Canadian Council on Animal Care
Conseil canadien de protection des animaux

Guide to the Care and Use of Experimental Animals

Volume 1, 2nd Edition

Sections of this document that have been revised are replaced by links to the relevant documents. The remaining sections are undergoing revision; however, they will continue to be used for CCAC assessments until revised guidelines are published.

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In keeping with the CCAC policy of revising statements and guidelines as needed, users of this *Guide* are encouraged to forward any comments to the Secretariat.

Citing certain devices or manufacturers is not to be perceived as the endorsement of the Canadian Council on Animal Care (CCAC) of one particular product over another.

Publication Date: 1993
Revision Date: April 2020

ISBN: 0-919087-18-3

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TABLE OF CONTENTS

APPENDICES

DEDICATION

The Canadian Council on Animal Care dedicates this 2nd Edition of Volume 1 of its *Guide to the Care and Use of Experimental Animals* to CCAC's founder and Executive Director until his retirement in 1992, Dr. Harry C. Rowsell. His vision and devotion to the cause of experimental animal welfare have set an example which many seek to emulate, but few achieve.

Guide to the Care and Use of Experimental Animals
Volume 1, 2nd Edition

PREFACE

In 1961, the Committee on Animal Care of the Canadian Federation of Biological Societies (CFBS) prepared a one-page placard outlining "Guiding Principles for the Care of Experimental Animals". These principles were quickly approved by most national scientific associations and, despite their brevity, addressed essentially the same basic principles of animal care embodied in this 2nd Edition of Volume 1 of the Canadian Council on Animal Care (CCAC) *Guide to the Care and Use of Experimental Animals*.

The hundreds of pages of information contained in the current two volumes of the *Guide* represent steps in the evolution of efforts by the CCAC to provide the means by which the use of animals in research, teaching and testing in Canada can be performed in accord with basic principles of humane treatment.

The CCAC is deeply indebted to the many veterinarians, animal care employees, humane society members, administrators, scientists, and others who have willingly contributed time and expertise to its programs and projects. This edition of Volume 1 of the *Guide* is only one example of the many CCAC directed activities that owe their existence and success to the tremendous generosity and good will of these Canadians. Their broad participation in animal welfare is one of the most important, and least-recognized, merits of the non-legislated, participatory, peer review system employed in Canada.

Donald P.J. Boisvert, MD, PhD
Executive Director
Canadian Council on Animal Care
April 1993

FORWARD

Since its inception in 1968, the Canadian Council on Animal Care (CCAC) has brought about enhanced animal care and use through education, voluntary compliance, and codes of ethics. The Council's unique flexibility allows it to readily respond to the concerns of both the scientific community and the general public, as exemplified by numerous amendments to CCAC's "living documents," such as its *Ethics of Animal Investigation*, which appear elsewhere in this *Guide*.

In line with increasing concerns for enrichment of the animal's environment (see Social and Behavioural Requirements of Experimental Animals), in addition to optimal physical standards, CCAC is placing increased emphasis on performance standards: it is of primary importance that the animal is comfortable and well-adjusted.

Local institutional Animal Care Committees (ACC) or Animal Research Ethics Boards (AREB) were introduced by CCAC in 1968, and are now embodied in American legislation. These committees serve as the "conscience" of the institution in order to ensure ethical concerns are addressed in the protocols for and conduct of the research being undertaken. As with its documentation, CCAC's assessment program and suggested terms of reference for ACCs continue to be subject to considerable change as experience is gained and new technology becomes available. Most of these changes have come in response to concerns expressed by the scientific community, although some have been influenced by concerns expressed by animal protection organizations.

Contemporary animal care programs address the comfort, health, safety and security of animals. At least to date, the numbers of animals needed has steadily declined, at least partially because of the scientific community's development of alternative techniques. Specific Pathogen Free (SPF) rodents, rabbits, etc., have been introduced. Microbiological and genetic monitoring have reduced animal disease, and thus diminished animal suffering.

The following, as included in the Foreword of Volume 1 of this *Guide* (1980) bears repeating:

> "The increasing use of cell cultures, microbial systems, computer simulation and other replacement techniques provides clear evidence of the scientific community's commitment to implementing the Russell-Burch tenet of 'reduction, replacement, and refinement' in the use of experimental animals. However, such methods are, of necessity, complementary to animal experimentation and are initially dependent on animal-based research. The applicability of such techniques depends on validation utilizing animal systems, and on clinical studies. Confirmation of the data frequently requires the investigator to 'return to the whole animal'."

In conclusion, it is not CCAC's responsibility to act as an advocate for the many contributions made through the use of animals in research. Its mandate is to develop programs to enhance animal care and to make

changes as required, based on sound expertise and input. However, the Council maintains the right to advocate the benefits of its voluntary control program. It is incumbent upon each institution to promulgate this program by supporting the decisions of its ACC and the researcher who has received the ACC's ethical approval for his/her studies.

Progress has been, and will continue to be made when the scientific community and those in the general public concerned with the welfare of animals join together to seek the middle ground. Through responsible and learned discussion, without acrimony, extravagant zeal for a cause, or polarized view, agreements will be made which will benefit the animals we utilize in research, teaching, and mandatory testing.

CCAC guidelines are not all-encompassing or "etched in stone". Their application requires good judgement and common sense, based on training and experience. CCAC's program encourages the development of consensus amongst those using the guidelines and those required to oversee their application.

General reference works and publications dealing with the care and use of experimental animals, if not available in institutional libraries or facility reading rooms, may often be borrowed for limited periods from the CCAC Secretariat library without charge, except for mailing costs.

Harry C. Rowsell, OC, DVM, PhD
Executive Director (1968-1992)
Canadian Council on Animal Care

ACKNOWLEDGEMENTS

The Secretariat would like to thank members of the Canadian Council on Animal Care (CCAC) for their careful perusal of and input into the material contained in the chapter on Social and Behavioural Requirements of Experimental Animals (SABREA). Directors of Animal Care Services, Chairpersons of Animal Care Committees (ACC), and members of the scientific community in Canada, the U.S. and abroad are also thanked for their suggestions.

We are particularly grateful to the following for comments regarding:

Nonhuman Primates:

Dr. Kathryn Bayne, U.S. Department of Health and Human Services
Dr. Irwin Bernstein, University of Georgia
Dr. Carolyn Crockett, University of Washington
Dr. James Else, Yerkes Regional Primate Research Center
Dr. Peter Gerone, Delta Regional Primate Research Center
Dr. Matt Kessler, Caribbean Primate Research Center
Dr. Scott Line, University of California, Davis
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Cats or Dogs:

Dr. Bonnie Beaver, Texas Veterinary Medical Center
Dr. Douglas Boeckh, Merivale Cat Hospital
Dr. Charles Povey, Langford Inc.

Animals Used in Agricultural Research:

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Ms. Patricia Barker, Memorial University of Newfoundland
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Dr. David Fraser, Agriculture Canada
Dr. Helene Guttman, U.S. Department of Agriculture
Dr. Ruth Newberry, Agriculture Canada
Dr. Suzanne Robert, Agriculture Canada
Dr. Joseph Stookey, University of Saskatchewan
Dr. Tarjei Tennessen, Nova Scotia Agricultural College
Dr. William Threlfall, Memorial University of Newfoundland

The Council would also like to thank Dr. Tanya Duke, University of Saskatchewan, for her contribution regarding the chapter on Anesthesia and Dr. Mardi Collins, Animal Disease Research Institute (ADRI), Ottawa, for her contribution regarding the chapter on Standards for Experimental Animal Surgery. Finally, the Council acknowledges with gratitude the efficiency and patience of the CCAC's staff through the many revisions of this volume of this *Guide*.

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I RESPONSIBILITY FOR THE CARE AND USE OF EXPERIMENTAL ANIMALS

A NATIONAL LEVEL

1. Evolution of the Canadian Council on Animal Care

This section has been revised. Please see "About the CCAC".

February 2017

2. The Contemporary Council

This section has been revised. Please see "About the CCAC".

February 2017

3. CCAC's Assessment Program

This section has been revised. Please see "Assessment and Certification".

February 2017

4. CCAC Position Statements

This section has been revised. Please see "Standards and Policies".

February 2017

5. Legislation Governing Experimental Animals

This section has been revised. Please see "Facts and Legislation".

March 2017

6. Animals in Secondary and Elementary Schools

This section has been revised. Primary responsibility for animals at the secondary and elementary school level lies with Youth Science Canada, which requires compliance with CCAC guidelines in the conduct of biological research, and regulates animal experimentation in science fairs and related or other events under its auspices.

February 2017

B. LOCAL LEVEL

This section has been revised. Please see the *CCAC policy statement for: senior administrators responsible for animal care and use programs* (2008) and the *CCAC policy statement on: terms of reference for animal care committees* (2006).

February 2017

II LABORATORY ANIMAL FACILITIES

A. INTRODUCTION

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

B. LOCATION

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

C. MECHANICAL SERVICES

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

D. DESIGN

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

E. MAJOR FUNCTIONAL DIVISIONS

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

F. SECURITY

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

G. CONSTRUCTION GUIDELINES FOR ANIMAL ROOMS

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

H. CAGING

This section is currently under revision and will be replaced by guidance in the relevant animal type guidelines.

February 2017

The size of caging chosen to house each species should be appropriate for that species (see Appendix I).

Cages and pens must not only confine the animals securely, but also ensure their comfort and safety by permitting normal postural and behavioural adjustments, and provide for environmental enrichment. Animals which are social by nature should not be singly housed unless this is a necessary requirement of the research protocol, and approved by the ACC (see also Social and Behavioural Requirements of Experimental Animals).

Cages must provide for adequate ventilation, satisfactory viewing and easy access to the animal. Food and water delivery systems should be designed and located so as to allow the animal ready access, but prevent contamination with excrement. Cage design should facilitate cleaning and disinfection.

The intensity of light perceived by the animal, the level of noise to which it is exposed, the ventilation and temperature of its microenvironment are affected by cage design and material. Considerable care should be used when choosing the appropriate caging for a particular species and usage. Caging for animals other than the conventional laboratory species requires special consideration.

Unless contra-indicated by the nature of the research (e.g., nutritional studies) solid bottom cages should be chosen (over suspended wire caging) for rodents and guinea pigs in that they permit creation of microenvironments and facilitate provision of environmental enrichment (see also Social and Behavioural Requirements of Experimental Animals).

1. Shoebox Cages

The shoebox cages used mainly for small rodents are particularly suited for breeding purposes. They are usually made of plastics such as polycarbonate, polystyrene, and polypropylene. Polycarbonate is clear, autoclavable, and resistant to most disinfectants. Polystyrene and polypropylene do not withstand high temperatures well. Polypropylene cages are translucent and offer animals more privacy, which may be beneficial for some breeds or wild species. However, opaque cages should not be placed on shelves above eye level since the animals within cannot be readily observed.

A contact bedding (e.g., woodchip, ground corncob, etc.) is used in the bottom of shoebox cages, allowing an animal to form its own microenvironment. These cages are considered comfortable for the animal, and the cage of choice for breeding. However, animals in these cages are in contact with their own excreta and airflow is restricted. Therefore, it is important to clean the cages frequently. Filter caps restrict the airflow even more if cages are not individually ventilated. Faster buildup of ammonia, carbon dioxide and moisture necessitates more frequent cleaning (up to three times per week may be required). Shoebox cages can be fitted with wire grid floors for certain projects which require that there be no contact with excreta.

2. Larger Solid Bottom Caging

Large plastic tubs have been used quite successfully for group housing guinea pigs and rabbits. These tubs must be strong enough to support the weight of the animals contained, have rounded corners to facilitate cleaning and be resistant to disinfectants. These are used with a contact bedding.

3. Suspended Cages

Suspended cages may be top or front opening. Most top opening suspended cages use the rack shelves as the top for the cage. The top opening cages are used primarily for smaller rodents, whereas the front opening cages are better suited to guinea pigs, cats, dogs, rabbits and nonhuman primates (NHP).

Most suspended cages have a floor of wire mesh, steel rod, perforated metal or plastic, above a collection tray or solid floor. It is extremely important that the size of the floor perforations be appropriate for the species housed. They should be large enough to permit excreta to freely pass through, but small enough to prevent foot and leg injuries. The gauge of wire should support the animal's weight without sagging. Floors should be designed so the animal's feet can grip during movement, so as to minimize slipping. Wire mesh floors are not suitable for guinea pigs nor for use in rodent littering cages.

In suspended cages, animals are not in contact with their own excreta and the cages are usually well-ventilated. The pans or trays can be cleaned more frequently than the cage, resulting in less disturbance of animals. The animals, however, do not have the opportunity to form their own microenvironment, and so control of the room environment becomes more critical.

It is recommended that these cages be fabricated from stainless steel or other woven metal alloys, corrosive resistant plastic and/or in the case of some front opening cages, fibreglass. Fibreglass is strong, warm-feeling, and more sound-resistant than other materials, making it especially suitable for post-operative care. NHP and cats should be supplied with one or more resting boards or perches at different levels. A squeeze device built into the cage facilitates restraint of NHP.

4. Other Cages

Many cages are designed to meet specific requirements. Examples include metabolism cages, mechanical exercise cages, gang cages, transfer cages, restraint cages and walk-in cages (used for housing groups of animals).

Additional information on housing large domestic animals and fowl may be found in the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).

For information on cages for wild animals, contact Canada's Accredited Zoos and Aquariums (CAZA).

Information on shipping crates and transport cages for a wide range of domestic, wild and laboratory animals may be obtained from the most recent volume of *Live Animals Regulations* of the International Air Transport Association (IATA).

February 2017

All cage types must take into consideration the well-being of the animal(s) during its confinement.

III THE ENVIRONMENT

There are many physical, chemical, and biological factors which may influence experimental animals and thus modify the results of the investigations (Melby, 1983; Small, 1983). The experimental results obtained are, in principle, only valid for the conditions under which they were obtained and only useful for comparison if all the relevant information concerning experimental conditions is made available.

Among the environmental factors which should be recorded for possible inclusion in scientific reports are: temperature (°C and range), relative humidity (% and range) and whether or not these are regulated; air exchanges/hour, proportion of fresh and recirculated air, and gas or particle concentrations in the air; lighting (natural and/or artificial, photoperiod, and intensity); water type, quality, and pretreatment; bedding type, quality, and pretreatment; housing density; housing equipment; and physical measures to protect microbiological status. The microbiological status of the animal should be reported [conventional, Specific Pathogen Free (SPF) for stated pathogens, or gnotobiotic with microorganisms specified] (WCBCLA, 1985).

A. CLIMATE CONTROL

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

1. Temperature

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

2. Humidity

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

3. Ventilation

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

4. Lighting

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

B. OTHER ENVIRONMENTAL FACTORS

1. Noise

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

2. Chemicals

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

3. Bedding

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

4. Population Density and Space Limitations

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

C. MICROBIOLOGICAL CONTROL

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

D. CHEMICAL AND RADIOISOTOPE UNITS

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

E. REFERENCES

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SMALL, J.D. Environmental and equipment monitoring. In: Foster, H.L., Small, J.D. and Fox, J.G., eds. *The mouse in biomedical research. III. Normative biology, immunology, and husbandry*. Toronto, Ont.: Academic Press, 1983: 83-100.

WORKING COMMITTEE FOR THE BIOLOGICAL CHARACTERIZATION OF LABORATORY ANIMALS/GV-SOLAS. Guidelines for specification of animals and husbandry methods when reporting the results of animal experiments. *Lab. Anim.* 1985; 19: 106-108.

IV FARM ANIMAL FACILITIES AND ENVIRONMENT

This section has been revised. Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).

February 2017

V LABORATORY ANIMAL CARE

A. INTRODUCTION

This section has been revised. Please see the *CCAC guidelines: Husbandry of animals in science* (2017)

March 2017

B. GENERAL PRACTICES

1. Reception

This section has been revised. Please see the *CCAC guidelines on: procurement of animals used in science* (2007).

February 2017

2. Conditioning/Quarantine

This section has been revised. Please see the *CCAC guidelines on: procurement of animals used in science* (2007).

February 2017

3. Holding (Maintenance)

This section has been revised. Please see the *CCAC guidelines on: procurement of animals used in science* (2007) and the *CCAC guidelines: Husbandry of animals in science* (2017).

March 2017

4. Identification and Records

This section has been revised. Please see the *CCAC guidelines on: procurement of animals used in science* (2007) and the *CCAC guidelines: Husbandry of animals in science* (2017).

March 2017

C. CARE OF THE ANIMAL

1. Food

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

2. Water

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

3. Exercise

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

D. CARE OF THE FACILITY

1. Cleaning and Sanitation

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

2. Waste Disposal

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

3. Vermin Control

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

4. Holiday and Emergency Care

This section has been revised. Please see the *CCAC policy statement for: senior administrators responsible for animal care and use programs* (2008).

February 2017

VI SOCIAL AND BEHAVIOURAL REQUIREMENTS OF EXPERIMENTAL ANIMALS

This section is currently under revision.

February 2017

A. INTRODUCTION

In the past, emphasis has been directed towards providing adequate caging for experimental animals in order to contain them hygienically, to facilitate husbandry, and minimize (husbandry) variables. However, increasing importance is now being placed on reducing the animal's stress, and improving its social and behavioural well-being. Provision of varied environmental enrichment may or may not result in increased cost of operation; however, it is considered that there is often immediate benefit to the animal and ultimately to the researcher and the research.

This chapter contains general principles rather than specifics. It is not infallible. Nor should it be taken literally at the expense of the animal (for example, it may be found that an otherwise desirable environment or social grouping is not suitable for an individual animal). This chapter, including a CCAC-approved policy statement, will receive continuing review, with changes made as needed. The ability to treat animals in the way we would wish requires sensitive and conscientious applications of knowledge. Critical, rigorous, scientific endeavour is required of us all in order to reach this goal. Management and housing situations that fulfil the animal's behavioural requirements should be interpreted as providing an ideal toward which we should aim.

1. What is Animal Well-being or Welfare?

Animal welfare is described by Broom (1986) as an animal's "state as regards its attempts to cope with its environment". Blood and Studdert (1988) define it as "maintaining appropriate standards of accommodation, feeding and general care, the prevention and treatment of disease..." The American Veterinary Medical Association (AVMA) enlarges on this to include "all aspects of animal well-being, including proper housing, management, nutrition, disease prevention and treatment, responsible care, humane handling, and, when necessary, humane euthanasia" (Anon., 1990).

Fraser (1989) notes that animal well-being encompasses "both the physical and psychological. These normally coexist. Physical well-being is manifested by a state of clinical health. Psychological well-being is reflected, in turn, in behavioural well-being. The latter is evident in the presence of normal behaviour and the absence of substantially abnormal behaviour."

The World Veterinary Association (WVA) states that animal ethology "puts the emphasis on knowledge which is scientifically based. Its aim is to clarify: a) needs that can be filled; and b) harm that can be avoided..." (WVA, 1989).

Hurnik (1988) defines animal well-being as "a state or condition of physical and psychological harmony between the organism and its surroundings." However, it is agreed that animal welfare is not a single phenomenon, and that no one definition will satisfy everyone (Moberg, 1992; Baxter, 1993; Duncan and Dawkins, 1983).

The Royal Society for the Prevention of Cruelty to Animals (RSPCA) has recently recognized the need to draw attention to stress in experimental animals and the necessity for alleviating this condition whenever it is associated with suffering (RSPCA, 1992). An annotated bibliography on animal welfare has recently been prepared (Murphy, Rowan and Smeby, 1991).

One must always remember, as well, Hollands's sensitive definition written more than a decade ago: "This then would be my definition of animal welfare: dignity-according to animals the natural dignity which is due them as living, sentient creatures" (Hollands, 1980).

2. Environmental Enrichment

Environmental enrichment is defined by Beaver (1989) as "additions to an animal's environment with which it can interact."

As a general rule, most experimental animals are social animals and benefit from the company of conspecifics or humans. As well, predictability in interactions usually enhances the animal's well-being, while the opposite results from frequent regrouping and restabilizing.

It should be remembered that an animal's experiences during the developmental phases determine social behaviour. Therefore, conditions of animal holding in a breeding facility will impact on the animal's future well-being.

The social needs of animals used in research, teaching, or testing, should be given equal consideration with environmental factors such as lighting, heating, ventilation and containment (caging). Particularly in the case of singly housed animals, daily observation provides an alternative form of social contact for the animal and commonly facilitates handling in that the animal becomes accustomed to the human presence.

A more complex environment, use of artificial appliances, and better use of existing space enhance stimulation. Simply increasing the number of square inches or centimetres available to an animal does not promote better space utilization (Line, 1987; Fajzi, Reinhardt and Smith, 1989); however, the amount of space should be appropriate to the species. In group housed animals, the size of the social group in relation to its available space should be regularly appraised.

3. Group Formation

When animals are introduced to each other and pairs or groups are established, there is an initial period during which they work out their social relationships (dominance ranks, etc.). There may be aggressive interactions; however, when conditions are right, the social organization will stabilize. Once the hierarchy

has been established the interactions are subtle, and based more on avoidance or ritualized threat than overt aggressive action. If their daily routine is disrupted, if resources such as food or resting spaces are limited, or the animals are poorly grouped, the hierarchy becomes disestablished and the number of aggressive interactions increases. The animal's well-being is threatened when:

a) space is insufficient for maintaining behaviourally adequate distance;

b) feeding or resting space for all individuals is insufficient; or when feeding and resting cannot be accomplished concurrently;

c) regrouping is performed so frequently that animals must repeatedly undergo the stabilization process; and

d) group sizes are inappropriate for the species.

The above statement challenges intense confinement practices which prohibit animals from engaging in their normal social-behavioural activities.

In addition to sufficient primary space for resting, animals also need what could be called secondary space, for freedom of movement at their own will. An important exception may occur at the time of parturition, when most individual animals should be given their own quarters.

Most animals should not be housed singly unless required by medical condition, aggression, or the dictates of the study. Singly housed animals should have some degree of social contact with others of their own kind. For most species, at the very least there should be potential visual contact. Olfactory and auditory contact with other animals is also usually desirable.

Protocols which involve single housing must describe proposed measures for meeting the social requirements of the isolated animal (e.g., where appropriate, increased positive human contact). Investigators must justify any deviations from the CCAC guidelines before an Animal Care Committee (ACC) and receive its approval, before any study can begin. All protocols must be reviewed at least annually by the ACC.

4. Position Statement

"SOCIAL AND BEHAVIOURAL REQUIREMENTS OF EXPERIMENTAL ANIMALS (SABREA)

Well-being in animals has two components: physical and behavioural. Physical well-being is manifested by a state of clinical health. Behavioural well-being is manifested by behaviour considered to be normal for that species and strain, together with the absence of significantly abnormal behaviour. Behavioural well-being is considered to reflect psychological well-being, and to that extent, the terms are considered to be synonymous in our usage.

In the interest of well-being, a social environment is desired for each animal which will allow basic social contacts and positive social relationships. Social behaviour assists animals to cope with circumstances of confinement. Caging, whether for single animals, pairs, or groups, should be enriched appropriately for the species.

It is necessary to recognize affiliations which commonly occur within and between species. Chronic isolation as a method of accommodation, should not normally occur. However, in exceptional circumstances, and with clear scientific and biological justification, some animals may be better kept alone. Positive interactions with human-beings are important in some species, and particularly in conditions of social isolation. Some individuals seem more readily accepted by animals than others; this concept should be used to maximize the benefits of these affiliations.

February, 1990"

B. ANIMALS USED IN AGRICULTURAL RESEARCH

This section has been revised. Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).

February 2017

C. ANIMALS (LARGE) HELD IN METABOLISM CAGES

This section is currently under revision and will be replaced by guidance in each of the relevant animal type guidelines.

For guidance on metabolism cages for farm animals, please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).

February 2017

The use of metabolism cages or crates necessarily reduces the animal's social and behavioural activities. This procedure should not, therefore, be used merely for the purpose of convenient restraint, but should be reserved for approved metabolic studies. Animals so housed should be under close and expert observation throughout the period of the study.

1. Conditioning

A seven to ten day conditioning period in a floor pen, to "acclimatize" the animal to a new diet (if this is necessary), and before its placement in the associated metabolism crate, is required, followed by three to four days' adjustment to the crate.

2. Size of Metabolism Crates

Enough space must be provided for the animal to rise and lie down normally. Some animals (e.g., calves and sheep) swing their weight forward when rising; therefore, the required length of crates should be greater than the simple length of the animal. Width of the crates must be sufficient to allow sternal recumbency.

Other postures for example shown by sheep, as well as serving to make the animal comfortable, also have a thermoregulatory function. If the dimensions of a metabolism crate do not permit such postures (e.g., lateral recumbency), then proper temperature and other environmental control becomes a responsibility of the research.

3. Contact with Other Animals

Many animals are highly social. An isolated animal is often not normal behaviourally, nor possibly metabolically. To minimize stress, crates should be designed and positioned so that there is good visual, auditory, and olfactory contact with conspecifics.

4. Pre-, During and Post-Experiment Checks

A physical and behavioural assessment of the animal should be done before, during, and after an experiment. Animal care personnel should observe the animal before and after eating in order to ascertain, for example, if intake has decreased.

5. Observing Changes in Behaviour

Strict attention should be paid to observing changes in behaviour, which can indicate a degree of stress or anxiety, or fear stereotypies (e.g., increased drinking in sheep). Noting such changes is important to good science as well as good animal care.

6. Duration of Confinement

Enforced immobility has a negative effect on bones, joints, and muscles. For this reason, animals should be released for periodic exercise or released from the metabolism crates for at least three hours per seven days.

Any period of study exceeding 21 days in a metabolism crate must be justified to the ACC by the investigator, on grounds of experimental design and scientific merit. However, the total period in the crate should not exceed 30 days.

7. Exceptional Circumstances

In exceptional circumstances (e.g., catheterization studies), it may not be possible to implement the recommended weekly exercise requirement. In such cases, variances to these guidelines require justification by the investigator, and review and approval of the institutional ACC.

D. CATS

1. Introduction

Various authors have proposed schemes to assist those who are attempting to enhance the welfare of research animals. Beaver (1989) proposes five basic methods which can be used to alter an animal's environment so as to permit the animal to live and produce to its full potential. These include behavioural enrichment, social peers, artificial appliances, food gathering activities, and control of the environment.

Spinelli (1989) in commenting on Beaver's five methods, disagrees with her definition of enrichment. However, he notes that there are a variety of strategies that will be useful singly or in combination to promote the psychological well-being of laboratory animals. Spinelli contends that environmental enrichment and an animal's psychological well-being "may be one of the most important areas of study in laboratory animal science over the next few years."

Beaver's five areas will be interpreted in light of recognized behaviour systems for cats (*Felis catus*). Such systems represent species-typical behaviours which are co-ordinated to serve a specific function that has adaptive value (Catcott, 1975). As such, they must all be integrated to a greater or lesser extent in any model which seeks to optimally meet the needs of, and avoid harm to, the animals in our care. These systems include:

- Social Behaviour
- Sexual Behaviour
- Feeding Behaviour
- Parental - Offspring Behaviour
- Eliminative Behaviour
- Comfort Behaviour
- Play Behaviour
- Resting – Locomotory Behaviour
- Exploratory Behaviour
- Agonistic Behaviour

Species-typical behaviours which occur in the domestic environment are co-ordinated to serve a specific function that has an adaptive value and therefore should not be a redirected response to some external stressor. For example, spraying is a normal behaviour in the wild environment, but is a sign of conflict behaviour in domestic animals kept in close quarters. An awareness of normal behaviour patterns in the species is essential in order for care-givers to identify and address abnormal behaviour. Both are extensively addressed by Hart and Pedersen (1991).

In the absence of scientific data to indicate a better management scheme, there is an underlying presumption that mimicking the wild habitat should be highly desirable for captive animals in general. Generally, this is accomplished in a modified fashion for most species, eliminating, for example, such features as predators which the species might encounter in the wild (Beaver, 1989). However, even in this latter regard, Markowitz and Laforse (1987) have discussed artificial prey as behavioural enrichment.

2. Behavioural Enrichment

Behavioural enrichment should, in general terms, foster and promote a full and extensive repertoire of normal behaviour (ethogram) for the domestic animals, whilst preventing the development of abnormal behaviour. The provision of physical stimuli and target objects that will promote the expression of species-typical behaviours should be incorporated into any plan for behavioural enrichment.

It may be possible to assess program success by the extent to which it prevents development of behavioural abnormalities and promotes normal behaviour, or minimizes the expression of or eliminates pre-existing abnormalities that an individual or group displayed prior to enrichment attempts.

The home range of domestic cats varies tremendously based on population density, need (hunger), desire (hunting, mating), and such natural and man-made barriers as rivers, fences, etc. While domestic cats living in rural areas may range over many tens of acres on a daily basis, as urban crowding intensifies, the territory commonly shrinks to a home range of one-fifth of an acre each or less (Morris, 1986).

Although cats have been portrayed as asocial loners (Leyhausen, 1990; Beaver, 1981), some authors now question this contention, as well as how much the social nature is being changed by selective breeding (Morris, 1986; Liberg and Sandell, 1990; Hurni and Rossbach, 1989). Even now, most cats are not highly social because they still need individual space and privacy. However, compatible individuals may share their first order home (house, room or even chair) as well as their home range (backyard, neighbourhood, or acres of farmland) (Morris, 1986; Leyhausen, 1990; Macdonald and Moehlman, 1982).

3. Social Peers

Insofar as "solitary confinement" is considered an unnatural condition for most species (Beaver, 1989), it is necessary to examine the role of conspecifics in promoting well-being and behavioural enrichment in domestic cats. A wealth of anecdotal information suggests that pairs and stable groups are successful alternatives to single cage housing for cats or other species. However, finding scientific data to demonstrate this and other social functions important to behavioural well-being in cats is a challenge.

Beaver (1981) reports that, although the socialization process is not well understood in cats, the critical window for their socialization may end as early as nine weeks of age. Cats weaned at an early age and raised in isolation later displayed excessive undirected activity, disorganized behaviour and fear of novel situations (Seitz, 1959).

Continued socialization with conspecifics is essential to the well-being of developing kittens. Blackshaw (1985a) notes that: "Kittens reared in the absence of other cats from the 7th week on – and so deprived of the possibility of social play – later showed poor control of attack and escape behaviours, sexual and parental encounters."

Similar findings regarding social deprivation have been reported for other species including calves (Broom and Leaver, 1978), rodents (Rosenzweig and Bennett, 1977), and dogs (Scott and Fuller, 1965).

Cats would be best adapted to the research environment when raised and socialized to research facilities and human handlers before seven weeks of age. Continued, regular human contact is also important (Beaver,

1989; Karsh and Turner, 1990) in order to maintain the human socialization. Beaver (1981) notes that excessive handling can be stressful to the unsocialized or asocial animal.

Animal caretaker styles can also affect the behaviour of animals (Beaver, 1981, 1989; Hurni and Rossbach, 1989; Fox, 1986). It is considered that calm, gentle, consistent keepers reduce the stress in a population.

Visual stimuli can also improve behavioural well-being.

In most animals, changes in routine should be avoided or minimized as much as possible. For example, even the introduction of a new technician can change liver enzymes in chimpanzees (Moor-Jankowski and Mahoney, 1989). Hemsworth and Barnett (1987) report that inconsistent behaviour has the effect of increasing pigs' fear of humans.

4. Enrichment Devices (Artificial Appliances)

Having recognized the need for adequately sized, appropriate caging that is clean, safe, secure, and suitably bedded, consideration is now being given to provision of species-appropriate activities through introduction of complexity within the cage space. Enrichment devices would include, for example, toys, scratch posts, climbing apparatus, PVC culverts for privacy and play, etc. Activity can be encouraged by hanging an object that can be swatted or watched, or by providing an object that will roll when batted (Beaver, 1981).

The concept of novelty is an important one when considering play-articles for cats. It is widely reported anecdotally that continued exposure to an item reduces the play value to the extent that the cat quickly becomes indifferent to the article, only to show renewed interest after a brief period of removal.

One must also consider the age of the cats. Kittens require a variety of articles with which to play. Play behaviour in kittens occupies almost 10% of total time and is considered to assist in the acquisition of information and skills includes an opportunity to learn the communicative value (message and meaning) of displays, particularly "graded displays" (Blackshaw, 1985a).

5. Food Gathering Activities

Food gathering activities can be manipulated to foster environmental and behavioural enrichment. Unfortunately, although much has been written about the food gathering activities of nonhuman primates (NHP), there is a relative dearth of literature for domestic cats. Until recently, it was assumed that if an animal had adequate supplies of nutritious food and clean water, its "feeding" needs were met. Clearly, this approach denies the complex range of behaviour exhibited by cats as part of a predator's feeding behaviour system, which includes, but is not limited to searching, chasing, catching, killing and consuming prey (food). Four of these five behaviours are redundant for animals provided with ample nutritious food, and they are deprived of the opportunity to express such behaviours.

The diet of feral cats includes small rodents, birds, etc., which have partially digested vegetable material in their intestinal tracts. The cravings many cats have to consume small amounts of grass, house plants, etc., may reflect a craving for plant material in a more natural form than as commercial pet food (Leyhausen, 1990; Beaver, 1981; Blackshaw, 1985b; Beaver, 1980). This need could be met in a variety of ways (e.g., by providing small amounts of fresh grass or other safe plant, or cooked vegetables which can be ingested without causing gastric irritation).

A cat's appetite may be affected by lighting and noise level, by the presence or absence of people, by the type and cleanliness of the container, and by the presence or absence of other cats (Scott, 1975).

Preference tests have shown that cats prefer their food at 30°C (86°F) (McKeown and Luescher, in press). Although it may not be possible or necessary to incorporate this documented preference in all feeding regimes, such knowledge forms the basis for enhanced care for individuals undergoing unusual stresses, (e.g., partial anorexia in the immediate post-operative period), or when introducing new individuals to a group, etc.

Most cats generally do not like to eat from narrow, deep bowls; however, some will only drink by dipping a paw in such a bowl and licking the foot. If an animal will not eat from a container on the floor, the bowl may be placed on the perch.

Some cats prefer fresh, clean water that has been allowed to stand for a time to permit the dissipation of chemical odours that result from water treatment. Other cats refuse to drink unless from a running source, such as a dripping faucet. Many cats are loath to eat or drink from any container which is contaminated with odour or saliva from another cat. Obviously these factors and countless others are significant in providing the optimal housing for cats under a variety of caging conditions.

Idiosyncrasies of behaviour which reflect the fastidious nature of felines should be considered in any effort to provide for their social and behavioural needs. For example, texture is important to cats: the texture of their food can affect appetite; the texture of resting and sleeping locations can determine preferences in this regard.

Many cats will not use a litter box that has been soiled by another cat. Indeed, many cats even have preferences for certain textures or types of litter and will not use others. Even the location of the food, water, and litter containers relative to each other, resting areas, doors, etc., can have a significant impact on the well-being of cats.

6. Control of the Environment

Assumptions are widely held that an animal's well-being is enhanced by affording some degree of control over its environment (Line, 1987). Whether this is expressed in the negative language of "reducing stress" or the positive language of "environmental enrichment" we continue to seek ways to allow animals to express their individual needs or desires. Radio broadcasts played during working hours make cats less frightened by sudden noises and more easily accustomed to strange human voices (Hurni and Rossbach, 1989).

The existence of a range of temperatures within the enclosures allows for an individual to seek preferred resting spots. Provision of safe indoor/outdoor enclosures permits further freedom of choice and therefore some degree of control. Choice of texture, height, temperature, and degree of enclosure are examples of a few methods of environmental enrichment for animals. Cats are noted for their enjoyment of a warm, sunny sleeping location.

Height (as provided by perches, for example) is also a desirable factor for many cats when seeking a resting spot (Beaver, 1989; Blackshaw, 1985a). In group housing, access to the individual's preferred vertical niche, with sufficient elevated resting places for all cats, will enhance the enrichment program.

Some prefer a dark, secluded spot for rest (Beaver, 1981); others may choose to sleep closely by another member of the group. Anecdotally, it is noted that some cats prefer to sleep on (sanitizeable) fleeces and soft blankets.

Many anecdotal observations regarding cats have been well documented in other species. For example, Chamove and Anderson (1989) report that such arboreal species of monkeys as the callitrichids rarely come to ground in the wild. Furthermore, they state that in captivity these monkeys almost never visit a bare floor (1% of the time); however, the time spent on the ground increases ten-fold if contact bedding such as a leaf-like substrate is used. Obviously, since the floor may encompass as much as 40% of the total usable surface area and more than 60% of the horizontal surface area, addressing the issue of texture preference can provide a potent tool for environmental enrichment for many species.

Both predictability and controllability are important variables to reduce stress. Therefore, when controllability cannot be provided, allowing the animal some degree of predictability is one coping strategy which should enhance well-being (Beaver, 1989).

The concept of predictability must be interpreted in light of species-typical behaviours. For example, while some species such as higher primates may respond positively to changes in time and content of their daily feedings (Line, 1987), other species can experience unnecessary distress from alterations to their routine. Changes in routine which may, for example, occur during weekend feeding and cleaning schedules, are known to be stressful in routine-oriented animals (Beaver, 1981).

7. Housing

The least stressful housing environment for research cats will usually be gang housing, especially if there are numerous perches on which individuals can rest (Beaver, 1989). When establishing pairs or small groups, compatibility can first be determined by observing which animals sit near each other.

Group pens or cages should be provided with adequate, usable, vertical space (e.g., shelves, or a tree-like structure with platforms). If kittens are present, access to higher levels can be provided through the use of a slanting board or similar object. Group housed cats prefer warmed floor areas on which to sleep (McKeown, Pers. Comm., 1990).

The housing should provide an area for eating and for elimination. In the latter regard, provision of a number of litter boxes can reduce the possibility of refusal by individual animals to use a particular box.

Aggression can occur between adjacent, individually housed animals. Provision of a dark, secluded hide-out (e.g., box) can allow a retreat from this type of stressful environment (Beaver, 1981). [This also proved beneficial in NHP which were provided with a privacy panel (Reinhardt, 1990).]

If animals must be singly housed for an experiment, then where possible and appropriate, they should be group housed with their original conspecifics between studies. Females are considered more appropriate for long-term holding, as they are generally more amiable towards one another and can be kept in groups after several days of limited exposure (Hurni and Rossbach, 1989).

