Guide to the Care and Use of Experimental Animals, Volume 2 (1984)

XX. NON-HUMAN PRIMATES

Please note that the *CCAC Guide to the Care and Use of Experimental Animals*, vol. 2 (1984) is out of date and currently under revision. In the interim, sections of this chapter have been replaced by reference to more recent CCAC publications where available. The sections that have not been replaced should be viewed alongside more recent literature, such as that available on the CCAC Three Rs microsite (http://www.ccac.ca/en/alternatives/species-resources_ressources-especes/primates.html).

A. INTRODUCTION

Non-human primates are exotic animals requiring special housing and knowledgeable care if they are to be successfully maintained and used in research. Measures to safeguard their psychological stability should take equal precedence to those concerning physical health (McGrew, 1980).

Many non-human primate species are threatened with extinction; others are in relatively short supply, difficult to procure and therefore expensive. The stresses of capture and transport predispose these animals to a variety of disease syndromes which often result in a high mortality prior to their arrival at the research facilities. Because non-human primates carry substantial zoonoses that pose a serious potential health hazard to personnel, and because of their susceptibility to a number of human diseases, special precautions must be taken in maintaining these animals. In light of these facts, it is clearly apparent that non-human primates should only be used for research purposes when no other species is suitable for the particular project and all other alternatives have been rejected.

Caging, diet, quarantine, conditioning and other practices will, of necessity, vary somewhat from facility to facility; however, the points presented here are basic and therefore apply to all non-human primate colonies.

B. ACQUISITION AND SUPPLY

Please refer to the *CCAC guidelines on: the procurement of animals used in science* (2007, http://www.ccac.ca/Documents/Standards/Guidelines/Procurement.pdf).

1. Sources

See Section 4 – Sources of Animals in the *CCAC guidelines on: the procurement of animals used in science*.

All non-human primates should be procured from reputable, and where legally required, licensed suppliers, or breeders. The importation of non-human primates must comply with the regulations established by Agriculture Canada and the Convention on International Trade in Endangered Species (CITES). The latter is administered in Canada by the Canadian Wildlife Service and enforced by Industry, Trade and Commerce through the Export and Import Permits Act.

2. Raw vs Conditioned Non-human primates

Non-human primates that are available commercially may be grouped into the following three categories:

a. **Raw or unconditioned non-human primates**: recently arrived from their country of origin and not yet adapted to captivity;

b. **Conditioned non-human primates**: ones which have been held by the supplier for a period of time and are, therefore, at least partly acclimatized to laboratory conditions. Animals in this category should have been tuberculin tested and treated for intestinal parasites and stress related diseases;

c. **Captive bred non-human primates**: these should be defined animals that can be purchased free of most disease conditions, including tuberculosis, salmonellosis and shigellosis.

C. RECEIVING

See Section 6 – Receiving Animals in the *CCAC guidelines on: the procurement of animals used in science*.

1. Initial Examination

New shipments of non-human primates should always be received by experienced personnel, familiar with non-human primates. The new arrivals should be placed immediately in a prepared isolation area located as distant as possible from the holding area of the colony (Wong and Gardell, 1982). The animals should be properly identified and their documents should be checked at the time of uncrating. An initial medical examination should be made at this point by a veterinarian experienced in the care of non-human primates. Overtly ill animals should be segregated for treatment, whilst any moribund animals should be euthanized. The latter animals, along with any that may have been dead on arrival, should be placed individually in plastic bags, securely tied, identified and refrigerated until necropsied by a pathologist or other qualified individual.

The vehicle used to deliver the animals to the facility should be thoroughly cleaned and disinfected immediately after use and prior to accommodating any other animal shipments. Care must be taken to properly sanitize the shipping crates if they are to be reused; however, it is preferable to dispose of used crates by incineration.

2. Health Records

It is extremely important to assure that a detailed health record is provided for each individual non-human primate. Such records should always accompany the animal and should be maintained throughout its life. This record becomes increasingly important for animals which may be transferred from one institution to another.

The health certificate of each non-human primate received from a supplier should have recorded on it all medications and vaccines given, as well as the results of any tests that have been carried out, with the dates on which each of these procedures was undertaken. Health certificates should record the date of arrival of the animal from its country of origin, or its birthdate and birthplace if domestic bred. It should also record tuberculosis tests, with certification by a veterinarian that the latest test was done within ten days of delivery to the purchaser. The test method, type and concentration of tuberculin should also be specified.

D. QUARANTINE

See Section 6 – Receiving Animals in the *CCAC guidelines on: the procurement of animals used in science*.

Every non-human primate should undergo a period of quarantine which, for raw non-human primates, should be for a minimum of eight weeks (Wong and Gardell, 1982). However, as a general rule, conditioned and captive-bred animals from reputable laboratories may be quarantined for somewhat shorter periods of time.

