible
<i>Trichophyton</i>					

* In the UK upgraded to 4 in 1998. For the nomenclature, current designations were used and recent names added in bold

Table 2 Laboratory diagnosis, testing intervals, proof of absence and suggested methods for eradication of microorganisms of current concern in non-human primates

Agent	Laboratory diagnosis (current methods used by specialized laboratories and referred to in publications)	Testing interval	Proof of absence after eradication measures or at the start of a testing programme	Eradication possibilities
(1) Viruses				
B virus, <i>Herpesvirus simiae</i> , <i>Cercopithecine herpesvirus 1</i>	Serology: • ELISA • CFR • Neutralization T • RIA PCR	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	Separation of positive animals from colony. Separation of weanling animals from potentially positive colonies
<i>Herpesvirus cercopithecus</i> , (SA 8), <i>Cercopithecine herpesvirus 2</i>	Serology: • ELISA • IFA	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	No efforts known to rid colonies of virus
<i>Herpesvirus papio</i> (HVP/2) <i>Cercopithecine herpesvirus 12</i>	Serology: • ELISA • IFA • Immunoblot	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	No efforts known to rid colonies of virus
Herpes T, <i>Herpesvirus platyrrhinae</i> , <i>Saimiriine herpesvirus 1</i>	Serology: • Neutralization T	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	No efforts known to rid colonies of virus. Strict separation of species
<i>Herpesvirus saimiri</i> , <i>Saimiriine herpesvirus 2</i>	Serology: • IFA	Initially 1 month, later annually or all outgoing animals	Four consecutive negative tests	No efforts known to rid colonies of virus. Strict separation of species
Hepatitis A virus	Serology: • ELISA	Initially 1 month, later annually or all outgoing animals	Four consecutive negative tests	Separation of positive animals from colony
Hepatitis B virus	Serology: • ELISA • Neutralization T	Initially 1 month, later annually or all outgoing animals	Four consecutive negative tests	Separation of positive animals from colony
SV 40	Serology: • IFA	Initially 1 month, later annually or all outgoing animals	Four consecutive negative tests	Separation of positive animals from colony
Simian immuno-deficiency virus (SIV)	Serology: • IFA	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	Formation of units with seronegative animals
Simian T-cell lympho-tropic virus-1 (STLV-1)	Serology: • ELISA • IFA • WB	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	Formation of units with seronegative animals
Simian retrovirus type D (SRV/D)	Serology: • IFA • WB Isolation from peripheral lymphocytes	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	Formation of units with seronegative animals
Foamy virus	Serology: • IFA • CFR	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	Formation of units with seronegative animals. Due to high preval- ence in existing colonies animals from less infected sources may have to be used

(continued)

Table 2 (continued)

Agent	Laboratory diagnosis (current methods used by specialized laboratories and referred to in publications)	Testing interval	Proof of absence after eradication measures or at the start of a testing programme	Eradication possibilities
Simian haemorrhagic fever	Serology: • IFA	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	Formation of units with seronegative animals
Filoviruses Reston Ebola Marburg	Serology: • ELISA • Ag capture PCR	Initially 3 months, later annually or all outgoing animals	Four consecutive negative tests	Formation of units with seronegative animals
Monkeypox virus	Serology: • ELISA • Neutralization T	Initially 1 month, later (only in endemic areas) annually or all outgoing animals	Four consecutive negative tests	Formation of units with seronegative animals from non endemic areas. Alternative: Vaccination
Yellow fever virus	Serology: • Neutralization T • ELISA • CFR	Initially 14 days, later (only in endemic areas) 6 months or all outgoing animals	Four consecutive negative tests	Formation of units with seronegative animals where vector transmission is excluded
(2) Bacteria				
<i>Campylobacter</i> spp.	Serology: • CFR Culturing of fresh faecal samples on selective media	Serology initially 2 weeks, later 6 months	After three negative tests	Treatment of all animals of the corresponding unit
<i>Leptospiralis interrogans</i> , various serovars	Serology: • CFR, ELISA, Agglut–Lysis Reaction Culturing of blood or urine samples	Initially 4 weeks later 6 months	After 12 weeks with three negative tests	Treatment of all animals of the corresponding unit
<i>Mycobacteria</i> spp.	Tuberculin test	Initially 2 to 4 weeks, later 6 months	After 12 weeks with at least three negative tests	Immediate culling of all infected animals and quarantine of affected unit
<i>Pseudomonas pseudomallei</i> (<i>Burkholderia pseudomallei</i>)	Serology: • ELISA	Serology initially 2 weeks, later 6 months	After three negative tests	Eradication of sick animals and treatment of unit
<i>Salmonella</i> spp.	Culturing of fresh faecal samples of selective media. Serotyping for species	Initially daily tests for 3 days repeated after 2 weeks. Later 6 months (3-day test)	After two negative test series	Treatment of all animals of the corresponding unit
<i>Shigella</i> spp.	Culturing of fresh faecal samples on selective media	Initially daily tests for 3 days repeated after 2 weeks. Later 6 months (3-day test)	After two negative test series	Treatment of all animals of the corresponding unit
<i>Yersinia pseudotuberculosis</i>	Serology: • HA	Serology initially 2 weeks	After three negative tests	Treatment of all animals of the corresponding unit
(3) Protozoa and parasites				
<i>Entamoeba histolytica</i>	Microscopy of faeces and typing for pathogenic strains	Initially 2 weeks later annually	Four consecutive negative tests	Treatment results only in transient disappearance