If possible, all animals not in large pens should be exercised daily, unless contra-indicated for health or experimental protocol reasons.

Some authors (e.g., Hurni and Rossbach [1989]), suggest that intact males be housed separately by four to six months unless they remain with litter mates and no stranger is introduced. However, Taylor (Pers. Comm., 1990) reports long-term success with several colonies of intact males housed in groups of 6-14. New individuals, carefully introduced, caused minimal disruption and in more than two years of observation only three to four episodes of aggression greater than ritual display were noted. None resulted in serious injury; however, in each of those cases it was only necessary to remove one individual to restore harmony.

Asocial individuals should also be singly housed, as the biggest stress to these cats is other cats. In addition, intact male cats not kept in a breeding harem, cats recuperating from surgery, and research animals being conditioned to a cage, are usually singly caged; however, cats can form bonds. This can be illustrated sometimes by the manifestation of separation anxiety (McKeown, Pers. Comm., 1990).

8. Maternal Behaviour

The duration of gestation in the cat ranges from 60 to 68 days, with an average of 65 to 66 days. During approximately the last third of pregnancy, obvious behavioural changes occur, although some queens have already been showing increased docility. Along with a rapid weight gain, due primarily to fetal growth, there is an accompanying increase in appetite, decrease in activity, and decrease in agility. Distention of the mammae may also occur.

In the week immediately preceding parturition, the queen will seek a dark, dry area where she can remain relatively undisturbed. A nesting box fills this need. During this period before delivery, the queen usually spends an increasing amount of time in self-grooming, particularly of her mammary and perineal areas. She may also become more irritable or defensive, possibly as a result of the extreme stress associated with this time of pregnancy.

As parturition becomes imminent, the female becomes increasingly restless, digs at the floor or nesting material, and assumes a defecation posture without defecating. There may be calling vocalizations, especially by Siamese cats, and a few queens become excessively anxious and even hysterical (Fox, 1974).

Each of the four phases of parturition is highly variable, although their order holds true for the majority of births. The initiation of each new phase is usually marked by an abrupt behavioural change, from contractions causing genitoabdominal licking to placental delivery resulting in the consumption of the placenta (Beaver, 1980).

Hurni and Rossbach (1989) suggest that queens in group housing be provided with a cage to which they be confined overnight and during mid-day; this would be made available from just before parturition until four to six weeks after. By letting them out for a few hours in the forenoon and afternoon into the stock pen, the female remains socialized to the community and the stress of changes in the population hierarchy is reduced.

9. Random-Source vs. Purpose-bred Animals

Since it is considered advantageous to house research animals in a social environment, the housing of animals which are genotypically sociable is a distinct advantage. Cats' tendency to socialize well is a trait which is carried genetically by the male (McKeown, Pers. Comm., 1990). Proper selection for genotypically social cats is therefore possible in purpose-bred populations. As well, kittens growing up with social conspecifics

become more social than those raised with non-social conspecifics (Schar, 1983). By culling animals which exhibit undesirable traits even after adequate socialization (Ringler and Peter, 1984), the population can be further selected to include more animals which are behaviourally adapted to the research environment.

For certain types of studies, use of purpose-bred cats provides advantages which enhance the quality and validity of the research. These include a known health status, and control over the animal's age, genetic factors, and environment. This allows the production and use of a much more uniform population of known status. Losses are less, results are more valid, and therefore fewer animals need be used. In addition, there are many advantages to the cats kept in the research environment, in terms of their social and behavioural well-being.

E. DOGS

1. Introduction

Dogs (*Canis familiaris*) have been human-beings' companions for over 12,000 years (MacArthur, 1987). In the laboratory, this potential for developing a close relationship with people may be realized through appropriate socialization of the animal at an early age. As well, most breeds of dogs used in research, teaching and testing are naturally gregarious and seek the companionship of other dogs (MacArthur, 1987; Beaver, 1981). This tendency is also seen in packs of feral or wild dogs travelling together (Dunbar, 1979). Therefore, unless contra-indicated by the protocol, medical condition, or the animal's aggressiveness, dogs should be paired or group housed with conspecifics in cages or runs, with space adequate for active normal behaviour. If this is not possible, dogs should be released at regular intervals into space adequate to permit this normal species-typical behaviour.

Social rearing of puppies is the most effective means of ensuring compatible conspecific behaviour as adults (Fox, 1972). Moreover, dogs that have been handled as puppies show greater resistance to stress and greater disease tolerance than those which are not handled (Fox, 1975).

The appropriate maintenance of dogs will be discussed under breed differences, criteria for assessing well-being, housing, socialization to people, and enrichments.

2. Breed Differences

The differences in size between Newfoundlands and Chihuahuas represent some of the extremes seen among the many breeds of dogs. These differences include not only morphology, but also temperament (e.g., terriers vs. labrador retrievers), conformation (e.g., beagles vs. greyhounds), urea metabolism (dalmatians), development of behaviour patterns (MacArthur, 1987) and other important considerations. Although every dog belongs to the single species (*Canis familiaris*), each breed has specific behavioural and social needs.

Interbreed morphological differences become important in selection of proper cage size (even though they have the same body weight, long, lean dogs are likely to require different cage sizes than short, stocky dogs). The decision to group house will depend to some degree upon breed differences. Much can be learned appropriate to the well-being of dogs from a basic knowledge of breed-typical behaviours; however, attention to the uniqueness of each individual animal is the only way in which well-being can be assured.

In addition to understanding breed differences, an understanding of intrabreed differences, which are the natural outcome of environmental and genetic factors, is also of great value. Litter mates, even when reared under the same conditions, may behave entirely differently.

3. Criteria for Assessing Well-being

Evaluation of animal well-being includes both engineering (environmental) standards (e.g., minimum cage size, temperature, light cycles, etc.) and performance or outcome measures (McCarthy, 1989) standards (the dogs' general state of health and their compatibility in social groups and with people).

The well-being of dogs is dependent on a number of factors which include: training and dedication of the scientific, animal care, and veterinary staff; a facility in compliance with this *Guide*; observations of the animal's physical health (does it appear healthy, alert, active?); observation of the dog's behaviour; pair or group housing of compatible animals; and socialization to people.

a) Clinical Observations

i) Eyes

Clarity and expressiveness of the eyes is a good indicator of general health. This should not be confused with non-eye contact, sometimes demonstrated by dogs raised as subordinate to people.

ii) Posture

Ill or distressed dogs may appear lethargic or cower in the rear of the cage or kennel. Abnormal gait or the carrying of a limb is suggestive of a localized trauma or infection.

iii) Hair coat

Ill or chronically distressed dogs will often manifest a rough, unkempt hair coat. Self-grooming may be absent.

iv) Stool

Presence of diarrhea, or stool with mucus, blood, or helminths (worm-like endoparasites) should be questioned.

v) Appetite

Inappetence or too-rapid ingestion of food should be questioned; sudden changes in weight, drinking or eating behaviour should also be questioned and investigated.

b) Behaviour

i) General

One should look for evidence of how well the dogs are adapted to the environment. Whether singly or socially housed, they should not normally exhibit highly repetitive or atypical behaviours. Dogs generally

perceive the cage or kennel as home territory and, when the threat is not too great (e.g., the door remains closed), they may bark in defence of the territory. Opening the kennel door may elicit very different behaviours; solicitation from human-bonded animals and fear from unsocialized ones. These differences may not be seen with the door closed; however, judgement about a fear-response to strange individuals must be made cautiously, for a certain degree of inquisitiveness or anxiety over the presence of unknown persons is normal.

ii) Toward cagemates

Compatible cagemates should demonstrate equal desire for attention when the cage is approached by familiar people. Overly dominant individuals (and dogs overly socialized to people and undersocialized to dogs) (Beaver, 1981) will prevent subordinate individuals from being touched by the person, which, at times, may lead to aggression that continues as long as the person remains at the cage door.

iii) Toward people

Dogs that bark excessively, remain in the rear of the cage, refuse to come to the cage door even for familiar technicians, or demonstrate aggressive tendencies when approached, are likely not well-socialized to people. Unsocialized dogs are fearful of people, may become "fear-biters," are difficult to catch and restrain, and may have physiological variability incompatible with some scientific studies. These manifestations are de facto evidence of distress and poor well-being. Such dogs are poor candidates for chronic studies.

iv) Maternal

Toward the end of gestation, the bitch will begin to seek seclusion, a safe, warm, dark and quiet place, and it is advisable to make such provisions by placing a whelping box in some corner that she will accept. She should be shown her whelping quarters early on in her pregnancy and be given amble time to become accustomed to them (Fox, 1972). Where possible, during the birth of the pups any kind of handling or interference should be avoided.

The behaviour of the pregnant bitch changes toward the end of gestation. She is generally more restless and appears uncomfortable. She may show nesting behaviour and start to tear up newspapers and to scratch at the floor of the whelping box. Often the bitch will go off her food, and some occasionally vomit during the few days immediately prior to parturition. It is not unusual for the bitch to pant a great deal and to regularly look apprehensively at her hindquarters (Dunbar, 1979).

Nest boxes for whelping bitches, provided with bedding materials and heat sources, keep homiothermic newborn pups warm and dry.

4. Housing

Housing should facilitate social group formation, human interaction, comfort, and sanitation. The use of modular cages or runs that can be converted to accommodate either pairs or groups of dogs is desirable.

Hite, Hanson, Conti *et al.* (1977) and Hughes, Campbell and Kenney (1989) discuss the effects of cage size on beagles (the most commonly used purpose-bred dog). Caging should permit ready access by personnel and permit visual, olfactory, and auditory contact with other dogs.

Resting boards made of non-conductive, non-permeable materials should be provided to permit animals to escape the floor, especially when temperature control and wetting may be a problem.

i) Social housing

Social housing is desirable for most breeds of dogs. Centuries of interaction with people and other dogs have developed species-typical behavioural patterns, which must be understood in order to evaluate and provide for their well-being (Beaver, 1981). Some breeds of dogs (e.g., hounds) are highly social; others such as terriers are not (Beaver, 1981). Single caging for most social breeds may be stressful.

Movement of an individual(s) away from compatible animals can be disruptive. Dogs that are removed from a social group (by virtue of health, protocol, or aggression) should remain in the same room, as close to the same social group as possible, and should be returned to the group as soon as possible. When the group is stable, positions within the room should not be changed without cause.

ii) Single housing

For those animals comfortably adapted to solitary living, introducing cagemates may induce distress. In these circumstances, exceptions to social housing may be appropriate, especially where human companionship is provided and they are in visual and auditory contact with other dogs.

If dogs must be housed singly, they should be in visual, auditory and olfactory contact with others in the room. It is likely that multiple social groups exist within such a room, with the most stable groups consisting of individuals immediately adjacent to or across from each other.

It should be remembered that dominance can be expressed across the aisle, so that an animal removed from a cagemate because of dominance aggression should not be placed directly across the aisle from its original cagemate, but moved to a location away from the overly dominant individual.

5. Socialization to People

Of all the common laboratory species, dogs are the most highly domesticated and adapted to live in intimate association with people. Socialization creates an attachment and trust of people, which assists in the development of coping strategies that serve to bridge periods of adaptation to new procedures and environments, thereby reducing stress and experimental variability.

Without early exposure to people (i.e., socialization), dogs rapidly become fearful of humans and manifest fear and distress in a variety of physiological and behavioural ways (e.g., "fear biting") (Beaver, 1981), all of which are incompatible with their well-being and can influence the reliability of research data derived from them.

The dog's ability to cope when a person enters the scene, or its environment changes, is a key criterion to well-being (Dunbar, 1979). Coping connotes the ability of the dog to adapt to stresses with minimal behavioural or physiological alteration (Archer, 1979).

Therefore, all dogs used in a facility, for whatever purpose, should be socialized to people, (either in the facility or by the supplier), or serious consideration be given to their euthanasia or use in acute non-survival

studies. Socialization (handling by people) should take place when pups are between 6-10 weeks of age (Wolfle, 1989a, 1989b; MacArthur, 1987; Fox, 1975). A number of other investigators believe the socialization period should extend to at least 12 weeks (Pfaffenberger, 1963; Bateson, 1987; Vanderlip, Vanderlip and Myles, 1985a, 1985b; Scott and Fuller, 1965). Fox (1968, 1990) contends that puppies deprived of human contact until after 10 weeks of age will be very difficult to handle later in life.

Adult dogs that demonstrate lack of socialization should not remain in the facility any longer than it takes to determine that the behaviour is unlikely to respond to remedial socialization, which, in any event is time and energy consuming and not at all sure of success (Dunbar, 1979). Such dogs should be either euthanized or used immediately in an acute, non-survival study. Socialization should be considered a critical part of every breeding program, and when animals are purchased from a supplier, socialization should be written into contract specifications.

Human/dog interactions will ensure continuation of the benefits gained from socialization. Quantification of contact during the socialization period, in terms of specific frequencies or durations, is less important than the quality of the interaction. Puppies are susceptible to attachment to humans or other animals. Thus, repetitive interaction with people during this period is more important than the exact nature, frequency, or duration of the interaction.

Wolfle (1990) described the socialization of large numbers of foxhound puppies with only five minutes per puppy per week. However, it should be noted that this was a complex, rich, bi-weekly socialization procedure where littermates were treated as a group and thus each pup benefitted from the interaction of people with the littermates. Nevertheless, it is clear that the amount of "hands-on" time required to socialize large numbers of puppies does not seem to be critical, and should be possible to accomplish with existing staff in most facilities.

Through observation, it should be established whether each dog in a social group is behaving normally (Beaver, 1981). By having a variety of people participate in the socialization of each dog and by reinforcing their socialization as adults, the problem of over-attachment to an individual (person) can be avoided.

Housekeeping routines should include recognition of each dog as the technician works about the room. Moments taken to speak to and pet the dogs will be repaid through reduction in the dogs' anxiety and physiological variability (Wolfle, 1990, 1985, 1989a, 1989b). The effects of animal caretaker styles may affect the animal (Fox, 1986) and thus experimental results.

6. Enrichment Devices (Artificial Appliances)

"Enrichments," often in the form of toys or other appliances, are frequently given to dogs to produce a desired change in behaviour. For example, abnormal or persistent grooming may be moderated by giving the dog rawhide or other treats on which to gnaw; however, this should be done only with the knowledge of the facility manager and investigator. Beaver (1989) notes that dogs respond well to running through mazes as a means of environmental enrichment.

Music has long been used to reduce stress in many laboratory animal facilities (Line, Clarke, Ellman *et al.* 1987) and dairy barns (Ewbank, 1968), (perhaps because of its initial stress-reducing effect on the attendant). However, few definitive data exist to recommend its use for dogs. If used, the volume should be placed at conversational levels. Levels exceeding 85 db for a sustained period may cause auditory damage. It

should also be remembered that many laboratory animals, including dogs, are able to hear frequencies above what humans can hear (Dunbar, 1979). If violin music, for example, is played at high volume, dogs may be in acute discomfort. Conversational (talk show) radio sound may accustom the animal to the human voice.

7. Exercise

Exercise for dogs has recently been mandated in American law which requires "that research facilities shall establish, in consultation with the attending veterinarian, written procedures and systems for exercise of dogs..." (USDA, 1989).

Dr. Dale Schwindaman, Assistant Deputy Minister for Regulatory Enforcement, Animal and Plant Health Inspection Services, U.S. Department of Agriculture, has stated that, in looking at exercise and socialization requirements, it may turn out that social contact with other dogs or with humans in the case of singly housed animals is more important than exercise. He reports that it has been proposed that, in addition to housing in compatible groups, the ability to see and hear other dogs will be required. Singly housed animals would receive positive physical contact with humans. Any exceptions to the requirement for exercise and socialization would have to be approved by the Institutional Animal Care and Use Committee (IACUC). It has also been proposed that animals held in (space that is) less than what is required for permanent housing as mandated by the *Guide for the Care and Use of Laboratory Animals* (USDHHS, 1985) would have to be released for exercise for at least thirty minutes daily (Schwindaman, 1990).

Scientific data have indicated that cage size had no significant effects on hematologic or serum biochemical values of purpose-bred beagles; that the dogs had little inclination to exercise when released alone into an exercise area, unless humans were present in the room; and that even a moderate exercise program had no demonstrable effect on biochemical parameters such as hematology, clinical chemistry or indicators of stress (Campbell, Hughes, Griffen *et al.* 1988; Hughes, Campbell, and Kenney, 1989; Campbell, 1990).

Studies demonstrated that on the average, dogs spend only 0.5 to 1.5 hours daily in any type of activity, regardless of the housing system. Most of the dog's activity takes place during the morning hours when there is the greatest amount of human activity in the area. Providing increased human contact will improve the handling and behavioural characteristics of the dog, but not its activity, because dogs that do not have enhanced human contact may move around the cage in an effort to attract attention (Hughes and Campbell, 1990). These authors contend that they have shown that "dogs are basically lazy. They do not like to exercise and have no particular inclination to run about an area." Fox (1986) reports that dogs that are well-fed and content do not exercise routinely.

Although, unlike the U.S., no legal requirements for the exercise of dogs exist in Canada, the concept of exercise, and perhaps more importantly communal housing and socialization of the animal, both with conspecifics and humans, is considered of great importance by the CCAC. Institutions are being asked to furnish documentation of ACC approval for any dog housed individually. Increasingly, the provision of environmental enrichment, in its various forms, will be strongly recommended by the CCAC.

In conclusion, it should be remembered that, as Erwin (1985) advised, reactions of animals to any type of environmental enrichment should be monitored to determine whether the desired outcome is achieved.

Beaver (1989) reminds us that studies have not determined the amount of activity that is actually beneficial to any species. Neither has it been shown whether stereotypic behaviour is beneficial or harmful (Fox, 1986).

Much knowledge of animal behaviour remains to be garnered and established in order to produce an environment that will enhance the dog's well-being.

F. NONHUMAN PRIMATES

This section is currently under revision and will be replaced by the *CCAC guidelines on: nonhuman primates* (in prep.)"

February 2017

1. Introduction

When animals are used, efforts must be made to provide a physical and social environment conducive to their well-being. As well, social structure makes many experimental animals sensitive to the ill effects of inappropriate housing conditions. In Canada, only four species of nonhuman primates (NHP) are currently used in research, teaching and testing: rhesus monkeys (*Macaca mulatta*), cynomolgus macaques (*Macaca fascicularis*), African green monkeys (*Cercopithecus aethiops*) and squirrel monkeys (*Saimiri sciureus*). Common and scientific names of a number of species are included as Addendum 1.

In focusing on NHP, emphasis must be placed on enhancing their social and behavioural well-being. As Markowitz and Line (1989) point out: "It is clearly possible to find methods by which environmental enrichment can be combined with a research protocol to enhance both."

Even though the animal may appear healthy, researchers "cannot be content with defending the status quo," says Line (1987). He challenges investigators to seek practical ways to expand opportunities for primates to display normal behaviour, "especially those housed singly". As Volume 2 (1984) of this *Guide* noted: "Any primate housed alone will probably suffer from social deprivation, the stress from which may distort processes, both physiological and behavioural." It is important, therefore, to provide the company of compatible conspecifics or other NHP species, and, if this is impossible, increased human company.

There is a growing body of scientific data on space/cage size appropriate for NHP. While enclosure size is an important variable, the primary emphasis should be on providing laboratory animals with the option for species-appropriate activities (Bayne, 1989; Bayne and McCully, 1989; Line, 1987; Bantin and Saunders, 1989; Fajzi, Reinhardt and Smith, 1989; Chamove, 1989; Markowitz and Spinelli, 1986; Segal, 1989a). Wilson (1982) found that in captive gorilla and orangutans, enclosure size had no effect on the level of activity. She suggested that objects within the environment were more important than the size or complexity of the enclosure. Primates maintained in the absence of external stimuli tend to display locomotion far more frequently than other categories of behaviour such as facial expressions, play, and inquisitive behaviour (Martinic, 1990). Chamove (1989) notes that many successful enrichment techniques act in a way similar to that of increasing physical space. Snowdon, Savage and McConnell (1984) note the adverse effects of too-small caging on reproduction, and the widely accepted fact that small cages increase the incidence of stereotyped movements and other non-locomotory abnormal behaviour.

Animals that are not housed properly and treated humanely "yield data that are clearly confounded with distress" (Markowitz and Spinelli, 1986), i.e., may yield unreliable data due to the effects of behavioural

stress (Levine, 1985) and introduce unwanted variables (Morton and Griffiths, 1985). It is important, therefore, that those using NHP should first acquaint themselves with the animal's distinctive characteristics and needs. Differences within and between species make the task difficult (Snowdon, 1990). Wolfle (1990) suggests that the researcher consult the psychological literature about animal cognition and perception. "The best tool of all for providing well-being begins with routine frequent observation of every animal," he concludes.

2. Interpretation of the Behavioural and Morphological Postures

Primate users sometimes misinterpret the meaning of the behavioural or morphological signals of NHP, as well as the effect of certain human behaviours on NHP. Inadequate animal husbandry practices are likely to increase the level of stress during cleaning, feeding and handling (Fox, 1986; Line, Morgan, Markowitz *et al.* 1989), and increase the risk of injuries to both humans and animals. Some of these misinterpreted signals are described below.

a) The Stare

The stare usually expresses an aggressive mood in NHP (e.g., rhesus). Threats are always initiated and accompanied by a stare, which usually precedes attack. This behaviour typically elicits one of the following responses by the recipient: a threat (in increasing order of intensity are staring back, staring with the mouth open, and grunting), an attack (lunging, hitting, biting), or a submissive reaction (avoiding to look, leaving, displaying a fear grimace). Primate users should keep in mind that when looking intensely at a monkey, they are threatening it and announcing an imminent attack.

b) The Fear Grimace

The fear grimace resembles an exaggerated smile; the mouth corners are fully retracted, showing all the teeth. This expression may be accompanied by a high-pitched, loud vocalization (Van Hoof, 1963, 1967). The fear grimace, or bared-teeth display is a ritualized signal of submissiveness emitted unidirectionally by subordinate to dominant individuals.

Thus, the fear grimace does not convey a playful mood or an aggressive motivation. The fear grimace is often inadvertently elicited by primate handlers when they move towards a monkey, while looking at it. The best way not to elicit a fear grimace is to avoid staring at the monkey, and to approach it indirectly.

c) Lip-Smacking or Teeth Chattering

In the many species in which it occurs (e.g., stump-tails), the teeth chattering face indicates a tendency to flee, the lip-smacking face a stronger sense of social attraction (Van Hoof, 1963). These are greeting gestures that express an affiliative mood, and probably include a submissive component, depending on the context.

d) Grooming

Removal of particles of dirt and ectoparasites in NHP is undertaken to establish, maintain or restore positive social bonds by expressing a state of non-aggression and by reducing tension. The cleaning function of social grooming is only secondary in importance. Grooming may pacify another animal, but is also used to maintain social bonds, as in mothers grooming infants or juveniles, and between members of a mated pair.

Grooming also serves to appease dominant individuals and prevent aggression, to provide contact-comfort (consolation) to the victims of attacks, to reconcile with an opponent after a fight, or to reassure subordinates. For example, grooming is directed by males to females in courtship, and is an important component of co-operative partnerships, such as coalitions and alliances.

e) Sexual Swelling

In many species, females in estrus manifest a reddening and/or swelling of the perineum. This signals their sexual receptivity to males. The extent of this swelling is highly variable among species. Sexual swellings are sometimes misinterpreted as injuries or symptoms of a pathologic condition. Blaffer-Hrdy and Whitten (1987) present comparative data on cycle length, duration of menstrual flow, visual signals, and the behaviour of males as well as females in estrus, for all species.

3. Distinctive Characteristics

a) Locomotion

In contrast with most other experimental animals, which are primarily terrestrial, NHP are characterized by a number of major morphological and behavioural adaptations to a three-dimensional arboreal life. These adaptations are stereoscopic vision, manipulative skills and specific modes of locomotion (climbing, leaping, etc.). Most primates show vertical flight reactions (Burt and Plant, 1990). For each species there is a defined behavioural repertoire, and for each species, preferred vertical limits in the wild should be considered.

b) Social Life

Most primate species, including the majority of those used in laboratories, are highly social (Boccia, 1989) and live in complex social groups; however, such social groups are not necessarily permanent. Species which are primarily solitary include some lemurs and orangutans (Jolly, 1985). The three major categories of societies are the family, the one male/multifemale group, and the multimale/multifemale group. Most laboratory primates belong to the third category.

Many studies have shown that NHP recognize individually every member of their group and that they establish long-term bonds, extending over years or a lifetime, with many of their kin and non-kin. Such relationships are bilateral and multidimensional, involving play, contact-comfort, grooming, sexual activity, protection, support during conflicts, etc.

Because of the social bonding that takes place in most species, social isolation is likely to affect individual animals. Studies have indicated that the effects of social isolation differ among rhesus, crab-eating macaques and stump-tailed macaques, with rhesus most severely affected (Sackett, Ruppenthal, Fahrenbruch *et al.* 1981).

The major contributions regarding social deprivation were made by Harlow in the 1960s. Animals raised in total social isolation were characterized as withdrawn, personally bizarre, and aberrant in social, sexual and exploratory behaviour (Harlow and Harlow, 1965). Goosen (1981) has discussed the isolation of rhesus, noting that individually housed monkeys have little opportunity to develop coping strategies, and may exhibit bizarre behaviour patterns (Novak and Suomi, 1988).

c) Cognitive Abilities

Intelligence is reflected in many of the NHP behaviours. For example, lion-tailed macaques, chimpanzees and capuchin monkeys are known to manufacture probing tools, and a number of species use "tools" to facilitate food acquisition such as cracking nuts (Beck, 1980). Research has also indicated that lion-tailed macaques manipulate objects, and use objects to serve as ladders, to create perches, and to apply leverage (Westergaard, 1988). *Macaca nemestrina* learn through the observation of others and pass on social traditions (Cole, 1963). They excel in the use and manipulation of third parties by forming coalitions and competing for the strongest allies, through the utilization of affiliative strategies. They are capable of some forms of deception (Smuts, Cheney, Seyfarth *et al.* 1987).

d) Emotions

Physical and emotional stress cause the release of various hormones, one of the main groups of which are the adrenal steroids, particularly cortisol (Moberg, 1985).

If it is accepted that humans and apes are related through evolution, it is considered that the African apes (the gorilla and two chimpanzee species) are humans' closest kin (Martin, 1988). NHP exhibit many external manifestations of emotions such as facial expressions, vocalizations, postures, gestures, and reactions, similar to those of humans.

Many of the ways in which NHP exhibit emotional responses, for example, separation and external threat, appear similar to ways in which humans react to comparable situations. Moreover, many of the abnormal behaviours displayed by captive NHP are similar to the behaviour patterns of institutionalized humans (Passingham, 1982).

4. Assessing Social and Behavioural Well-being

Psychological well-being can be defined as "a state of harmony, both physical and psychological of an animal with itself and with its environment" (Coelho and Carey, 1990). Dresser (1988) points out that an animal's well-being "...connotes not only the absence of pain and distress. It implies as well that an individual's physiological, security and behavioural needs are fulfilled."

Although we cannot measure psychological well-being in NHP, the following criteria serve as indications that such a state exists: a) good physical health; b) no signs of pain, distress or discomfort; and c) no abnormal behaviours.

Moberg (1985) proposes that an animal's well-being is compromised only when it is stressed by events in its environment, and suggests that researchers should look for changes in the animal's immune competence, reproductive function or growth and development: "The existence of pre-pathological states in these systems would indicate the animal's well-being was threatened."

a) State of Physical Health

Poor health and physical injuries are not compatible with psychological or physical well-being. Physical health should be routinely assessed by a qualified veterinarian.

Some of the most obvious external signs that can be monitored are the condition of the coat and skin, the appearance of the eyes, and, if the size of cage permits, the gait pattern.

Examples of abnormalities include unresponsiveness and hypersubmissiveness, hair pulling-and-eating (Reinhardt, Reinhardt and Houser, 1986), and may include the crouching posture.

b) Absence of Signs of Pain, Distress and Discomfort

Although NHP express fear through high-pitched screams, when experiencing pain they are unlikely to emit loud vocalizations. Instead, they display a hunched or crouched posture, an abnormal or slow gait. They stop self-grooming and avoid conspecifics. They may moan, refuse to eat and drink, and often attract the attention of conspecifics (Hinde and Rowell, 1962) (see Control of Animal Pain).

c) Absence of Abnormal Behaviours

Laboratory primates may exhibit abnormal behavioural disorders in both a barren cage or in a compatible group (Reinhardt, Reinhardt and Houser, 1986). However, Reinhardt (1990b) reports that most behave in normal ways even in an impoverished environment.

Every species of NHP is characterized by a specific behavioural repertoire. Ethograms or descriptive lists of species-typical behaviours, have been published for many species (Van Hoof, 1967; Bertrand, 1969; Fedigan, 1976; Skinner and Lockard, 1979; O'Keefe and Lefshitz, 1985; Walsh, Bramblett and Alford, 1982; Erwin and Deni, 1979). A vast body of information on the social behaviour of NHP living in the wild or in large outdoor enclosures is also available. For geographical distribution, ecology, diet, reproduction and social behaviour of a representative sample of taxonomic subgroup of NHP see Smuts, Cheney, Seyfarth *et al.* (1987).

Despite the existence of a fair degree of interspecific and intergroup variation, it is possible to identify general categories of abnormal behaviours observed in captive species of NHP. Examples are summarized below. More details and a description of idiosyncratic variants may be found in the literature (Goosen, 1981; Walsh, Bramblett and Alford, 1982; Erwin and Deni, 1979).

d) Examples of Abnormal Behaviour Patterns

i) Bizarre postures and behaviours

Self-biting, self-clasping, self-grasping, hair pulling-and-eating, feces spreading, face or eye poking, penis sucking, and "floating limb" accompanied by attack of the limb.

ii) Stereotypical behaviours

Pacing, "saluting," head tossing or weaving, walking or bouncing in place, somersaulting, rocking, and cage charging.

iii) Appetitive disorders

Coprophagia (ingestion of animal's own feces), urine drinking, hyperphagia (excessive over-eating), and polydipsia (excessive, long-term thirst).

iv) Abnormal levels of activity

Inactivity, depression.

v) Abnormal social behaviours

Maternal neglect of infants, maternal over-protectiveness of infants, high levels of fearfulness and over-dependence of infants, inappropriate sexual behaviour, hyperaggressiveness, hypersubmissiveness, and avoidance of social interactions.

5. Ways of Promoting Social and Behavioural Well-being

There are a number of ways to alter or improve an animal's environment. Beaver (1989), for example, suggests five basic means: behavioural enrichment (by creating an environment similar to the wild habitat), social peers, artificial appliances, food gathering activities, and control of non-food items. Some of these will be described below.

a) Social Peers

The best psychological enrichment is social enrichment (Crockett, 1990). Providing opportunities for social interactions is by far the best way to help NHP cope with the two main categories of problems associated with captivity: boredom (understimulation) and fear. Social interactions appear to provide the richest source of stimulation and the best source of emotional security. Segal (1989b), in editing a new publication on NHP noted that several authors independently reached the conclusion that "the single most important thing one can do to enrich the life of a captive primate is to provide it with a companion animal." Moreover, it is believed that more social interaction may take place in an environmentally enriched milieu (Martinic, 1990).

b) Housing

i) Single housing

The reasons commonly cited for housing primates singly are reviewed, and contested, by Reinhardt (1990a); these include wounding, disease transmission, dominance hierarchies, social distress, and undernourishment of a lower-ranking partner. Reinhardt concludes that chimpanzees, orangutans, rhesus monkeys and stump-tailed macaques have been resocialized without undue risks or disadvantages: "There is no reason to suspect that other primate species are less suitable for careful resocialization programs." He warns, however, that such programs must be tested for each species before social housing is implemented. Fritz (1989) reported that resocializing singly caged chimpanzees caused neither wounding nor death.

Single housing is strenuously discouraged, except in those situations when it is necessary for the experimental protocol, in the case of aggression, or to prevent or contain disease. When single housing is required for an experimental protocol, the institutional ACC must be very diligent in assuring this aspect is necessary to achieve the experimental objectives. **ACCs should require the investigator to submit scientific justification for environmental impoverishment, e.g., as a result of regulations or the demands of the study protocol**.

Singly housed animals have exhibited depressed heart rates and elevated blood pressure similar to the elevated blood pressure noted in humans diagnosed as being depressed (Coelho and Carey, 1990).

If single caging must be used, every effort should be made to enrich it (Reinhardt, Houser, Eisele *et al.* 1987; Bayne, Mainzer, Dexter *et al.* 1991), although strategies for so doing are apparently still very limited (Chamove, 1989). If possible, NHP should be given the opportunity to take part in species-typical activities. In the case of singly housed NHP, the role of the animal care technician takes on added importance (Chamove, 1989; Wolfle, 1990). Familiarity with the handler, surrounding and procedure can significantly reduce anxiety. Positive reinforcement, using rewards such as food, encourage animals to accept manipulations without apprehension.

In order to preclude the need for single housing to facilitate sampling of body fluids and chronic monitoring of physiological parameters, a system of social tethering has been developed (Coelho and Carey, 1990).

ii) Pair housing

Novak and Suomi (1988) claim that pair-housed primates enjoy a state of physical health that is usually superior to that of many free-ranging monkeys. Pairing of 700 captive cynomolgus breeding females (and subsequent offspring) was successfully pioneered in 1983 in the Ottawa colony of the Health Protection Branch of Health and Welfare Canada (McWilliam, 1989). Although pair housing is not advocated as universally beneficial (Crockett, 1990; Rupenthal and Walker, 1989), the benefits appear to outweigh the risks (Crockett, 1990).

Most all age-sex combinations of pair housing are possible. Reinhardt (1987, 1988, 1991) and Reinhardt, Houser, Eisele *et al.* (1988) have successfully paired rhesus unrelated adult females, unrelated adult males, and adults of both sexes with infants.

Pairing provides social stimulation and makes it possible to avoid some of the problems associated with larger groups (Erwin, 1979; Crockett, 1990). It elicits most species-typical social interactions for the sexes and ages concerned, except for the multi-animal interactions.

In an interesting innovation, Reinhardt (1990c) in a recently controlled study provided isosexually paired (male-male, female-female) adult rhesus monkeys with privacy panels. It was found that they spent more time in close proximity and more time grooming each other and huddling, while the incidence of agonistic conflicts was significantly reduced.

Monkeys that are paired should be compatible. Compatibility can be defined as an affiliative relationship in which such interactions as grooming occur and in which both members appear relaxed. This only occurs after a dominance relationship has been established. Reinhardt (1987) suggests compatibility is shown when neither animal exhibits signs of depression, and neither has inflicted serious injury on the other. Before being paired, prospective cagemates should be allowed to become familiar with each other in adjacent cages permitting visual and auditory communication. Dominance signals, such as staring, open-mouth threat, displacement, or fear grimaces, may be displayed in this situation or soon after the monkeys have been put together.

The pair may be formed in a third cage in order to avoid aggression (Erwin, 1979) which to some species such as gibbons may be related to territoriality. They should be monitored regularly for signs of incompatibility, such as injuries, avoidance of contact, or inappetence. Once pairs have been established, they should not be disrupted unless dictated by an experimental protocol.

iii) Group housing

Larger groups usually offer a much richer social environment and should be favoured over pairs when groups will remain relatively stable. However, it should be noted that chimpanzees associate in temporary parties, unlike stable groups of most large primates (Nishida and Hiraiwa-Hasegawa, 1987). For troop-living primates such as rhesus, the best way to promote their well-being in the laboratory may be to rear them with partners or in social groups (Novak and Drewsen, 1989). When groups are being formed, observers must adjust group composition so the units show minimal aggression (Wolff and Ruppert, 1991).

There are drawbacks to group housing which should be considered, however. Increased social interaction may result in disease transmission as well as the risk of injury and death (Beaver, 1989; Line, Clarke and Markowitz, 1989; Novak and Suomi, 1988; Wolverton, Ator, Beardsley *et al.* 1989; Line, 1987). Snowdon (1990) notes that the various species have different responses to group housing. Group formation may be stressful; Sapolsky (1989) contends that it takes up to 12 to 15 months for animals' stress markers to return to normal levels; however, Reinhardt, Cowley, Scheffler *et al.* (1990) disputes this as regards to rhesus. Erwin (1979) notes that "fighting is a fairly common occurrence in primate groups even in natural settings, but trauma due to aggression is an especially pressing problem in captive groups of macaques and baboons."

NHP are prompt to form coalitions through which they establish their dominance ranks and compete for food and sexual partners. Removing a monkey from its group may disrupt the existing network of alliances and induce rank changes, which may be associated with vicious fighting, resulting in injuries (Kaplan, Manning and Zucker, 1980; Reinhardt, Reinhardt, Eisele *et al.* 1987). Animals that are to be reintroduced should be kept away from the group for as short a time period as possible.

c) Social Interaction with Humans

It is suggested that there be as much interaction as possible between the NHP and the investigator or technician (Hearn and Dixson, 1984; Bayne, 1989). The interaction, however, must not involve handling other than what is necessary for the maintenance of the animal or for investigational procedures. The necessary precautions are described in Volume 2 of this *Guide* (CCAC, 1984).

Direct physical contact between humans and NHP should be evaluated from facility to facility. In many instances it should be kept to an absolute minimum for example, because of the need to break the human/animal bond when staff changes occur or when an animal must be euthanized, as well as the hazards posed by zoonotic diseases. Some of the most significant diseases are Herpesvirus simiae infection (B-Virus) and infectious hemorrhagic fever viruses. Also, many NHP have extreme physical strength in relationship to body size, and can inflict serious injury on personnel. Furthermore, humans can transmit infectious diseases to primates, e.g., measles, tuberculosis.

Forced physical contact between humans and NHP can be extremely stressful to the monkey. Moor-Jankowski and Mahoney (1989) have reported that even the introduction of a new technician can change the NHP's liver enzymes to the point that it can compromise a study. Many animals react to the presence of a human observer with anti-predator behaviour such as mobbing and alarm calling (Caine, 1989), and threat behaviour toward observers (Wolff and Ruppert, 1991). Talking to the monkeys, combined with the physical presence of the human, will accustom the NHP to the human presence, and may thus reduce stress. Burt and Plant (1990) suggest that use of mesh cage fronts are preferable to the barred variety aiding interaction between animals and staff.

d) Diet Supplementation and Food Gathering Activities

The core diet of the NHP should be a complete, well-balanced commercial diet, or alternatively a diet of equal quality prepared in the diet kitchen of the institution. This diet should be supplemented to suit the nutritional requirements of the primate species being used (Jones, 1972).