The purpose of quarantine is to isolate new arrivals from other animals in the colony until it has been established that their health status is satisfactory in accordance with acceptable veterinary practices. During both quarantine and conditioning, non-human primates should be caged individually to minimize disease spread and fighting (Hunt, 1970; Committee on Non-Human Primates, 1980). This precaution is particularly applicable to rhesus monkeys (*M. mulatta*); however, it may be better to house certain species of New World monkeys and prosimians in group caging, providing the animals are all part of one shipment.

In addition to the required total separation of quarantine from regular holding areas, species should be maintained separately at all times (Hunt, 1970). Rhesus, in particular, should be isolated from other species due to their relatively high incidence of tuberculosis and specific viruses (e.g., SV40, SV5, foamy virus). During the quarantine period, as at all times, adequate provision must be made for the further isolation and treatment of animals that may become sick.

E. CONDITIONING

See Section 6 – Receiving Animals in the *CCAC guidelines on: the procurement of animals used in science*.

Conditioning may take place prior to, during, or following quarantine. In raw animals, these procedures are usually undertaken concurrently.

1. General Objectives

The purpose of conditioning is to prepare the animal for the use to which it is to be put and acclimatize it to its new environmental conditions.

As a general rule, raw or unconditioned non-human primates should undergo a minimum conditioning period of six weeks prior to use. Longer conditioning periods may be required depending on the nature and requirements of the research for which the animal is intended.

Non-human primates that are obtained as so-called "conditioned" animals have, by definition, undergone a preliminary period of conditioning prior to their arrival. However, they should always be held for at least an additional 14 days prior to use, in order to allow them to become accustomed to their new environment. Captive bred animals should be allowed to adjust to their new environment for a minimum of one week, but otherwise will not normally need further conditioning.

2. Specific Considerations

During the conditioning period, the animal is being "acclimatized" to its new home, food, water, climate control, etc. Food and water intake should be monitored carefully. A half orange may be given daily as a dietary supplement. Abnormalities in behavior, as well as health, should be reported to the veterinarian for evaluation (Wong and Gardell, 1982). In addition, the health and well-being of both colony and staff should be safeguarded as outlined in Volume 1 of this Guide (CCAC, 1980) with special attention being given to the following steps:

a. All non-human primates which have not been tuberculin tested should pass three consecutive negative tests at two week intervals before being transferred to a "conditioned colony".

b. Examination for and, where indicated, treatment of internal and external parasites should be undertaken. Newly arrived animals should be allowed a reasonable period of time to adapt before being treated for the former.

c. Many institutions administer an appropriately chosen, long acting antibiotic to newly arrived non-human primates. This is instituted as a prophylactic measure to minimize emergence of latent disease as a consequence of travel induced stress.

d. All non-human primates must be considered as potentially infected with Herpesvirus simiae (B-virus). Serologically negative animals should not be considered

unquestionably free of this virus, as it is not uncommon for animals' sera to convert to positive, especially over an extended period of time.

F. HOUSING

Facilities for housing non-human primates should conform to the recommendations for small animal containment facilities in the *Containment Standards for Veterinary Facilities* published by Agriculture and Agri-Food Canada, Minister of Supply and Services Canada (1996, http://www.inspection.gc.ca/english/sci/bio/anima/convet/convete.shtml).

See also Chapter VI – Social and Behavioural Requirements of Experimental Animals in the *CCAC Guide to the Care and Use of Experimental Animals*, vol. 1, 2nd ed. (1993, http://www.ccac.ca/Documents/Standards/Guidelines/Experimental_Animals_vol1.pdf).

1. General Environment

Consideration must be given for the behavioral, emotional and social needs of laboratory non-human primates when planning their housing. Any non-human primate housed alone will probably suffer from social deprivation, the stress from which may distort processes, both physiological and behavioral (McGrew, 1980).

Lighting should be controlled so as to provide light and dark periods that mimic those of the animals' natural environment. When in doubt, 12 hours of light and 12 hours of darkness will usually be satisfactory. The fact that most prosimian species are nocturnal should be taken into account when these animals are to be housed.

Ventilation should provide a minimum of 12-15 air changes per hour. If the population density is high, consideration should be given to increasing this to 18-20 changes per hour. There should be no re-circulation, and effluent air should be incinerated, or at least passed through HEPA or charcoal filters before being discharged to the outside.

The ideal room temperature will vary with the species. Most Old World monkeys can adapt easily to a temperature of 19°C (66°F), while some species, such as baboons (*Papio anubis*) and Japanese macaques, can adapt to much lower temperatures. Most New World monkeys and prosimians should be maintained at a temperature between 22°C-26°C (72°F-79°F). To mimic wild conditions, it is desirable, where possible, to lower the environmental temperature overnight.

During the conditioning period, all non-human primates should be maintained at a temperature of between 22°C-26°C.

Relative humidity should be maintained between 45 and 60% for most species, and must never be permitted to fall below 30%, as low humidity predisposes animals to respiratory disorders. Relative humidity should be higher than 60% for tropical New World species such as the marmoset (*Callithris* spp).