(continued)

Table 2 (continued)

Agent	Laboratory diagnosis (current methods used by specialized laboratories and referred to in publications)	Testing interval	Proof of absence after eradication measures or at the start of a testing programme	Eradication possibilities
Plasmodia	Haematology, Giemsa	Initially 2 weeks later annually	Three consecutive negative tests	Medical treatment of infested animals, Anti-mosquito programme
<i>Toxoplasma gondii</i>	Serology: • Sabin-Feldmann • IFA • ELISA PCR	Initially 2 weeks later annually	After three negative consecutive tests	Elimination of positive animals. Prevention of rodent or cat contact
<i>Pneumonyssus simicola</i>	Thorough post-mortem inspection of lungs of adult animals	Continuous	No findings during one year, provided it has been possible to examine at least 10 animals per unit	Treatment of all animals of the corresponding unit
<i>Prosthenorchis elegans</i>	Sedimentation techniques of faecal samples	Initially 2 weeks later annually	Four consecutive negative tests	Separation of positive animals, effort to treat all animals of unit. Control of insect transmission
<i>Strongyloides stercoralis</i>	Microscopy of faeces	Initially 2 weeks later annually	Four consecutive negative tests	Treatment of all animals of the corresponding unit
Other endoparasites	Microscopy of faeces	Initially 2 weeks later annually	Four consecutive negative tests	Treatment of all animals of the corresponding unit
Ectoparasites	External inspection of animals	Continuous	One year no findings, provided it has been possible to examine at least 10 animals, and animals from all units	Treatment of all animals of the corresponding unit
Trichophyton	Clinical inspection, scanning with Wood's lamp, microscopy of scrapings from skin lesions in KOH	Continuous clinical inspection	One year no findings, provided it has been possible to examine at least 10 animals, and animals from all units	Separation and treatment of infected animals

Ag. Capture: antigen capture; CFR: complement fixation reaction; ELISA: enzyme linked immunosorbent assay; HA: haemagglutination test; IFA: immunofluorescence antibody assay; PCR: polymerase chain reaction; RIA: radio immune assay; WB: Western blot

HEALTH STATUS REPORT FOR NON-HUMAN PRIMATE COLONIES

in accordance with FELASA recommendations

(Sample specimen for *Macaca mulatta*. Reports for other species to be adapted according to lists in Part 3 of this Report)

Date of issue: _____

Name and address of institute: _____

Tel: _____ Fax: _____ E-mail: _____

Standard operating procedures available from: _____

Species: *M. mulatta* Designation or number of unit: _____

Date of colony foundation or sanitation: _____

Test dates (D)¹ and results (R=number of positive animals vs number tested). Method applied (M) and diagnostic laboratory (L); reference to attachment possible.

		Previous test	Previous test	Previous test	Latest test	Remarks ²
1. VIRAL INFECTIONS						
Cercopith herpesvirus 1	D/R	
	M/L	_____	_____	_____	_____	_____
Hepatitis A virus	D/R	
	M/L	_____	_____	_____	_____	_____
SIV	D/R	
	M/L	_____	_____	_____	_____	_____
STLV-1	D/R	
	M/L	_____	_____	_____	_____	_____
SRV/D	D/R	
	M/L	_____	_____	_____	_____	_____
Filoviruses	D/R	
	M/L	_____	_____	_____	_____	_____
On request						
.....	D/R	
.....	M/L	_____	_____	_____	_____	_____
.....	D/R	
.....	M/L	_____	_____	_____	_____	_____
2. BACTERIAL AND FUNGAL INFECTIONS						
Mycobacteria	D/R	
	M/L	_____	_____	_____	_____	_____
Salmonella	D/R	
	M/L	_____	_____	_____	_____	_____
Shigella	D/R	
	M/L	_____	_____	_____	_____	_____
Leptospira	D/R	
	M/L	_____	_____	_____	_____	_____
Dermatophytes	D/R	
	M/L	_____	_____	_____	_____	_____
On request						
.....	D/R	
.....	M/L	_____	_____	_____	_____	_____
.....	D/R	
.....	M/L	_____	_____	_____	_____	_____

3. PARASITIC INFECTIONS

<i>Entamoeba histolytica</i>	D/R
	M/L	_____	_____	_____	_____	_____
<i>Toxoplasma gondii</i>	D/R
	M/L	_____	_____	_____	_____	_____
Pneumonyssus	D/R
	M/L	_____	_____	_____	_____	_____
Helminths	D/R
	M/L	_____	_____	_____	_____	_____
Ectoparasites	D/R
	M/L	_____	_____	_____	_____	_____
On request						
.....	D/R
	M/L	_____	_____	_____	_____	_____
.....	D/R
	M/L	_____	_____	_____	_____	_____

ABBREVIATIONS:

¹If samples of sufficient size (at least 10 animals per unit) are not gathered at same date (e.g. necropsies or samples from outgoing animals, the test period should be indicated.

²REMARKS: **A:** no further testing because agent is known to be present in unit
B: region is officially free of disease carriers
C: animals are vaccinated against disease
X: others (e.g. identified helminths or 'apathogenic strain')