Supplementation and innovative ways of presenting the food to the monkey are effective ways of enhancing well-being, particularly of those in individual caging. Examples of items used for supplementation are raisins, fruit, chicken scratch feed, and Prima-Treats (Addendum 2). Fresh branch clippings may be used for supplementation, providing toxic plants are avoided and the dust and pesticides are washed off the branches.

e) Exercise

The diet supplement can also be provided as food puzzles (e.g., Kong Toys) containing frozen juice, peanut butter or raisins (Addendum 2). Seeds, etc., can be hidden in deep litter. These methods of supplementation require the monkey to search and/or work for the food (Anderson and Chamove, 1984). This challenge will simulate the foraging activity which the NHP pursue in their natural habitat, and has been found to reduce stereotypies and increase exploratory behaviour (Anderson and Chamove, 1984; Boccia, 1989).

The majority of NHP in their natural environment move widely and regularly within their established home ranges. Except for owl monkeys and many prosimians, primates are diurnal, spending large portions of the day foraging for food or participating in grooming and other social activities. For this reason, NHP housed in standard cages over long periods of time, whether they are held singly or in pairs, appear to benefit from species-appropriate activities reminiscent of those in the wild (Hearn and Dixson, 1984; Chamove, 1989; Burt and Plant, 1990).

It has not been demonstrated that simply enlarging the amount of available space will improve the well-being of the animal (Novak and Suomi, 1988; Fajzi, Reinhardt and Smith, 1989; Novak and Meyer, 1988). Indeed, an increase in aggression has been associated with an increase in space for some captive primates (Novak and Meyer, 1988).

Exercise cages for NHP were introduced over a decade ago (Tolan, Malone and Rogers, 1980). However, it is considered that environmental complexity, rather than size alone should be increased (Line, 1987; Line, Clark and Markowitz, 1989; Bryant, Rupniak and Iversen, 1988). Wolff and Ruppert (1991), reporting on an exercise program involving rhesus, cynomolgus and capuchins, note that the majority of animals interacted in a positive fashion. Constant observation prevented fights and thus minimized injury. Much of the aggressive behaviour was non-physical (e.g., vocalizing or teeth baring rather than biting).

The NHP entering an exercise area for the first few occasions will usually exhibit a fear response (Wolff and Ruppert, 1991). However, exercise can be stimulated by synchronizing it with feeding. Deep litter in which food can be hidden can also be used in the exercise cage and will stimulate the monkeys to forage. To instill a feeling of security, freedom of movement between the exercise cage and the home cage is preferable.

If more than one monkey is exercised at the same time, the animals should be cage mates. However, it is sometimes possible that singly housed or paired monkeys can be exercised in larger groups if they have been confined in the same room, and are exercised together on a regular basis. These animals must, however, first be tested for compatibility.

f) Physical Enrichment of the Cage Environment

It is important that the animal be given as much control (or even the perception of control), as possible over its environment (Line, 1987). Guidelines for minimum cage size have been established by the CCAC (see Appendix I). Life in cages can be enriched and activity promoted by the installation of devices such as small branches (O'Neill, 1989), toys (Line, Clarke and Markowitz, 1989), perches (Crockett, 1990), swings (Bayne, Suomi and Brown, 1989) and food puzzles (Beaver, 1989; Chamove and Anderson, 1989). Such enrichment is particularly important to the singly caged animal (Fajzi, Reinhardt and Smith, 1989), where devices which encourage foraging appear most successful (Crockett, 1990; Bayne, Mainzer, Dexter *et al.* 1991). Jerome and Szostak (1987) contend that foraging devices are used more frequently than play objects by baboons. Climbing is an especially good exercise. Bryant, Rupniak and Iversen (1988) contend that enrichment of the home cage could benefit the animals more than exposure to a playpen routine. Enrichment devices and their suppliers are listed in Addendum 2.

Wolfle (1990) notes that choice tests permit the animal to indicate that one environment or toy is preferred over another. Other tests measure the frequency of use of new space or new "toys." It has been suggested that toys be rotated in order to minimize understimulation (McWilliam, 1989).

Because of the importance of vision to the NHP, particularly *M. nemestrina*, (Cole, 1963), cages should be positioned so that the monkeys can see animals of like species. Solid-sided caging prevents visual contact. If physical contact is possible, there must be assurance that the animals are compatible.

There is a diversity of opinion with respect to the use of audiovisual devices (radio, video, television) as a means of enhancing the well-being of NHP. They appear to be of most benefit if the monkey can turn the equipment on and off at will (Beaver, 1989; Line, Clarke, Ellman *et al.* 1987). In some situations, audio may serve as a contentment device for the primate; however, it is possible for some sounds to be irritating and stressful.

Visual means of enrichment may be stressful to the animal if the monkey perceives the picture to be threatening. This may be circumvented by the preparation of tapes or videos especially prepared for primate entertainment. It has been reported anecdotally that monkeys are particulary fascinated by visuals depicting their natural environment, or animals that are found in their natural habitat. NHP are fascinated by videos of themselves (Chapais, Pers. Comm., 1990).

6. Disposition

Following completion of the study, consideration should be given to further use of NHP utilized in non-invasive research, in an effort to minimize the numbers of animals used. However, monkeys used in invasive or stressful projects should not be subjected to further stressful procedures or conditions and should be humanely killed according to CCAC euthanasia guidelines found elsewhere in this *Guide*. Maximum utilization of NHP tissues, histological specimens, etc., is encouraged.

Following completion of research, retention of an animal in the laboratory, on the assumption that it may be required for future studies, is rarely justifiable.

7. Summary

In considering all the factors related to well-being of NHP, we should remember that "because well-being is subject to past experiences, present circumstances, and future expectations, it is a dynamic and changing phenomenon" (Wolfle, 1990).

G. RODENTS AND RABBITS

This section is currently under revision and will be replaced by the *CCAC guidelines on: mice* (in prep.) and the *CCAC guidelines on: rats* (in prep.), as well as future guidelines on other rodents and rabbits.

February 2017

1. Introduction

Over the course of the past 25 years, standards have been established which are considered to represent optimum housing requirements for laboratory animals. Many of the improvements in housing and management standards were primarily designed to reduce variables and enhance the reproducibility of experimental results (Lang and Vessell, 1976). However, during the past decade, increased emphasis has been placed on the behavioural and social needs of animals kept in the laboratory setting. Most investigations into enhancement of the animal's environment have concentrated on the "higher mammals," particularly NHP. This document's conclusions have been based on contemporary concerns.

Laboratory rodents and rabbits are frequently perceived to have relatively few requirements other than basic housing, husbandry, and dietary needs. Thus, control of the environment has frequently been the primary consideration, with little (or no) emphasis on other areas.

"Well-being" is frequently difficult to assess objectively in these species. Weight gains, general behaviour, and adrenal weights are examples of criteria which have been used in studies of this type (Chamove, 1989).

Housing conditions should be evaluated carefully for each species, and consideration given, wherever possible, to innovative group housing in species such as guinea pigs and rabbits.

Qualified investigators should be encouraged to do additional objective, controlled studies on the environmental needs and preferences of rodents and rabbits in the laboratory setting.

Awareness of normal behavioural patterns in each species is essential. For example, coprophagy (reingestion of feces) is a normal function in several species, including rabbits and rats (Smelser, 1985; Newton, 1978). Rats normally ingest 35-65% of their feces on a daily basis. Deprived of this opportunity, 15-25% reductions in weight gains have been observed (Newton, 1978).

Beaver (1989) suggests that five aspects in particular may contribute to environmental enrichment: behavioural enrichment, social peers, artificial appliances, food gathering activities, and control of the environment. Some of these are discussed below.

2. Behavioural Enrichment and Social Peers

Social interaction with peers is recognized to be a desirable, if not an essential aspect of laboratory animal well-being.

a) Mice

Mice thrive when housed in groups of two or more per cage. In one study, evidence of "stress" was minimal in mice housed at four per cage, compared with groups of two or eight per cage (Peng, Lang and Drozdowicz, 1989). A high incidence of stress-related tail lesions has been observed in cages housing up to 40 mice which were placed together after weaning. The problem was resolved when the groups were reduced to five per cage (Les, 1972).

As another example, female C3H/He mice in an intensive breeding program, and housed under conditions of severe social stress, had an incidence of spontaneous mammary tumours considerably different from counterparts kept under ideal conditions. At 400 days of age, approximately 90% of animals maintained under adverse conditions had mammary tumours, while the incidence of tumours was around 10% in females housed and mated under optimum conditions (Riley, 1975).

Compatibility is a critical consideration. It may be impossible to house male mice together after puberty, particularly those of more aggressive strains.

b) Rats

Rats are frequently housed singly for certain types of studies; however, it is desirable that two or more compatible rats be housed together in an appropriate cage. Post-puberal males are usually compatible, particularly if they have been together since an early age. It has been shown that even groups of highly standardized male rats exhibit a high level of variability of behavioural patterns (Gärtner, Ziesniss, Karstens *et al.* 1991).

c) Guinea Pigs

Guinea pigs live in groups of five to ten individuals in the wild (Sutherland and Festing, 1987) and thrive under group housing, although it is unlikely that two or more sexually mature males will live together without incident unless they have been together since birth. In their natural environment, guinea pigs exhibit a strong herd or family orientation, and this should be maintained in the laboratory setting, if at all possible. The one boar per harem arrangement is the recommended procedure in breeding colonies. Guinea pigs should not be housed singly; however, if this is necessary, Sutherland and Festing (1987) recommend a minimum of 700 cm^2. Vocalization appears to play an important part in guinea pig social behaviour, and they call for attention from human caretakers (Sutherland and Festing, 1987).

d) Hamsters

Adult hamsters are frequently caged separately because of their tendency to fight, with the exception of the female during the time she is ready to mate. However, they have been housed together under certain circumstances, particularly if they have been weaned and raised together since birth (Hobbs, 1987); nonetheless, the European hamster becomes more aggressive as it grows older. Hamsters spend more time in social proximity if they have had prior group housing experience. Singly housed hamsters show more agonistic

behaviour with conspecifics, and lower weight gains than group-housed animals. Early housing experience can profoundly affect later social preferences and behaviour.

e) Gerbils

Most gerbil species are gregarious and live in large groups (Norris, 1987). Therefore, they should be housed in pairs or in larger groups wherever possible. If animals are placed together before they reach puberty, fighting should not be a problem. Gerbils usually mate for life; thus, it is advisable that single pairs be kept together throughout life. Most are normally docile, although aggression may be noted after pairing for mating.

Mature mongolian gerbils of either sex may show a characteristically severe form of epileptiform seizure (Norris, 1987).

f) Rabbits

In their natural habitat in the wild, rabbits of the genus *Oryctolagus* are social animals, frequently living in warrens of up to 100 or more rabbits of various ages. In the laboratory, convention has dictated that sexually mature animals be housed singly: a) to avoid fighting injuries; and b) to prevent ovulation and subsequent pseudopregnancy due to physical interaction in mature does. Male rabbits, if penned together, become increasingly aggressive from about 90 days (Adams, 1987). However, group housing for adult rabbits has been under study, both in the laboratory setting, and in commercial rabbitries (Stauffacher, 1992; Love, 1988; Anon., 1989a).

Group housing in larger enclosures has provided animals with the opportunity to live a more natural lifestyle, including ample opportunity for adequate exercise, mutual grooming, and general improved well-being (Love, 1988; Boyd, 1988). Breeding colonies have been established, using the group housing approach (Anon., 1989b). In some facilities, compatible rabbits are allowed to exercise in a designated floor area several times per week.

3. Enrichment Devices (Artificial Appliances)

a) Mice

Mice have used empty plastic water bottles placed in the cage for a "urinal," and an additional bottle for nesting and as a "bolt hole". It was concluded that provision of the bottle was beneficial in several respects, including improved sanitation, and an opportunity to establish their own optimal environment in the nesting bottles (Boyd, 1988). However, in one study, the addition of objects such as flower pots and bricks has been reported to increase aggression among male mice (Ayling, 1989), presumably because of territorial instincts.

b) Rabbits

The use of resting boards has been shown to have a calming effect on rabbits, which use them to hide beneath (Anon., 1989a), and the use of tubing as "bolt holes" has been suggested.

c) Hamsters

Hobbs (1987) states that wheel-running has not been shown to be beneficial; however, a raised top to the cage provides opportunity for climbing and exercise.

d) Gerbils

It has been recommended that gerbils be supplied with appliances such as PVC plastic pipe since they are burrowers in their natural habitat, and retain this behavioural pattern, as well as food hoarding, in the laboratory (Norris, 1987). It is likely that other small rodents would also benefit from these additions.

4. Caging and Bedding

i) **Floor space** per animal is an important consideration, and requirements for individual species have been identified in Appendix I [the U.S. and the U.K. have developed standards as well (USDHHS, 1985; UFAW, 1987)]. Although ample floor space per animal is essential, there is some evidence that the actual needs for group-housed guinea pigs, for example, may be less than current guidelines indicate (White, Balk and Lang, 1989).

ii) **Solid bottom cages** are strongly recommended for housing rodents, particularly for long-term studies. Solid floors with appropriate bedding are particularly critical for breeding rodents (Weihe, 1987). Wire bottom cages, although less labour intensive to use, are far removed from the natural environment.

iii) **Bedding** is also an important consideration. For example, gerbils are active burrowers, and prefer bedding that can be used for digging and tunnel making, an important activity in this species. There have been studies of bedding preferences in small rodents (Iturrian and Fink, 1968). Straw bedding has been recommended for rabbits (Adams, 1987) who also notes that breeding females kept in metal cages must be provided with nest-boxes some days before parturition. In metal caging, Adams (1987) found that 16 mm mesh, 2 mm gauge wire was satisfactory in preventing sore hocks.

a) Rats

It is now recognized that rats like to run, stand on their hind legs, and jump (Weihe, 1987); unfortunately, presently available caging does not permit this. Weihe (1987) recommends addition to the caging of paper, wood, pellets or grain as a means of environmental enrichment. He also suggests caging of solid plastic with a wire mesh lid, and criticizes use of wire mesh-floored cages. Rectangular cages are more satisfactory than square caging, with 20 cm high cages suggested (Weihe, 1987).

b) Mice

In one study conducted in mice, vertical dividers were placed in cages, and the animals' performance and well-being compared with that of animals housed in conventional cages. Mice preferred the complex cages, and appeared to be "less emotional" than were the mice kept in regular cages. It was concluded that the divided cage represented a more natural housing arrangement, and that its use would lead to healthier animals (Chamove, 1989).

c) Gerbils

Any cage suitable for rats and golden hamsters is satisfactory for gerbils. As gerbils often stand erect on their hind legs, the cages should have a solid bottom, with floor to lid height at least 15 cm. A monogamous breeding pair requires a floor area of about 700-900 cm^2 and gerbils caged in large groups need about 100 cm^2 floor area per animal (Norris, 1987).

d) Rabbits

Adams (1987) suggests that, for laboratory purposes, rooms designed to accommodate units of 50-60 rabbits are best. If metal caging is used, 16 mm mesh, 2 mm gauge wire is satisfactory in order to preclude sore hocks.

These are often built with portable sides with or without a roof or raised grid floor. They may be used to house a variety of species such as cats, dogs and NHP. Rabbits and guinea pigs have also been successfully housed in floor pens. In Swiss studies, near-to-nature surroundings for rabbits have been replaced by manageable artificial substitutes (Stauffacher, 1992).

e) Guinea Pigs

In guinea pigs, easily sanitized boxes with an end opening, placed in the floor pens, have proven to be an unqualified success. These boxes serve as a place to hide and as a secure place for farrowing, and provide some variety in the environment (White, Balk and Lang, 1989).

5. Food Gathering

Good quality legumes or appropriate vegetables (e.g., carrots, cabbage, etc.) are useful supplements to commercially available diets for guinea pigs, rabbits and gerbils. Seed mixtures are recommended additions for species such as gerbils and hamsters although Norris (1987) warns that gerbils will eat sunflower seeds and exclude other seeds. He also suggests feeding seed mix to young animals on the cage floor. Nutritious food items of this type will provide a pleasant diversion, as well supply additional nutrients to these species. However, quality control of such materials is essential since there is the potential for biological or chemical contamination. This practice could be contra-indicated in animals in nutritional or toxicology studies.

Rabbits are said to prefer pelleted commercial feed rather than meal, and to have a higher requirement for fibre than other species (Adams, 1987).

6. Control of the Environment

Ambient temperature, humidity, air changes, frequency of cage cleaning, light-dark cycles, noise and daily routines, are examples of environmental conditions that affect the welfare of animals in a research facility (Clough, 1982; Gamble, 1982; Riley, 1975; Peterson, 1980; McSheehy, 1983; Everitt, McLaughlin and Helper, 1987; Besch, 1980; Gärtner, Büttner, Döhler *et al.* 1980; Anon., 1989b).

Significant variations in certain blood constituents were observed in rats subjected to various handling and experimental procedures. On the other hand, the presence of a familiar animal attendant in the room in the absence of manipulations had minimal influence on the blood characteristics under study (Gärtner, Büttner, Döhler *et al.* 1980). Sudden changes in humidity may adversely affect rabbits (Anon., 1989b).

In laboratory rodents and rabbits, stimuli and conditions have been identified which may have adverse effects on psychological well-being and general health. Animal rooms may not be used for performing any experimental procedures requiring manipulation, particularly those likely to evoke fear and/or vocalization.

a) Noise

Levels of 50-70 DBA or higher are considered likely to be detrimental to the hearing of rodents and rabbits. Adverse effects have included audiogenic seizures in young mice (Bevan, 1955; Gamble, 1982), and reduced fertility in mice and rats (Newton, 1978).

b) Lighting

Light intensity can influence rodent activity, maternal behaviour, and various other aspects of reproductive physiology (Clough, 1982). Reproductive disorders have been identified in mice and rats housed under inappropriate light/dark cycles, or in the absence of such a cycle (Newton, 1978). In albino rats, continuous exposure to light levels of greater than 700 Lux can cause severe retinal degeneration over a period of time (Everitt, McLaughlin and Helper, 1978; Clough, 1982; Semple-Rowland and Dawson, 1987), and there are other reports of light-associated retinal damage in albino rats (McSheehy, 1983). Data on acceptable light levels for laboratory rodents are available (ILAR, 1977).

H. WILDLIFE HELD IN THE LABORATORY

Wildlife species which are threatened, endangered or Convention on International Trade in Endangered Species of flora and fauna (CITES)-listed must be conserved, and every effort should be made to replace these animals after study, either through reintroduction to the environment of origin, or placement in captive breeding-release projects.

Researchers planning to use large numbers of animals should, where feasible, breed replacement stock rather than continuing to remove animals from the wild.

The *CCAC guidelines on: the care and use of wildlife* (2003) is comprehensive and wide-ranging, and should constitute the primary source of information and guidance, for short-term holding of wildlife in the field. When animals are to be held for a longer period in field facilities (i.e. more than a few days), and in particular in the laboratory, additional husbandry practices are required to address the animals' needs, such as enrichment opportunities for physical and psychological stimulation.

February 2017

Wild animals should only be brought into an institution after the investigator proposing to use them has demonstrated adequate knowledge of the animals' social and behavioural requirements or those of a closely related species. Those who will be responsible for such animals must also be able to provide for appropriate management and housing before the animals are introduced into the laboratory.

A number of recent, excellent publications are listed under Additional Reading.

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ADDENDUM 1
COMMON AND SCIENTIFIC NAMES OF NONHUMAN PRIMATES

COMMON NAME	SCIENTIFIC NAME
African Green monkey	*Cercopithecus aethiops*
Assamese macaque	*Macaca assamensis*
Baboon	*Papio spp.*
Bush baby	*Galago spp.*
Capuchin monkey	*Cebus apella*
Chimpanzee	*Pan troglodytes*
Common marmoset	*Callithrix jacchus*
Cynomolgus macaque	*Macaca fascicularis (M. irus)*
Gibbon	*Hylobates spp.*
Japanese macaque	*Macaca fuscata*
Lion-tail macaque	*Macaca silenus*
Owl monkey	*Aotus trivirgatus*
Rhesus monkey	*Macaca mulatta*
Squirrel monkey	*Saimiri sciureus*
Spider monkey	*Ateles spp.*
Stump-tailed macaque	*Macaca arctoides (M. speciosa)*
Tamarin	*Saguinus spp.*
Pig-tail macaque	*Macaca nemestrina*

VII SPECIAL PRACTICES

A. ANIMAL ACQUISITION

1. Procurement

This section has been revised. Please see the *CCAC guidelines on: procurement of animals used in science* (2007).

February 2017

2. Transportation

This section has been revised. Please see the *CCAC guidelines on: procurement of animals used in science* (2007).

February 2017

3. Breeding

This section has been revised. Please see the *CCAC guidelines on: procurement of animals used in science* (2007).

February 2017

4. Breeding Transgenic Animals

This section has been revised. Please see the *CCAC guidelines on: transgenic animals* (1997).

February 2017

5. Animal Models with Special Needs

Animal models of human disease are used to study the causes and therapeutic and preventive methods for human disease, as well as to develop new drugs (Nomura, Katsuki, Yokoyama *et al.* 1987). Models are available for many diseases and conditions, e.g., hemophilia (Moake, 1988) atherosclerosis (Reddick, Read, Brinkhous *et al.* 1990; Farrell, Saunders, Freeman *et al.* 1986), Pasteurellosis (Morck, Costerton, Bolingbroke *et al.* 1990), intestinal disease (Pfeiffer, 1985), hepatic degeneration (Hultgren, Stevens and Hardy, 1986), enteric diseases such as *Campylobacter jejuni* (Fox, Ackerman, Taylor *et al.* 1987), cardiomyopathy (Wagner, Reynolds, Weisman *et al.* 1986) and neurological disease (Barnes, 1986). Animal models for advancing understanding of diseases such as hypertension, gastrointestinal tract and cardiovascular disease were discussed at a symposium of the British Laboratory Animals Veterinary Association (BLAVA) (Anon., 1986). Another meeting addressed the challenges facing researchers into the human immunodeficiency virus (HIV) and the need for animal models in this regard (Groopman, 1991).

Animal models of some conditions or diseases have special needs beyond those of normal, healthy laboratory animals. These special needs must be recognized and accommodated when such animal models are going to be used in research. It should be the responsibility of the principal investigator to take into consideration the special needs of the animals before embarking on the research project. These special needs will no doubt impact on the research budget in terms of additional animal care time, materials, and equipment. ACC reviews of research proposals should include an assessment of these extra considerations for the animals.

The principle that encompasses this responsibility to attend to the special needs of animal models could be stated as follows: that any pain, suffering, distress, or deficits in function that negatively affect the animal's well-being, not scientifically "necessary" for the study, should be alleviated or minimized. Cost or convenience should not deter from this. Further, as soon as the study is done, the animal suffering should be terminated (Olfert, 1992).

6. Identification of the Sexes

This section has been revised. Please see the relevant animal type guidelines.

February 2017

B. RESTRAINT AND MANIPULATIONS

1. Physical Restraint

This section has been revised. General guidance is provided in the *CCAC guidelines: Husbandry of animals in science* (2017), with further details provided in the relevant animal type guidelines.

March 2017

2. Implantation, Cannulation and Sampling

For further details, please see the relevant animal type guidelines.

February 2017

Chronic studies involving the implantation of electrodes, cannulae and catheters will require that the animal be anesthetized at the time of implantation, and restrained awake when sampling is undertaken.

Electrode implantations must be undertaken by, or under the direct supervision of personnel experienced in the techniques involved, and must utilize proper surgical and anesthetic procedures (Meyer and Meyer, 1971; NIH, 1991) (see also Standards for Experimental Surgery and Anesthesia). Detailed descriptions of stereotaxic surgical techniques may be found in several sources (Hart, 1969; Pellegrino and Cushman, 1971; Skinner, 1971; Singh and Avery, 1975).

3. Bleeding

For further details, please see the relevant animal type guidelines.

February 2017

Guidelines for blood removal from laboratory mammals and birds have recently been published in Great Britain (BVA/FRAME/RSPCA/UFAW Joint Working Group on Refinement, 1993). Efforts should constantly be made to refine scientific techniques so as to reduce the volume of the blood sample. In small animals such as mice, volume and frequency are of particular importance. If the animal's welfare is threatened by the volume of the sample required, either more animals should be used, or compensatory blood transfusion considered.

Rather than multiple sampling carried out by repeated needle punctures, a butterfly needle or a percutaneous (over the needle) cannula taped in position, should be utilized.

In removing volumes greater than 0.1 ml, as large a bore as possible should be used in order to ensure rapid blood withdrawal without collapsing the vein, with the constraint of avoiding hematomata formation. Before taking a sample, it is important to accurately locate the vein and dilate it by gentle obstruction or warming. If general body warming is used, the animal must be constantly observed to prevent hyperthermia, as evidenced by more rapid breathing, panting or salivating. The use of xylene (xylol, dimethylbenzene) as a dilator is not recommended as it causes skin rashes and is easily misused.

Common bleeding sites may be found in Appendix VIII of this *Guide*.

4. Motivation Procedures

This section has been revised. Please see the relevant animal type guidelines.

February 2017

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VIII OCCUPATIONAL HEALTH AND SAFETY

For further details, please see the relevant animal type guidelines. In addition, current regulatory requirements for the containment of human and terrestrial animal pathogens and toxins is available in the *Canadian Biosafety Standard* (2015).

February 2017

Those working with experimental animals risk exposure to physical hazards (e.g., heat, noise, radiation), chemical hazards (e.g., disinfectants, cleaning solutions), as well as intestinal parasites, enteric bacteria, pathogenic organisms, and animal bites (Soave and Brand, 1991). As well, those working with swine in confinement buildings may suffer future chronic and irreversible lung damage, according to Donham and Leininger (1984). Those working with nonhuman primates (NHP) must take special precautions. Guidance for these individuals may be found in Volume 2 of this *Guide*.

A. REGULATORY REQUIREMENTS

As is the case with other laboratories, the animal care facility should have an Occupational Health and Safety program. All persons using the facility should also be familiar with the requirements of relevant federal, provincial and municipal legislation. This would include, for example, the federal *Health of Animals Act* (38-39 Elizabeth II, Chapter 21, pgs. 387-421), which replaced the *Animal Disease and Protection Act* and which governs control of animal diseases and toxic substances. Those working with animals should also be cognizant of institutional and/or facility safety programs (see also Volume 2 of this *Guide* [CCAC, 1984a]).

The Workplace Hazardous Materials Information System (WHMIS), which resulted from federal and provincial co-operation, was instituted in 1988. Federal government laboratories are governed by federal WHMIS and the Canada Labour Code. The following publications are available free of charge from Labour Canada: *The Employer and WHMIS*; *Introduction to the WHMIS Program*; *Exercise WHMIS in the Workplace*, and a relevant poster.

Elsewhere, provincially enacted Health and Safety legislation specifies the accountability of owners and directors and the rights and responsibilities of employers, supervisors and workers in the workplace. The right to refuse unsafe work is a part of the *Occupational Health and Safety (OHS) Act*. WHMIS regulations are also a section of this legislation and require that each employer provide safe working conditions and that employees be informed about all hazards they will face in the course of their duties. Employees are also given the right to withdraw from the workplace if faced with an unsafe condition. All hazardous substances, including microorganisms, must be labelled in a specified manner, and a Material Safety Data Sheet (MSDS) must be available to accompany each hazardous substance. Each province has adapted these federal government guidelines for its own purposes. WHMIS material may be obtained from provincial Ministries of Labour.

All personnel working with animals must understand how to handle the species involved, both for their own safety and health, and for that of the animals. Training for this should be provided.

B. BIOLOGICAL HAZARDS

Guidelines for working with biohazards (e.g., bacteria, viruses, parasites, fungi and other infectious agents), are provided in the *Health and Welfare Canada/Medical Research Council Laboratory Biosafety Guidelines* (HWC/MRC, 1990). The guidelines include such items as biohazard containment, laboratory design, personal hygiene and safety facilities, and can be used to provide training for employees as mandated by WHMIS.

The biosafety guidelines apply to all research carried out or supported by the federal government and have been adopted by many industries.

Standard Operating Procedures (SOP) based on the guidelines, aimed at minimizing risks to humans in biohazard risk areas, should be developed and enforced.

Personal cleanliness is an important barrier to infection and washing of hands after handling any animal will reduce the risk of disease spread and self-infection. All employees working with animals, as well as visitors to the facility, should wear protective clothing, minimally a lab coat.

All contaminated material must be decontaminated before disposal. Necropsy of animals infected with highly infectious agents should be carried out in certified and tested biological safety cabinets. Necropsy material for disposal should be sealed in plastic bags, properly labelled and incinerated. The necropsy room should be properly equipped to provide adequate refrigeration and hand-washing facilities.

C. ZOONOSES

Those infections that are "secondarily transmitted from animals to humans" are referred to as zoonoses (Schnurrenberger and Hubbert, 1981; August and Loar, 1987; Acha and Szyfres, 1989) and can seriously affect research (Hamm, 1986; Bhatt, Jacoby, Morse *et al.* 1986; ILAR/NRC, 1991).

While most infectious agents show a considerable degree of species specificity, they also may, from time to time, vary widely in virulence and in their capacity to break through species barriers. Thus, infections that have not commonly been considered to be zoonotic hazards may sporadically affect susceptible persons or animals. Persons potentially at higher risk are those who suffer from defective immune systems and those who are under severe stress or who have non-overt clinical disease. Numerous pathogenic microorganisms, such as those responsible for tuberculosis, brucellosis, rabies, etc., which are normally perpetuated by direct transmission from one or more species of vertebrate animals, are also readily transmissible to humans.

Transmission of infections from animals to humans can generally be avoided through proper veterinary care and adherence to SOPs for control of transmission. However, when animals are obtained from areas in which zoonotic diseases are known to exist, e.g., in NHP acquired from the wild (Houghton, 1986) special attention is required.

Work involving exposure to hazardous microorganisms might require prior immunization of the staff, if a vaccine is available. It is recommended, for example, that all personnel handling random-source dogs and

cats, including dealers and handlers, should receive routine rabies vaccination (see also Special Animal Colonies, Infectious Disease Units).

Serological testing and banking of reference serum samples from all personnel working in the animal facility is advisable. This is of particular importance where NHP are being handled and/or agents infectious to humans are being used.

Caution should be exercised in assigning women of childbearing status to animal care duties that might expose them to potential or known teratogens. For example *Toxoplasma gondii*, a protozoan that infects most species of warm-blooded animals, including humans, is spread primarily by oocysts shed in cat feces. These oocysts sporulate in two to four days and may survive for more than a year (Fraser and Mays, 1986). Human toxoplasmosis can result in spontaneous abortion, prematurity, stillbirth or congenital defects (Schnurrenberger and Hubbert, 1981).

The life cycle of the causative organisms implicated in a number of indirect zoonoses may involve transmission through one or more other vertebrate and/or invertebrate intermediate hosts before affecting humans (for example, in taeniasis, tularemia, and vesicular stomatitis). Amongst invertebrate vectors of zoonotic disease, the biting insects are the main offenders. A list of some of the diseases transmitted to humans from animals is included in Appendix VII.

The role of cold-blooded vertebrates in the epidemiology of zoonoses should not be overlooked. In particular, turtles infected with salmonella may constitute a human health hazard in the student laboratory as well as in the animal facility (Sherris, 1990).

D. PROCEDURES FOR WORKING WITH NONHUMAN PRIMATES

All animals must be regarded as potential sources of zoonoses, although the risk of this occurring will vary widely with the class, species, and source of the animal involved. In general, the more closely related phylogenetically a species is to humans, (Anon., 1987a, 1987b; FRAME, 1987; Rice, 1987a, 1987b), the greater the likelihood of zoonoses. It is for this reason that special precautions must be followed for NHP (Love, 1980; Wong and Gardell, 1982; Richter, Lehner and Henrickson, 1984; Else, 1988).

Each institution that maintains a NHP facility is responsible for providing the proper veterinary and human medical services to safeguard the health and safety of both personnel and animals. International guidelines have been prepared for those working with NHP (FRAME/CREA, 1987; Kaplan, 1987; Anon., 1989; MRC, 1985).

Outbreaks of viral diseases, e.g., Callitrichid Hepatitis Virus (Anderson, 1991) recently "rocked the primatologist's world," and current procedures for the rapid diagnosis of primate viral diseases include serology, virus isolation, direct visualization using electronmicroscopy or immunofluorescence, and detection of viral components (Kalter and Herberling, 1990).

The most reasonable and effective approach in reducing occupational infection risks is to develop and follow SOPs that preclude or minimize overt occupational exposure among personnel working with NHP or biological samples therefrom. SOPs should be established for an Occupational Health and Safety Program for personnel which would include serological screening and vaccination, use of protective clothing, con-

tainment, stress on personal hygiene, procedures for accidents including bite wounds and/or other exposure to potential risk, and for quarantine and quality control procedures for confined animals.

Guidelines have been prepared for prevention of *Herpes Simiae* (B-Virus) infection by a B-Virus Working Group which convened at the Centers for Disease Control (Anon., 1987c; Kaplan, Balk, Brock *et al.* 1987; Schulhof, 1990). *Herpes Simiae* is fatal in humans (Kalter and Herberling, 1989).

Similarly, because of the expanding use of Simian Immunodeficiency Virus (SIV), which is closely related to the Human Immunodeficiency Virus (HIV), guidelines in this regard have been prepared as well (Anon., 1989). Standard serological procedures to identify SIV antibody are used in laboratories conducting research with the virus, and the National Institutes of Health (NIH) and World Health Organization (WHO) have expanded their diagnostic services (Kalter, 1987).

In addition to NHP from the wild, those within the colony may also carry indigenous latent infections (Baulu, Everard and Everard, 1987; Dance, King, Aucken *et al.* 1992). It is important to establish rigid quarantine and quality control procedures for the animal colony and to better define and be more aware of the potential risks. The Ebola-like virus outbreak in the U.S. in 1989 exemplified such risks (Anon., 1990; Anderson, 1990a, 1990b; Dalgard, Hardy, Pearson *et al.* 1992).

Adherence to the following list of precautions is recommended:

a) all NHP must be considered as potentially carrying a disease transmissible to humans;

b) NHP, or anything that has been in direct contact with them, should not come in contact with the skin;

c) protective clothing, including coveralls, boot covers, surgical caps, masks and gloves should be worn when working with NHP, and removed when leaving the NHP quarters;

d) smoking and bringing food and drink into NHP rooms are strictly forbidden;

e) facilities for washing hands must be made available and used by all personnel immediately upon leaving NHP rooms;

f) personnel with sores, cuts, and other lacerations should not come in contact with NHP. However, if this is unavoidable, then the lesion must be adequately covered prior to and during any activity in a room containing NHP, and dressings must be changed immediately upon leaving. These dressings and any other disposable items so exposed must be treated as biological hazardous waste;

g) all cuts, bites, scratches, or needle punctures acquired while working with or in proximity of NHP must be reported to the medical authority designated by the institution. SOPs for all wounds so encountered should be developed and followed accordingly. Immediate treatment must ensure that the wound is made to bleed freely and thoroughly scrubbed and cleansed with soap and water. A flushing of the wound area with a provodine iodine solution is recommended. In the event that sterility has been breached (e.g., tearing or puncture of a surgical glove) the hands must be re-scrubbed before leaving the room and re-gloved before continuing the procedure.

   Following injury by a NHP, the animal concerned must immediately be immobilized and examined for excessive salivation and for lesions of the oral cavity which may be characteristic of Herpes (B-Virus). SOPs must be followed for dealing with this type of accident. Procedures for sampling for Herpes B of the animal and of the injured person must be followed. The results of the examination must be commu-

nicated to the previously designated medical authorities, along with information on the species of NHP, length of time in the colony, and contacts with other species;

h) special precautions should be taken whenever conducting necropsies on NHP that have died during the conditioning period; necropsy procedures should include the wearing of protective clothing, surgical caps, and masks, gowns and surgical gloves. The use of biosafety cabinets for conducting all necropsy of NHP tissue is recommended;

i) because of the possible danger of contacting Hepatitis A, it is recommended that personnel working with newly imported chimpanzees receive hyper-immune serum globulin prophylactically. Animals should be tested for human hepatitis antigens and, if positive, strictly quarantined;

j) all personnel having contact with NHP must be free of tuberculosis and should receive a tuberculin skin test not less than once yearly and X-ray examination as prescribed. It should be noted that it has recently been reported that misleading positive tuberculin reactions were caused in squirrel monkeys that had received Freund's Complete Adjuvant (FCA) (Pierce and Dukelow, 1988);

k) protective leather gauntlets should be worn when handling conscious NHP. Several varieties are available commercially;

l) all laundry that has been in direct contact with NHP or their excreta should be autoclaved prior to being sent out for washing.

E. ALLERGIES

Allergies to laboratory animals are a significant occupational health concern for people regularly working with the common laboratory animal species (Aoyama, Ueda, Manda *et al.* 1992; Olson, 1986; Bland, Levine, Wilson *et al.* 1986; Botham, Davies and Teasdale, 1987; Kibby, Powell and Cromer, 1989; Lutsky, 1987; Slovak and Hill, 1987; Venables, Tee, Hawkings *et al.* 1988). Laboratory animal allergy (LAA) is an immediate-type hypersensitivity reaction, IgE-mediated, which develops upon exposure to a laboratory animal, its fur or dander, its urine, saliva, serum or other body tissues. Typical symptoms range from mild (e.g., upper respiratory signs such as sneezing, itchy and/or runny nose and eyes, and skin reactions such as red, raised and itchy wheals after contact with animals, their tissues or their excreta), to severe [e.g., wheezing, shortness of breath, and a feeling of chest tightness (asthma)]. Persons experiencing such symptoms should be advised to contact their physician for diagnosis and treatment.