2. Non-Human Primate Rooms

Non-human primates should be housed in areas and rooms as remote as possible from other animal quarters. Moreover, as noted under Quarantine, it is important that species separation be maintained in order to minimize disease transmission. In this regard, it should be noted that squirrel monkeys (*Saimiri sciureus*) are a reservoir for *Herpesvirus saimiri* which can induce fatal infection in owl monkeys (*Aotus*), marmosets and tamarins (*Saguinus* spp.) (Ablashi, Gerber and Easton, 1979).

Rooms housing non-human primates must be provided with a vestibule or other arrangement to ensure that there are always two doors between the non-human primate cage and the building corridor or the outside. All windows, ceilings, and fixtures should be provided with heavy, protective screens.

Non-human primate rooms and cages should be kept locked at all times and be accessible only to authorized persons. Signs should be posted designating the rooms as hazardous areas.

The names and telephone numbers of experienced non-human primate handlers or the person responsible for the facility should be posted in a conspicuous place in each room and throughout the holding area. These notices should include instructions to service and security personnel in the event of an emergency.

3. Individual Caging

The marked variety in body conformation, postural preferences, and locomotor characteristics amongst non-human primates, calls for the careful application of professional judgment in the selection of caging. Cages must always be of sufficient size and height to provide for normal postural and behavioral adjustments.

Cages must have sufficient strength to assure that they cannot be damaged by their occupants. Cage doors should be provided with closing devices that cannot be opened by the non-human primates; padlocks with keys have proven very effective for this purpose. Direct contact between non-human primates in adjacent cages should be prevented.

With the exception of certain of the prosimians, cages for non-human primates should be equipped with wire mesh floors and a smooth surfaced shelf or perch upon which to rest or sleep. The strength of the floor must be sufficient to support the weight of the animal. The size of the mesh openings should permit the passage of feces, yet assure that arms and legs cannot be caught. The non-human primates should not be able to reach their excreta. Dropping pans should be locked in place so that the animals cannot slide them out onto the floor.

Watering devices must be such that the water cannot be contaminated with excreta. Automatic watering systems, are labour efficient and quite satisfactory. Water bottles and tubes are more commonly used in small colonies and are satisfactory if properly and regularly sanitized.

Food receptacles are not usually necessary for species with cheek pouches. However, where food dishes are used, they must be so designed and located that the food will not become soiled by excreta and so that they are not easily moved by the animals.

Cages should be equipped with sliding or false backs (squeeze cages) permitting non-human primates to be compressed to the front of the cage for administration of injections, tranquilizers, medications, etc. It is desirable that cages be fitted with a sliding panel in the door to permit the easy transfer of the animal into a transport cage.

4. Species Requirements

Baboons of 5-12 kg require a minimum single floor area of 0.74 m^2 with a minimal height of 0.91 m. Animals of more than 15 kg require 1.39 m^2 and 1.22 m. Group housed animals require 2.8 m^2 per occupant.

Macaques of less than 7 kg require a single floor area of 0.4 m^2 and height of 0.9 m^2. Animals of more than 15 kg require a single floor area of 0.75 m^2 and height of 1.2 m. Group housing should provide 2-3 m^2 with perches (CCAC, 1980).

Smaller animals of less than 1 kg such as tamarins, tupaias and infants of various species require a minimum floor area per animal of 0.15 m^2 and minimum height of 0.51 m.

Cebus and similar species weighing less than 3 kg require 0.3 m^2 minimum floor area per animal, and minimum height of 0.76 m. Great apes and brachiating species require a minimum floor area per animal of 2.32 m^2 and a minimum height of 2.2 m (Committee on Non-Human Primates, 1980).

The minimum heights noted refer to the height from resting board to cage top. The minimal cage height for brachiating species such as gibbons, spider and woolly monkeys should be such that the animal can swing from the cage ceiling without having its feet touch the floor of the cage when fully extended. Resting perches and nesting boxes, and escape barriers necessary for the well-being of the particular animals, should also be provided (Committee on Non-Human Primates, 1980).

Numerous commercial non-human primate cages which meet all the existing requirements for the housing of the common laboratory species are available. There are also many commercial cages especially designed to accommodate specific sampling procedures and research (e.g., convertible cage/chair, etc.).

5. Group Caging

If non-human primates are housed in group pens, only compatible animals should be kept together.

The caging requirements for New World monkeys with prehensile tails are somewhat different from those of the tail-less or non-prehensile tailed non-human primates. The former animal hangs by its tail and extends its arms to cover an area almost four times the length of its body (McGrew, 1980). Group or gang housing of these species is most practical and desirable.

Group caging of non-human primates is an economic alternative to single caging that should be exploited when appropriate, and may be necessary or desirable once the animals have completed quarantine. Care must be exercised in gang caging some species, especially adult macaques, as fighting often occurs among animals that have not been housed together from infancy (Committee on Non-Human Primates, 1980). The provision

of deep woodchip litter, particularly with food added, reportedly reduced aggressive behavior in eight different non-human primate species (Chamove, Anderson, Morgan-Jones *et al.* 1982). When utilizing group cages, it is important that factors such as the population dynamics of the species, male-female ratios, dominance and social behavioral patterns be taken into consideration. Perches and/or swings of varying heights should be provided within gang or group cages and also, as previously noted, where possible within individual cages. Similar precautions to prevent contamination of water and feed should be practiced as in individual caging.