Measures which can reduce the degree of exposure to laboratory animal allergens include:

a) use of protective gear such as gloves, face masks, gowns, shoe covers, etc., worn only in animal rooms;

b) regular hand-washing, and showering after work;

c) use of improved filtration in animal room ventilation systems, and the use of special filtered caging systems; and

d) educational programs for employees identifying high risk (e.g., high allergen load) areas and tasks, and strict use of preventive measures, as set out by the institution's SOPs.

Institutions are encouraged to include a consideration of LAA in their Occupational Health and Safety programs. As noted above, identifying high risk areas and tasks (Eggleston, Newill, Ansari *et al.* 1989; Gordon, Tee, Lowson *et al.* 1992; Swanson, Campbell, O'Hallaren *et al.* 1990), and the use of SOPs in these areas, along with education of staff, are useful in reducing the severity of the problem (Botham, Davies and Teas-

dale, 1987). Procedures for monitoring exposure, health-monitoring of staff at risk, and for dealing with staff who become allergic should also be considered (Botham, Davies and Teasdale, 1987; Lutsky, 1987; Newill, Evans and Khoury, 1986).

F. PHYSICAL INJURIES AND CHEMICAL HAZARDS

Physical injuries related to the handling of animals may be kept to a minimum by ensuring that:

a) all staff are trained and experienced in handling the species with which they work, and that they know the particular hazards associated with each species;

b) all staff are familiar with the hazards of the experiment, and are provided with (and use) a proper working area, protective clothing and equipment;

c) a mechanism is in place in every unit to deal with animal-inflicted injury, and for referral for any further medical treatment if this is required.

Responsibility for ensuring that first aid kit(s) are available and always properly stocked must be clearly identified. The location of the first aid kit(s) should be prominently marked and all personnel using the facility should be made aware of these locations.

Injuries from chemicals can be avoided by treating all chemicals with care, by knowing their properties and adhering to the accepted safety practices for handling that type of product. WHMIS, legislative and institutional requirements must be met.

Care should always be taken in handling such common chemicals as industrial detergents used in cage washers, cleaning agents, and powerful disinfectants. These substances should be stored separate from animal feed and bedding materials. Volatile liquids used as anesthetics or for euthanasia, and other toxic and volatile materials, should be stored in well-ventilated fume hoods or cabinets designed for that purpose.

G. RADIATION AND ULTRAVIOLET LIGHT

Radioactive materials present special hazards. All persons working with these materials should know the properties of each, and be familiar with the appropriate safe handling techniques. The possession of radioactive materials is authorized by Radioisotope Licences issued by the (federal) Atomic Energy Control Board (AECB) to the institutions. The Radiation Safety Program is administered by a Radiation Safety Officer, who the AECB recommends sit as an *ex-officio* member of the institution's Occupational Health and Safety Committee. Use of X-rays is governed by Occupational Health and Safety Acts under provincial Ministries of Labour.

Isotope-treated animals may pass radioactive material in their excrement, which should therefore be disposed of in an approved manner, as must the animal itself after death. Complete records should be kept through to the final disposition of these animals.

The eye and skin are critical areas for exposure to ultraviolet (UV) light. The eye, in particular, can be seriously injured. Staff should not be exposed to UV rays; however, if they must be, they should be warned of the hazards and provided with "wraparound" safety glasses. As well, the source of illumination should be suitably marked. The maximum intensities tolerated by sensitive faces for a seven-hour day, range from 0.1 to 0.5 milliwatt per square foot.

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IX STANDARDS FOR EXPERIMENTAL ANIMAL SURGERY

A. INTRODUCTION

Distress resulting from inappropriate or inadequately performed surgical technique or post-operative care constitutes "unnecessary pain". Adequate knowledge of topics such as animal physiology, pharmacology and anatomy is essential for the success of any research program involving the use of experimental animals, especially where surgical techniques are required. Good surgical techniques, appropriate anesthesia, proper instrumentation and competent pre- and post-operative care are all essential to the welfare of the experimental animal and the success of the surgical component of the research project, as are correctly designed surgical facilities.

All persons performing surgical techniques should have demonstrated ability in the surgical procedures required. In this respect, it is essential that institutions provide the opportunity for basic training and practice in required procedures before experimental surgery is conducted. Cadaver practice and non-survival trials can help train investigators. Adequate training and practice will help minimize anesthetic and surgical time and contribute to faster recovery of the animal.

Medical training does not include training in the husbandry, medicine or surgery of laboratory animals. It cannot be assumed, therefore, that prior human surgical experience will result in good experimental animal surgery because there are significant differences in both anesthesia and surgical technique. The guidelines of the Academy of Surgical Research (ASR, 1989) should be consulted regarding the training necessary for the various groups of professionals. In large experimental surgery programs, a key member of the team should be an experienced veterinary surgeon. The primary objective is always responsible use of the experimental animal. It is important that all personnel involved in acute or chronic surgery treat the animals humanely and with dignity at all times. It is the responsibility of the principal investigator to ensure that proper procedures and precautions are observed.

Also see the *CCAC guidelines on: training of personnel working with animals in science* (2015).

February 2017

B. FACILITIES FOR SURVIVAL SURGERY

This section has been revised. Please see the *CCAC guidelines on: laboratory animal facilities – characteristics, design and development* (2003).

February 2017

C. PRE-OPERATIVE PLANNING AND ANIMAL PREPARATION

This section is currently under revision. Please also see the relevant animal type guidelines.

February 2017

All persons involved in an experimental surgery program should be identified to ensure that they are properly trained in the principles and practice of aseptic technique, proper instrument use, tissue handling, closure and suturing techniques, anesthesia and analgesia.

The primary investigator must develop a written protocol for the operative procedure in which possible complications or special maintenance requirements arising from the procedure are anticipated. The protocol should clearly identify the responsibilities of all persons involved in the project; support staff, animal care staff, research technicians and investigators. Adequate staff must be available for proper care of each animal during the peri-operative period. For some projects, the surgical facility may need to be staffed on a 24 hour basis.

It is recommended that pre-operative care, operative technique and post-operative care practices be developed in consultation with a veterinarian. A laboratory animal veterinarian must be consulted to ensure that there is a**dequate veterinary care for the animal**, including appropriate anesthesia and analgesia.

Only healthy, disease-free animals should be used in an experimental surgery program. Specific Pathogen Free (SPF) rodents and rabbits are available commercially. Random-source animals must undergo a conditioning period as recommended by the laboratory animal veterinarian.

A period of **acclimatization**, in which the animal can adjust to new environments, special housing, tethers, slings, other forms of restraint or frequent handling, is very important. This will greatly decrease the amount of distress or disorientation experienced by the animal and ensure the validity of experimental results.

Surgical records should be kept for all experimental animals. The degree of detail recorded will vary with the procedure and the species. The amount of information recorded for a calf undergoing heart transplantation will be very different from that recorded for a group of rats undergoing adrenalectomy, for example.

Each species has a different **fasting time before surgery.** Food is usually withheld for 12 hours before surgery in dogs, cats, ferrets, nonhuman primates (NHP) and pigs (Flecknell, 1987). Water should be withheld only for two to three hours (if at all) before the actual surgery so that dehydration does not result. Fasting ruminants for 24 to 48 hours prior to surgery helps to reduce the incidence of rumenal tympany (bloat) (Flecknell, 1987). It is unnecessary to withhold food and water from rodents and rabbits except in special circumstances such as surgery of the lower bowel.

If fasting is required, it can be done overnight in large rodents, or for up to 24 hours in rabbits, as they retain their food longer. Mice or other small rodents with similarly high metabolic rates should not be fasted for more than three or four hours (see also Anesthesia).

D. SURGICAL PROCEDURES AND INTRA-OPERATIVE NURSING CARE

This section is currently under revision. Please also see the relevant animal type guidelines.

February 2017

Methods for restraining animals for injections or the collection of body fluids are described in Volume 2 of this *Guide* (CCAC, 1984). Table 1 provides a summary of the injection sites, needle sizes and volumes to be introduced for the smaller common laboratory species.

All species undergoing surgery should receive a similar level of care and attention. Recovery surgery in all species of animals should be performed using aseptic technique. Instruments should be sterile. Objects introduced into the animal, such as telemetry implants, osmotic minipumps, vascular access ports, cannulae and any other biomedical devices, must be sterile. Suitable preparation of the surgeon will include wearing a scrub suit, performing a surgical scrub, wearing a cap, mask, sterile gown and sterile surgical gloves. For minor recovery surgery in rodents, a minimum of a clean lab coat, hand scrub, mask and sterile surgical gloves is required of the surgeon.

Surgery in field conditions should be performed in as clean an environment as possible, with sterile instruments, sterile surgical gloves and aseptic technique.

Every effort must be made to minimize infection. The rat may exhibit increased resistance to post- surgical infection compared to other rodents; however, this should not be an excuse for less-than-adequate sterilization of implants, cannulae, etc., or for non-sterile technique. Routine use of antibiotics is inappropriate.

Those performing "multiple run" surgeries, in which a large number of rodents are undergoing the same procedure, should also use aseptic technique. Several sets of sterile instruments will be required. Instruments, if used more than once, should be kept in a germicidal solution between animals.

General publications are available that describe in detail the pre-surgical preparation of the animal and the incision site, the preparation and sterilization of instrument packs, drapes, fluids, etc., and the draping of the animal. For surgeries that are frequently performed in veterinary practice (e.g., rumenotomies, thoracotomies, castrations), clinical approaches may be used. For experimental surgery, guides to approaches for each body system are available (Gay, 1986a, 1986b, 1989; Swindle and Adams, 1988).

TABLE 1 For Each Species, Site of Injection, Maximum Normally Accepted Volume and Needle Size*

SPECIES	SUBCUTANEOUS	INTRAMUSCULAR	INTRAPERITONEAL	INTRAVENOUS
MOUSE	Scruff, 2-3 ml, <20 G	Quadriceps/posterior thigh, 0.05 ml, <23 G	2-3 ml, <21 G	Lateral tail vein, 0.2 ml, <25 G
RAT	Scruff, back, 5-10 ml, <20 G	Quadriceps/posterior thigh, 0.3 ml, <21 G	5-10 ml, <21 G	Lateral tail vein, sublingual vein, penile vein (jugular vein, femoral vein--cut down), 0.5 ml, <23 G
HAMSTER	Scruff, 3-4 ml, <20 G	Quadriceps/posterior thigh, 0.1 ml, <23 G	3-4 ml, <21 G	Femoral or jugular vein (cut down), 0.3 ml, <25 G
GUINEA PIG	Scruff, back, 5-10 ml, <20 G	Quadriceps/posterior thigh, 0.3 ml, <21 G	10-15 ml, <21 G	Ear vein, saphenous vein, dorsal penile vein, 0.5 ml, <23 G
RABBIT	Scruff, flank, 30-50 ml, <20 G	Quadriceps/posterior thigh, lumbar muscles, 0.5-1.0 ml, <20 G	50-100 ml, <20 G	Marginal ear vein, 1-5 ml, (slowly) <21 G
CAT	Scruff, back, 50-100 ml, <20 G	Quadriceps/posterior thigh, 1.0 ml, <20 G	50-100 ml, <20 G	Cephalic vein, 2-5 ml, (slowly), <23 G
DOG	Scruff, back, 100- 200 ml, <20 G	Quadriceps/posterior thigh, 2-5.0 ml, <20 G	200-500 ml, <20 G	Cephalic vein, 10- 15 ml, (slowly), <21 G
BIRD (domestic fowl)	--	Pectoral muscles, 1-2 ml, <21 G	Midline, halfway between cloaca and sternum, 10-15 ml, <21 G	Brachial (wing) vein, 2-3 ml, <21 G

* In intravenous administration for infusion, the amount of fluid replacement may exceed recommended maximum volumes, particularly in dogs and cats.

TUFFERY, A.A., ed. *Laboratory animals: An introduction for new experimenters*. J. Wiley & Sons Ltd. 1987

When selecting a surgical approach, it is important that the surgeon consider the anatomy and normal body posture of the animal. This is especially important in ruminants. In this way, the least painful approach or the one promoting a speedy recovery can be chosen. The surgeon should also be familiar with the behaviour of the animal species being used, so that the appropriate closure technique can be used.

During surgery, it is important that the physiological condition of the animal be monitored and kept stable. The degree of monitoring will depend on the equipment available. Basic monitoring of the cardiovascular system, respiratory system and core temperature requires very little equipment. These observations should

be recorded in the animal's surgery record. It is essential that the animal be clinically examined at least twice per day in the immediate post-operative period.

Attention should be paid to the fluid requirements of the animal. Careful attention should be paid to hemostasis during surgery, to avoid hypovolemic shock, especially in small animals. Prolonged surgical procedures or those in which there will be significant blood loss require intravenous electrolyte replacement and/or blood transfusion.

The animal should be positioned on the table so as to avoid compromising cardiovascular or respiratory function and pressure point tissue necrosis. It should be protected from hypothermia and firmly, but carefully restrained in the operative position.

The use of a single animal in multiple survival surgeries is strongly discouraged. Multiple major surgery protocols must be approved by the institution's Animal Care Committee (ACC), and allowed only if for scientific reasons. **Multiple major surgeries on a single animal are not to be performed in order to save money.** A second major surgery may be performed if it is non-survival.

Minor procedures such as biopsies may be performed more than once. However, it is important that animals recover completely between procedures.

The subject of anesthesia is covered elsewhere in this *Guide*; however, the following points should be noted by experimental surgeons:

a) all surgical procedures are to be carried out under anesthesia;

b) those doing surgery have an obligation to be aware of the efficiency of the anesthetic technique being used;

c) it is the responsibility of the surgeon and anesthetist to ensure that this animal is spared discomfort during the entire peri-operative period. This includes the period during the induction of anesthesia, for the entire surgical period and for the post-surgical recovery period.

d) in no case is it acceptable to use muscle paralytics without appropriate anesthetics. No ACC should approve the use of a "paralysed-awake animal" (see also *Ethics of Animal Investigation*) in a surgical or other procedure which might involve pain or distress.

E. POST-OPERATIVE RECOVERY AND SUPPORT

This section is currently under revision. Please also see the relevant animal type guidelines.

February 2017

Recovery from anesthesia can be hazardous and requires frequent, perhaps continuous monitoring. Depending on the anesthetic regime, recovery may take from a few minutes to several hours. Qualified staff must be available to monitor the animal throughout the entire recovery period. In the case of recovering

neonatal rodents, care must be taken to prevent maternal cannibalism. **Under no circumstances should any animal be allowed to recover unattended**.

A number of nursing activities will be required during the **immediate post-operative period**, e.g., removal of endotracheal tube if used, maintenance or removal of intravenous lines, frequent turning of the animal to avoid bruising and vascular and respiratory problems, and recording of physiological parameters. All these should take place in a designated area suitable for intensive care.

When normal eating and drinking behaviour has resumed, and physiological parameters have been stabilized or are within expected limits, the animal may be removed from intensive care to more standardized husbandry. However, the animal must continue to be monitored carefully; the wound will need attention, sutures need to be removed, catheters flushed, etc. Depending on the model created, **long-term post-operative care** may involve special diets, daily medication, physiotherapy or some other form of specialized treatment. All animals must be monitored for signs of post-surgical infection or other complications.

The goal of the surgery team must be to minimize any pain or distress. The degree of post-operative pain will vary; however, in all cases, every attempt must be made to relieve pain with appropriate use of analgesics and good nursing care. **Investigators must consult with a veterinarian to set up an analgesic regime for ALL species of animals used**. The type of analgesic, the dose and duration of treatment will depend on the species and temperament of the animal and the type of surgery it has undergone. Most analgesics in use are relatively short acting and require administration every few hours. **It is the responsibility of the investigator to make sure that the necessary staff are available to administer analgesics as prescribed**. The laboratory animal veterinarian will have the necessary expertise to advise on the newer analgesics and methods of administration.

All personnel in the project should be familiar with the animal's behaviour and posture when normal and when in pain.

a) Responsibility for Surgical Standards

i) The responsibility for the animal in each surgical case lies with the person doing the surgery who, in turn, should be accountable to the institutional ACC for his/her adherence to these standards and for demonstrating an acceptable level of expertise.

ii) The responsibility for supervision of the experimental animal surgical facility should be clearly defined.

iii) Where supportive treatment is required (analgesics, tranquillizers, antibiotics, etc.), the surgical investigator must institute suitable treatment in consultation with a veterinarian.

iv) If the animal, as a result of the experimental manipulation, is in distress that cannot be relieved, authorized personnel, e.g., the laboratory animal veterinarian, should be contacted immediately and procedures instituted for euthanasia.

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X CONTROL OF ANIMAL PAIN IN RESEARCH, TEACHING AND TESTING

This section is currently under revision. Please also see the relevant animal type guidelines.

February 2017

A. INTRODUCTION

> "Many of the advances made in our knowledge of the basic mechanisms of pain and advances in pain therapy would have been impossible without experiments in animals, which have yielded enormous benefits for both humans and animals. The knowledge gained has resulted in more effective methods of pain control in both humans and animals, has brought about a decrease in suffering, and has thus improved the quality of peoples' lives" (Bonica, 1992).

The assessment and management of pain and suffering is a challenge that must be faced if animals are to be treated ethically and humanely (Fosse, 1991). A landmark publication on animal pain was Dawkins' (1980) *Animal Suffering: The Science of Animal Welfare*. Recent valuable additions include *Animal Pain: Ethical and Scientific Perspectives* (Kuchel, Rose and Burrell, 1990), *Animal Pain* (Short and Van Poznak, 1992), and a handbook, *Recognition and Alleviation of Pain and Distress in Laboratory Animals*, prepared by the Committee on Pain and Distress in Laboratory Animals of the Institute of Laboratory Animal Resources (ILAR), which discusses stressors in the laboratory and the animal behaviours they cause, the physiology of pain and distress, drug dosages and euthanasia (ILAR, 1992).

The first symposium on animal pain was presented in 1982 by the Federation of American Societies for Experimental Biology (FASEB) (Kitchell, Erickson, Carstens *et al.* 1983). It was quickly followed by other publications, symposia, and guidelines related to pain relief in animals (Zimmerman, 1983; RSPCA, 1983; Wall and Melzack, 1984; Flecknell, 1984; Gibson and Paterson, 1985; Morton and Griffiths, 1985; AVTRW, 1986; Frenk, Cannon, Lewis *et al.* 1986; AVMA, 1987; Beynen, Baumans, Bertens *et al.* 1987; Rowan, 1988; Anon., 1990; Balls, 1989, 1990; Arena and Richardson, 1990; Dawkins, 1990; Goyd, 1990; LASA, 1990; Bateson, 1991; Moberg, 1992).

Sackman (1991) has prepared a review article on control of pain in cats and dogs.

B. WHAT IS ANIMAL PAIN?

In addition to ethical concerns, poor health, pain or distress in animals interject unwanted variables into research that can greatly interfere with interpretation of the studies (Montgomery, 1990). Pain research often requires the production of the same sensations and behaviour in animals that ethical guidelines say must

be eliminated (Amyx, 1990). Wall (1992) suggests that instead of agonizing over an undefinable concept of pain, we simply study the animal's efforts to stabilize its internal environment and then aid it, or at least not intrude on those efforts without good reason.

The question of distress in animals and how to define and measure it is still quite perplexing (Olfert, 1992; Lewis, 1942; Brown, 1988; Molony, 1985).

Reduction or alleviation of stress or pain is considered by Flecknell (1987) as a refinement in animal care, as part of Russell and Burch's (1959) "3Rs" of refinement, reduction and replacement (Smyth, 1978; Rowsell and McWilliam, 1986). Poor anesthetic techniques, for example, can adversely affect research and may produce unnecessary pain (Flecknell, 1987). Animal suffering includes stress, distress, discomfort, and deprivation, (Smith, 1988) as well as anxiety and fear. Freedom from discomfort and freedom from pain, injury or disease are two of the animal's Five Freedoms, as promulgated by the U.K.'s Farm Animal Welfare Council (FAWC) (Seamer, 1993).

In the absence of evidence to the contrary, it may be assumed that any stimuli or experience which produces pain and discomfort in humans, also does so in animals (LASA, 1990; RSPCA, 1983), as first promulgated by the Littlewood Committee in 1965. Amyx (1990) suggests that when Animal Care Committees (ACC) are reviewing protocols which involve aversive stimuli, members test the stimulus on themselves.

Discomfort may not be sufficient to manifest observable pain. However, it is important to be able to assess discomfort, because this provides the first steps towards avoiding it.

Attempts to define what constitutes stress have been made for some time, with little agreement (Levine, 1985). However, it was recently defined by ILAR (1992) as "the effect produced by external (i.e., physical or environmental) events or internal (i.e., physiologic or psychologic) factors, referred to as stressors, which induce an alteration in an animal's biologic equilibrium." The presence or absence of stress appears to be the only acceptable indicator of animal well-being (Duncan, 1992).

In addition to stress in the research setting, the stress of animal transportation, even for short distances, has been demonstrated in laboratory animals (Gärtner, Büttner, Döhler *et al.* 1980; Clark, Mason and Moberg, 1988; Toth and January, 1990) and farm animals (Fraser and Broom, 1990).

Sherrington (1947) originally defined a noxious stimulus as one which was actually or potentially damaging to the skin, to which Lineberry (1981) added production of escape behaviour in animals. The receptors specifically responsive to noxious stimuli are termed "nociceptors" (Kitchell, Erickson, Carstens *et al.* 1983). However, Wall (1992) states that there is evidence that the Central Nervous System (CNS) can extract information relevant to pain from afferents other than specific nociceptors.

The strongest intensity of noxious stimulation that a human-being will permit is called the "pain tolerance threshold" (Kitchell, Erickson, Carstens *et al.* 1983). Bateson (1991) notes that the subjective experiences of an animal, if it has any, may be totally different from humans, reflecting its different way of life and the different ways in which its body works. For example, most clinical veterinary neurologists are amazed by the high pain thresholds of some dogs (Kitchell, Erickson, Carstens *et al.* 1983).

In pain research, the vast majority of animals used are rodents, specifically rats (Amyx, 1990). Silverman (1991) notes, however, that "pain detection in rodents is not easy. Slight behavioural changes, vocalizations,

abnormal use of body parts may signal pain, but we may not be able to evaluate its magnitude." In rodents, important indicators are recumbency and changes in the hair coat and brightness of the eyes (Montgomery, 1990).

Criteria for assessing morbid and moribund conditions in oncologic and toxicologic research include impaired activity, change in temperament, restlessness, decreased feed or water intake, abnormal vocalization, abnormal posture, self-mutilation and changes in bowel or urinary activity (Montgomery, 1990).

One of the characteristics of pain or distress in animals is a change in behaviour and reflex attributes (Amyx, 1990). Animal care personnel and research investigators must be familiar with the normal behavioural characteristics of the experimental animal, for the success or failure of the study can depend on the expertise of the technician observing the animals to minimize pain and distress (Montgomery, 1990; Bateson, 1991). Moreover, familiarity with the handler, surroundings and procedures can reduce anxiety in the animal, as can positive re-enforcement (LASA, 1990).

C. GUIDELINES

The first code of laboratory procedures regarding animals in North America was formulated by Walter B. Cannon in 1909, and was adopted and enforced in the laboratories of American medical schools, and later served as the basis of American Physiological Society's (APS) *Guiding Principles in the Care and Use of Animals* (Cecil and Samuels, 1987).

In both Britain and The Netherlands, suffering is categorized as mild, moderate or substantial in severity (Smith, 1988).

A working party of Britain's Laboratory Animal Science Association (BLASA) has discussed the assessment and control of pain in experimental animals (LASA, 1990). Barclay (1988) has developed a disturbance index for rodents. The Laboratory Animal Science Association's (LASA) Working Party on Assessment and Control of Severity has developed a Severity Index (SI). This has been applied to such areas as administration of substances, collection of tissues and body fluids, surgical techniques and restraint. The SI is reached by means of assigning scores based on consciousness, anesthesia, preparation (preparatory manipulation), restraint (ranging from brief manual restraint to whole body restraint), duration, tissue sensitivity, organ risk and mortality. As well, the consequences in terms of pain, distress and deprivation are evaluated. Procedures are judged on a scale of up to 34 points. Examples ranged from two points for intravenous perfusion in an anesthetized animal, to 24 points for parabiosis (reversible suspension of obvious vital activities or anatomical and physiological union of two organisms) (LASA, 1990).

It is LASA's contention, based on Maslow (1970) and Curtis (1985) that interference with the basic physiological functions or needs presents a greater risk to well-being or survival than interference with behavioural requirements (LASA, 1990). The Canadian Council on Animal Care (CCAC) believes, however, that at least as regards nonhuman primates, "measures to safeguard psychological stability should take equal precedence to those concerning physical health" (CCAC, 1984).

This *Guide* includes the *Categories of Invasiveness in Animal Experiments* which were originally based on those of the Washington-based Scientists Center for Animal Welfare's (SCAW) *Categories of Biomedical Experiments Based on Increasing Ethical Concerns for Non-Human Species* (Orlans, Simmonds and Dodds, 1987). The Categories of Invasiveness document has since been amended nine times. In the management

of animal pain, see also the CCAC statement on *Ethics of Animal Investigation* which is found elsewhere in this *Guide*.

D. THE ROLE OF THE VETERINARIAN IN REDUCING PAIN

Veterinary training and expertise play a vital role in fulfilling an institution's responsibilities to prevent and minimize pain and suffering in all animals used for research, teaching and testing (Gorham, 1991; Rowsell, 1992). The Canadian Association for Laboratory Animal Medicine (CALAM) in 1990 adopted a document-*Adequate Veterinary Care*, which the CCAC considers a basis for its own policy on this topic. The document covers the prevention and relief of animal pain.

The contribution of trained animal technicians has already been noted. The Canadian Association for Laboratory Animal Science (CALAS) sets standards, examines and registers laboratory animal technicians in Canada.

E. SIGNS OF PAIN AND DISTRESS*

There are numerous stereotypical responses to stress or pain stimuli in animals, particularly in mammals. Nevertheless, species differences do exist. Recognition of changes in behaviour and physical appearance in the species under study will allow early identification of an animal experiencing pain or distress. Some species specific observations are presented in this section.

Nonhuman Primates (NHP)

Monkeys often show remarkably little reaction to surgical procedures or to traumatic injury. Obvious signs of pain are not readily seen. Loud and persistent vocalization, for example, commonly signifies only alarm or anger. The animal in pain may be huddled in a crouching posture with a "sad" facial expression and glassy eyes, or it may sit hunched with its head forward and its arms across its body. It may avoid its companions and may stop grooming itself. A monkey in pain may also attract increased attention from its cage mates, which can vary from social grooming to attack. Acute abdominal pain may be shown by facial contortions, clenching of the teeth, restlessness, and shaking accompanied by grunts and moans. Food and water intake is usually diminished or absent.

Key Signs: hunched position, failure to groom, refusal of food or water, dejected appearance.

* With acknowledgement to: Association of Veterinary Teachers and Research Workers. *Guidelines for the recognition and assessment of pain in animals.* Potters Bar, Herts: Universities Federation for Animal Welfare (UFAW), 1989; Laboratory Animal Science Association Working Party. The assessment and control of the severity of scientific procedures on laboratory animals. *Lab. Anim.* 1990; 24: 97-130; Hansen, B., Hardie, E. and Young, M. Recognition of acute pain and distress in the dog. *Humane Innovations and Alternatives to Animal Experimentation* 1990; 4: 170-173; Morton, D.B. and Griffiths, P. H.M. Guidelines on the recognition of pain, distress and discomfort in experimental animals and a hypothesis for assessment. *Vet. Rec.* 1985; 116(16): 431-436.

Dogs

Dogs in pain generally appear quieter, less alert, and withdrawn, with stiff body movements and an unwillingness to move. In severe pain, the dog may lie still or adopt an abnormal posture in order to minimize its discomfort. In less severe states, it may appear restless and the immediate response to acute, but low intensity pain may be an increased alertness. There may be inappetence, shivering, and increased respirations with panting. Spontaneous barking is unlikely; the dog is more likely to whimper or howl, especially if unattended, and may growl without apparent provocation. A dog may lick or scratch at painful areas of its body. When handled, it may be abnormally apprehensive or aggressive. The animal exhibits anxious glances; it seeks cold surfaces. Its tail is often between its legs.

Penile protrusion and frequent urination may also be noted.

Key Signs: inappetence, bites at pain regions, abnormally apprehensive.

Cats

Cats in pain are generally quiet, with an apprehensive facial expression; the forehead may appear creased. There may be crying or yowling and the cat may growl and hiss if approached or made to move. There is inappetence and a tendency to hide or to separate from other cats. The posture becomes stiff and abnormal, varying with the site of the pain. A cat with head pain may keep its head tilted. If the pain is generalized in the thorax and abdomen, the cat may be crouched or hunched. With thoracic pain alone, the head, neck, and body may be extended. In abdominal or back pain, the cat may lie in lateral recumbency with its back arched. If the animal is standing or walking, the back is arched and the gait stilted. Incessant licking is sometimes also associated with localized pain. Pain in one limb usually results in limping or holding up of the affected limb.

A cat in severe pain may show demented behaviour and make desperate attempts to escape. If a painful area is touched or palpated, there may be an instant and violent reaction. There may be panting, with an increased pulse rate and pupillary dilatation. A cat in chronic pain may have an ungroomed appearance and show a marked change from its normal behaviour. The animal exhibits tucked in limbs, hunched head and neck, and utters a distinctive cry or hissing and spitting sound. Its ears are flattened. It shows fear of being handled and may cringe.

Key Signs: stiff posture, demented behaviour, lack of grooming, hunched head and neck, inappetence.

Mice

After procedures which cause pain, mice may increase their sleeping times. Reduced food and water intake, with resultant weight loss, dehydration and wasting of the muscles on the back may be observed. Piloerection (erection of hair) and a hunched appearance indicate pain or distress. The animal fails to groom, but scratches more frequently. Sick mice are often isolated from the remainder of the group. Aggressive vocalization is observed in the early stages, decreasing where pain or stress reduces the ability to move and respond.

The eyes appear sunken, and ocular and nasal discharge may be noted as the animal's condition worsens. The respiration rate increases and breathing may be forced or laboured. Defecation/urination are immedi-

ate reactions to stress in the mouse, and increase or decrease as stress continues. The movement of vibrissae (muscle hairs) becomes less evident as pain or stress continues. Affected mice become more timid and apprehensive; however, as pain or stress increases, they may become aggressive, with a tendency to bite. The animal may attempt to bite the source of pain or affected area, and may self-mutilate the affected part.

Writhing movements are noted when the pain is abdominal. There is gradual assumption of a hunched, 'sleeping posture' away from any light source. Where limbs or feet are affected, sudden running movements are exhibited as an escape mechanism; there is increasing difficulty in maintaining posture. The mouse may show unsteady gait, difficulty in moving in straight line, and circling movements where balance is affected. A rolling gait is often noted with developing ascites.

As its condition worsens, the animal becomes quiet and unresponsive, separates from the group and eventually becomes unaware of its surroundings. Hypothermia is observed with increasing deterioration in condition; the animal feels 'cold' to the touch.

Key Signs: withdrawal, biting response, piloerection, hunched back, sunken eyes and abdomen, dehydration, weight loss.

Rats

Rats are generally docile and less aggressive than mice towards members of their own species and humans. Acute pain or distress is usually accompanied by constant vocalization and struggling. Rats will often lick or guard a painful area. Increased scratching can indicate chronic pain. A rat in pain will often sit crouched with its head turned into its abdomen. Sleeping periods will be disturbed and increase if pain or distress are present. An elevated respiratory rate associated with sneezing occurs where the respiratory system is affected. Increasing piloerection (staring coat) is noted, along with an increasingly untidy appearance as the animal fails to groom itself. There may be some hair loss. The animal ceases to eat and drink normally. There is poor skin tone, and evidence of muscle wasting along the back-- indicative of dehydration and weight loss.

During repeated painful or distressing procedures, animals may become more aggressive and resist handling, which will increase with increasing pain or distress. The eyelids rapidly assume a half-closed or almost-closed position. The eyes may appear sunken, and ocular discharge is common, often progressing to red-coloured hematoporphyrin exudate which may encircle the eye. Nasal discharge, if present, may be red-coloured as well (Harkness and Ridgway, 1980).

Constipation or diarrhea may occur depending on the organ system(s) affected. Urination decreases with reduced water intake; however, frequency may increase where urinary infection or hormonal disturbance is present. Animals in pain initially show increased awareness/aggressive responses and a tendency to bite, but eventually become depressed and unresponsive. Exploratory behaviour lessens. Aversive behaviour is shown towards other animals. There is possible self-mutilation of affected parts in later stages. Abdominal contraction and stilted movements may occur if abdominal pain is present. There may be increasing pain associated with locomotion. Lameness in one of the limbs or simply careful gait may be noted. A "waddling" gait occurs where abdominal enlargement take place as a result of intestinal obstruction or ascites. Circling often occurs where balance is disturbed.

Initially, the rat exhibits increased angry or aggressive vocalization, especially on handling. There is a gradual reduction in vocal response as the pain or stress continues, and movement ceases unless a sudden painful

stimulus is experienced. Hypothermia indicates significant deterioration in the animal's condition. A pale appearance indicates anemia or blood loss.

Key Signs: vocalization, struggling, licking/guarding, weight loss, piloerection, hunched position, hypothermia.

Guinea Pigs

Guinea pigs are alert, but timid and apprehensive animals which will try to avoid capture and restraint. Rarely is there any aggression towards humans. Any sign of acceptance indicates the animal is unwell. Loud vocalization will accompany even minor and transient pain. Guinea pigs often appear sleepy when in pain. Initially, there is an increased level of response to painful or stressful stimuli. However, this gradually subsides and the animal becomes unresponsive. It gradually appears more apprehensive. The eyes may be sunken and dull. The respiratory rate increases as a painful or stressful stimulus increases or continues; where the respiratory system is affected, respirations become increasingly forced and laboured. Often loss of weight occurs as well as hair loss, scaly skin, and dehydration. Where the gastrointestinal tract is affected there may be evidence of diarrhea. There is a tendency to 'barbering' under dietary stress with failure to eat or drink. Group aggression may occur and damage to the skin of the back may result from fighting. There is excessive salivation where abnormal teeth cause eating difficulties, a tendency to an arched back where abdominal pain is present, and failure of the "righting" reflex in seriously ill animals. There may be pain associated with locomotion, lameness, and careful gait due to sore feet in older animals.

Key Signs: withdrawal, vocalization, failure to resist restraint, staring coat, unresponsive.

Mongolian Gerbils

Gerbils are highly active, nervous animals and usually attempt to avoid restraint. Signs of pain and distress are difficult to assess, as gerbils apparently object to any interference. There is an increased level of response under painful or stressful stimuli. Ocular discharge is common. Under stressful conditions, the eyelids may be half closed, with dry matting of the eyelids. The increased respiratory rate associated with lung involvement is difficult to assess by eye. Loss of coat condition occurs. Loss of hair from the tail may be seen in overcrowded animals. Facial lesions and sores may result from excessive burrowing in the corners of the cage.

Dehydration is rarely seen, since the gerbil's normal metabolism enables full utilization of the water content of the diet. Only small quantities of urine are voided under normal conditions. Feces are normally firm, dry pellets. Constipation is rare. Diarrhea, if it occurs, may quickly lead to death from fluid loss.

Gerbils are normally extremely active and nervous. Under severe stress, there may be temporary collapse and apparent shock syndrome; however, the animals recover, given time. Changes in exploratory behaviour and increased aggressive response may occur. A hunching up and arching of the back may be observed, especially with abdominal involvement. Abnormal gait is associated with locomotion or abdominal involvement.

Key Signs: hunched appearance, weight loss, shock syndrome.

Syrian (golden) Hamsters

Under normal conditions, hamsters will sleep for long periods during the day, and little activity will be seen. They often appear aggressive towards their cage mates and emit loud screeching noises, disproportionate to the degree of interference, when handled. This response increases under painful or stressful stimuli. Ocular discharge is commonly associated with stress. An increased respiratory rate is associated with lung involvement. Loss of coat condition is seen where the diet is deficient in Vitamin E and short chain fatty acids. Loss of body condition occurs with decreased food and water intake. Constipation is unusual in the hamster. Diarrhea, when it occurs, is profuse and liquid, staining the perineal region. Increasing depression takes place when the animal is left undisturbed. Daytime sleep periods may be extended and increasing lassitude may be seen except when the animal is being handled. Exploratory behaviour is reduced. A hunched appearance is noted, as is an unwillingness to move, especially where abdominal organs are involved. Lateral recumbency can indicate that the animal is moribund. Normal gait is affected when pain is associated with locomotion. Stilted movements are sometimes associated with abdominal involvement, e.g., ascites following cirrhosis of the liver.

Key Signs: weight loss, hunched appearance, increased aggression or depression, extended sleep periods.

Rabbits

The rabbit presents significant difficulties in recognition of pain and distress, as it often quietly accepts apparently painful or distressing procedures; this may relate to its feral behaviour where concealment is important to survival. Even healthy rabbits may not move frequently or indulge in exploratory behaviour. Pain is usually characterized by a reduction in food and water intake (and thus weight loss and dehydration) and limited movement. Although rabbits frequently become ill and distressed without showing much apparent loss of condition, careful examination will reveal a loss of muscle mass on the lower back. Ocular discharge is a common response to stress in the rabbit, with protrusion of the nictitating membrane.

Under continued pain or stress, rabbits assume a 'sleepy' appearance. The animal exhibits increased depression, progressive unawareness and lack of response. The animal will often face the back of cage, away from light. An increased respiratory rate is associated with either apprehension or lung involvement. There is fecal staining of the coat. Night time pellet production may be interrupted. Constipation and diarrhea are common responses to pain or stress. Excessive self-grooming may precipitate hair balls in the stomach. Where foot soreness is involved, weight may be thrown forward or backward to reduce discomfort. Body stretching and lying flat are common indications of abdominal discomfort. Pain may be associated with locomotion, especially with sore feet.

Key Signs: reduced eating and drinking, faces towards back of cage, limited movement, apparent photosensitivity.

Horses

Periods of restlessness are noted in horses experiencing pain or distress. Food is held in the mouth uneaten. The horse exhibits an anxious appearance with dilated pupils and glassy eyes; increased respiration and pulse rate with flared nostrils; profuse sweating and a rigid stance. In prolonged pain, behaviour may change from restlessness to depression with the head lowered. In pain associated with skeletal damage, limbs may

be held in unusual positions and there is a reluctance to move, with the head and neck "fixed." There may be a pain-induced tachycardia.

In abdominal pain, a horse may look at, bite or kick its abdomen; it may get up and lie down frequently; walk in circles; or roll. When near collapse, the horse may stand very quietly, rigid and unmoving, but with signs of deteriorating circulatory status such as mucosal cyanosis and prolonged capillary filling time. Horses in pain generally show a reluctance to be handled.

Key Signs: anxious appearance, restlessness, biting at site of pain, depression, fixed position.

Cattle

Cattle in pain often appear dull and depressed, with the head held low and showing little interest in their surroundings. There is inappetence, weight loss and, in milking cows, a sudden drop in milk yield. Severe pain often results in rapid shallow respirations. On being handled, they may react violently or adopt a rigid posture designed to immobilize the painful region. Grunting and grinding of the teeth may be heard. Acute pain may be associated with bellowing. Generally, signs of abdominal pain are similar to those seen in the horse, but are less marked. Rigid posture may lead to a lack of grooming due to an unwillingness to turn the neck. In acute abdominal conditions, such as intestinal strangulation, the animal adopts a characteristic stance with one hind foot placed directly in front of the other. Localized pain may be indicated by persistent licking of an area of skin, or kicking at the offending area.

Key Signs: dull, depressed, inappetence, grunting, grinding of the teeth, rigid posture.

Sheep and Goats

In general, signs of pain in these species are similar to those in cattle. Changes in posture and movement are apparent, and a change in facial expression may be indicative of pain or distress. There is a general reluctance to move. Goats are more likely than cattle to vocalize in response to pain. Grinding of the teeth and grunting are also heard. Sheep, in particular, tolerate severe injury without overt signs of pain or distress. Following procedures such as castration and tail docking, lambs may show signs of discomfort such as standing up and lying down repeatedly, tail wagging, occasional bleating, neck extension, dorsal lip curling, kicking, rolling and hyperventilation.

Key Signs: rigid posture and reluctance to move.

Pigs

Pigs in pain may show changes in gait and posture. They normally squeal and attempt to escape when handled; however, these reactions may be accentuated when the animal is in pain. Adult pigs may become aggressive. Squealing is also characteristic when painful areas are palpated. Handling of chronic lesions may not elicit signs of pain. Pigs will often be unwilling to move and may hide in bedding if possible.

Key Signs: vocalization and the lack of normal social behaviour may be helpful indicators of a pig in pain.

Birds

Birds in pain may show escape reactions with vocalization and excessive movement. Head movements increase in extent and frequency. There may be an increase in heart and respiratory rates. Prolonged pain will result in inappetence and inactivity with a drooping, miserable appearance. The eyes may be partially closed, the wings held flat against the body, and the neck retracted. When handled, the escape reaction may be replaced by a state of tonic immobility. Birds with limb pain will avoid use of the affected limb and will "guard" it from extension.

Key Signs: escape reactions, atonic immobility, inappetence, avoidance of use of pain site.

Reptiles

Acute pain in reptiles may be characterized by flinching and muscle contractions. There may be aversive movements away from the unpleasant stimulus, and attempts to bite. More chronic and persistent pain may be associated with anorexia, lethargy and weight loss, although it is difficult to associate any of these signs of lack of well-being specifically with pain.

Key Signs: flinching and muscle contractions, weight loss, anorexia.

Fishes

It is difficult to determine the nature of the response to pain in fish. Although they exhibit a pronounced response to injuries or to contact with irritants, their response to chronic stimuli may be small or absent. Fish with severe wounds which would cause immobility in a mammal, will often appear to behave completely normally, even resuming feeding. Fish will react to noxious stimuli, such as that administered by a hypodermic needle, by strong muscular movements. When exposed to a noxious environment, such as a strong acid, they show abnormal swimming behaviour with attempts to jump from the water, their colouring becomes darker and their opercular movements become more rapid. Such effects are indicative of some degree of distress; however, it is not possible to describe these unequivocally as signs of pain.

F. ANALGESIC AGENTS

The appropriate use of analgesics during or after a painful procedure is an integral part of a protocol plan. The following general information, as well as details of administration and dosages by species, are given in several references (Sawyer, 1985; Sackman, 1991; Flecknell, 1984) in addition to the anesthetic textbooks listed in the additional reading.

The opioids (morphine-like drugs) are the most widely used analgesic agents. Opioids act by binding to specific receptors. The main classes of receptors are mμ.

1. Opioid Agonists

Opioids produce potent hypnotic and analgesic effects including significant depression of the cardiovascular and respiratory systems and an alteration in the thermoregulatory mechanism. The euphoria and addiction associated with opioids in human is not a problem in animals when the drugs are used properly. Some opioids induce vomiting in dogs and NHP and rapid intravenous injection may occasionally result in an

excitatory phase in most species. In farm animals, as well as in the cat and mouse, the effects of opioids are less predictable, and undesired excitement may occur. Avoidance of the excitement phase in species with an enhanced sensitivity to opioids can often be achieved by the use of very low dosages (Green, 1982).

Opioids used in the veterinary medicine include morphine, meperidine, fentanyl, oxymorphone, etorphine (M99) and carfentanil. They are pure or relatively pure mμ agonists and are all good analgesics.

a) **Morphine** is most frequently used clinically for the control of post-operative pain in dogs and NHP, providing up to four hours of pain relief. In dogs, its use is complicated by undesirable gastrointestinal effects. Intravenous bolus administration in dogs may cause histamine release which may contribute to morphine's hypotensive action (Hall and Clarke, 1991). As a pre-medicant, morphine's stimulatory effect on the vagus nerve may induce bradycardia, unless atropine is given in advance. Profound respiratory depression occurs rapidly and is dose-related. Intracranial and intra-ocular pressure are increased (Sackman, 1991).

b) **Meperidine** has effects similar to morphine and is the drug of choice for premedication in the dog, as very little gastrointestinal stimulation is induced. However, severe hypotension may occur after intravenous use. As analgesia lasts only one to two hours, it is not recommended for alleviating post-surgical pain. This drug has also proven useful as a post-operative sedative for NHP and horses.

c) **Fentanyl** is a very potent short-acting opioid. It is combined with droperidol to make a neuroleptanalgesic that provides profound analgesia. New synthetic compounds of fentanyl include alfentanil, which has an ultrashort half-life, and sufentanyl with a half-life shorter than fentanyl, but with fewer peripheral side effects (Flecknell, 1984).

d) **Oxymorphone** is more potent than morphine and produces more sedation in the dog than morphine or meperidine. Post-surgical pain relief lasts two to six hours. Cardiovascular stability is much greater than with the other opioids. It is frequently combined with diazepam or acepromazine for anesthesia and analgesia in old or sick animals. An anticholinergic should be given to prevent severe bradycardia.

e) **Etorphine (M99)** is an extremely potent morphine derivative with a high tendency to produce initial excitement followed by depression. Because of its potency, it has been widely used in dart guns for the capture and immobilization of zoo animals and wild game (Fowler, 1986; Green, 1982). The drug has also been used successfully in certain cold blooded animals (Fowler, 1986; Green, 1982). It is extremely dangerous to humans; therefore, diprenorphine (M5050) must be available for immediate reversal should accidental human exposure occur (Fowler, 1986).

f) **Carfentanil** is currently preferred to etorphine by many zoo veterinarians because of its higher potency, which allows administration by swabbing or spraying of the buccal or nasal mucosa. It can be reversed by cyprenorphine (M285) or diprenorphine (M5050) (Lumb and Jones, 1984) and naltrexone. Carfentanil can be fatal in humans if accidentally injected (partial immobilizing dose).

2. Opioid Agonist/Antagonists

The search for analgesic agents with fewer side effects than pure mμ agonists led to the development of partial mμ agonists and kappa agonists such as butorphanol and buprenorphine. This group of drugs may also be used to reverse the depressant effects of an opioid while preserving the analgesic qualities.

a) **Butorphanol** is a synthetic analgesic with five times the potency of morphine. A degree of sedation occurs and the respiratory depression has a ceiling effect that does not increase with higher doses. Car-

diovascular effects are minimal and it is a poor opioid antagonist (Dyson, 1990). Analgesia lasts two to five hours following subcutaneous injection, and may be accompanied by some dysphoria.

b) **Buprenorphine** is a long-acting analgesic that antagonizes the depressant effects of the opioid agonists, while still maintaining long-term post-operative analgesia of 8-12 hours in many species (Flecknell, 1984).

c) **Pentazocine lactate** is a poor analgesic with a very short duration (approximate half-life in the dog of 22 minutes). It has minimal cardiovascular effects and is a mild respiratory depressant.

d **Nalbuphine** is slightly less potent than morphine, with a wide safety margin and minimal cardiovascular and respiratory depression. Analgesia lasts three to eight hours. It has also been used as an opioid antagonist to reverse sedation and respiratory depression of opioids while maintaining analgesia (O'Hair, Dodd, Phillips *et al.* 1988).

3. Opioid Antagonists

Naloxone hydrochloride, an effective antagonist, is available to reverse the effects of opioids (this includes the analgesia). It has no agonist properties and does not produce respiratory or cardiovascular depression. It has an antagonistic effect for one to four hours, and can be used to reverse the effects of any of the opioid agonist/antagonist group. Nalorphine or diprenorphine must be available when using etorphine, in case of accidental human administration (Lumb and Jones, 1984). Naltrexone is a long-acting derivative of naloxone. At present, its use in veterinary medicine is limited; however, should a pure long-acting antagonist be required, it could prove useful (Hall and Clarke, 1991).

4. Non-steroidal Anti-inflammatory Drugs (NSAIDS)

These agents produce analgesia by reducing inflammation and thus peripheral sensitization. They have little, if any, central analgesic action. Side effects are interference with platelet and renal function and gastric ulceration. Cats metabolize these agents slowly and must be dosed infrequently to prevent toxicity. Those commonly used in dogs are the carboxylic acid group (aspirin, naproxen, meclofenamic acid, flunixin) and the enolic acids (phenylbutazone, dipyrone, and piroxicam). In cats aspirin, phenylbutazone and dipyrone are frequently used at low dosages (Sawyer, 1985).

a) **Aspirin** relieves pain associated with peripheral inflammation, but is ineffective for visceral pain. In cats, it should be given only every 48 to 72 hours.

b) **Naproxen** is used when aspirin does not relieve the pain, and the once daily administration is convenient. As is the case with aspirin, gastric ulcers are listed as a side effect.

c) **Meclofenamic acid** is popular for treating musculoskeletal pain that is refractory to aspirin. It has 1.5 times the potency of phenylbutazone.

d) **Flunixin** is reported to have greater analgesic properties than phenylbutazone, meperidine or codeine, and is used for osteoarthritic pain. Its use in large animals is well established. Its use in small animals is expanding. In dogs, it has the potential to produce serious gastrointestinal effects (bleeding) if a maximum of three doses is exceeded (Hall and Clarke, 1991).

e) **Phenylbutazone** relieves musculoskeletal pain, but has been associated with blood dyscrasias, gastrointestinal disturbances, nephropathies and hepatitis.

f) **Dipyrone** is an analgesic, antipyretic, anti-inflammatory that also may cause blood dyscrasias with prolonged use.

g) **Piroxicam** is popular in human medicine for its once daily dosage and very effective relief of osteoarthritic pain. Toxicity is similar to that of other non-steroidal anti-inflammatory drugs (Sackman, 1991).

5. Analgesia provided by Local Anesthetics

As an alternative to systemically administered agents, analgesia can be provided by use of local anesthetics. Bupivacaine, a long-acting local anesthetic, is preferred for post-operative analgesia (Flecknell, 1992). It can either be injected around specific nerve trunks which supply the surgical site, or infiltrated into the muscular and subcutaneous tissue layers during closure of a surgical incision. Use of local anesthesia to infiltrate the surgical wound is a simple technique that can provide 4-12 hours analgesia.

Selective blocking of the intercostal nerves two to three intercostal spaces on either side of a thoracotomy incision has recently been recommended for relief of pain following thoracotomy in dogs. Bupivicaine hydrochloride is used before incision closure, and provides four to five hours of analgesia. The respiratory pattern of dogs recovering from thoracotomies is not significantly changed. This provides a distinct advantage over opioid analgesics which may cause significant respiratory depression. This technique, while providing relief of pain associated with the surgical incision, does not elevate visceral (intrathoracic) pain (Sackman, 1991).

6. Neuroleptanalgesics

Neuroleptanalgesia is a state of sedation and analgesia produced by the combined use of a tranquillizer (neuroleptic) and an opioid. Minor surgery can be performed; however, the patient remains rousable and responds to certain stimuli. Moderate respiratory depression occurs, and muscle relaxation tends to be poor, but can be counteracted by combination of the neuroleptanalgesic with a benzodiazepine (Flecknell, 1987). The most commonly used preparation is Innovar-Vet, (droperidol 20 mg/ml and fentanyl 0.4 mg/ml), which should not be confused with Innovar, prepared for human use (droperidol 2.5 mg/ml and fentanyl 0.0005 mg/ml).

Innovar-Vet has been used extensively in the dog and is reported useful in many other species. It has a wide margin of safety, is well tolerated by animals in poor physical condition, and is partially reversible with naloxone. Significant bradycardia may be avoided by prior use of atropine. Its use is contra-indicated in the cat, cow, horse and sheep due to CNS stimulation. Animals remain responsive to auditory stimuli, and aggressiveness during recovery and other disposition changes lasting several days have been reported in the dog (Lumb and Jones, 1984).

A variety of other opioids and tranquillizers can be combined to produce neuroleptanalgesia; among these, mixtures of morphine/promazine and etorphine/acepromazine have proven useful in a variety of animals (Flecknell, 1987). Meperidine/acepromazine (Lumb and Jones, 1984) and oxymorphone/ acepromazine (Short, 1987) have also been used for the dog and cat.

G. AREAS FOR FUTURE STUDY

Farm animal welfare, transgenic animals, amphibians, reptiles and invertebrates all constitute areas of increasing concern.

The welfare of domestic animals is of great importance, and it is claimed by Spira (1986) that, because of their numbers, 95% of all animal suffering takes place in intensive management ("factory farming") practices; thus, every 1% reduction in their suffering will accomplish more than all other protection campaigns for other species of animals put together. Animal behaviour and applied animal ethology are increasingly becoming areas of great importance (Maxie, 1987; Fraser, 1988; Fraser and Broom, 1990; McKeown and Luescher, 1988; Duncan, 1992).

Another area that will become of increasing concern is the production of transgenic animals (Jaenisch, 1988; Baker, 1988; Ewing, 1990; Cross, 1990; McLaren, 1990; Page, 1990) and the possible pain and distress that may be caused them. Their uses in research have recently been discussed (Saffer, 1992; Merlino, 1991) as well as management of their colonies (Geistfeld, 1991). The CCAC, foreseeing the need for guidelines on animal biotechnology, has recently established a committee comprising knowledgeable scientists, and representatives of industry and animal welfare, to develop such guidelines to include embryo manipulation, fetal research and transgenic animals. Agriculture Canada is also considering a proposed framework for regulating the production and use of transgenic animals (Sethi, 1992).

Only recently has the analgesia, anesthesia and euthanasia of amphibians, reptiles and fish been addressed (UFAW, 1989; Johnson, 1992; Iwama, 1992; Davis, 1992). Evaluation of pain and stress has been discussed in reptiles (Lance, 1992), cold-blooded vertebrates (Arena and Richardson, 1990; Fiorito, 1986), and birds (Gentle, 1992). It has been contended that fish can experience pain and fear to a degree which can be compared with human reactions (Anon., 1988).

In addition to studies involving vertebrates, the use of invertebrates in research is governed in Canada by CCAC's Categories of Invasiveness found elsewhere in this *Guide*. It states that cephalopods and some other higher invertebrates have nervous systems as well developed as some vertebrates and therefore may warrant inclusion in the Categories under B, C, D and E. In Great Britain, only one species of cephalopod, the common octopus (*Octopus vulgaris*), is only now being brought under the Animals (Scientific Procedures) Act (Anon., 1993). Handling, anesthesia and surgery of cephalopods are outlined in a recent Universities Federation for Animal Welfare publication (Boyle, 1991).

Other areas of concern to the scientific community and ACCs include, for example, the effects of blood loss (McGuill, 1989) and the use of Freund's Complete Adjuvant (FCA) (Broderson, 1989). An expert committee of CCAC has been established especially to examine this latter issue and investigate replacements for FCA. The *CCAC policy statement on: acceptable immunological procedures* appears elsewhere in this *Guide*, and are revised as new knowledge becomes available.

In the development of research in the future, the scientist should consider the importance of refinement and should address those studies which are known to cause the most pain and suffering (Rowsell, 1992).

We have a considerable distance to go before animals need no longer be used. However, as Medawar (1972) notes: "We must grapple with the paradox that nothing but research on an animal will provide us with the knowledge that will make it possible for us, one day, to dispense with the use of them altogether." And to paraphrase Wall (1984): "So long as one animal remains in pain and we cannot help, our knowledge of pain remains inadequate."

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XI ANESTHESIA

This section is currently under revision. Please also see the relevant animal type guidelines.

February 2017

This chapter provides guidance and information on anesthesia and relief of pain in experimental animals. It is not meant to be comprehensive, and non-veterinary users should consult with a veterinary anesthesiologist or laboratory animal veterinarian when such drugs are to be administered. Information on common dosages and means of administration of analgesic, tranquillizing and anesthetic agents are given in the Appendices. **The agents described in this chapter are all prescription and/or controlled drugs. Non-veterinary users may obtain prescription drugs from a licensed veterinarian, and should contact the Bureau of Dangerous Drugs, Health and Welfare Canada regarding the use of controlled drugs in research**.

Methods for assessing the depth of anesthesia vary with the species and the drug, and are discussed in Green (1982). Specific details are available in the textbooks and review articles listed in the references.

A. MANAGEMENT OF ANESTHESIA

1. General

Sedatives, analgesics, and general anesthetic agents must be utilized for the control of pain and distress unless contrary to the achievement of the objectives of the study. **In the latter case, approval of the institutional Animal Care Committee (ACC) is mandatory**.

Anesthetic agents frequently affect the cardiovascular, respiratory and thermoregulatory mechanisms, in addition to the central nervous system (CNS). Every effort should therefore be made to maintain the circulation, respiratory function and the body temperature of the anesthetized subject within normal physiological limits (Parker and Adams, 1978). Endotracheal intubation ensures that the airway remains patent and free from obstruction.

Hypothermia may occur during exposure to anesthetic gases and during intra-abdominal surgery, particularly in small animals. This may result in death or a greatly prolonged recovery from the anesthetic. The degree of hypothermia may be reduced by placing the animal on a circulating warm water blanket or other device that assists in conserving body heat (Muir and Hubbell, 1989; Lumb and Jones, 1984; Flecknell, 1987).

2. Handling the Patient

The animal should always be handled gently and calmly in order to minimize struggling and fright. Prolonged excitement will disturb the circulatory and metabolic state of the patient and induce a degree of shock. Furthermore, attempts to anesthetize a struggling animal present physical problems in addition to enhancing the likelihood of an abnormal response to the anesthetic agents. These points are particularly important when restraining and anesthetizing wild animals (Fowler, 1986).

3. Fasting

Cats, dogs, nonhuman primates (NHP), ferrets and pigs should receive no food during the 8-12 hours prior to induction of anesthesia in order to minimize the risk of vomiting during induction or recovery from anesthesia (Flecknell, 1987). Very small or immature mammals should be subjected to a much shorter fast, usually from two to four hours, due to their higher metabolic rate. Withholding food from ruminants for 12-24 hours may help reduce the incidence of ruminal tympany (bloat); however, reduction of the volume of digesta in the rumen requires much longer periods of starvation (36-72 hours). Water should be withheld for 12 hours before surgery to prevent gorging and increase in the volume of rumen contents. Pre-anesthetic fasting of small rodents or rabbits is unnecessary since they do not vomit during induction (Flecknell, 1987). Guinea pigs should be fasted 6-12 hours before anesthesia to allow time to clear their mouths of the food bolus commonly carried at the base of the tongue. Small birds often are not fasted at all, in order to maintain energy during the stress of the procedure (Muir and Hubbell, 1989; NRC [U.S.], 1977). Fasting pregnant animals of all species, particularly ruminants, can produce severe metabolic disturbances. Other than ruminants, every animal should be provided with drinking water until approximately one hour before induction of anesthesia (Flecknell, 1987).

4. Anticholinergics

Anticholinergics block parasympathetic stimulation to the cardiopulmonary system and reduce salivary secretion. They are used in combination with sedatives and analgesics as pre-medication to general anesthesia. Anticholinergics are no longer routinely administered to each animal undergoing anesthesia. They are administered selectively, after a pre-anesthetic clinical examination of the animal, and according to the determined needs of the individual patient, the anticipated response to the anesthetic medication, and the tendency to develop bradycardia or excessive salivation (Short, 1987).

a) **Atropine** is the most commonly used anticholinergic agent; however, routine administration is controversial due to the high incidence of associated cardiac dysrhythmias (premature ventricular contractions and sinus tachycardia) (Lumb and Jones, 1984; Flecknell, 1987). It is most commonly recommended for use in NHP, pigs, guinea pigs and chinchillas in order to decrease airway secretions, but should not be given if a marked tachycardia is already present (Green, 1982).

b) **Glycopyrrolate** is a quaternary ammonium anticholinergic. Although its mechanism of action is similar to that of atropine, its effects last longer. Glycopyrrolate seems to be less likely than atropine to produce sinus tachycardia (Paddleford, 1988). It does not penetrate the CNS because of its difficulty in crossing the blood-brain barrier. It is also less likely than atropine to cross the placental barrier, indicating that it is a selective peripheral anticholinergic agent (Short, 1987).

B. TRANQUILLIZERS AND SEDATIVES

Tranquillizers produce a calming effect without sedation (Green, 1982). They have no analgesic properties, and even at the high doses that cause ataxia (failure of muscular co-ordination) and depression, animals are easily aroused. Tranquillizers are useful over a wide range of species, often in combination with other drugs, to lessen the dose of a general anesthetic and produce a smoother induction and recovery. Sedatives are used to produce drowsiness and reduce fear and apprehension (Flecknell, 1987).

The psychological state of the animal prior to administration of tranquillizers may markedly affect the degree of sedation achieved. Animals that are vicious, intractable and in a state of excitement may not become manageable except with very high (incapacitating) doses.

a) **Phenothiazines (promazine, acepromazine)** produce sedation and reduce the dose of drugs needed for general anesthesia, but also cause moderate hypotension and hypothermia (Lumb and Jones, 1984; Flecknell, 1987).

b) **Benzodiazepines (diazepam, midazolam)** produce variable sedation depending on the species (Lumb and Jones, 1984; Flecknell, 1987; Green, 1982). They are good muscle relaxants and have no marked undesirable side effects. Diazepam cannot be mixed with other water soluble agents, while midazolam can (Flecknell, 1987).

c) **Butyrophenones (azaperone, droperidol)** have similar effects as phenothiazines, but are more potent and cause less hypotension (Lumb and Jones, 1984; Flecknell, 1987; Green, 1982). Droperidol is used in combination with an opioid to produce neuroleptanalgesia (Flecknell, 1987).

d) **alpha-2-adrenergic agonists (xylazine, detomidine, medetomidine)**

i) **Xylazine (Rompun)** is a sedative and analgesic that acts as a CNS depressant and induces muscle relaxation by inhibiting the transmission of impulses in the CNS. Its major use in laboratory animal anesthesia is in combination with ketamine to produce surgical anesthesia. This combination has been used in dogs, cats, NHP, large farm animals and wild animals (Olson and McCabe, 1986; Lumb and Jones, 1984). It causes respiratory depression and a bradycardia which may progress to heart block (Flecknell, 1987). It also increases the susceptibility of the myocardium to circulating catecholamines during halothane anesthesia (Short, 1987). Vomiting may occur in dogs and cats, and gas accumulation due to gastrointestinal atony (lack of normal tone or strength) may be a problem in both large dogs and ruminants (Lumb and Jones, 1984). Xylazine produces profound physiological changes and its safe use requires knowledge of these effects which are often species specific. Yohimbine and 4-aminopyridine reverse most of the effects of xylazine without relapse in many species (Jernigan, Wilson, Booth *et al.* 1988), with the exception of NHP (Lynch and Line, 1985).

ii) **Detomidine** is marketed for use in horses, and has the same cardiovascular effects (bradycardia and hypotension) as xylazine, but is more potent and has a longer-acting effect.

iii) **Medetomidine** is being evaluated for use in dogs and cats, and has cardiovascular effects similalr to xylazine. A medetomidine/ketamine combination in cats has the advantage over xylazine/ketamine in that a lower dose of ketamine is needed, the duration of action is longer and the analgesia better (Verstegen, Fargetton, Donnay *et al.* 1990).

C. GENERAL ANESTHETICS

1. Dissociative Anesthetics

Dissociative anesthetics produce a state of chemical restraint and anesthesia characterized by muscle rigidity and dissociation of the mind from the external environment. The eyes remain open, necessitating use of protective ointment. Various reflexes, including the blinking reflex and laryngeal reflex, remain intact, and adequate respiration is normally maintained. An increase in heart rate, blood pressure and intracranial pressure frequently occurs. Thus, their use is contra-indicated in head injuries or intra-ocular surgery. While the use of dissociative anesthetic agents is most common with NHP and cats, they have also been used in most other mammalian species as well as birds and reptiles (Jones, 1977). Combination with a tranquillizer is recommended in most species to enhance analgesia and reduce muscle tone (Flecknell, 1987; Green, 1982).

a) **Ketamine hydrochloride** is the most commonly used member of this group. Depth of anesthesia is dose related. Side effects include excessive salivation which may be controlled with atropine (Flecknell, 1987), a tendency toward convulsions, and a recovery characterized by excitement, disorientation, and hallucinations which may be controlled by tranquillizers and barbiturates (Lumb and Jones, 1984). In all cases, a smooth recovery will be facilitated if the patient is left undisturbed in a quiet, darkened environment.

b) **Tiletamine** is similar to ketamine, but is longer lasting and more potent; therefore, a smaller dose volume is needed. It is most commonly sold in combination with the tranquillizer zolazepam (Telazol), which improves muscle relaxation, CNS depression, and emergence from anesthesia. It also prevents tiletamine seizures. Cats may take 12-36 hours to be clinically "normal" following tiletamine anesthesia. Tiletamine/zolazepam has proven successful in rats and gerbils, but not in mice or hamsters (Hrapkiewicz, Stein and Smiler, 1989). Tiletamine causes nephrotoxicity in rabbits (Brammer, Doerning, Chrisp *et al.* 1991; Doerning, Brammer, Chrisp *et al.* 1992).

2. Barbiturates

Barbiturates differ from tranquillizers and opioids in that increasing the dose progressively increases the depth of depression until a state of general anesthesia is reached. They are poor analgesics. Their primary use is in the induction and/or maintenance of general anesthesia. Barbiturates are potent respiratory depressants and their effects on the cardiovascular system are variable. At intermediate dosages, excitement is sometimes induced (Green, 1982).

The barbiturates are grouped according to duration of action into long acting (e.g., phenobarbital), short- or intermediate-acting (e.g., pentobarbital) and ultrashort-acting (e.g., thiopental, thiamylal, methohexital) (McLaughlin, 1988). The short- and ultrashort-acting drugs are commonly used for anesthesia. Anesthetic duration varies widely with species; however, in general, short/intermediate barbiturates produce approximately 2-3 hours of anesthesia and ultrashort barbiturates range from 10 to 20 minutes (McLaughlin, 1988).

Variation in dose response and duration of effect of barbiturates is extreme within and between species (Olson, 1986a; Green, 1982; McLaughlin, 1988). The following are examples of the variation found with pentobarbital (intermediate) anesthesia:

i) cats frequently having a considerably prolonged sleeping time (McLaughlin, 1988);

ii) mice on hardwood bedding take almost twice as long to recover as mice on softwood bedding, and male mice sleep longer than female mice (McLaughlin, 1988);

iii) the anesthesia produced in adult horses and cattle is of relatively short duration; however, the recovery period is long and difficult (Lumb and Jones, 1984).

Whenever possible, barbiturates should be administered intravenously, slowly, to effect. Administration by other routes is far less satisfactory, as dosage is more difficult to judge and the anesthetic effects are less predictable. Any of the barbiturates can cause skin sloughing if perivascular injection accidently occurs (McLaughlin, 1988).

Although barbiturates are commonly used, they are often poor choices for general anesthesia due to poor analgesia, profound cardiovascular effects, high mortality and numerous external factors that can affect dose response and sleeping time. Adequate anesthesia can be obtained by combining a barbiturate with a tranquillizer, sedative or an opioid (Olson, 1986a; Lumb and Jones, 1984; McLaughlin, 1988).

3. Chloralose

Chloralose may be used for **non-survival experiments** requiring prolonged anesthesia and **minimal surgical interference** (Flecknell, 1987; Holzgrefe, Everitt and Wright, 1987). There is disagreement about whether chloralose is a true anesthetic agent or a hypnotic with little analgesic action. It is used primarily for physiological studies to preserve the vagal and central baroreceptor reflexes or in acute cardiovascular studies to preserve myocardial function. While chloralose is generally considered to have no application in survival studies or in clinical veterinary medicine (Lumb and Jones, 1984), one recent study used chloralose repeatedly over a long time period in puppies without any signs of toxicity (Grad, Witten, Quan *et al.* 1988).

4. Urethane (Urethan, Ethyl Carbamate)

Urethane produces long periods of anesthesia, has a wide safety margin and little effect on normal blood pressure and respiration. It produces sufficient analgesia to allow surgical manipulations (Flecknell, 1987). **However, the drug should be handled with extreme care as it is considered to be cytotoxic, carcinogenic and immunosuppressive.** It also causes profound changes in gastrointestinal function and is stimulatory to the hypothalamus and pituitary (Olson, 1985). **Animals should not be allowed to recover following urethane anesthesia.**

5. Saffan

Saffan is a combination of two steroids, alphaxalone and alphadolone dissolved in a surfactant (vehicle), Cremaphor EL, to solubilise it. It is administered intravenously or intramuscularly, although the latter route gives more unpredictable results. Muscle relaxation is good, and recovery rapid. It is rapidly metabolized and is an excellent agent for long-term maintenance (Flecknell, 1987). It has been used for the cat, pig, large farm animals, small NHP, rodents, birds and exotics (Lumb and Jones, 1984; Flecknell, 1987; Green, 1982). It is not recommended in the dog due to the associated massive histamine release caused by the Cremaphor EL vehicle that often occurs (Flecknell, 1987). Saffan must not be used with barbiturates (Flecknell, 1987).

6. Tribomoethanol (Avertin)

The use of Avertin is controversial because of the wide variation in results between laboratories. Although no longer available in Canada, it may be introduced in a different formulation. Purchased as a powder, it must be dissolved in amylene hydrate and then diluted with distilled water at 40°C immediately prior to use.

Great care must be taken to use only fresh solutions as it decomposes very rapidly in light or temperatures above 40°C, producing byproducts that are severe tissue irritants. In rodents, it is given intraperitoneally (Green, 1982), resulting in good muscle relaxation and moderate respiratory and cardiovascular depression (Flecknell, 1987; Green, 1982); however, post-operative fatalities are often high due to peritoneal adhesions. Even if a freshly prepared solution is used, mortality is often high after administration of a second anesthetic at a later date (Green, 1982; Norris and Turner, 1983).

7. Non-specific Injectable Anesthetic Antagonists

Several agents have the ability to reverse many of the effects of non-opioid injectable anesthetics through non-specific antagonistic properties.

a) **Yohimbine** blocks central alpha-2-adrenoreceptors, and partially antagonizes barbiturates, xylazine, ketamine, benzodiazepines and phenothiazines (Fowler, 1986; Lumb and Jones, 1984).

b) **4-aminopyridine (4-AP)** partially antagonizes xylazine, ketamine and barbiturates. Yohimbine and 4-AP are often combined for a more effective reversal (Lumb and Jones, 1984).

c) **Doxapram** is a respiratory stimulant and not a reversal agent per se; however, it has been used to partially antagonize the respiratory depression produced by barbiturate anesthesia in dogs (Hatch, Jernigan, Wilson *et al.* 1986).

8. Inhalant Anesthetics

Inhalant anesthetics have the advantage of requiring minimal detoxification by the body, as they are exhaled through the lungs, and the level of anesthesia can be easily and rapidly controlled. However, their use requires specialized equipment for administration, and constant monitoring of the patient (Stimpfel and Gershey, 1991). Some are explosive or inflammable, or tissue irritants. Chronic exposure to some agents is hazardous to the health of the operating room personnel (Lumb and Jones, 1984).

The speed of induction and recovery depend on the solubility of the anesthetic in blood. Highly soluble anesthetics (methoxyflurane) are slow to reach an equilibrium in the blood; therefore, induction and recovery are prolonged. Insoluble anesthetics (halothane) reach an equilibrium rapidly, making manipulation of anesthetic depth easier, but also more hazardous due to the potential for rapid overdose (Flecknell, 1987).

The use of inhalation anesthesia requires the following equipment:

i) a vaporizer for the volatile anesthetics;

ii) a source of carrier gas (usually oxygen or air);

iii) a breathing system from which the anesthetic mixture is inhaled;

iv) a mask or endotracheal tube for connecting the breathing system to the patient (Sedgwick and Jahn, 1980; Gilroy, 1981). Exceptions are discussed with the individual agents. Numerous simple systems have been devised and reported in the laboratory animal literature for use in small laboratory animals (Dudley, Soma, Barnes *et al.* 1975; Skartvedt and Lyon, 1972; Rich, Grimm, Wong *et al.* 1990; Olson, 1986b; Levy, Zwies and Duffy, 1980; Mulder and Hauser, 1984).

Unnecessary exposure of personnel to gases from volatile anesthetics must be avoided by use of appropriate scavenger systems (Muir and Hubbell, 1989). Several reports have suggested a health risk associated with

prolonged and repeated exposure to low concentrations of halothane (hepatocellular toxicity), methoxyflurane (renal toxicity), nitrous oxide (neurologic disease and pernicious anemia) and to the chronic ingestion of chloroform (renal and hepatic tumours in rodents) (Rettig, 1987; Stimpfel and Gershey, 1991). Expired gases should be vented to the exterior or adsorbed onto activated charcoal (Mitchell, 1976).

a) Ether-based Volatile Agents

i) **Diethyl ether** is a highly volatile agent of relatively low potency and wide range of safety. Ether produces good muscle relaxation and analgesia; however, it is very irritating to mucous membranes. The vapours are highly explosive, necessitating extreme caution in its use and storage. **Due to the risk of explosion, the use of ether is discouraged as excellent alternatives are now available** (Flecknell, 1987; Stimpfel and Gershey, 1991).

ii) **Methoxyflurane (Metofane)** is a highly soluble, potent ether-based anesthetic. Because of its low volatility, it may be used safely for induction with anesthetic chambers, and nose cone maintenance. Methoxyflurane produces some respiratory and cardiovascular depression, but less than halothane at comparable depths of anesthesia. Myocardial sensitization occurs, but is not as severe as with halothane. Muscle relaxation and analgesia are good, and it is neither irritating nor explosive in anesthetic concentrations. In animals, methoxyflurane anesthesia for less than one hour is not usually associated with hepatorenal toxicity, especially if periods of hypoxia and/or hypercapnia are avoided (Stimpfel and Gershey, 1991).

iii) **Enflurane** provides rapid induction and emergence from anesthesia. It provides moderate levels of analgesia and muscle relaxation, the latter decreasing as anesthetic concentrations increase. It produces profound depression of respiratory functions and myocardial performance (Short, 1987). It is largely eliminated via the lungs. Unlike halothane, very little of the drug is metabolized by the liver. This may offer some experimental advantages; otherwise, there is little to choose between enflurane and halothane in terms of efficacy (Flecknell, 1987). Enflurane is expensive and requires a special vaporizer.

iv) **Isoflurane** is less potent than halothane or methoxyflurane. It is relatively insoluble which leads to fast inductions and recoveries. It may be used in halothane vaporizers that have been recalibrated. It produces a slightly more severe respiratory depression than does halothane, but slightly less depression of the cardiovascular system (Flecknell, 1987). There is very little myocardial sensitization to catecholamines; in fact, isoflurane has the greatest margin of safety with the cardiovascular system of all the inhalant anesthetics. Isoflurane produces better muscle relaxation than halothane, but has poorer analgesic properties. It undergoes even less biotransformation than enflurane and is almost completely eliminated in exhaled air (Flecknell, 1987). Isoflurane has a pungent odour which may cause breath holding during induction. It has no known toxicities, but it is expensive (Raper, Barker, Burwen *et al.* 1987).

b) Halogenated Hydrocarbons

i) **Halothane**, a halogenated hydrocarbon, is highly potent and volatile. It should be used only with a finely calibrated precision vaporizer. It produces dose-dependent depression of the cardiopulmonary system and hypotension (Flecknell, 1987). There is direct myocardial depression and sensitization to circulating catecholamines. The analgesia offered by halothane is reasonable, as is muscle relaxation. The vapours are neither explosive nor irritating, but can be hepatotoxic to man (Lumb and Jones, 1984).

c) Other Agents

i) Nitrous oxide has very low anesthetic potency. Induction of a state of general anesthesia or even unconsciousness is not possible in most animal species (Flecknell, 1987; Mahmoudi, Cole and Shapiro, 1989). As it exerts minimal effects on the cardiopulmonary system, it can be used to reduce the required concentration of other agents and so reduce the degree of depression at a particular depth of anesthesia (Flecknell, 1987). It has some analgesic properties in animals; however, the potency is less than half that experienced in humans (Short, 1987). Following cessation of nitrous oxide administration, 100% oxygen must be administered to the animal to prevent hypoxia caused by the rapid diffusion of the gas from the body (Flecknell, 1987; Short, 1987). **Because it presents numerous occupational hazards, nitrous oxide should be scavenged**. If a carrier gas is required 100% oxygen is effective and non-toxic as well as being vital to life (Stimpfel and Gershey, 1991).