Some space requirements for group housing were given under species requirements above.

G. NUTRITION

Please refer to the *Nutrient Requirements of Nonhuman Primates, 2nd ed.* (National Research Council, 2003; http://www.nap.edu/catalog.php?record_id=9826).

Most non-human primates used in biomedical research can adapt to a wide variety of laboratory diets; however, careful planning should go into the preparation and feeding of the daily dietary requirements. Raw or recently imported, unconditioned non-human primates, will invariably be under-nourished. Protein and vitamin deficiencies can be expected to be common in these classes of animals.

Most commercial non-human primate chows are satisfactory, although special formulae may be required by marmosets and tamarins. Portions of fresh fruits and raw vegetables may be given at regular and frequent intervals. It is important to remember that, in the wild, non-human primates are omnivores and eat a variety of foodstuffs. Variety is particularly important for non-human primates on long-term studies; however, abrupt dietary changes should be avoided as these often lead to enteric upsets. The mortality during quarantine of wild caught rhesus monkeys is reported to be significantly reduced when an open formula diet with a 7% crude fibre content is fed (Morin, 1980).

It is most important that all non-human primates receive supplementary Vitamin C and that all New World monkeys receive a supplement of Vitamin D3 as well.

Non-human primates have a tendency to waste food; consequently, it is best to feed them small portions two or three times each day. When non-human primates refuse to eat, they can often be tempted with a variety of foods, such as fresh fruit or peanuts. Concentrated, high caloric feed or Vitamin B complex injections are useful in treating anorexic animals.

Foods which contribute to increased dental caries should be avoided. This condition can be a problem in species maintained on chow.

H. BREEDING

1. General Considerations

Non-human primate breeding programs should only be undertaken in those institutions with proper facilities specifically designed for breeding purposes and with competent, experienced attendants and handlers.

2. Systems

The three main types of breeding arrangement in general use in the breeding of non-human primates, are briefly described below. The particular breeding program that is adopted will be dependent upon the species to be bred, the facilities that are available, and, particularly, upon investigator preference and experience. For example, it is generally felt that baboons breed more satisfactorily under group or harem conditions, while cage breeding of macaques is considered by many, but by no means all, to be the system of choice.

a. **The Free Ranging System**: This is commonly practiced in breeding programs in zoos and safari park compounds. Animals should be accommodated at a ratio of one male to six females, except for monogamous species such as marmosets and gibbons where a one to one ratio should be maintained. Often, the actual breeding performance within a compound will be found to be more in the ratio of one male to 20 females. Nevertheless, it has been shown that the additional males are needed to stimulate the dominant male.

   Advantages of the free ranging program are a more efficient utilization of space, less labour and the provision of continuous exercise for the animals. Care must be taken to adhere to the normal social organization found in the wild, particularly if the offspring are themselves to be retained as breeding stock. The disadvantages of the system include greatly increased risk of injury to the young and reduced accessibility. The latter enhances the problem of maintaining a close check on individuals, thus increasing the difficulty of detecting illnesses.

b. **The Harem System**: This is a modified free ranging system which, again, usually involves one male to approximately six females. These animals are housed together within a small compound which, besides being more labour efficient, allows for the effective utilization of maternity caging. Its disadvantages include the difficulty in determining the conception date and thus parturition date, and the fact that the individual animal is not readily available for clinical evaluation. It is not necessarily the most efficient breeding system, as estrous females will not always be bred at the desired time. Prolonged menstrual cycles and weaning periods are, however, not reported to occur under harem conditions.

c. **Caged Breeding**: Although labour intensive, this may be the system of choice, particularly for the smaller facility. In this system, females are individually caged, or perhaps caged in small groups away from, but in plain sight of, the male. The female is reintroduced to the male each estrus until pregnancy occurs. The advantages of this system lie in the precision of the breeding program and the better individual records that it facilitates. Individuals are readily available for clinical evaluation and it is

possible to more readily identify non breeders and thus eliminate them from the breeding program. Its disadvantages are those of increased labour and considerably greater capital outlay requirements for caging.

Females not accepted by the male may be in some danger from him in the confinement of a cage; consequently close observation is important and may be critical.

3. Parturition

With many of the non-human primate species there are few or no signs to the onset of labour. Parturition is most frequently nocturnal. Depending on the breeding system employed, the pregnant female may be placed in a maternity cage, although she may also be left to give birth within the harem or compound without undue risk.

Offspring are either raised by their mother or in specially equipped nurseries. Under harem and free ranging conditions, the problem of kidnapping of infants from subservient females by old, dominant, but dry, females may be encountered as a source of infant mortality.

While rhesus and cynomolgus usually refuse to accept their infants after caesarian delivery, it has been indicated that smearing the infant with the mother's vaginal secretions at the conclusion of the operative procedure results in acceptance (Lundbland and Hodgen, 1980).