D. MUSCLE RELAXANTS

1. Glyceryl Guiacolate

Glyceryl guiacolate (guaifenesin) is a centrally acting muscle relaxant, with its action on the internuncial neurons of the spinal cord. As the drug has little effect on the diaphragm, it produces muscle relaxation without respiratory paralysis. A state of sedation and hypnosis is produced; however, the degree of analgesia is in dispute. Guaifenesin is most often used as part of induction technique in large farm animals. It is useful in combination with thiobarbiturate for short surgical procedures and for intubation prior to the administration of an inhalant anesthetic (Lumb and Jones, 1984). Guaifenesin has been added to ketamine and xylazine to produce effective anesthesia in ponies, dogs and pigs with minimal cardiovascular and respiratory depression. This same combination has also been used in a continuous infusion for long term anesthesia in cats (Brown, McCarthy and Bennett, 1991).

2. Neuromuscular Blocking Agents

Succinylcholine (a depolarizing agent), curare, pancuronium, gallamine, atacurium and vecuronium (non-depolarizing agents) are neuromuscular blocking agents which act peripherally at the neuromuscular junctions. Anticholinesterases such as neostigmine, pyridostigmine and edrophonium are antagonistic to the non-depolarizing agents, but ineffective against the depolarizing agents (Lumb and Jones, 1984). Neuromuscular blocking agents are used as adjuncts to general anesthetics where profound muscle relaxation is desired.

These agents produce motor paralysis only. There is no sedation or analgesia. Their use on conscious animals is prohibited (see also *Ethics of Animal Investigation*).

The use of neuromuscular blocking agents abolishes some of the signs used to judge the depth of anesthesia. Autonomic functions remain intact with the newer agents (atacurium, vercuronium); therefore, increases in heart rate and arterial blood pressure may indicate the perception of pain. Animals must be artificially ventilated as the respiratory muscles are paralyzed. Should neuromuscular blocking agents be a component of an anesthetic protocol, it is extremely important that proper equipment and personnel with experience in the use of these agents be available.

E. LOCAL AND REGIONAL ANESTHETICS

Local anesthetics such as lidocaine, procaine, bupivacaine and tetracaine may be used to block the nerve supply to a limited area for the performance of minor or rapid procedures. Local anesthesia is also frequently used as an adjunct to various sedative and hypnotic agents in more prolonged and invasive procedures, such as caesarian section. Local anesthetic agents may be used for the regional infiltration of a surgical site, field blocking, nerve blocks, and for epidural and spinal anesthesia (Green, 1982; Elmore, 1981; Kero, Thomasson and Soppi, 1981; Gray and McDonell, 1986). Veterinary assistance should be sought in the initial use of the last three procedures (Lumb and Jones, 1984; Gray and McDonell, 1986). A combination of lignocaine/prilocaine has also been used topically for pain-free venipuncture in some laboratory animals (Flecknell, Liles and Williamson, 1990).

F. ANIMAL HYPNOSIS (Tonic Immobility)

A state of hypnosis or tonic immobility can be readily induced in a variety of animals including rabbits, birds, small rodents and reptiles (Prestrude and Crawford, 1970; Danneman, White, Marshall *et al.* 1988). It is characterized by a lack of spontaneous movement or overt response to external stimuli for up to several minutes, and is usually exhibited under stressful or fearful conditions. There is evidence that animals remain aware of external events and hypnosis can be interrupted by mild tactile or auditory stimuli. It is usually induced by placing the animal on its back and gently extending the neck and hind legs to place traction on the spine. Recent work indicates that some degree of analgesia is produced with hypnosis; however, individual animal susceptibility to hypnosis varies greatly and in consequence **hypnosis cannot be recommended as a suitable alternative to appropriate analgesics when painful procedures are to be performed** (Danneman, White, Marshall *et al.* 1988).

G. SPECIES CONSIDERATIONS

a) Canine

General anesthesia: sedation, followed by intravenous induction with an ultrashort-acting barbiturate, intubation and maintenance with an inhalant anesthetic. Alternatively, intermediate or long-acting barbiturates may be used but are poor analgesics and can result in profound respiratory and cardiovascular depression (Flecknell, 1987; Green, 1982). Minor surgical procedures can be carried out using neuroleptoanalgesics, xylazine combinations and diazepam combinations (Green, 1982).

b) Feline

General anesthesia: sedation, induction using an injectable agent, intubation and maintenance with an inhalant anesthetic (Green, 1982). The larynx should be sprayed with a local anesthetic such as 2% lidocaine (without epinephrine) prior to intubation (Flecknell, 1987). Mask induction with an inhalant anesthetic is also well tolerated if the cat is sedated previously and handled expertly. Ketamine and ketamine combinations have proven very useful for restraint and minor surgical procedures (Flecknell, 1987; Ingwersen, Allen, Dyson *et al.* 1988). Saffan or xylazine also produce sedation and anesthesia for minor surgical procedures (Flecknell, 1987; Green, 1982).

c) Ferrets

Administration of intravenous drugs can be difficult in the awake ferret; therefore, alternate routes are usually used. Intramuscular ketamine and ketamine combinations are useful (Muir and Hubbell, 1989; Moreland and Glaser, 1985), as are fentanyl/ droperidol and intravenous Saffan (Flecknell, 1987; Green, 1982). For induction with inhalation anesthetics, a special induction chamber is usually used, with maintenance by mask or intubation (Poole, 1987; Moody, Bowman and Lang, 1985).

d) Rabbits

Neuroleptanalgesics and ketamine combinations with xylazine, acepromazine or azaperone have been used successfully (Muir and Hubbell, 1989; Olson, 1986a; Flecknell, 1987; Lipman, Marini and Erdman, 1990). Ketamine alone does not produce adequate anesthesia or analgesia (Lumb and Jones, 1984; Flecknell, 1987). The degree of analgesia produced by Saffan is generally low. At the higher dose rates needed to produce medium or deep surgical anesthesia, there may be sudden apnea followed by cardiac arrest (Flecknell, 1987). A technique of continuous intravenous infusion of ketamine and xylazine has been reported to maintain a light anesthetic plane for up to 4 hours, although hypoxemia and hypotension are marked (Wyatt, Scott and Richardson, 1989). Inhalant anesthetics and mask induction are readily tolerated (Peeters, Gil, Teske *et al.* 1988). Endotracheal intubation in the rabbit is relatively difficult for anatomical reasons. Barbiturates alone are not recommended in rabbits, as the dose required to produce surgical anesthesia is very close to the lethal dose. Respiratory arrest frequently occurs before the onset of surgical anesthesia. They may be used, if combined with a sedative or tranquillizer (Olson, 1986a; Peeters, Gil, Teske *et al.* 1988). If atropine is used it must be at high dose levels to counteract the presence of serum atropinase (Muir and Hubbell, 1989).

e) Small laboratory rodents (rats, mice, guinea pigs, gerbils, hamsters and wild rodents)

Withholding food and water is unnecessary prior to anesthesia, since vomiting normally does not occur (Flecknell, 1987). Anesthetic agents used include barbiturates, ketamine, ketamine combinations (Muir and Hubbell, 1989; Flecknell, 1987; Wixson, 1987a, 1987b), neuroleptoanalgesics (Muir and Hubbell, 1989; Green, 1982; Parkes, 1987; Olson, 1986a), tiletamine/zolazepam (Muir and Hubbell, 1989) and Saffan (Green, 1982). Ketamine alone produces severe respiratory depression at doses high enough for surgical anesthesia in small rodents (Flecknell, 1987). Intramuscular ketamine/xylazine causes muscle necrosis in Syrian hamsters and is not recommended in that species (Gaertner, Boschert and Schoeb, 1987). The same problem has been noted with fentanyl/droperidol in guinea pigs (Holmes, 1984). Ketamine combinations and pentobarbital are poor anesthetics in the gerbil, but fentanyl/metomidate (Flecknell, John, Mitchell *et al.* 1983) and tiletamine/zolazepam have proven effective (Hrapkiewicz, Stein and Smiler, 1989). Barbiturates are still in common use, but are very poor analgesics, and often cause high mortality, especially when given intraperitoneally or when full-strength commercial solutions are used intravenously (dilution is recommended). When combined with a sedative, tranquillizer or an opioid, adequate anesthesia results (Olson, 1986a).

Induction of anesthesia with an inhalational agent is best accomplished with an induction chamber. Anesthesia may be maintained with a face mask. Endotracheal intubation is difficult in small rodents and requires purpose-made laryngoscopes (Flecknell, 1987).

The safe administration of general anesthesia to the guinea pig is notoriously difficult, since they often maintain their pedal reflex and make squirming movements even when deeply anesthetized (Holmes, 1984).

Their response to many injectable anesthetics is very variable. Post-anesthetic complications such as respiratory infections, digestive disturbances, and generalized depression, are seen (Flecknell, 1987). Spinal anesthesia offers a useful alternative (Green, 1982).

Very brief procedures (e.g., orbital blood sampling) may be performed on rodents by using a 50:50 mixture of carbon dioxide and oxygen, if the animal is removed from the gas chamber as soon as the pedal reflex has disappeared (Green, 1982; Fenwick and Blackshaw, 1989).

Hypothermia may be used to anesthetize neonatal mice and rats (1-2 days old). The pup is placed in an ice water slush for 20-30 minutes (Green, 1982).

f) Nonhuman Primates

Ketamine and its combinations are most often used for restraint, particularly where rapid recovery is desired. Neuroleptanalgesics have also been used, and Saffan is useful for small species such as marmosets. The NHP can be intubated and inhalation anesthesia administered using techniques similar to those used for the human (Flecknell, 1987; Sainsbury, Eaton and Cooper, 1989).

g) Horses

Both induction and recovery from anesthesia may be associated with excitement. Due to their size and strength, special facilities are required for induction and recovery in horses. Veterinary consultation should be sought. Xylazine and acepromazine are most commonly used as pre-anesthetics, followed by an induction agent (thiamylal sodium, guaifenesin, etc.) and inhalation anesthesia (Muir and Hubbell, 1989; Green, 1982).

h) Ruminants

This section has been revised. Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).

February 2017

i) Swine

This section has been revised. Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).

February 2017

j) Avian

Hypothermia is a frequent problem in general anesthesia, especially for small birds. Small birds are also prone to handling shock, and small friable vessels make intravenous injection difficult (Green, 1982). Ketamine is an effective pre-anesthetic, and ketamine/xylazine (Muir and Hubbell, 1989) or ketamine/ diazepam (Fowler, 1986) are two of the safest injectable anesthetics. Tiletamine/zolazepam is an alternative to ketamine/xylazine (Muir and Hubbell, 1989; Green, 1982). Diazepam combined with chloropent (chloral hydrate, sodium pentobarbital, magnesium sulfate) provides surgical anesthesia for 60-90 minutes in the domestic fowl (Christensen, Fosse, Halverson *et al.* 1987). Saffan has been used in a variety of avian species (Lumb and Jones, 1984). However, it should only be administered intravenously, and even then used with great caution due to associated cardiac arrhythmias (Green, 1982; Short, 1987).

Inhalant anesthesia with mask induction can be used fairly safely and effectively; however, because of the efficiency of the avian respiratory system, changes in anesthetic depth tend to occur very rapidly, especially in small birds (Muir and Hubbell, 1989; Lumb and Jones, 1984; Green, 1982). Resuscitation is complicated due to accumulation in the air sacs (Fowler, 1986; Ludders, Mitchell and Schaefer, 1988). Inhalants cannot be used for thoracic procedures because the gas leaks through the opened air sacs (Christensen, Fosse, Halverson *et al.* 1987), and positive pressure ventilation is necessary for abdominal procedures due to an incomplete diaphragm. Restraint must allow free movement of the sternum for respiration. Isoflurane is the safest inhalation anesthetic, followed by halothane (Muir and Hubbell, 1989).

k) Cold Blooded Animals

Agents commonly used include tiletamine/zolazepam, ketamine, Saffan, tricaine methanesulfonate (MS-222) and inhalant anesthetics. Dosage varies widely between species. Absorption and excretion of injectable anesthetics are directly related to environmental temperature.

For fish, please see "Additional information related to the *CCAC guidelines on: the care and use of fish in research, teaching and testing*".

February 2017

Reptiles and amphibians can be effectively anesthetized with local anesthetics, immersion in a solution containing an anesthetic agent, injectable or inhalation anesthetics (Muir and Hubbell, 1989). Hypothermia should only be used for restraint in non-painful procedures, as it is not known whether or not analgesia is induced. Secondary tissue damage also results from the practice. Hypothermia is not a suitable anesthetic for major surgery (Muir and Hubbell, 1989). Amphibians can be anesthetized by immersion in MS-222, which provides excellent muscle relaxation and analgesia (Muir and Hubbell, 1989; Green, 1982). Preferred injectable anesthetics for reptiles include ketamine and tiletamine/zolazepam, although Saffan and etorphine have also been used successfully (Muir and Hubbell, 1989; Fowler, 1986).

Inhalation anesthesia is induced by soaking a cotton ball with a volatile anesthetic and placing it with the animal in a box or bag, or using an induction chamber or face mask (Muir and Hubbell, 1989). Halothane, isoflurane and methoxyflurane are preferred to ether (Muir and Hubbell, 1989). Reptiles are relatively easy to intubate, as the larynx is readily visualized. Their slow respiratory rates and ability to breath-hold con-

stitute complicating factors (Muir and Hubbell, 1989). Inhalants are not recommended for turtles (Green, 1982).

Johnson (1992) warns that in administering anesthetics to amphibians and reptiles, one must consider the structure of the reptilian respiratory system. Respiratory movements are different in snakes, which have one lung, crocodiles which have diaphragms, and lizards which have pleuroperitoneal cavities. He suggests that, because their respiratory movements may be weak, if a volatile anesthetic is used, one may have to assist respiration because they have a poor way of expelling air. Johnson also notes that, if anesthesia is to be done for a long period of time, amphibians must be kept moist; as they are all poikilotherms, keeping them at their preferred optimum temperature zone will have an effect on the absorption and excretion of the anesthetic.

l) Invertebrates

Volk (1986) discusses methods of evaluating anesthetic depth in various invertebrates and includes a complete list of anesthetics.

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XII EUTHANASIA

This section has been revised. Please see the *CCAC guidelines on: euthanasia of animals used in science* (2010).

February 2017

F. SPECIFIC SPECIES

This section has been revised. Please see the *CCAC guidelines on: euthanasia of animals used in science* (2010).

February 2017

G. TISSUE EFFECTS OF EUTHANASIA METHODS

This section has been revised. Please see *Additional Information on Effects of Euthanasia Methods on Research Results*. This information is intended to support the implementation of the guidelines but is not used as a basis for recommendations made in CCAC assessment reports.

February 2017

H. EFFECT ON OBSERVERS

This section has been revised. Please see the *CCAC guidelines on: husbandry of animals in science* (2017).

March 2017

I. EUTHANASIA STATEMENTS–OTHER AGENCIES

This section has been revised. Please see the *CCAC guidelines on: euthanasia of animals used in science* (2010).

February 2017

XIII THE USE OF ANIMALS IN PSYCHOLOGY

The focus of psychology is the organization of behaviour. It is concerned with processes that control and direct adaptive and maladaptive activity, and so the range of phenomena studied is broad, and the paradigms and research settings employed are varied. The study of behaviour may incorporate physiology, pharmacology, ethology, or even sociology, and for that reason the distinction between psychology and closely related disciplines is often blurred. Through the history of the discipline, extending back, for example, to nineteenth century work on reflex organization, through Pavlov's fundamental discoveries about conditioning, and more recently to the identification of motivational and reward systems through electrical stimulation of the brain, animal behaviour has played a central role in research and conceptualization. Although there are clearly recognized limitations to the use of animals in research (e.g., no access to verbal report), it does permit a control of hereditary and experiential variables that could seldom be achieved in other ways. Furthermore, animal research places humans in an evolutionary context and makes possible a comparative and biological perspective on human behaviour.

Basic animal research in psychology has played a significant role in advancing our understanding of processes of learning, memory, perception, motivation, and emotion, and of behavioural adaptations of individuals and species to their environments. While much of this work has addressed theoretical issues, it can have direct implications for contemporary applied problems. Examples of such problems that affect animals directly include captive and domestic animal care, non-lethal means of predator control, and the reintroduction of endangered species to their former habitats. Examples of problems that have a direct effect on human welfare include the control of depression, phobias, pain, addiction, and the pathological effects of stress and anxiety.

Although it may be convenient to dichotomize research activities as basic and applied, it is important to recognize that there is a continuum and that it is difficult to know a priori where along that continuum the implications of some research program will fall. Applications sometimes follow quite directly from basic research, and fundamental discoveries often arise in applied research. It is also important to appreciate, as Hebb (1966) has pointed out: "Before we can have applied science, we must have a science to apply." This is a position shared by many researchers who, while cognizant of applied implications, orient their work toward the elucidation of issues that are basically scientific and theoretical in nature.

Since psychological research approaches a wide range of topics with a diversity of methodologies, it is not surprising that animal research in psychology may not be well understood outside the discipline. The following points are directed at research strategies and general experimental procedures that have apparently been sources of misunderstanding:

1. Many problems studied by psychologists deal with the understanding and control of psychopathology, such as depression, phobias, psychosomatic disorders, psychoses, hyperactivity and learning disabilities, obesity and addiction. Many aspects of these problems cannot be studied satisfactorily in human patients because of the difficulties associated with non-experimental paradigms in determining the causal relationship among variables. In other words, when one studies patients with a form of psychopatholo-

gy, all one can establish is that some variable, X, is correlated with the pathology, P. Yet an understanding and control of the problem requires knowing more than correlations. It is necessary to establish whether that variable X in some sense causes or is an antecedent of the pathology P, whether the pathology P is an antecedent for the change in variable X, or whether the two variables are related only indirectly and non-causally through their relationship to some common underlying variables yet to be determined. Seldom is it practicable to study these kinds of important issues in human patients using the necessary experimental (as opposed to correlational) research designs. One alternative and productive research approach has been to use animal models. In the present context, such models refer to "the production, under controlled conditions, of phenomena analogous to naturally occurring disorders."

A more extensive discussion of the concept of animal models in psychology may be found in the literature (Abramson and Seligman, 1977).

Using such models, it becomes possible to conduct experimental studies involving the active manipulation of variables, and this permits clarification of the relationships among variables. It is important to recognize, however, that a model is simply that, and requires validation through a detailed study of its essential features and an analysis of its similarities to the psychopathology in question.

2. In addition to their use in applied problems, animal models play an important role in the development of fundamental behaviour theory. Research may study, for example, the behaviour of animals pressing a lever in an isolated chamber, in order to examine the way in which the frequency or patterning of lever presses is controlled by the schedule of food reward or reinforcement. No one is terribly interested in lever pressing as a behaviour in itself; however, this simple and easily quantified behaviour can be viewed as a model or analogue of more complex forms of behaviour. The assumption is that if one can understand the basic principles that control a simple behaviour, one will have at least a place to start in developing principles that govern more complexly organized behaviour systems.

   Similarly, when researchers use electric shock as a means of producing stress or of motivating animals to escape or avoid, they are fully recognizant that electric shock does not normally occur in nature. They do assume, however, that this particular easily controlled aversive event can serve as a model or analogue of other unpleasant events that do occur naturally and affect behaviour. This use of models in psychology is often misunderstood by those outside the discipline. It is important that they note that questions of the validity of the assumptions and the adequacy and generalizability of a model cannot be answered a priori and are more productively approached through empirical* research than logical argument.

   * It should be noted that the word empirical has two quite different, but equally correct meanings of which the reader should be aware. The first refers to work that is based on a systematic observation and the application of scientific principles in methods. It is in this sense that the word is normally used in psychology (although there also occurs the word **empiricism**, which refers to a philosophy of knowledge). The second meaning of empirical is found in the medical sphere, and refers to work that "relies on or is based on practical experience without reference to scientific principles as, an empirical remedy". It is related to the noun, **empiric**, which refers to one "ignorant of scientific principles" and who "lacks regular training and proper qualifications" (*Webster's New World Dictionary*, Second College Edition, 1970). The reader should be aware of these two quite opposite meanings and of what is implied by the psychologist when characterizing research as "empirical".

3. A basic assumption of contemporary psychology is that the brain is the organ of the mind, a term which simply refers to the internal processes that determine the organization of complex behaviour. Accordingly, one approach to the study of the properties of mind is to study the functioning of the brain. Such research is sometimes correlational in that it relates indices of brain function (e.g., electroencephalo-

grams [EEG], evoked potentials) in humans and animals to behavioural processes. Often, however, and for reasons related to the control and sorting out of relationships among variables discussed under point 1), the research involves an experimental study of the effects of manipulation of the brain on behaviour. No one assumes that the brains of experimental animals are miniature human brains; however, it is assumed that the basic principles of brain organization are common across mammalian species and that the brain of the particular animal species **may** serve as a model for certain aspects of human brain function.

4. Psychologists incorporate and manipulate motivational variables in their research for three somewhat dissimilar reasons. The first is when the subject of study is the motivational system in question, e.g., the control of feeding or drinking behaviour. In such a context, it is obvious to all why an animal might be on a water or food- restricted regimen. The second is when the motivational system in question is being used as a model for other appetitive or aversive motivational systems, as discussed under point 2). A third reason, and one that is often not well appreciated by those outside the discipline, is that such manipulation represents an effective means of facilitating the controlled study of phenomena only indirectly related to the motivational manipulation.

   Behaviour that is oriented towards obtaining access to food and water, or escaping or avoiding an aversive event, can form the basis of sound inferences about non-motivational processes associated with, for example, learning, memory or perception. The origin of the misunderstanding is that, although motivation is manipulated, the dependent variables of the study relate to learning. The misunderstanding is compounded by the fact that although sometimes the interest is in learning as a process itself, other times it is in learning as a process that is affected by sensory, perceptual, motor or other processes that are in fact the principal foci of the study. As a simple example, consider the case of studying the capacity of an animal for pattern discrimination. One approach might be to place the animal repeatedly into a chamber with two doors. Behind the door with pattern A, food is always to be found. Behind the door with pattern B, there is no food. The animal is then taught to enter one of the doors each time it is placed in the chamber. To learn to enter the door behind which the food is located requires the animal to be motivated and interested in finding and consuming the food, and that is why motivation is manipulated. When the animal can consistently perform the correct response, i.e., when it has learned to go to the door with pattern A, one is in a position to make some statement about the perceptual capability of the animal, even though what was measured was learning, and what was manipulated was motivation. The analysis of learning is central to experimental psychology, and motivation is necessary for that analysis. The rationale for the choice of motivation manipulated is not always obvious, but the later discussion of Guideline 7 attempts to identify some of the considerations that are made. Often these considerations relate to practicability and minimization of behavioural variability, which promotes the economical and efficient use of animal resources.

   Over the years, members of the general public, the discipline of psychology itself, and other disciplines, have expressed concerns about aspects of psychological research involving animals. In part, this may be due to psychology including as subjects of study phenomena to which one can easily relate on a highly personal level (e.g., stress, pain, anxiety, motivation, etc.). In part, this may be due to a poor understanding of the nature of the model systems as a research tool, and we have tried to address that in these introductory remarks. However, in large measure, this is undoubtedly due to a language, vocabulary, or jargon used to characterize phenomena, events, or hypothetical processes that can sometimes conjure unrealistic, distressing images. Those with concerns are to be encouraged to become fully informed about the nature of psychological research, and those engaged in research are to be encouraged to be

sensitive to these concerns and to discuss openly their work and its implications with concerned individuals outside their discipline.

Certain procedures used in the study of psychological problems undoubtedly do produce some distress in animal and human subjects, and this places directly on the investigator a responsibility to question seriously what is being done, why it is being done, and where the work will lead. The Canadian Council on Animal Care (CCAC) and the scientific community have had a continuing concern for these and other issues related to the care and use of experimental animals. In the recognition that there are certain aspects of behavioural research that are misunderstood and can be problematic with respect to research ethics, the Canadian Psychological Association (CPA), in consultation with the CCAC, has prepared the following set of guidelines to assist psychologists as researchers and instructors in making the ethical decisions viewed to be an integral part of behavioural research with animals. It is hoped that these guidelines will complement those of the CCAC and facilitate the conduct of ethically responsible research that will promote our understanding of basic processes underlying behaviour.

GUIDELINES FOR THE USE OF ANIMALS IN RESEARCH AND INSTRUCTION IN PSYCHOLOGY: COMMENTARY AND ELABORATION

The discipline and profession of psychology in Canada shares with contemporary society a deep concern for the welfare and humane treatment of animals, especially in scientific research and instruction. While it is recognized that animal research is essential to the further development of scientific knowledge, it is also recognized that there are limits to what should be done to animals in the conduct of that research. In response to this concern, the Canadian Psychological Association (CPA), in consultation with the Canadian Council on Animal Care (CCAC), has formulated these guidelines to assist psychologists as researchers and instructors in making the ethical decisions that are an integral aspect of working with animals. These have been published in a form suitable for posting in laboratories. The purpose of this commentary is to provide some elaboration of considerations that psychologists should give with respect to implementation of the preamble and each guideline.

Psychologists have an obligation to advance knowledge and promote welfare through the competent conduct of research, the accurate communication of findings, and the effective instruction of students. However, their values and goals as scientists sometimes come into conflict with their values related to the treatment of living organisms. Dilemmas posed by the conflict cannot be resolved by rigid rules and regulations, but require a careful weighing of values and alternatives. In many cases, the decisions reflect a relative judgement of the value of the research and the effects of the procedures on the animals. Psychologists using animals for research or instruction should be prepared to make such decisions and to explain the bases of their decisions to an informed audience. The following guidelines are intended to assist the scientist in making these ethical decisions.

The CPA's *Guidelines for the Use of Animals in Research and Instruction in Psychology* were formulated from the ethical perspective advocated by Diener and Crandall (1978a) in their book *Ethics in Social and Behavioural Research*. They consider research ethics to be a process of decision-making rather than one of devising explicit rules and regulations intended to govern the conduct of all research under all circumstances. Their approach is well represented in the following passage:

> "The ethical or moral scientist makes individual judgements about research practices in light of his/her own values. According to this approach to ethics, the moral person is not

> one who blindly follows ethical codes, no matter how enlightened. The ethical decision-maker is one who realizes that his/her choices are related to values, and weighs these values carefully when making important decisions. For the moral person there may be a few moral absolutes (Szasz, 1967); however, he or she realizes that most moral decisions must be made individually in each case (Smith, 1969). This meaning of ethics emphasizes the process by which the decisions are made as well as the final choice. The decision is made by a person **who is educated about ethical guidelines, carefully examines moral alternatives, exercises judgement in each situation and accepts responsibility for his/her choices** (Diener and Crandall, 1978b) (emphasis added)."

As reflected in the Preamble to these Guidelines, this ethical framework clearly places the responsibility for the careful consideration of personal, social, and professional values on the individual scientist. A corollary of this is that the individual researcher or instructor must accept responsibility for choices through accountability to an informed public. Specifically, the investigator must be able to explain the rationale for both the research problem and its methodology to informed colleagues, peers, and institutional committees. If necessary, the investigator must be able to defend the research against the criticisms that suffering inflicted on animal subjects was unnecessary in view of the objectives of the research, or unconscionable in view of the balance between the suffering inflicted and expectation of gain in scientific knowledge or education. The present commentary is intended to provide the scientist with an indication of problematic issues and concerns that require special attention and consideration.

A. THE SCIENTIST

1. **Prior to undertaking a research or instructional project with animals, the scientist has a responsibility to be sufficiently knowledgeable to ensure compliance with these guidelines. When in doubt about compliance, the scientist should consult with informed colleagues and the institutional Animal Care Committee (ACC) and give due regard to their advice**. Investigators are reminded that it is the policy of the major granting agencies, e.g., Medical Research Council (MRC) and the Natural Sciences and Engineering Research Council (NSERC), of government departments and of most universities that ACC approval must be received prior to commencing any project with animals.

   The position that the ethical scientist is one who can make informed decisions and who is prepared to give a reasoned judgment for the values and appropriateness of the objectives and procedures of the research or teaching assumes a considerable depth and breadth of knowledge by the scientist. The decisions involved are usually complex and multifaceted. If they are to be informed, scientists must be familiar with the recent literature relevant to the problem, aware of the current status of the problem, familiar with procedures involved, either through study of the literature or direct experience with the techniques, and aware of potential risks. When undertaking research in a new area, or when the research involves severe stress, pain, or privation, the investigator may have doubts about the breadth and depth of his/her knowledge and experience. Under such circumstances, there is an obligation to consult with informed colleagues and/or the ACC and to give due regard to their advice. Such consultation does not absolve the investigator from responsibility for the decisions; however, it is evidence of a responsible attitude towards becoming sufficiently knowledgeable to undertake research in an ethical manner.

2. **A scientist trained in research methods and experienced in the care of laboratory animals should ensure that the comfort, health and humane treatment of experimental animals are given appropriate consideration.**

Psychological research frequently requires that an investigator interact with animal subjects over an extended period of time. Accordingly, the psychologist has a vested interest, quite apart from humane considerations, in ensuring that experimental animals are well treated and healthy; otherwise, it is likely that behavioural data will be unreliable and the research objectives not achieved. Although the day-to-day maintenance and/or behavioural testing of animals may be done by trained technical staff, it is the responsibility of the individual scientist to be able to recognize good and poor practices by staff and students. This ability requires training in research methods and experience in animal care procedures. While our attention is naturally drawn to practices that involve pain or physical illness, the scientist should be sensitive to problems that can arise from the capacity of some animals to form human attachments (e.g., the distress that might be experienced by the animal when returned to isolated quarters at the end of a prolonged study).

3. **The scientist should ensure that all individuals under his/her supervision have the training and competence needed to carry out their responsibilities for experimental procedures, care, maintenance, and handling of the species being used.**

   A variety of technical skills is required in any laboratory to ensure proper care and handling of animals, and it is the responsibility of the scientist to ensure that all supervised individuals have the skills and attitudes required to carry out competently their assigned duties. Since every species has unique biological and social needs, the design of experimental and maintenance protocols should take into consideration the species' normal ecology, evolutionary history, and behavioural adaptations to the natural environment. It is the responsibility of the scientist to acquire sufficient expertise in these regards, and to ensure that the training of technical staff, students, and research associates is adequate to meet their respective responsibilities. This is necessary, not only from the point of view of the humane treatment of animals, but also from the scientific perspective of generating reliable data.

4. **The scientist should be fully cognizant of the CCAC's guidelines and of current federal, provincial, and local laws and regulations concerning the acquisition, care, use, and disposal of animals.**

   This guideline is self-explanatory. As professionals and as members of society, psychologists have a responsibility to be aware of and to follow federal, provincial, and local laws and regulations concerning animals. In cases of doubt, the scientists should consult with the chairman of the ACC or with the CCAC. Compliance with this *Guide* is a requirement of Canada's major granting agencies, many journals in Canada, and ACCs.

B. RESEARCH

5. **There must be a reasonable expectation that studies involving animals will: a) increase understanding of structures and processes underlying behaviour; b) increase understanding of the particular animal species used in the experiment; or c) result eventually in benefits to the health and welfare of humans or other animals.**

   This guideline outlines the general spheres to which psychological research should contribute if animals are legitimately to be involved. It specifically recognizes the value of research, the implications of which are largely theoretical or philosophical, and is consistent with the CCAC guidelines in that there is a reasonable expectation that the development of new scientific knowledge and conceptualization may result in eventual benefits to the health and welfare of humans or other animals.

   This guideline refers more to research programs than to individual studies. It is intended to recognize that there is no such thing as the "definitive study" and that the significance of any individual experi-

ment, especially when viewed after the fact, is not always immediately apparent and can be easily trivialized. Accordingly, a particular experiment must be judged within the context of a research program as to whether it will contribute in a meaningful way to a systematic empirical or theoretical base.

An integral part of any research program is the use of small pilot studies, the results of which are at best suggestive, but which are important for decisions about directions to proceed, research design, parameters, etc. The value of such studies is often indirect, and therefore must be evaluated in the broader context of a research.

This guideline bears also on the problem of replication or reproducibility of results in psychological research. Replication is a necessary and desirable aspect of science when it is seen as a manipulation of a special class of factors (e.g., different laboratories, different experimenters, different times of the year, etc.), which can provide new scientific knowledge of value in understanding a phenomenon. As with the case of pilot studies, replications must be seen within the broader context of a research program. To the extent that there is a reasonable expectation that a replication will contribute to new scientific knowledge, it is consistent with this guideline.

6. **Procedures subjecting animals to pain, stress, privation, or death should be used only when an acceptable alternative procedure is unavailable.**

   In psychological research, the subjection of animals to procedures involving pain, stress, privation, or death occurs in two broad contexts. The first is when the subject of study is pain, stress, motivational systems, or aspects of death, all of which are legitimate and important areas of the discipline. In such a context, there are seldom realistic alternatives, and the attention of the scientist must focus on ways of minimizing discomfort. For example, the study of stress must necessarily involve manipulations that will produce stress; nevertheless, the investigator must consider ways to minimize the trauma of these manipulations. In the second context, procedures are employed to induce motivational states that facilitate the controlled study of phenomena only indirectly related to the motivational manipulations (for example, learning discrimination, memory, sensory thresholds, etc.). Under such circumstances, the scientist has an ethical obligation to consider whether the research objectives could be met using broad alternatives not involving pain or discomfort.

7. **Scientists should examine methodological and procedural techniques for the purpose of minimizing discomfort, illness, and pain to animals.**

   When acceptable alternative procedures to ones that involve pain or privation are not available, there remains a responsibility to examine methodologies and procedures that will minimize discomfort, illness, or pain, and that are consistent with the objectives of the research. The judgement involved clearly requires considerable knowledge of the species and its behavioural repertoire, as well as the research problem. Issues that may arise in considering this guideline include: Is the species appropriate for the study? Have the motivational systems and the biological/social needs of the species been assessed so that a reasonable judgment can be made about the relative discomfort and stress produced by various potentially painful procedures or different kinds of levels of privation? Can motivational states in the given species be better controlled through appetitive motivation (e.g., water or food deprivation) or through aversive motivation (e.g., mild electric shock)? Have parameters of the aversive stimuli or the deprivation been selected judiciously so as to be optimal in light of the behavioural requirements of the research and the principle of minimizing discomfort? Could lower levels of shock or privation be used and still produce reliable behaviour? Could a lower level of aversive stimulation or privation be used, even though more animals might be required because of less reliable or stable behaviour? In studies involving food motivation, is privation to a fixed percentage (e.g., 80%) of ad lib body weight required,

or would controlled daily access to food (e.g., every 23 hours), perhaps in combination with a preferred incentive, be sufficient?

Manipulations involving surgery can be problematic with respect to discomfort, and issues that may arise in this regard include: Is the method of an anesthetization optimal? Are the surgical procedures sufficiently aseptic to minimize post-operative infection and other stress? Is an analgesic required during post-operative recovery? Does the manipulation, such as implantation of a chronic cannula or electrode assembly, cause irritation, and if so are there ways to minimize this? Does a physiological or pharmacological manipulation (including administration of toxins) cause a generalized deterioration of the well-being of the animal, and if so, how can this be minimized in a manner consistent with the research objectives?

It is sometimes suggested that one approach to minimizing discomfort is to minimize the number of animals used in the research. However, since the detection of treatment effects is against a background of uncontrollable behavioural variance, one must be careful to ensure that there is sufficient power to detect those effects when they are there. Otherwise, the animals that were used would have suffered needlessly. However, investigators should consider single-subject designs, repeated measures designs, and other techniques to minimize variance, all of which could lead to fewer total subjects being required for the research.

8. **An experiment should be terminated whenever it becomes apparent to the scientist or the institutional ACC, that its continuation will result in injury or suffering that is incompatible with these guidelines.**

   With the best of planning, some experiments simply do not work out as expected. This can be due to various reasons, such as equipment failure, procedures having unforeseen effects, experimenter error, or behavioural variance so large as to obliterate any possible treatment effects. Also, on occasion, new research results become known and may make ongoing research redundant. In such situations, the experimenters must give careful consideration to whether it is worthwhile to continue the work, and do so only if they are satisfied that it is justified in light of these guidelines.

9. **The killing or other disposition of experimental animals at the termination of the experiment must be accomplished in a humane manner.**

   At the end of most experiments in psychology, experimental animals are killed. This must be done in a humane manner, as described in this *Guide*, and in Volume 2 (CCAC, 1984). While this is obvious and is the accepted practice, problems can arise when research animals are not killed. For example, releasing trapped animals back into the wild may or may not be humane depending on the species, its territorial behaviour, feeding habits, time of year, etc. As noted earlier, some animals can form human attachments and problems can arise after experiments involving long-term interaction with them if they are returned to isolated laboratory housing. The responsibility of the scientist to his/her animals extends beyond the actual termination of the experiment, and careful consideration must be given to whether the means of disposing of the experimental animal is actually humane.

C. INSTRUCTION

10. **The decision to use animals for instructional purposes must be based on a consideration of educational objectives rather than contributions to new scientific knowledge. In other respects, ethical practices in the care and treatment of animals are the same as those that apply to the use of animals in research.**

A committee of the British Psychological Society (BPS) has commented that, "...No psychology undergraduate can for long remain unaware of the extent to which the empirical basis of much psychological theory is derived from experimental work with animals. Accordingly, it is appropriate that, as a matter of course, all undergraduate students of psychology should receive specific instruction on the issues which arise from animal experimentation, issues scientific, intellectual, methodological, practical, and ethical" (BPS, 1979).

The CPA shares the view that instruction on the use of animals in psychology is desirable and necessary. On occasion, the actual use of animals in instruction is required to achieve educational objectives. In such cases, the same general considerations must apply to animal use in instruction as in research, that is, a balancing of the expected benefits against the costs, with the benefits seen in terms of advancing education rather than incrementing scientific knowledge. Clearly, classroom demonstrations of animal behaviour by their very nature involve phenomena which may not intrinsically advance scientific knowledge. However, to the extent that they assist the student's understanding of existing knowledge, they make a substantive contribution. As contained in the BPS position, there is an obligation to incorporate material on ethical issues into discussions of animal use. In this way, instructors can, by example, promote the ethical use of animals by future scientists and instill in students an appropriate sensitivity to associated issues.

11. **Classroom demonstrations involving animals should only be used when instructional objectives cannot be achieved through the use of videotapes, films, or other alternative methods. Careful consideration should be given to whether the type of demonstration is warranted by the anticipated instructional gain.**

    Videotapes and films represent effective means of demonstrating principles of animal behaviour and experimentation. However, there are often advantages of using real animals, not the least of which is to convey the realism of the phenomenon. In deciding on the medium of instruction, instructors have an obligation to evaluate carefully their instructional objectives and to decide if those objectives warrant the use of animals.

    In making the evaluation, the instructor should be sensitive to the possible trauma that the animals may experience in being brought into a classroom, and to the possibility of disease transmission to or from the animal. The instructor must also consider whether the animal will be used solely for the demonstration, or whether it has already been used in experimentation, or is breeding stock, or is maintained for the purpose of demonstrations.

    The guideline makes reference to "type of demonstration" to alert the instructor to the possibly adverse reactions that a demonstration, live or filmed, may produce in unprepared students. Procedures which to the naive viewer may appear to involve pain or stress (e.g., showing animals with chronic cannulae or electrode assemblies, animals having epileptic seizures, animals being operated on, injected with drugs or social animals raised in isolation, etc.) are especially problematic.

12. **Student projects involving pain or distress to animals should be undertaken judiciously and only when the training objectives cannot be achieved in any other way.**

    Student research projects fall along a continuum from casual classroom projects at one end, to doctoral dissertation research (which should contribute to new scientific knowledge) at the other. The value of such projects is seldom to be found in their making substantive new contributions to knowledge, but is found in their advancing knowledge through communication. If students are to acquire the knowledge and expertise required by these guidelines, it is necessary that they gain experience in working with ani-

mals. Especially in the case of students who show every indication of embarking on a research-oriented career, that experience may involve using procedures that involve minimal pain or distress. If so, the instructor must consider very carefully the appropriateness of the project and its procedures against its training objectives for the individual student and the development of student sensibilities towards animals. Students and instructors are reminded that ACC approval must be received prior to commencing any project with animals.

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These guidelines shall be conspicuously posted in every laboratory teaching facility and applied setting where animals are being used.

The CPA recommends that a copy of the guidelines and this commentary be included in laboratory manuals as well as that selected sections be posted in all laboratory facilities. It is hoped this will not be seen as an empty formality, but rather as an invitation for all laboratory personnel to become acquainted with the ethical process. Like science itself, ethical procedures are advanced by communication and discussion.

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In any situation involving decisions and judgment, there will, on occasion, be disagreements and misunderstandings. When these arise in the context of the use of animals in research or instruction in psychology, they should be resolved as quickly as possible so as not to impede legitimate research nor to prolong unacceptable procedures. The well-being of the animal must be a paramount concern. In general, there are two classes of problems. In the first, there may be allegations by students, colleagues, or the public that some on-going or completed research or instruction is inappropriate in light of these guidelines. In this case, the concerned individual should attempt to work through the ACC of the institution in which the research is carried out. In the second, individual psychologists may find their ACC or a granting agency unwilling to approve some research which they feel is scientifically and ethically warranted. The CCAC has developed a formal appeal mechanism of which researchers may take advantage. Part of this mechanism will involve consultation with the CPA.

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XIV GUIDELINES ON THE USE OF ANIMALS IN NEUROBIOLOGICAL RESEARCH*

A. INTRODUCTION

Research in the neurosciences contributes to the quality of life by expanding knowledge about living organisms. This improvement in quality of life stems in part from progress toward ameliorating human disease and disability, in part from advances in animal welfare and veterinary medicine, and in part from the steady increase in knowledge of the abilities and potentialities of human and animal life. Continued progress in many areas of biomedical research requires the use of living animals in order to investigate complex systems and functions because, in such cases, no adequate alternatives exist. Progress in both basic and clinical research in such areas cannot continue without the use of living animals as experimental subjects. The use of living animals in properly designed scientific research is therefore both ethical and appropriate. Nevertheless, our concern for the humane treatment of animals dictates that we weigh carefully the benefits to human knowledge and welfare whenever animal research is undertaken. The investigator using research animals assumes responsibility for proper experimental design, including ethical as well as scientific aspects.

The scientific community shares the concern of society at large that the use of animals in research should conform to standards that are consonant with those applied to other uses of animals by humans. While it is unlikely that any particular set of standards will satisfy everyone, it is appropriate for scientific societies to formulate guidelines that apply to the humane use of laboratory animals in particular areas of research. Ideally, such guidelines should also be acceptable to society at large as reasonable and prudent.

Most of the more specific sections of this document were formulated with respect to research using warm-blooded vertebrates. As a general principle, however, ethical issues involved in the use of any species, whether vertebrate or invertebrate, are best considered in relation to the complexity of that species's nervous system and its apparent awareness of the environment, rather than physical appearance or evolutionary proximity to humans.

B. FACTORS THAT RELATE TO THE DESIGN OF EXPERIMENTS

The primary factor used to evaluate humane treatment in animal research is degree of distress or discomfort, assessed by anthropomorphic judgements made by reasonable and prudent human observers. **The fundamental principle of ethical animal research is that experimental animals must not be subjected to avoidable distress or discomfort**. This principle must be observed when designing any experiment that uses live animals.

Although most animal research involves minimal distress or discomfort, certain valid scientific questions may require experimental designs that inevitably produce these effects. Such situations, while uncommon,

* Reproduced with permission of the Society for Neuroscience from *Handbook for the Use of Animals in Neuroscience Research* (1992). References to American publications and to American states are not relevant to Canadian researchers.

are extremely diverse and must be evaluated individually. It is critical that distress and discomfort be minimized by careful experimental design. It is also important to recognize that there is no difference between distress and discomfort that may be inherent in a valid experimental design and that which may occur as an unintended side effect. It is therefore incumbent on the investigator to recognize and to eliminate all avoidable sources of distress and discomfort in animal subjects. This goal often requires attention to specifics of animal husbandry as well as to experimental design.

Invasive procedures and paralytic drugs should never be employed without benefit of anesthetic agents unless there is a very strong scientific justification and careful consideration is given to possible alternatives. Advances in experimental techniques, such as the use of devices chronically implanted under anesthesia, can offer alternative approaches. If these are not feasible, it is essential to monitor nociceptive responses (for example, recordings of EEG, blood pressure and pupillary responses) that may indicate stress in the animal subject, and to use these as signals of the need to alleviate pain, to modify the experimental design, or to terminate the experiment.

When designing research projects, investigators should carefully consider the species and numbers of animals necessary to provide valid information, as well as the question of whether living subjects are required to answer the scientific question. As a general rule, experiments should be designed so as to minimize the number of animals used and to avoid the depletion of endangered species. Advances in experimental methods, more efficient use of animals within-subject designs, and modern statistical techniques all provide possible ways to minimize the numbers of animals used in research. This goal is completely consistent with the critical importance of replication and validation of results to true progress in science.

C. FACTORS THAT RELATE TO THE CONDUCT OF EXPERIMENTS

Research animals must be acquired and cared for in accordance with the guidelines published in the *NIH Guide for the Care and Use of Laboratory Animals* (National Institutes of Health, Publication No. 85-23, Revised 1985). The use of an animal scheduled for euthanasia by a pound or shelter saves the life of another; therefore, the use of pound or shelter animals is endorsed for research projects in which they are suitable subjects. In using animals acquired from a pound or shelter, as with all other aspects of research, investigators must adhere to the relevant local, state and federal law. (The reference to pound or shelter animals was added to the Guidelines following the recommendation by the Committee on Animals in Research and approval by Council.) The quality of research data depends in no small measure on the health and general condition of the animals used, as well as on the specifics of the experimental design. Thus, proper animal husbandry is integral to the success of any research effort using living animal subjects. General standards for animal husbandry (housing, food quality, ventilation, etc.) are detailed in the *NIH Guide*. The experienced investigator can contribute additional specifics for optimum care for particular experimental situations, or for species not commonly encountered in laboratory settings.

Surgery performed with the intent that the animal will survive, (for example, on animals intended for chronic study), should be carried out, or directly supervised, by persons with appropriate levels of experience and training, and with attention to asepsis and prevention of infection. Major surgical procedures should be done using an appropriate method of anesthesia to render the animal insensitive to pain. Muscle relaxants and paralytics have no anesthetic action and should not be used alone for surgical restraint. Post-operative care must include attention to minimize discomfort and the risk of infection.

Many experimental designs call for surgical preparation under anesthetic agents with no intent that the animal should survive. In such cases, the animals ordinarily should be maintained unconscious for the duration of the experiment. At the conclusion of the experiment, the animal should be killed without regaining consciousness and death ensured before final disposition.

Certain experiments may require physical restraint, and/or withholding of food or water, as methodological procedures rather than experimental paradigms. In such cases, careful attention must be paid to minimize discomfort or distress and to ensure that general health is maintained. Immobilization or restraint to which the animals cannot be readily adapted should not be imposed when alternative procedures are practical. Reasonable periods of rest and readjustment should be included in the experimental schedule unless these would be absolutely inconsistent with valid scientific objectives.

When distress and discomfort are unavoidable attributes of a valid experimental design, it is mandatory to conduct such experiments so as to minimize these effects, to minimize the duration of the procedure and to minimize the numbers of animals used, consistent with the scientific objectives of the study.

APPENDIX I
HOUSING AND ENVIRONMENT

The following charts are based on successful experiences and professional judgement ever cognizant of the performance evaluation of the animals being maintained. As there are few objective data available on the ideal space requirements for individual laboratory species, veterinary judgement must be considered in evaluating housing requirements. The Social and Behavioural Requirements of Experimental Animals chapter provides additional guidelines for specific species.

SPECIES (weight)	SPACE PER ANIMAL			TEMPERATURE °C		R.H.%	Ventilation Changes/ Hour	B.T.U. Animal/ Hour
	Single-Floor Area	Minimal Height	Group or Loose Housing	Room/ Cage °C	Pen/Free Ranging			
CAT >4 kg	0.28 m^2 0.37 m^2	0.76 m Perch	0.56 m^2 Perches	20-22	15-25	45-60	10-18	25-30
CATTLE Calf Cow	Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).							
CHICKEN	Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).							
DOG <12 kg 12-30 kg >30 kg	 0.75 m^2 1.20 m^2 2.23 m^2	 0.8 m 0.9 m pen-2.0 m	 1.5 m^2 2.0 m^2 3.0 m^2	18-21	5-25	45-55	8-12	80-150
GERBIL	116 cm^2	15 cm	pair + litter 900 cm^2	15-24		40-50	8-10	4.0
GOAT	Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).							
GUINEA PIG <350 g >350 g	 300cm^2 650cm^2	 18 cm 22 cm	 500 cm^2 800 cm^2	18-22		50-60	4-8	5-6
HAMSTER >100 g	 100cm^2 120cm^2	 18 cm 18 cm	 fem. + litter 900 cm^2	21-24		45-65	6-10	2.5
HORSE	4-5 cm^2	3 m	13-17 m^2	10-24	2-27	25-75	4-8	
MOUSE	Please see the *CCAC guidelines: Mice* (2019).							

SPECIES (weight)	SPACE PER ANIMAL			TEMPERATURE °C		R.H.%	Ventilation Changes/ Hour	B.T.U. Animal/ Hour
	Single-Floor Area	Minimal Height	Group or Loose Housing	Room/ Cage °C	Pen/Free Ranging			
NON-HUMAN PRIMATE	Please see the *CCAC guidelines: Nonhuman primates* (2019).							
OPOSSUM	0.56 m^2	0.75 m		21-25	10-27	45-65	10-12	
PIGEON	0.18 m^2	0.38 m		16-20	5-27	45-70	12-15	1.2
QUAIL	400 cm^2	15 cm max . 30 cm	200 cm^2	21-22	20-30	45-70	10-15	
RABBIT <4 kg >4 kg	 0.37 m^2 0.46 m^2	 0.40 m 0.45 m	 fem. + litter 0.93 m^2	16-22	10-28 shade	40-50	10-20	30-40
RAT	Please see the *CCAC guidelines: Rats* (2020).							
SHEEP	Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).							
SWINE	Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).							

APPENDIX II
BREEDING AND REPRODUCTION DATA

SPECIES (age and weight)	Breeding Age Range female-male	Cycle Type* Length (days)	Duration of Sexual Receptivity	Breeding Behaviour** and Season**	Gestation mean (d) range	Litter Size and Range	Optimal*** Reproductive Span (yrs/mos)	Light Hours
CAT	7-10 mos	14-24 S.P.	3-8 d irregular	Ph (f. to m.) Jan. to Sept.	62 57-65	2-6	6-7 yrs	12-14
CATTLE	16-24 mos	18-24 P	10-24 hrs	Ph (A1) all year	283 279-290	1	8-10 yrs	8-12
CHICKEN	4-6 mos			Poly all year	21 incubation		9-12 mos	13-14
DOG	10-14 mos	21 M	4-8 d	Ph (f. to m.) Biannual	63 58-68	4-10 breed dependent	6-7 yrs	10-12
GERBIL	9-12 wks	4-6 P	14-18 hrs	MP all year	25 24-26	4-5	15 mos	12-14
GOAT	15-18 mos	14-21 S.P.	48-72 hrs	Poly Sept. to Feb.	151 149-153	1-2	4-5 yrs	8-12
GUINEA PIG	3 mos	15-19 P	6-14 d	H (1 to 6) all year	65 59-72	2-6	2 yrs	12-15
HAMSTER	6-8 wks	4 P	6-20 hrs	M.P. or H (1 to 5) all year	16 15-18	5-8	15 mos	12
HORSE	36-60 mos	19-24 S.P.	3 d 2-6	Ph (f. to m.) Feb. to Aug.	335 320-360	1	12-15 yrs	8-12
MOUSE	6 wks	4-5 P	10-20 hrs	H (1 to 4) all year	20 19-21	6-12	7-8 mos	14
NON-HUMAN PRIMATE Baboon (*Papio* sp)	48-66 mos	31-32	3-4 day menses day 15-17 optimal breeding period	H (1 to 6) all year	175 154-185	1	5-20 yrs	12-14
(*Macaca* sp)	36-48 mos	28	3-4 day menses day 10-12 optimal breeding time	H (1 to 8) or Ph (f. to m.) all year	165 150-180	1	5-20 yrs	10-14

SPECIES (age and weight)	Breeding Age Range female-male	Cycle Type* Length (days)	Duration of Sexual Receptivity	Breeding Behaviour** and Season**	Gestation mean (d) range	Litter Size and Range	Optimal*** Reproductive Span (yrs/ mos)	Light Hours
OPOSSUM	8-12 mos	22-27 P	7-14 d post-partum	M.P.	marsupial 12-13	1-12	5 yrs	
PIGEON	6 mos			M.P. all year	13 incubation		2 yrs	12-14
QUAIL	6 wks			H (1 to 3) or poly all year	16 incubation		5-6 mos	14
RABBIT	6-9 mos	induced P	ovulation variable	Ph (f. to m.) all year	31 28-34	6-10	3 yrs	12-14
RAT	10-12 wks	4-5 P	10-20 hr	H (1 to 6) all year	21 20-22	7-14	9-10 mos	12-14
SHEEP	18-24 m	16-17 S.P.	1-1 1/2 d	Poly mid-Sept. to mid-Jan.	145 144-148	1-3	4-5 yrs	12
SWINE	9-11 mos	21 P	2-3 d	Poly all year	114 112-116	6-16	3-4 yrs	10-12

* P = Polyestrus; S.P. = Seasonal Polyestrus; M = Monoestrus

** H = Harem mating (1 male (m) to # females (f)); Poly = Polygamous; Ph = Polygamous but usually hand mated, take (male to female) or (female to male); A.I. = Artificial Insemination; M.P. = Monogamous Pair, set up at weaning for life.

*** Optimal Reproductive Span - refers to that period of the female's life during which fertility and litter size are maximal and reproductive complications minimal. Breeding stock will usually be replaced at the end of this span of time for economic reasons.

APPENDIX III
PHYSIOLOGICAL AND NUTRITIONAL PARAMETERS*

SPECIES	Rectal Temp. °C +0.5	Resp. Rate/ Mean and (range)	Heart Rate/ Mean and (range)	Average Daily Water Consumption	Urine Excreted Daily	Daily Feed Recommendations	Digestible Protein** %
CAT	38.5	31 (20-40)	150 (110-226)	150 ml 100-200	50-120 ml	110-225 g	30
CATTLE	38.5	29 (26-35)	58 (46-55)	45-65 L	14-23 L.	7.5-12.5 kg	8.5-10
CHICKEN	39.5	(12-36)	300 (150-400)	ad lib		85-115 g	13-17
DOG	39.0	24 (20-34)	110 (77-138)	25-35 ml/kg body wt	65-400 ml breed dependent	250-1200 g breed dependent	20
FERRET	38.5	34 (33-36)	240 (200-400)	75-100 ml	26-28 ml	140-190 g	9.5
GERBIL	38.5	90 (70-120)	360 (260-600)	3-4 ml or green feed	few drops	10-15 g	15
GOAT	39.0	19 (12-35)	90 (70-135)	1.5-4 L	1-2 L	1-4 kg	15
GUINEA PIG	39.0	86 (42-104)	280 (230-380)	12-15 ml/100 g body wt	15-75 ml	20-35 g + Vit. C supp.	25-30
HAMSTER	39.0	77 (35-135)	332 (250-500)	8-12 ml	6-12 ml	7-15 g	16
HORSE	38.0	12 (10-14)	44 (23-70)	25-55 L	3-15 L	8-16 kg	5.5-14
MOUSE	37.5	138 (94-163)	470 (325-780)	3-7 ml	1-3 ml	3-6 g	12
NONHUMAN PRIMATE Baboon (*Papio* sp)	39.0	25 (22-35)	115 (105-150)	400-600 ml	150-400 ml	1-1.5 kg + Vit. C supp.	17
Cynomolgus (*M. fascicularis*)	39.0	40 (30-54)	220 (165-243)	350-950 ml	150-550 ml	350-550 g + Vit. C supp.	17
OPOSSUM	34.5	36-65	(140-220)	100-200 ml		85-150 g	20-25
PIGEON	41.0	25-30	(140-244)	40-50 ml		25-75 g	10-15

SPECIES	Rectal Temp. °C +0.5	Resp. Rate/ Mean and (range)	Heart Rate/ Mean and (range)	Average Daily Water Consumption	Urine Excreted Daily	Daily Feed Recommendations	Digestible Protein** %
RABBIT	39.0	40 (32-60)	260 (130-325)	80-100 ml/kg body wt	50-90 ml/ kg body wt	75-100 g	14
RAT	37.0	92 (70-115)	350 (250-450)	20-45 ml	10-15 ml	10-20 g	12
SHEEP	39.5	25 (20-34)	76 (70-80)	600-1800 ml	400-1200 ml	1-2 kg	5
SWINE	39.0	40 (32-58)	70 (60-75)	4.5-6.5 L	2.5-4.5 L	1.5-3 kg	14

* Averages and ranges derived from literature mean values for **young adult animals** under various conditions (from various sources).

** Refers to (ideal or digestible protein required; crude protein (CP)) levels in most prepared laboratory animal diets may be considerably higher.

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APPENDIX IV HEMATOLOGY*

SPECIES	RBC X 10^{12}/L	Hb g/L	PCV L/L	Platelets X 10^9/L	WBC X 10^9/L	Neutrophils 10^9/L	Lymphocytes 10^9/L	Blood Vol. (ml/kg)
CAT	7.5 5.0-10.0	120 80-150	0.37 0.24-0.45	190-400	12.5 5.5-19.5	7.5 2.5-12.5	4.0 1.5-7.0	66.7 45-75
CATTLE	7.0 5.0-10.0	110 80-150	0.35 0.24-0.46	220-640	8.0 4.0-12.0	2.0 0.6-4.0	4.5 2.5-7.5	57 55-60
CHICKEN	3.0 2.5-3.5	90 70-130	0.3 0.22-0.35	14-60	12.0 12.0-30.0	3.0-6.0	14.0 7.0-17.5	83 60-90
DOG	6.8 5.5-8.5	150 132-193	0.45 0.38-0.57	145-440	11.5 6.0-17.0	7.0 3.9-12.0	2.8 1.0-4.8	83-101
GERBIL	8.5 7.0-10.0	150 121-169	0.48 0.41-0.52	638	4.3-21.6	0.3-4.1	3.2-9.7	60-85
GOAT	13.0 8.0-18.0	100 80-120	0.35 0.24-0.48	250-750	9.0 4.0-13.0	3.2 1.2-7.2	5.0 2.0-9.0	70 55-80
GUINEA PIG	5.2 4.8-5.9	110-140	0.43 0.37-0.46	450-630	3.8-13.5	2.6 2.0-3.1	6.4-7.5	65-90
HAMSTER	7.5 5.0-9.2	168 146-200	0.5 0.46-0.52	300-570	7.6 5.0-10.0	1.5-3.5	6.1-7.0	65-80
HORSE	9.0 6.8-12.9	144 111-190	0.41 0.32-0.53	80-397	9.0 5.4-14.3	4.7 2.3-8.6	3.9 1.7-6.8	72 75-100
MOUSE	9.1 7.9-10.1	110-145	0.37-0.46	600-1200	5.0-13.7	0.4-2.7	7.1-9.5	70-80
NONHUMAN PRIMATES Baboon (*Papio* sp)	5.0 4.0-6.0	120 90-150	0.42 0.36-0.49	135-400	3.0-11.4	2.7-7.3	2.6-5.9	50-70
Cynomolgus (*M. fascicularis*)	5.0 3.9-7.1	116-145	0.38-0.50	90-140	8.1-21.3	1.3-8.1	3.5-8.3	55-75
OPOSSUM	5.0 3.4-7.1	121-198	0.42 0.30-0.58	235-1235	3.0-27.0	1.5-6.5	1.9-9.2	45-65
QUAIL	4.7 4.0-5.5	110-150	0.42 0.3-0.45		12.5-25.0	2.5-5.0	5.0-7.0	55-75
RABBIT	6.5 4.5-8.5	94-175	0.40 0.31-0.50	468 180-750	4.0-13.0	3.0-5.2	2.8-9.0	57-65
RAT	5.4-8.5	115-160	0.37-0.49	450-885	4.0-10.2	1.3-3.6	5.6-8.3	50-65

SPECIES	RBC X 10^{12}/L	Hb g/L	PCV L/L	Platelets X 10^9/L	WBC X 10^9/L	Neutrophils 10^9/L	Lymphocytes 10^9/L	Blood Vol. (ml/kg)
SHEEP	12.0 9.0-15.0	115 90-150	0.35 0.27-0.45	250-750	8.0 4.0-12.0	2.4 0.7-6.0	5.0 2.0-9.0	58-66.4
SWINE	6.5 5.0-8.0	130 100-160	0.42 0.32-0.50	300-700	16.0 11.0-22.0	4.0-7.5	6.0-10.0	52-69

* The normal values may vary according to age, sex, breed and function of animals.

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APPENDIX V
CLINICAL BIOCHEMISTRY REFERENCE VALUES[a]

SPECIES	Glucose mmol/L	Urea mmol/L	Cholesterol Total mmol/L	Protein			Aspartate Amino-transferase (AST, SGOT) U/L	Alanine Amino-transferase (ALT, SGPT) U/L	Alkaline Phosphatase U/L
				Total g/L	Albumin g/L	Globulin g/L			
CAT[b]	3.89-6.11 (5.05±0.42)	14.28-21.42	2.46-3.37	54-78 (66±7)	21-33 (27±2)	26-51 (39±7)	26-43 (35±9)	6-83 (26±16)	25-93 (50±35)
CHICKEN[b]		(9.30)		(56)	(25)	(31)	(175)		
COW[b]	2.5-4.16 (3.19±0.38)	14.28-21.42	2.07-3.11	67-75 (71±2)	30-35 (33±1)	30-35 (32±2)	78-132 (105±27)	14-38 (27±14)	0-488 (194±126)
DOG[b]	3.61-6.55 (5.05±0.67)	7.14-19.99 (12.14 ±2.86)	3.50-6.99 (4.61±0.98)	54-71 (61±5)	26-33 (29±2)	27-44 (34±5)	23-66 (33±12)	21-102 (47±26)	20-156 (66±36)
GOAT[b]	2.78-4.16 (3.49±0.39)	7.14-14.28 (10.71 ±1.43)	2.07-3.37	64-70 (69±5)	27-39 (33±3)	27-41 (36±5)	167-513	24-83	93-387 (219±76)
GUINEA PIG[c] Hartley (500-800g)	4.94-5.29 (5.12)	15.35-17.99 (16.67)		48-56 (52)	24-27 (25)		46-48 (47)	38-45 (41)	66-74 (70)
HAMSTER[c] Syrian (100g)	3.61-4.07 (3.84)	14.85-21.49 (18.33± 3.08)	4.71-6.13 (5.42)	64-73 (67±5)	32-37 (35±2)		53-124 (79±32)	21-50 (35±11)	8-18 (13±5)
HORSE[b]	4.16-6.39 (5.30±0.47)	7.14-17.14	1.94-3.89 (2.88±0.04)	52-79 (63±6)	26-37 (31±3)	26-40 (33±7)	226-366 (296±70)	3-23 (14±11)	143-395 (244±101)
MOUSE[d] CD-1 [Crl:CD-1 (ICR)BR][e]	9.71-18.60 (15.00)	12.14-20.59 (16.07)	1.27-2.48 (1.89)	42-60 (51)	21-34 (28)	18-82 (22)	55-251 (139)	28-184 (95)	28-94 (67)
CF-1 [Crl: CF-1BR][e]	9.10-20.48 (14.46)	8.57-19.99 (14.99)	2.72-4.16 (3.49)	54-65 (60)	30-40 (35)	18-31 (24)	30-314 (177)	76-208 (143)	67-303 (167)
B6C3F1 [B6C3F1/ CrlBR][f]	7.6-26.0 (17.3)	4.3-13.5 (7.85)	1.53-3.63 (2.29)	47-60 (52)	26-34 (30)	17-29 (22)	0-111 (43)		46-289 (207)

SPECIES	Glucose mmol/L	Urea mmol/L	Cholesterol Total mmol/L	Protein			Aspartate Amino-transferase (AST, SGOT) U/L	Alanine Amino-transferase (ALT, SGPT) U/L	Alkaline Phosphatase U/L
				Total g/L	Albumin g/L	Globulin g/L			
NON-HUMAN PRIMATE Baboon (*Papio sp*)[c]	(6.72±1.16)			(63±6)	(37±4)		(25±3)	(16±4)	
Cynomolgus (*M. fascicularis*)[g]	2.20-4.70	3.80-10.00	1.91-4.52	68-86	34-45	27-47	9-68	0-138	102-1163
Rhesus (*M. mulatta*)[c]	(3.89±0.57)	12.07-14.85 (13.46)	3.31-4.43 (3.87)	66-80 (70±8)	43-44		27-79 (55±27)	27-42 (35)	(149)
PIG[b]	4.72-8.33 (6.61±0.96)	7.41-21.42	0.93-1.40	79- 89 (84 ±7)	(26±7)	53-64 (59±6)	32-84 (61±26)	31-58 (45±14)	118-395 (194±84)
RABBIT[b]	2.78-5.18 (4.08±0.53)	(10.21± 2.14)	0.14-1.86 (0.69±0.41)	(64±3)	(27±3)		(47)	(79)	(120±14)
RAT[d] Wistar[Crl: (W)BR][h]	4.71-7.33 (6.22)	11.42-19.28 (14.64)	1.20-2.38[f] (1.79)	63-86 (73)	33-49 (47)	24-39 (31)	39-92 (64)	17-50 (32)	39-216 (123)
F-344[i] [CDF(F-344) CrlBR]	4.24-20.04 (10.85)	7.85-19.99 (10.00)	0.54-2.22 (1.29)	60-78 (66)	34-43 (39)	24-35 (29)	56-436 (233)	108-375 (232)	147-399 (248)
CD[Crl:CD (SD)BR][j]	5.55-16.71 (11.69)	9.28-22.13 (14.64)	1.18 (0.52-1.914)	59-79 (70)	28-44 (38)	26-39 (32)	39-262 (129)	110-274 (216)	46-264 (161)
SHEEP[b]	2.78-4.44 (3.80±0.33)	5.71-14.28	1.34-1.97 (1.66±0.31)	60-79 (72±5)	24-30 (27±2)	35-57 (44±5)	(307±43)	(30±4)	68-387 (178±102)

a Ranges with the means and standard deviations in parenthesis. Reported in S.I. units.

b KANEKO, J.J., ed. Clinical chemistry of domestic animals. Academic Press, 1989: 886-891.

c LOEB, W.F. and QUIMBY, F.W., eds. The Clinical Chemistry of Laboratory Animals. Pergamon Press, 1989: 417-476.

d Sexes combined, 19-21 weeks.

e Baseline haematology and clinical chemistry values for Charles River outbred mice: Crl:CD-1(ICR)BR. Crl:CF-1BR. Charles River Laboratories Techn. Bull., 1986.

f Values from Parke Davis Research Institute, Mississauga, Ontario.

g CLARKE, D., TUPASI, G., WALKER, R. and SMITH, G. Stability of serum biochemical parameters in Beagle Dogs and Cynomolgus monkeys. Clin. Chem. Newsl. (In press).

h Baseline haematology and clinical chemistry values for Charles River Wistar rats (CRL:(W)BR) as a function of sex and age. Charles River Techn. Bull., Vol. 1, No. 2, 1982.

i Baseline haematology and clinical chemistry calues for Charles River Fischer-344 rats - CDF(F-344)CrlBR as a function of sex and age. Charles River Techn. Bull., Vol. 3, No. 1, 1984.

j Baseline haematology and clinical chemistry values for Charles River CD[Crl:CD(SD)BR] rats as a function of sex and age. Charles River Techn. Bull., Vol. 3, No. 2, 1984.

APPENDIX VI
SERUM ELECTROLYTE REFERENCE VALUES[a]

SPECIES	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Bicarbonate mmol/L	Phosphorus mmol/L	Calcium mmol/L	Magnesium mmol/L
CAT[b]	147-156 (152)	4.0-4.5 (4.3)	117-123	17-21	1.45-2.62 (2.00)	1.55-2.55 (2.06±0.24)	(0.90)
CHICKEN[b]					(2.52)	(7.10)	
COW[b]	132-152 (142)	3.9-5.8 (4.8)	97-111 (104)	17-29	1.81-2.10	2.43- 3.10 (2.78±0.15)	0.74-0.95 (0.84±0.10)
DOG[b]	141-152	4.37-5.35	105-115	18-24	0.84-2.00 (1.39±0.29)	2.25-2.83 (2.55±0.15)	0.74-0.99 (0.86±0.12)
GOAT[b]	142-155 (150±3.1)	3.5-5.4	99-110 (105±2.9)		(4.62+0.25)	2.88-3.20 (2.58±0.15)	0.90-0.31 (1.03±0.12)
GUINEA PIG[c] Hartley (500-800g)	122-125	4.7-5.3	92-97	22-24	1.71-1.72	2.40-2.67	0.97-1.01
HAMSTER[c] Syrian (100g)	128-145	4.9-5.1	94-99	(30±2.9)	1.71-2.13	2.60-3.09	0.91-1.03
HORSE[b]	132-146 (139±3.5)	2.4-4.7 (3.5±0.6)	99-109 (104±2.6)	20-28	1.00-1.81	2.80-3.40 (3.10±0.14)	0.19-1.15 (1.03±0.13)
MOUSE[d] CD-1 [Crl:CD-1(ICR)BR]e	143-150 (148)	3.8-10.0 (6.3)	96-111 (105)		2.68-3.62 (3.08)	2.77-3.02 (2.90)	
CF-1 [Crl:CF-1BR]e	139-157 (148)	4.8-8.9 (6.9)	104-119 (111)		2.91-4.65 (3.76)	2.25-2.89 (2.57)	
NONHUMAN PRIMATE Baboon (*Papio* sp)[c]	(142±3.5)	(3.8±0.5)	(107±3.7)		(2.26±0.48)	(2.10±0.02)	
Cynomolgus (*M. fascicularis*)	142-153[f] (149)	3.0-4.8[f] (3.9)	101-112[f] (107)		1.18-2.30[g]	2.17-2.55[g] (2.36)	
Rhesus (*M. mulatta*)[c]	154-158	3.6-4.6	110-114		1.41-1.62	2.42-2.70	0.68-0.75
PIG[b]	135-152	4.4-6.7	94-106	18-27	1.71-3.10	1.78- 2.90 (2.41 +0.25)	1.11-1.52 (1.31+0.20)
RABBIT[b]	(141±0.93)	(5.3±0.5)	85-105.3 (96.5±6.7)	(47)	(1.34±0.15)	1.46-3.60	(0.92±0.07)
RAT[d] Wistar[Crl:(W)BR]	141-150[h] (145)	5.2-7.8[h] (6.2)	99-114[h] (106)		1.99-3.77[f] (2.95)	2.67-3.43[f] (3.05)	1.07-1.28[c]

SPECIES	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Bicarbonate mmol/L	Phosphorus mmol/L	Calcium mmol/L	Magnesium mmol/L
F-344[i] [CDF(F-344)CrlBR]	139-150 (145)	3.9-7.5 (5.7)	82-99 (93)		2.42-5.62 (4.13)	2.47-3.32 (2.82)	
CD[Crl:CD(SD)BR][j]	139-150 (145)	3.6-8.4 (5.7)	84-99 (93)		2.42-5.62 (4.13)	2.47-3.22 (2.82)	0.66-1.79[c]
SHEEP[b]	139-152	3.9-5.8	95-103	20-25	1.62-2.36	2.88-3.20 (2.78±0.07)	0.90-0.31 (1.03±0.12)

a Ranges with the means and standard deviations in parenthesis. Reported in S.I. units.

b KANEKO, J.J., ed. Clinical chemistry of domestic animals. Academic Press, 1989: 886-891.

c LOEB, W.F. and QUIMBY, F.W., eds. The clinical chemistry of laboratory animals. Pergamon Press, 1989: 417-476.

d Sexes combined, 19-21 weeks.

e Baseline haematology and clinical chemistry values for Charles River outbred mice: Crl:CD-1(ICR)BR. Crl:CF-1BR. Charles River Laboratories Techn. Bull., 1986.

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g CLARKE, D., TUPASI, G., WALKER, R. and SMITH, G. Stability of serum biochemical parameters in beagle dogs and cynomolgus monkeys. Clin. Chem. Newsl. (In press).

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i Baseline haematology and clinical chemistry values for Charles River Fischer-344 rats - CDF(F-344)CrlBR as a function of sex and age. Charles River Techn. Bull., Vol. 3, No. 1, 1984.

j Baseline haematology and clinical chemistry values for Charles River CD[Crl:CD(SD)BR] rats as a function of sex and age. Charles River Techn. Bull., Vol. 3, No. 2, 1984.