I. HANDLING AND RESTRAINT

Please refer to the *The Laboratory Biosafety Guidelines: 3rd ed.* published by The Public Health Agency of Canada. See Section 7.1.2 – Non-human Primates (2004, http://www.phac-aspc.gc.ca/publicat/lbg-ldmbl-04/ch7-eng.php#jmp-lan712).

1. General Precautions

One should never underestimate the dangers posed by the strength, tenacity, and viciousness of the non-human primate. These animals are, at best, unpredictable in their reaction in handling, particularly by inexperienced attendants. In addition to the zoonotic implications associated with non-human primate induced injuries, their long canine teeth and powerful jaws can inflict serious and painful lacerations.

Whenever possible, non-human primates should be immobilized before handling. If tranquillization is not possible, special protective gloves must be worn. Two types of protective gloves are available commercially: a special high gauntlet leather catching glove with a false first finger[1]; and a high gauntlet chain mail glove[2] worn under soft, high leather gloves[3].

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[1] Primates Imports Inc., 34 Munson St, Port Washington, Long Island NY 11050, USA.

A fibre glass padded device to protect the forearm is also available[3].

2. Capture and Removal

Non-human primate cages should be equipped with a squeeze mechanism to facilitate the injection of immobilizing or tranquillizing agents into the animal prior to its removal from the cage.

A scissor mesh net is an alternative method of restraining individually caged, untranquillized non-human primates.

A "butterfly" net is sometimes used to capture and restrain non-human primates from a group cage. Netting in this way is a frightening experience for most animals which tends to exhaust them and may result in injury. It is preferable to entice such group animals into a small catching cage with a squeeze back, from which they may be tranquillized or otherwise readily restrained.

In many cases, transfer cages may be used. The animal voluntarily enters this cage, which is generally smaller and from which it may be more readily restrained manually.

3. Immobilization and Handling

The smaller non-human primate should be grasped by its forearms above the elbow, with the arms held behind its back and with its legs extended. This will completely immobilize the animal and put it in such a position that it is impossible for it to bite the holder. Care must be taken not to fracture arms and legs when removing the animal from its cage. Nutritional bone disease is not uncommon in newly imported animals, and the long bones in animals so afflicted may fracture quite readily and unexpectedly.

Chemical immobilization is generally advisable when larger non-human primates are to be removed from their cages. Suitable tranquillizing and immobilizing agents and analgesics are listed in Volume 1 of this guide (CCAC, 1980). Extreme caution is advised, however, when using these agents on overtly ill, weak, or debilitated animals.

The commonly-used dissociative anesthetic, ketamine hydrochloride, affects or alters the hemogram of rhesus is affected, compared with that of comparable non-human primates under physical restraint (Loomis, Henrickson and Anderson, 1980). Recent studies also note that diazepam used in conjunction with ketamine in baboons, suppressed or eliminated the epileptoid movements characteristic of anesthesia with ketamine alone (Woolfson, Foran and Freedman et al. 1980).

Precautions in handling are particularly pertinent to wild caught non-human primates, as these animals fear humans and will often be carriers of disease. On the other hand, animals raised in captivity often become "trained" to capture, restraint, and having

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[2] Whiting and Davis, Pakinsville MA, USA.

[3] Safety Supply Canada, 214 King St E., Toronto ON, Canada.

samples taken. It is tempting, to ignore many of the recommended precautions such as use of gloves and proper restraint. This is most inadvisable, and due caution should always be exercised, regardless of the apparent tameness of the animal. The non-human primate that has lost its fear of humans is, nonetheless, potentially just as dangerous and unpredictable as a wild caught animal.

J. ANESTHESIA

Please see Chapter XI – Anesthesia in the *CCAC Guide to the Care and Use of Experimental Animals*, vol. 1, 2nd ed. (1993), http://www.ccac.ca/Documents/Standards/Guidelines/Experimental_Animals_vol1.pdf, and the *CCAC training module on: anesthesia* (2003), http://www.ccac.ca/en/education/niaut/vivaria/anaesthesia.

1. Preanesthetic Management and Medication

Small species of non-human primates such as squirrel monkeys and marmosets should be fasted six to 12 hours prior to anesthesia. Medium size and larger species should be fasted for a minimum of 24 hours. Water should be available at all times before anesthesia. Providing that it is practical to physically restrain the animal, a hematology and biochemistry profile should be performed before major surgery is undertaken.

Chemical restraint is best achieved and preanesthetic therapy is facilitated by injecting ketamine hydrochloride at a dose level from 5-25 mg/kg i.m. (to a maximum of 40 mg/kg if further increments are needed). Atropine sulfate at 0.05 mg/kg s.c. or i.m. may then be administered to help to reduce secretions from the respiratory tract and salivary glands and to counteract vagal stimulation of the cardiovascular and respiratory systems.

The steroid combination of alphaxolone-alphadolone at a dose of 12-18 mg/kg i.m. is a very valuable agent for use on marmosets, squirrel and cynomolgus monkeys as well as many other species. At the above dose, this agent produces a light surgical anesthesia which can be enhanced and prolonged by drip administration of a volatile anesthetic to effect. Other neuroleptanalgesic combinations that have also been used for these purposes on non-human primates are fentanyl-droperidol, pethidine-xylazine, and ketamine-xylazine (Green, 1979; Soma, 1971).

2. Surgical Anesthesia

During surgical anesthesia, it is mandatory that vital signs be monitored throughout the entire procedure. To this end, it is important that the anesthetist be fully familiar with the biological data for the species utilized. An intravenous infusion of Ringer's lactate or dextrose-saline solution delivered via drip at a rate of 15 mg/kg/hr should be given to maintain the fluid balance. Heat conservation must be assured by maintaining the animal on a heating pad.

The surgical plane of anesthesia can be reached by using an injectable agent such as a barbiturate, or a sedative-analgesic and an inhalation gas mixture. The most commonly used injectable anesthetics are pentobarbital sodium at a dose of 25-35 mg/kg i.v. and

thiopental at a dose of 25 mg/kg i.v. Use of the intraperitoneal route is strongly discouraged, as anesthesia following delivery by this route is not as predictable or readily controllable as when administered i.v. Access to a vein, even in the smaller species of non-human primates, for i.v. injection is easy to achieve.

Inhalation anesthesia is best achieved following endotracheal intubation. The latter procedure does not pose any major problem in the average size non-human primate if an appropriate preanesthetic agent has been used. N_2O:O_2 (one to one) and 0.5-1% halothane or methoxyflurane may then be administered using an anesthetic machine to ensure a proper level of anesthesia.

3. Post-Operative Care

The endotracheal tube and intravenous catheter should be removed as soon as the animal regains its reflexes. The animal should be allowed to recover in a warm, quiet, well ventilated environment. The recovery area should be readily accessible for observation and suitably equipped for emergency therapy. Observation at frequent intervals will minimize post-surgical complications. Proper analgesics and supportive medicines should be utilized when deemed necessary.

K. SPECIAL CONSIDERATIONS

Please see Chapter – Social and Behavioural Requirements of Experimental Animals in the *CCAC Guide to the Care and Use of Experimental Animals*, vol. 1, 2nd ed. (1993, http://www.ccac.ca/Documents/Standards/Guidelines/Experimental_Animals_vol1.pdf).

1. Boredom

Captive non-human primates kept in bare cages without access to a continually changing array of manipulatable objects will rapidly come to suffer from sensory, motor, and intellectual deprivation. Lack of variation in the diet (e.g., one consisting largely or entirely of artificial biscuits), will compound these problems. Non-human primates, no less than humans, suffer pathogenic boredom, which may be expressed in such signs as depilation, coprophagy, and self-mutilation (McGrew, 1980).

The beneficial effects of deep-litter substrates, seeded with small cereal grain, mealy worms or fruit, in counteracting boredom has been clearly demonstrated. This is a simple, efficient and economical technique for providing opportunities to forage in group housed non-human primates (Chamove, Anderson, Morgan-Jones *et al.* 1982; Chamove and Anderson, 1979).

The provision of television has a salutary effect on boredom for the closely housed non-human primate and its use is particularly recommended where the practice of chronic restraint is essential to the experimental protocol.

2. Euthanasia

The information previously presented in this section will be superceded by the *CCAC guidelines on: euthanasia of animals used in science* (in prep.). This guidelines document is based on recommendations made by the International Council for Laboratory Animal Science (ICLAS) Working Group on Harmonization (Demers et al., 2006. Harmonization of animal care and use guidance. *Science* 312:700-701) and the two international reference documents on euthanasia recommended by ICLAS: the *AVMA Guidelines on Euthanasia 2007* (http://www.avma.org/issues/animal_welfare/euthanasia.pdf); and the *Recommendations for euthanasia of experimental animals* Part 1 (1996; http://www.justitsministeriet.dk/fileadmin/downloads/dyreforsoegstilsynet/reco1.pdf) and Part 2 (1997; http://www.justitsministeriet.dk/fileadmin/downloads/dyreforsoegstilsynet/reco2.pdf).

L. PERSONNEL SAFETY

Please refer to the *The Laboratory Biosafety Guidelines: 3rd edition* published by The Public Health Agency of Canada. See Section 7.1.2 – Non-human Primates (2004, http://www.phac-aspc.gc.ca/publicat/lbg-ldmbl-04/ch7-eng.php#jmp-lan712).

See also the *Occupational Health and Safety in the Care and Use of Non-human Primates*, published by the National Research Council (2003, http://www.nap.edu/catalog.php?record_id=10713).

See also Appendix VII – Zoonoses—Experimental Animals to Man in the *CCAC Guide to the Care and Use of Experimental Animals*, vol. 1, 2nd ed. (1993, http://www.ccac.ca/Documents/Standards/Guidelines/Experimental_Animals_vol1.pdf).

1. Precautions and Procedures

Because of their relatively high levels of intelligence, strength, dexterity, and the special health problems that they pose, non-human primates should only be handled by dependable and properly trained (experienced) personnel.

The hazards posed to personnel by the various non-human primate zoonoses cannot be over-emphasized (Hubbert, McCulloch and Schnurrenberger, 1975; Mayr, 1980). Because of the potential danger to animal handlers and researchers, as well as to the animal themselves, the following safety precautions must always be observed when working with non-human primates:

a. One must assume that every non-human primate is carrying a disease which is transmissible to humans.

b. Protective gloves should be worn at all times and at no time should a non-human primate, or anything that has been in direct contact with non-human primates, be touched with bare hands.

c. Protective clothing should be worn at all times and should include a surgical quality face mask, coveralls or operating gown, boot or shoe covers and a surgical cap or other hair protection. Because of the prevalence of enteric diseases, it is not uncommon for one to be sprayed on the face and hands with feces or urine when attempting to restrain a non-human primate so afflicted.

d. It is important that provision be made for removal of protective clothing and hand washing immediately upon leaving a non-human primate room. Such facilities should be used diligently.

e. Smoking and the consumption of food or drink should not be allowed in the non-human primate areas.

f. All sores, cuts or other lacerations must be adequately covered while in the non-human primate rooms, and the dressings changed upon leaving the area.

g. All cuts, bites, scratches, and needle punctures acquired while working with or in the proximity of non-human primates should be reported to the appropriate medical authority within the institution or community. It is advisable that such a wound be made to bleed freely and 2 1/2% tincture of iodine applied as quickly as possible. If the wound is in the nature of a bite or scratch from a non-human primate, the animal concerned must be immediately immobilized and its oral cavity examined for lesions characteristic of *Herpesvirus simiae* (B-virus). The result of this examination should be communicated immediately to the appropriate medical authority, along with all pertinent information regarding the species of animal, its health record, contact with other species, etc.

h. Comparable precautions regarding protective clothing must be undertaken when performing necropsies, performing elective or research surgery, or treating any injured non-human primate.

i. Visitors, particularly children, should not be permitted access to the non-human primate rooms as non-human primates are highly susceptible to several human diseases commonly encountered in young people.

j. Several species of non-human primates are particularly susceptible to tuberculosis. Therefore, all non-human primate handlers and investigators should be chest x-rayed or tuberculin tested at least once a year. All new employees should be TB tested, and have a serum reference sample taken and stored by the health services of the institution.

A more detailed treatment of this and other topics relating to the management of non-human primates may be found in the "Standard Operative Procedures- Nonhuman

Primates" developed, used by and obtainable from the Animal Resources Division, Health and Welfare Canada[4]

2. Decontamination

Special precautions in decontamination should be observed in non-human primate colonies. Leather gloves used to restrain non-human primates or to handle equipment should be routinely decontaminated by the use of formaldehyde gas or ethylene oxide. The excreta from non-human primates invariably contain a variety of infectious agents (bacterial, viral, protozoan and parasitic) that pose a potential public health hazard. All non-human primate excreta must be handled in a manner to ensure their safe disposal, e.g., liquid decontamination, incineration of bedding, disinfecting of cages, etc.

Instruments, syringes, needles, and other equipment used with non-human primates must be autoclaved prior to routine washing and sterilizing. If a chemical disinfectant is used, compounds that have tuberculocidal and virucidal properties should be selected. The quaternary ammonia compounds must not be used as they are not effective against the tuberculosis organism.

All laundry, including attendants' protective outerwear that has been soiled by non-human primates or their excreta, should be autoclaved prior to being sent for washing.

M. DISEASE PREVENTION AND CONTROL

Please refer to the *The Laboratory Biosafety Guidelines: 3rd edition* published by The Public Health Agency of Canada. See Section 7.1.2 – Non-human Primates (2004, http://www.phac-aspc.gc.ca/publicat/lbg-ldmbl-04/ch7-eng.php#jmp-lan712).

1. General Procedures (See also Quarantine and Conditioning)

Health evaluations of the animals within a non-human primate colony must be carried out at frequent and regular intervals. All animals should be observed a minimum of once daily and notations made of any irregularities, medication needed and administered, etc. Regular bacteriological and parasitological examinations should also be carried out and adequate treatment provided where necessary.

Visitor access to the non-human primate colony should be strictly restricted and carefully monitored because of the susceptibility of many non-human primates to human infectious diseases and because of the everpresent hazard from zoonoses.

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[4] Animal Resources Division, Health Protection Branch, Health and Welfare Canada, Sir Frederick G. Banting Research Centre, Tunney's Pasture, Ottawa, Ontario, K1A 0L2

2. Tuberculosis

Evaluations should include regular tuberculin testing, which should be done at least three times a year. It is essential that a thorough health examination by a veterinarian experienced in non-human primate diseases be performed, along with proper tuberculin testing, as advanced cases of tuberculosis may not react to the tuberculin test.

Tuberculosis is a common problem in non-human primates. Old World monkeys are more susceptible than those species from the New World. TB testing is mandatory upon arrival at the facility whether or not it as been done previously by the supplier. A new shipment of non-human primates should be negative to at least three tests which have been given at no less than two week intervals, preferably at 30 to 60 day intervals, using alternate eyelids for each test.

The dosage and type of tuberculin is important, and expert advice should be sought before doing the test. Generally, 0.1 ml of Old Tuberculin at a concentration of 250 mg/ml is injected intrapalpebrally as close to the margin of the eyelid as possible. Sterile water is injected into the other eyelid as a control. The test is read at 24, 48 and 72 hours after injection and results recorded (Wong and Gardell, 1982). A positive reaction is characterized by edema, erythema and occasional necrosis. Positive reactors should be isolated and tested further (by radiology, sputum tests, etc.). Upon confirmation of the reaction, the animal should be destroyed and the diagnosis confirmed through necropsy.

3. Respiratory Infections

Essentially all non-human primates, and particularly the great apes (chimpanzee, gorilla, orangutan), are extremely sensitive to the human respiratory viruses such as measles. Therefore, no human so infected or who has been in immediate contact with these diseases (having a sick child at home, for example), should ever be permitted to work with these animals. Even mild human respiratory illness, such as colds or flu, can be deadly to non-human primates and may rapidly decimate a colony. It is of paramount importance that the seriousness of the above risk be made absolutely clear to all scientific and technical personnel working in the non-human primate colony.

Pneumonia has been encountered frequently in non-human primate colonies. The disease is usually preceded by exposure to poor husbandry or the stresses associated with capture and transportation. Pulmonary acariasis is a common condition in some non-human primate species such as *M. mulatta*, but is considered of minor significance unless the animal is to be used in studies involving the respiratory system. Organisms frequently implicated as causing pulmonary disease include *Diplococcus pneumoniae*, *Klebsiella pneumoniae* and *Pasteurella* species.

4. Gastrointestinal Problems

Enteritis is probably the most commonly encountered problem in non-human primates. Organisms of the genus *Salmonella* and *Shigella* are the major causative agents, but *E. coli*, *Campylobacter* sp. and other enteric organisms are frequently encountered. Many enteric disorders of non-specific origin may be related to the stress of capture and transportation. Unfamiliar diets, the stresses of laboratory conditioning, and even

endoparasites may also be causative factors. Regardless of the etiology of gastrointestinal disturbances, good husbandry is essential to their prevention and control.

5. Herpes Viruses

Please visit the Viral Immunology Centre's National B Virus Resource Centre (http://www2.gsu.edu/~wwwvir/) and the Centers for Disease Control and Prevention – B Virus (http://www.cdc.gov/herpesbvirus//index.html).

See also the Centers for Disease Control and Prevention's updated recommendations report: Cohen J.I., et al (2002) Recommendations for Prevention of and Therapy for Exposure to B Virus (*Cercopithecine Herpesvirus 1*). *Clinical Infectious Diseases.* 35(10):1191-203.

Non-human primates are susceptible to Herpes viruses. Herpes B affects the Old World monkey, primarily the rhesus, but it has been observed in other species of macaques and also the African Green (*Cercopithecus aethiops*). Herpes B usually produces a sub-clinical or mild disease in the non-human primate host, resembling a cold sore (*Herpes simplex*) lesion in humans. However, Herpes B virus causes a fatal encephalitis in humans and strict isolation of non-human primates with any unidentified oral or facial lesions is therefore mandatory. Although the incidence of the infection is usually low, occasionally an entire group of newly arrived non-human primates can be infected. The lesions of Herpes B virus in non-human primates usually develop over a period of 14 days, with the small, initial vesicle rupturing and becoming ulcerated. The tongue is the most common site of ulceration; however, the mucous membranes of the inner lips and gums can also be involved. A tentative diagnosis can be made serologically and by finding typical Herpes intranuclear inclusion bodies in cells around the border of the ulcer.

This virus is known to be transmitted to humans by bites and by scratches from infected non-human primates. It has also been transmitted to humans from skin-penetrating wounds caused by equipment contaminated with the virus.

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APPENDIX
COMMON AND SCIENTIFIC NAMES OF NON-HUMAN PRIMATES

COMMON NAME	SCIENTIFIC NAME
African Green Monkey	*Cercopithecus aethiops*
Assamese macaque	*Macaca assamensis*
Baboons	*Papio* spp.
Bush Baby	*Galagos* spp.
Capuchin monkey	*Cebus capucinus*
Chimpanzee	*Pan troglodytes*
Common Marmoset	*Callithrix jacchus*
Cynomolgus macaque	*Macaca fascicularis (M. irus)*
Gibbons	*Hylobates* spp.
Japanese macaque	*Macaca fuscata*
Owl monkey	*Aotus trivirgatus*
Rhesus monkey	*Macaca mulatta*
Squirrel monkey	*Saimiri sciureus*
Spider monkey	*Ateles* spp.
Stump-tailed macaque	*Macaca arctoides (M. speciosa)*
Tamarins	*Saguinus* spp.