APPENDIX VII
ZOONOSES: EXPERIMENTAL ANIMALS TO MAN

A. BACTERIAL DISEASES:

Disease in Man	Causative Agent	Vertebrate Hosts[1]	Means of Spread	Vectors and Notes on Cycle
Anthrax Woolsorters disease	*Bacillus anthracis*	Farm animals wild and zoo animals	contact, inhalation, ingestion	Spores: long lived in soil
Brucellosis[2] Undulant Fever Malta Fever Zang's disease	*B.suis*	swine	contact and ingestion of milk, milk products, raw meat	
	B.abortus	cattle, sheep, buffalo		
	B.melitensis	sheep, goats		
	B.ovis	sheep	direct contact primarily with semen	
	B.canis	dogs	contact with infected semen, fetuses, fetal membranes and vaginal secretions	
Campylobacteriosis	*C.fetus* *C.jejuni*	cattle, sheep, pigs, dogs, nonhuman primates, poultry	ingestion	may survive inadequate heating
Chlamydiosis[3] Psittacosis	*Chlamydia* spp.	Psittacine birds, poultry, pigeons	inhalation	recovered nestlings
Colibacillosis[4]	*E.coli*	cattle, swine, poultry, misc. animals	ingestion	
Leptospirosis Weil's disease	*Leptospira* spp.	rodents, dogs, farm and wild animals	contact, urine contaminated soil and water	
Pasteurellosis	*P.multocida* *P.hemolytica* *P.pneumotropica*	cats, dogs, rabbits, misc. mammals, birds	contact, bite wounds, inhalation	
Plague	*Yersinia pestis*	rodents	contact, flea bites, inhalation	fleas
Pseudotuberculosis	*Yersinia pseudotuberculosis*	rodents, lagomorphs, pigeons, turkeys, canaries, wild birds	contact, contaminated food and water ingestion	
Rat Bite Fever	*S.moniliformis* *Spirillum minus*	rodents	rodent bites, ingestion	infected saliva
Salmonellosis	*Salmonella* spp.	farm animals, rodents, reptiles, amphibians, zoo and wild animals	ingestion, inhalation, contact	

Disease in Man	Causative Agent	Vertebrate Hosts[1]	Means of Spread	Vectors and Notes on Cycle
Shigellosis Bacillary dysentery	*Shigella* spp.	nonhuman primates	contact, fecal contamination, ingestion	direct or by fomites
Tetanus[5]	*Cl.tetani*	dog, cat, equine spp.	bite wounds, contaminated puncture wounds	soil
Tuberculosis	*M.tuberculosis* *M.bovis* *M.avium*	nonhuman primates, cattle, dogs cattle, dogs poultry, swine, sheep	contact, ingestion, inhalation	Anthropozoonotic[6]
Tularemia Rabbit fever	*F.tularensis*	lagomorphs, wild rodents, birds, dogs	inhalation contact, tick and insect bites, ingestion of contaminated food and water	biting insects and ticks

B. RICKETTSIAL DISEASES:

Causative Agent	Disease in Man	Common Vertebrate Hosts[1]	Means of Spread, Vectors and Cycle Notes
Coxiella[8]	Q fever	cattle, sheep, goats	inhalation, ingestion of contaminated raw milk, blood sucking anthropods, contact with amniotic fluid or placenta
R.akari	Rickettsial pox	wild mice, rats	mite bites: *A. sanguineus*
R.rickettsia	Rocky mountain spotted fever	wild rodents, rabbits, dogs	tick bites: *Dermacentor* spp., American dog tick
R.siberica	Asian tick fever	various wild rodents	tick bites: ticks themselves may act as reservoirs with tick to tick passage
R.typhi	Murine typhus	wild mice, rats	flea bites from rat fleas, rat to rat spread by lice, ingestion of contaminated food

C. ARBOVIRUS DISEASES:

Causative Agent	Diseases in Man	Common Vertebrate Hosts[1]	Means of Spread, Vectors and Cycle Notes
Asian arboviruses	various tickborne hemorrhagic fevers	wild rodents, hares, wild-caught monkeys	tick bites, sub-tropical climate conditions favour cycle
California encephalitis	California encephalitis	wild rabbits, rodents	natural cycle wild rabbits and rodents/ mosquito
Colorado tickborne virus	Colorado tick fever	ground squirrels, *Deromyscus* spp.	tick bite, tick/small rodent natural cycle
E.E.E.	Eastern equine encephalitis	horses, birds	mosquito bites: bird/mosquito/horse natural cycle
Powassan virus	Powassan encephalitis	wild rabbits, rodents	tick bites
S.L.E.	St. Louis encephalitis	birds	natural cycle bird/mosquito only
V.E.E.	Venezuelan equine encephalitis	horses	natural cycle horse/mosquito only
W.E.E.	Western equine encephalitis	horses, birds	mosquito bites: bird/mosquito/horse natural cycle

D. OTHER VIRUS DISEASES:

Causative Agent	Diseases in Man	Common Vertebrate Hosts[1]	Means of Spread, Vectors and Cycle Notes
Filovirus	Marburg disease Ebola hemorrhagic fever	African green monkey *Macaca* sp.	direct contact with monkey tissues
Hemorrhagic fever virus	S. American and Korean hemorrhagic fever	wild rodents *Mastomys ratalensis*	contact, contamination of food, etc., with rodent excreta; direct contact
Hepatitis virus	Hepatitis A	chimpanzees	contact, anthropozoonotic diseases[9]
Herpes simiae	Herpes B. encephalitis	rhesus; other Macaca	contact, bite wounds, Old World monkeys
L.C.M. virus	Lymphocytic Chorio - Meningitis	rodents; numerous other mammals	contact, inhalation; congenital transmission, tissue culture transmission
Rabies virus	Rabies	dogs, cats, bats and many others	bites; saliva contact, virus concentrate in saliva

E. FUNGAL AND PROTOZOAN DISEASES:

Causative Agent	Diseases in Man	Common Vertebrate Hosts[1]	Means of Spread, Vectors and Cycle Notes
Balantidium coli	Balantidiasis	nonhuman primates	ingestion by contamination of food or fomites
Coccidioides immitis	Coccidioidomycosis	cattle, dogs and occasionally other spp.	inhalation of air-borne spores; fungus present in desert soil
Entamoeba histolytica	Amebiasis Amebic dysentery	nonhuman primates, dogs	contamination of food, usually by man (natural host) to dogs
Giardia intestinalis	Giardiasis	nonhuman primates, dogs, beaver	man is main reservoir, ingestion of cysts in contaminated water or food
Histoplasma capsulatum	Histoplasmosis	dogs, other domestic and wild species	inhalation of fungi; may also grow in soil
Toxoplasma gondii	Toxoplasmosis	cats; occasionally other domestic and lab spp.	ingestion of oocysts from cats; inhalation infected meat; fetal transmission may occur
Trichophyton spp. *Microsporum* spp. Other dermatophytes	Ringworm, dermatomycosis	dog, cat, guinea pig, other rodents and farm animals, rabbits	direct contact, ringworm of man can be transmitted to animals and visa-versa; soil may be reservoir
Trypanasoma spp. *Plasmodium* spp. *Leishmania* spp.	Blood protozoan diseases	nonhuman primates, rodents, domestic and wild spp.	insect vectors—saliva transmission; some few species direct transmission

1 Only more common host species are listed.

2 *Brucella abortus* has also been reported in bactrian and dromedary camels, alpacas, and caribou. *B.suis* has been reported in African rodents, European hares (it is the reservoir). Brucellosis has also been reported in desert rats in the U.S. and in foxes and mustelids in S. America.

3 One case of cat to human transmission causing conjunctivitis.

4 *E.coli* has many serotypes; those with capsular K antigen are especially pathogenic to man and animals. Some serotypes are species specific. Man is the main reservoir of colibacillosis for humans with the route of infection the handling of human feces or not washing hands after using the bathroom.

5 Tetanus is not considered a true zoonoses.

6 Man is the primary vertebrate host.

7 In addition to the G.I. signs, this organism is associated with abortion in women.

8 Organism concentrated in placenta and fetal membranes and fluids.

9 Man is primary host. Measles (Rubeola) is another anthropozoonotic virus to nonhuman primates.

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APPENDIX VIII
COMMON BLEEDING SITES

SPECIES	ANT, VENA CAVA	CEPHALIC VEIN	EAR VEIN	FEMORAL VEIN	HEART	JUGULAR VEIN	ORBITAL SINUS	TAIL V/A	TOE/TAIL NICK	WING VEIN
BIRD					Xc,f	Xc				Xc,f
CAT		Xc		Xc,r,t		Xc,r,t				
COW	Please see the *CCAC guidelines on: the care and use of farm animals in research, teaching and testing* (2009).									
DOG		Xc,r,t,u		Xc		Xc,r,t,u				
FERRET					Xl	Xl		Xl	Xl	
FISH	Please see the *CCAC guidelines on: the care and use of fish in research, teaching and testing* (2005).									
FROG					Xg					
GERBIL					Xv		Xv	Xv		
GUINEA PIG	Xaa		Xn,o		Xo		Xo		Xc,o	
HAMSTER	Xx		Xp		Xp,x		Xx		Xx	
MOUSE	Please see the *CCAC guidelines: Mice* (2019).									
NHP				Xc,w		Xc				
OPOSSUM						Xk		Xk		
PIG	Xq,t		Xq,t							
RABBIT			Xa,c,b,n		Xa,c,b					
RAT	Please see the *CCAC guidelines: Rats* (2020).									
SMALL RUMINANT		Xt				Xt				
SNAKE					Xm					
TURTLE					Xm				Xm	

X Recognized bleeding site, followed by reference.

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APPENDIX IX
TRANQUILIZER, SEDATIVE AND ANTICHOLINERGIC DRUG DOSAGES

SPECIES	Acepromazine Maleate (Atravet)		Xylazine (Rompum)[d]		Midazolam[a] (Versed)		Diazepam[a] (Valium)		Atropine Sulfate[c]		Glycopyrrolate[c]	
	Mg/Kg	Route[b]	Mg/Kg	Route	Mg/Kg	Route	Mg/Kg	Route	Mg/Kg	Route	Mg/Kg	Route
CAT	0.2-0.5 1-3	IM IV PO	1-3	IM SC	0.2-0.5	IM IV	1.0-max 5 mg		0.02-0.05	SC IM IV	0.011 0.005	IM IV
CATTLE	0.1	IV	0.1	IM					not effective			
DOG	0.1-0.5	IM IV SC	1-2	IM	0.2-0.5	IM IV	1.0 max 20.0	IM IV	0.02-0.05	SC IM IV	0.011 0.005	IM IV
GUINEA PIG					5.0	IP	2.5	IM IP	0.02-0.05	SC IM IV		
HAMSTER/ GERBIL					5.0 5.0	IP IP	5.0	IP	0.02-0.05	SC IM IV		
MOUSE					5.0	IP	1.0	IM IV	0.1-0.2	SC IM IV		
NON-HUMAN PRIMATE	0.5-1	SC IM	1-2	IM			1.0	IM IV	0.05	SC IM IV		
RABBIT	1.0	SC IM	1-3.0	IM	2.0	IP	1.0	IM IV	0.1-0.2	SC IM IV	0.1	SC
RAT					2.5	IP	2.5	IP	0.02-0.05	SC IM IV		
SHEEP/ GOAT	0.1-0.2	IM IV	1.0 0.05	IM IM					0.05	SC IM		
SWINE	0.2	IM IV					1-2	IM IV	0.05-0.1	SC IM IV		

a The tranquillizers listed are not marketed in Canada under veterinary labels. These are human Schedule F, Part II (H&W Canada) drugs requiring prescription.

b PO = oral; SC = subcutaneous; IM = intramuscular; IP = intraperitoneal; IV = intravenous.

c Atropine and Glycopyrrolate should be administered 35-50 minutes prior to surgery, SC or IM.

d Xylazine–is an analgesic as well as a sedative.

APPENDIX X
ANALGESIC DRUG DOSAGES

SPECIES	Acetylsalicylic Acid (Aspirin)		Meperidine HCl (Pethidine) (Demerol)		Fentanyl + Droperidol** (Innovar-vet)*		Morphine		Butorphanol		Buprenorphine	
	Mg/Kg Route	Duration	Mg/Kg Route	Duration	Mg/Kg Route	Duration	Mg/Kg Route	Duration	Mg/Kg Route	Duration	Mg/Kg Route	Duration
CAT			2-6 IM SC	2-3 hr			0.05-0.1 SC	4 hr	0.4 SC	3-4 hr	0.005-0.01 SC IV	8-12 hr
CATTLE												
DOG	10 PO	8-12 hr	2-6 SC IM	1-2 hr	0.2- 0.5 IM		0.3-2.0 SC IM	2-4 hr	0.2-0.4 SC IM	3-4 hr	0.01-0.02 IM SC IV	8-12 hr
GOAT			up to 200 total dose IM	4 hr		up to 10 total dose IM	4 hr				0.005 SC IM	8-12 hr
GUINEA PIG	85 PO	4 hr	10-20 SC IM	2-3 hr			2-5 SC	2-4 hr			0.05 SC	6-12 hr
HAMSTER					0.02-0.05 ml/100 g IM 0.1 of 1:10 dilution IP						0.5 SC	6-8 hr
MOUSE	120-300 PO	4 hr	10-20 SC IM	2-3 hr	0.02-0.05 ml/100 g IM		2-5 SC	2-4 hr	1-5 SC	4 hr	0.05-0.1 SC	6-8 hr

SPECIES	Acetylsalicylic Acid (Aspirin)		Meperidine HCl (Pethidine) (Demerol)		Fentanyl + Droperidol** (Innovar-vet)*		Morphine		Butorphanol		Buprenorphine	
	Mg/Kg Route	Duration	Mg/Kg Route	Duration	Mg/Kg Route	Duration	Mg/Kg Route	Duration	Mg/Kg Route	Duration	Mg/Kg Route	Duration
NON-HUMAN PRIMATE	10-20 PO	6 hr	2-4 IM	3-4 hr	0.05-0.2 IM	required dosages vary greatly with different NHP species	1-2 SC IM	4 hr	0.025 IM	4 hr	0.01-0.05 IM IV	8-12 hr
RABBIT	10 PO	4 hr	10-20 SC IM 5 IV	2 hr 2-4 hr	0.15-0.3 IM		2-5 SC IM	2-4 hr	0.1- 0.5 IV	4 hr	0.02-0.05 SC IV IM	8-12 hr
RAT	100 PO	4 hr	10-20 SC IM	2-3 hr	0.10-0.25 IM 0.2- 0.5 IM	Sedation/ Anesthe-sia. Dilute to 10% solution prior to adminis-tration	2-5 SC	2-4 hr	2 SC	4 hr	0.01-0.5 SC IV	8-12 hr
SHEEP			up to 200 total dose IM	4 hr			up to 10 total dose IM	4 hr			0.005 IM	4-6 hr
SWINE	10 PO	4 hr	2 IM	4 hr	0.5 IM 0.03 IV		up to 10 total dose IM	4 hr	0.1-0.3 IM	4 hr	0.1 IV IM	8-12 hr

* Innovar-vet = Fentanyl 0.4 mg/ml + Droperidol 20 mg/ml.

** Neurolepranalgesic.

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APPENDIX XI
INJECTABLE ANESTHETIC AGENTS: DOSAGE

SPECIES	Pentobarbital		Thiopental		Ketamine HCl[a]		Urethane[b]		Ketamine/ Xylazine		Alphaxalone/ Alphadolone (Saffan)[c]	
	Mg/Kg	Route	Mg/Kg	Route	Mg/Kg	Route	Mg/Kg	Route	Mg/Kg	Route	Mg/Kg	Route
CAT	25	IV	10-15	IV	20	IM	1250	IV	15/ 1	IM IM SC	9-12 12-18	IV IM
DOG	20-30	IV	25	IV			1000	IV			contraindicated	
GOAT	30	IV	15	IV	20	IM						
GUINEA PIG	37	IP	20	IV	100-200	IM	1500	IP IV	40-100/ 4-5	IM IM SQ	40	IP
HAMSTER	50-90	IP	20-40	IV IP							150	IP
MOUSE	30-40	IP	30-40	IV IP	100-200	IM			200/ 10	IM IP	10-15	IV
NON-HUMAN PRIMATE	5-15	IV	15-20	IV	5-25	IM			7/ 0.6	IM IM	6-9 12-18	IV IM
RABBIT	45	IV	20	IV	50	IM	1000	IV IP	35-50/ 5-10	IM IM	6-9	IV
RAT	40	IP	20-40	IV IP	60-100	IM	1000	IP	10/ 5-10	IP IM IP IM	10-12	IV
SHEEP	30	IV	15	IV	20	IM						
SWINE	30	IV	6-8	IV	10	IM			20/ 2	IM IM	2 5	IV IM

a Ketamine useful for birds at 15-20 mg/kg for immobilization and from 40-100 mg/kg for anesthesia in healthy birds, alone or in combination with a suitable tranquillizer.

b May only be used for non-survival surgery–gives prolonged anesthesia. CAUTION: Urethane is carcinogenic.

c Saffan useful as anesthetic for birds given IV rapidly at 12-14 mg/kg body weight.

APPENDIX XII
ANESTHETIC AND SEDATIVE DRUG DOSAGE: AMPHIBIANS AND REPTILES*

Species	Agent	Dosage and Administration
Chemical Restraint of Amphibians		
Frog	MS-222 (Tricaine methane-sulfonate)	1:1000 adult by immersion 1:5000 juvenile by immersion • prepare 1:1000 stock solution by adding 1 gm MS-222 to 1 liter of water • buffer with 2 grams Na bicarbonate; use of unbuffered acidic MS-222 has caused acidosis, increased BUN, ACTH and cholesterol and is believed to be a stressor in other aquatic species • for recovery use administer at holding or ambient temperature to avoid shock and use an air-stone to oxygenate solution, induction 15 minutes • for rapid induction, use warmed solution; however, may induce shock • for maintenance, dilute induction concentration 50 percent, cover animal with paper towel soaked in solution • recovery 30 to 90 minutes
Newt/Salamander	MS-222 (Tricaine methane-sulfonate) Benzocaine	1:2000-1:7500 by immersion • prepare and administer solution as for frog • induction more rapid; 3-5 minutes 1:10,000 by immersion • dissolve 100 mg crystalline solid in 5 ml ethanol, add to1 liter of water • 5 minute induction at room temperature
Chemical Restraint of Reptiles		
Crocodilian	Ketamine Pentobarbital Halothane/Isoflurane	40-60 mg/kg IM • administer in forelimb muscles • induction 15-30 minutes • require adjunct anesthesia for surgery 7.5-15 mg/kg IP; recovery up to 5 days, unpredictable effects • not recommended for recovery use • use after premedication with ketamine; otherwise, apnea results in prolonged induction in diving species • use nasal mask, preoxygenate for 3 minutes with 100% oxygen, then give 4% halothane or isoflurane until jaw tone slackens • block mouth open, intubate and maintain on positive pressure ventilation, use 100% oxygen and 0.5-2% anesthetic gas • do not exceed 10 cm water pressure during PPV; ventilate 4-6 times per minute 10-20 ml/kg tidal volume

Species	Agent	Dosage and Administration
Turtle	Ketamine	40-80 mg/kg IM in forelimb • results highly variable, prolonged induction common, resp. arrest and death at doses over 110 mg/kg common, prolonged recovery 6 hours - 3 days • use at low dose to abolish apnea during gas anesthesia
	Halothane/Isoflurane	• use after ketamine premedication • mask induction using N_2O as with crocodilian or direct intubation and maintain on gas anesthesia • can spontaneously ventilate, if in dorsal recumbency use PPV at 6 breaths per minute, maintain at 0.5-1.0 percent gas
	Pentobarbital	60 mg/kg IP • dilute stock solution to 25 mg/kg to lessen irritation • prolonged induction (1-3 hours) and recovery (3 days) • may have no effect in 10 percent of turtles
Lizard	Ketamine	20-30 mg/kg IM in forelimb • apnea common after induction, intubate and ventilate as for turtles with oxygen during apnea
	Halothane/Isoflurane	• mask induction with oxygen or nitrous oxide/oxygen and 4 percent gas, apnea common; use ketamine premedication • maintain at 0.5-2.0 percent gas • recovery rapid (30 minutes or less)
Snake	Ketamine	40-80 mg/kg IM in dorsal epaxial muscles • 3-5 minute induction, muscle rigidity common • recovery dose-dependent, 30-90 minutes
	Halothane/Isoflurane	4 percent by mask/chamber • apnea uncommon, use of N_2O will hasten induction which is rapid (5-10 minutes) • maintain at 0.5-2 percent, intubate and allow to spontaneously ventilate • exercise caution if using PPV due to fragility of snake air sac

* BENNETT, R.A. A review of anesthesia and chemical restraint in reptiles. J. Zoo. Wildlife Med. 1991; 22 (3): 282-303.

APPENDIX XIII
ANESTHETIC AND SEDATIVE DRUG DOSAGE: FISHES

This section has been revised. Please see "Additional information related to the *CCAC guidelines on: the care and use of fish in research, teaching and testing*".

February 2017

APPENDIX XIV
METHODS OF EUTHANASIA BY SPECIES

This section has been revised. Please see the *CCAC guidelines on: euthanasia of animals used in science* (2010).

February 2017

APPENDIX XV
CCAC POSITION STATEMENTS

A. ETHICS OF ANIMAL INVESTIGATION

Please see the *CCAC policy statement on: ethics of animal investigation* (1989).

February 2017

B. CATEGORIES OF INVASIVENESS IN ANIMAL EXPERIMENTS

Please see the *CCAC policy statement on: categories of invasiveness in animal experiments* (1991).

February 2017

C. CCAC GUIDELINES ON ACCEPTABLE IMMUNOLOGICAL PROCEDURES

For procedures related to antibody production please see the *CCAC guidelines on: antibody production* (2002).

February 2017

When beginning an immunization, choosing the correct adjuvant may be difficult. As a general suggestion, Freund's Complete Adjuvant (FCA) may be used when only small amounts of soluble immunogens are available. FCA is considered to be an emulsion consisting of equal volumes of FCA to antigen (1 part FCA or less to 1 part antigen). If large amounts of particulate, or highly immunogenic immunogens are available, other adjuvants should be considered.

An important aspect in immunization procedures is the utilization of skilled, competent, technical staff experienced in the handling of the species being used and in performing the technique. They must be knowledgeable and capable of recognizing signs of distress in all injected animals, and be responsible for taking action when necessary.

FCA should be used only for the most problematic immunization situations. It must never be given either intravenously or in repeated doses. FCA must not be used in horses.

Intradermal Route

Sound scientific evidence and justification must be available if the intradermal route of injection of FCA is to be used, because of the frequent ulceration and infections that occur at the site of such injections. The use of the intradermal route may be justified only when the purpose is to induce cell-mediated response.

In rabbits, volumes of inoculum in excess of 0.05 mls (50 microliters) per site should not be used. The location of the site(s) should be carefully selected so as to prevent mutilation. A minimal number of sites should be selected, and the distance between each site be maximized.

The intradermal route is inappropriate in the mouse. Nor is it recommended in other rodents.

Subcutaneous Route

In guinea pigs, up to a total volume of 0.4 ml (400 microliters) of inoculum may be injected subcutaneously dorsally in the neck, in one or divided into several sites. In rabbits, the site of choice is the interscapular region (between the shoulder blades) on the dorsum (back), administering up to 0.25 ml of inoculum (250 microliters) per site, to a maximum of four sites. The distance between sites should be maximized. In the mouse, up to 0.1 ml (100 microliters) may be administered in the neck region.

Intramuscular Route

In rabbits, intramuscular injections of FCA may be administered in the thigh muscle; up to 0.5 ml (500 microliters), preferably in one site. Intramuscular injection of FCA is not recommended for small laboratory animals such as rats, mice, hamsters, gerbils, etc.. For larger animals such as cats, dogs and poultry, up to 1 ml of FCA injected into the thigh muscles is acceptable. In livestock such as pigs, cattle, sheep and goats, the intramuscular route is acceptable.

Intraperitoneal Route

The intraperitoneal route for injection of FCA is permitted in small rodents only. FCA should be administered only once, and be limited to minimal volumes of up to 0.1 ml (100 microliters).

Intravenous Route

FCA is not to be injected intravenously.

Footpad Injection

FCA should not be injected in the feet of rabbits. Footpad injection of FCA in rodents is not permissible unless there is scientific evidence indicating this route is essential as a specific requirement for the production of immune response. In rats and mice, only one footpad may be used. Animals should be maintained on soft bedding and not on wire-bottomed cages.

Induction of Ascites Fluid in Animals

Pristane or other recognized priming agent(s) (excluding FCA) may be used.

Ascites may be collected only for as long as the animal is not experiencing pain or distress, is in good body condition, and does not show signs of debilitation, dehydration or other complications from the procedure. Upon recognition of loss of condition, pain, or distress the animal must be euthanized according to a method approved by the Canadian Council on Animal Care (CCAC).

Observation of Injection Sites

The injection site(s) must be observed by the investigator or his/her designate, a minimum of three times per week, for four weeks after each injection.

If a lesion(s) develops at any injection site, it must be reported through established channels, e.g., the animal resources supervisor or veterinarian, and must receive appropriate veterinary treatment. Such lesions should be inspected at least three times per week by the investigator or his/her designate, until all lesions are healed.

Revised June 1991

APPENDIX XVI
JOURNALS HELD BY CCAC

The CCAC no longer maintains a library of journals and newsletters for public access.

February 2017

APPENDIX XVII
GLOSSARY

***ABNORMAL BEHAVIOUR** – Behaviour that deviates from a defined, comparable standard. Such a standard may be a behavioural inventory typical for a given genotype, age group, sex, nutritional level, housing condition or management system, etc.

AD LIBITUM – Free choice.

ADJUVANT – A substance which non-specifically enhances the immune response to an antigen.

AMBIENT TEMPERATURE – The temperature surrounding the animal: under caging conditions may refer to the temperature in the microenvironment inside the cage as opposed to temperature outside the cage in the room or enclosure.

ANALGESIC – Substance which reduces or ameliorates the sensation of pain.

ANESTHESIA – The loss of sensation in a part or portion (local) or all (general) of the body, usually produced by the administration of a chemical or a drug.

ANTIBODY – A molecule produced by animals in response to antigen, and which has the particular property of combining specifically with the antigen which induced its formation.

ANTICOAGULANT – A substance added to whole blood to prevent clotting.

ANTIGEN – A foreign material or substance that stimulates the formation of antibodies when introduced into the tissues and blood stream.

ANTISEPTIC – 1. Preventing decay or putrefaction; 2. A substance which will inhibit the growth and development of microorganisms.

ANXIETY – An aroused state in which there is involuntary and voluntary nervous activation.

ASEPTIC – The absence of living germs, free from septic or poisonous putrefactive products.

AXENIC – Free of foreign organisms; germ-free.

BACK CROSS – The cross of an F1 hybrid to either of its parents (see F1 below).

BARRIER HOUSING – Housing for research animals that protects them from outside contamination through both procedure and facility design. In contrast, containment housing protects the outside environment from contaminants within the animal housing facility.

BIOSAFETY CABINET – A special exhaust hood with an enclosed work surface used for biological testing and experiments. Biosafety cabinets protect the surrounding room, and they protect workers from hazardous materials being used in the cabinet.

BIOTECHNOLOGY – The use or development of techniques using organisms or parts of organisms to provide or improve goods or services.

BIOPSY – The surgical removal of a cell or sample of tissue for diagnostic purposes.

BREED – A population of animals within a species, which differs from those in other populations within the same species in respect to definite genetically determined traits.

CANNULA – A tube (may be plastic or glass) which is inserted into the intravascular compartment or into the body to facilitate administration or withdrawal of gases or liquids.

*__CIRCADIAN__ – Referring to cyclic rhythmicity corresponding closely to a 24 hour interval.

CLOSED COLONY – A colony not recruiting breeding animals from outside itself.

***COGNITION** – A process of perception, reasoning and development of expectations.

COLONY (HERD, FLOCK) – An animal population maintained under some degree of control for the purpose of reproduction. A group of animals representing a single genetic pool produced at a single site under identical conditions of management.

CONDITIONING – Term applied to examination and preparation of animals for research.

CONGENIC – Animals which genetically differ at one particular locus.

CONJUNCTIVITIS – Inflammation of the conjunctiva (the membrane that lines the eyelids and covers the exposed surfaces of the eyeball).

CONTAGIOUS – A disease or disorder easily transmitted from individual to individual.

CONTAINMENT HOUSING – Housing for research animals that protects the environment from contaminants within; accomplished through procedure and facility design.

***DEPRIVATION** – Removal of needed substances (feed deprivation, water deprivation), perceptual isolation from things desired (social isolation) or prevention of the performance of necessary behaviours (sleep deprivation, exercise deprivation). Deprivation frequently is used experimentally to induce a detectable drive.

DIFFERENTIAL PRESSURE – The difference between pressures measured at two points or levels in a system.

DOMINANT – Controlling. Usually applied to controlling trait or gene governing genetic patterns.

DRIVE – An internal state causing increased activity, e.g., hunger drive.

EDEMA – The presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body; usually applied to accumulation of fluid in subcutaneous tissues.

EMBRYO – The early or developing stage of any organism, especially the developing product of fertilization of an egg.

***ENVIRONMENTAL COMPLEXITY** – The diversity and intensity of environmental stimuli relevant to a given organism, age group, species, etc. Environmental complexity may range from very low to very high, and thus be characterized as insufficient, adequate, or excessive.

ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA) – Rapid, sensitive and cost-effective test for screening large numbers of serum samples. ELISA kits are commercially available.

ESTRUS – The period when mating may occur.

ETHICS – A system of moral principles or standards governing conduct.

ETHOLOGY – The scientific study of animal behaviour.

F1 HYBRID – The first generation cross between two strains, between two inbred strains, between two lines, etc.

FARROW – The act of giving birth by sow (guinea pigs or swine).

FERTILIZATION – The union of the sperm of the male with the ovum (egg) of the female leading to reproduction.

FETUS – A developing embryo in utero.

FOMITE – Non-living objects that can carry disease organisms (e.g., restrainers, feeders, mops, etc.).

FREUND'S COMPLETE ADJUVANT (FCA) – An emulsion of aqueous antigen in oil. Contains killed Mycobacterium tuberculosis while Incomplete Freund's Adjuvant does not.

FULL SPECTRUM LIGHTING – Fluorescent lighting that very closely matches the spectral energy distribution of sunlight.

FUME HOOD – A negative airflow cabinet designed to prevent exposure of personnel to hazardous materials being handled in it, chemical or microbiological.

GENE – The hereditary unit that occupies a fixed chromosomal locus, which through transcription has a specific effect upon phenotype.

GENOME – The total genetic material contained within the cell.

GENOTYPE – The genetic constitution of an animal, as distinguished from its phenotype.

GESTATION – The period between conception and birth which includes embryonic and fetal life.

GNOTOBIOTES – Animals which are completely germ-free or may have one or more clearly-identified microorganisms existing in the animal.

GOOD LABORATORY PRACTICES (GLP) – Standards for conducting non-clinical research studies as published by the U.S. Federal Food and Drug Administration (USFDA).

GROSS SQUARE METERS – All of the floor space inside building measured from the outside surface of exterior walls.

HAREM MATING – Mating of one male with more than two females.

***HEALTH** – A relative state of physical, psychological and social well-being.

HEAT – The period during which the mating desire is prominent in the female.

HEMATOCRIT – The volume percentage of erythrocytes (red blood cells) in whole blood. Also Packed Cell Volume (PCV).

HEMOGLOBIN – The oxygen carrying pigment of erythrocytes (red blood cells) composed of iron complex and protein.

HIGH EFFICIENCY PARTICULATE AIR (HEPA) FILTER – Used in cleanrooms, biological safety cabinets, laminar flow units, etc., to filter out contaminating particles as small as 0.5 microns in diameter.

HERITABILITY – A measure of the degree to which a phenotype is genetically determined.

HUMIDITY (RELATIVE) – The ratio of the quantity of water vapour actually present in the air to the amount of water vapour that air is capable of holding at the given temperature.

IMPRINTING – The learning process involved in developing, during an early sensitive period, the tendency to follow or otherwise approach an object.

INFECTION – Disease process caused by the invasion of microorganisms into the body tissue.

INBRED – Inbreeding - resulting from mating between closely related animals.

INFLAMMATION – The condition into which tissues enter as a reaction to injury or an infectious agent.

INTRADERMAL – Delivered into the dermis or skin.

INTRAPERITONEAL (IP) – Delivered into the peritoneal or abdominal cavity.

INTRAVENOUS (IV) – Delivered into a vein.

LAMINAR AIRFLOW – Uniform direction movement of air. Laminar airflow is generally associated with fume hoods or biological safety enclosures that utilize this characteristic to capture and carry away airborne particles.

LATENT OR MASKED INFECTION – An infection or condition which is not clinically expressed in the animal but may, under stress or certain conditions, develop into an overt, recognizable diseased state.

LITTER – a) numerous young born at one time of a single female; b) in reference to bedding may mean straw, hay or other material used for the purpose of bedding.

MAJOR SURGERY – A surgical procedure in which there is direct visual access to a major body cavity (cranium, spinal canal, thorax, abdomen, pelvis) and/or exposure of major vascular, muscular, skeletal, neural, lymphatic or glandular structures and/or removal of, or alteration to, a functionally significant amount of tissue. There is no clear boundary between Major and Minor Surgery; thus Animal Care Committees (ACC) should use definitions of these terms only as adjuncts to the "Categories of Invasiveness", and should seek additional professional judgment when the level of invasiveness and injury is unclear.

MALIGNANT – Tending to become progressively worse and to result in death.

MASS AIR DISPLACEMENT CLEANROOM (MADC) – A cleanroom used in conjunction with animal housing in research facilities to keep the environment free of hair, dandruff and other airborne contaminants. The level of cleanliness is determined by the number of air changes per hour and the numbers and types of animals held in the cleanroom.

MATERIAL SAFETY DATA SHEETS (MSDS) – Technical documents that provide detailed and comprehensive information on controlled products related to health effects of overexposure to the products; hazard evaluation related to the products handling, storage or use; measures to protect employees at risk of over-exposure; and emergency procedures.

MICROENVIRONMENT – A small, isolated habitat, usually within a cage.

MICROINJECTION – A technique used for the insertion of genes from one cell into another cell.

MICROISOLATION CAGING – A caging system that protects animals from becoming contaminated via other lab animals or personnel by placing the barrier at cage level and never allowing that barrier to be opened except in a protected class 100 environment by personnel whose pertinent body surfaces are covered and decontaminated with a sterilant.

MICROORGANISM – A microscopic living agent, often a producer of disease.

MINIPUMP – A small device, implanted in the body (usually subcutaneously or intraperitoneally), which through osmotic pressure on a drug-containing chamber, provides continuous controlled delivery of drugs to the body.

MINOR SURGERY – A surgical procedure that does not result in removal of, or alteration to, a functionally significant amount of tissue. There is no clear boundary between Minor and Major Surgery; thus Animal Care Committees (ACC) should use definitions of these terms only as adjuncts to the "Categories of Invasiveness", and should seek additional professional judgment when the level of invasiveness and injury is unclear.

MORBIDITY – The occurrence of sickness.

MORIBUND – Close to death.

MUTANT – An organism bearing a mutant gene that expresses itself in the phenotype of the organism.

MYCOTIC INFECTION – Disease caused by a fungus.

NECROPSY – Systematic dissection of an animal after death to elucidate the cause of death. Same as post-mortem examination. Necropsy preferred term for animal postmortem examinations as opposed to autopsy for human-beings.

NECROSIS – The death of a portion of tissue or organ.

NET ASSIGNABLE SQUARE METERS – The net floor space in a building measured from the inside surfaces of exterior walls and excluding interior walls and partitions, mechanical equipment rooms, lavatories, janitorial closets, elevators, stairways, major circulation corridors, aisles, and elevator lobbies.

NONHUMAN PRIMATES – Any nonhuman member of the order primates of mammals including prosimians, monkey, apes. Synonyms: infrahuman primate, sub-human primate.

NON-SENTIENT MATERIAL – Material that fails to visually demonstrate pain, without or almost devoid of nervous and sensory systems.

NUDE MOUSE – A genetically athymic mouse, it also carries a closely-linked gene producing a defect in hair production.

ORAL OR PER OS (PO) – The act of administering a substance through the mouth.

OVUM – Egg or germ cell produced by the female reproductive organ, the ovary.

PATHOGEN – An organism which causes disease.

PARTURITION – The act or process of giving birth.

PHENOTYPE – The outward visible expression of the hereditary constitution of an organism.

***PICA** – Abnormal appetite for unusual and often inappropriate feed, e.g., dirt, hair, feces, etc.

PLASMA – The fluid portion of blood, without cells, in which anticoagulants have prevented clotting.

***POLYDIPSIA** – The consumption of large amounts of liquids (frequently used interchangeably with the term, excessive thirst).

***POLYPHAGIA** – Consumption of an unusually broad variety of foods. Compare: Hyperphagia.

***POLYURIA** – Excessive excretion of urine.

POST PARTUM – The immediate period following parturition or birth of young.

PROGENY – The young of a species.

PROGNOSIS – The prospect as to recovery from a disease as indicated by the nature and symptoms of the case.

PROPHYLAXIS – Prevention.

PUBERTY – The onset of sexual maturity.

QUARANTINE – The segregation or isolation of animals from all others to prevent the spread of disease.

RESTRAINT – Holding or securing to reduce activity in order to prevent the animal from causing harm to itself or harm to the handler.

***REWARD TRAINING** – A type of operant conditioning in which a reward (positive reinforcer) is directly contingent on the performance of the subject. According to the training objectives, the performance resulting in reward may be either a produced response or a withheld response.

RISK – The probability of adverse effects, their nature and their severity over a range of exposures.

ROUGHAGE – Food that is high in fibre and low in digestible nutrients.

RUMINANT – A cud-chewing polygastric animal having usually four digestive compartments; includes such animals as cows, goats, sheep.

SANITIZE – To reduce the level of microorganisms to an acceptable health level.

SEMEN – The ejaculate of the male reproductive organs containing spermatozoa and including material from accessory glands and the testes.

SERUM – Non-cellular components of blood which remain after clotting.

SERVICE – In reference to animal breeding, refers to the act of copulation by the male animal. The male animal serves (breeds) the female.

SEVERE COMBINED IMMUNE DEFICIENCY (SCID) MOUSE – Mice that possess a genetic autosomal recessive mutation. SCID mice lack functional lymphocytes, a defect that is manifested in a number of ways including lymphopenia, agammaglobulinemia and a high susceptibility to infection. SCID mice are desirable research models for implantation of foreign tissues and tumours.

SEXUAL MATURITY – The age at which the animal is first able to reproduce.

***SOCIAL DOMINANCE** – Ascendency of an individual over another individual(s).

SPECIFIC PATHOGEN FREE (SPF) – Defines the health status of animals raised free of specific disease organisms.

STANDARD OPERATING PROCEDURES (SOP) – Written documents specifying the procedures that must be followed to ensure the quality and integrity of the study.

***STEREOTYPED BEHAVIOUR** – Behaviour repeated in a very constant way. The term generally is used to refer to behaviour that develops as a consequence of a problem situation such as extended social isolation, low level of environmental complexity, etc.

STERILIZATION – The complete destruction of microorganisms by heat, chemical compounds, mechanical or physical means. In animal breeding, refers to any procedure which renders the animal incapable of reproduction.

STOCK – A collection of outbred animals being grown or maintained for breeding or for experimental use.

STRAIN – A group of animals of known ancestry maintained by a planned inbreeding mating system; generally with some distinguishing characteristics.

STRESS – A strain upon the normal physiological or psychological processes or functions of the body, organ or tissue. Some stresses may cause pathology or diseased states or weaken the normal body defences.

SUBCUTANEOUS (SC) – Occurring beneath the skin.

SUSCEPTIBLE – Lacking in resistance to infection or injury or permitting a weak defense.

SYNDROME – A group of signs (animals) or symptoms (humans) occurring together designating a state or a disease.

SYSTEMIC – A condition occurring throughout the entire system of the entire animal body.

THRESHOLD LIMIT VALUE (TLV) – An airborne concentration of a substance to which indoor workers may be exposed repeatedly without adverse effects.

TISSUE CULTURE – The propagation of tissue removed from organisms in a laboratory environment that has strict sterility, temperature and nutrient requirements.

TOXIN – A product poisonous to the animal, arising from a plant or animal cell. It may be produced by the cell itself and excreted from the cell or it may be contained within the cell, such as the bacterial cell, and released only on the death of the cell.

TRANQUILLIZER – An agent, usually a drug, capable of making the animal quiet and docile.

TRANSGENIC ANIMALS – Animals whose hereditary DNA has been augmented by the addition of DNA from a source other than parental germplasm, usually from another animal or a human, using recombinant DNA techniques.

TRAUMA – An injury.

VACCINE – A substance used to stimulate the production of antibodies against a specific disease-producing agent, usually as a preventive measure.

VASCULAR ACCESS PORT – Catheters terminating subcutaneously in "ports" which allow transcutaneous access with needles.

VECTOR – A living thing that is capable of carrying and transmitting infectious agents.

VERMIN – Any undesirable or disturbing offender such as flies, lice, fleas, cockroaches, ticks, mice, rats, weasels.

VIABILITY – Usually refers to the ability of the young to live after birth.

VIRUS – Any of a large group of organisms containing genetic material, but unable to reproduce outside a host cell.

VITAL CENTER – Any one of a various group of nerve cells located in the medulla oblongata of the central nervous system (CNS) which co-ordinates functions essential to life, e.g., respiration, heart beat.

***WELL-BEING** – A state or condition of physical and psychological harmony between the organism and its surroundings. Good health and manifestation of a normal behavioural repertoire are the most commonly used indicators of (an) animal's well-being.

WHELP – The act of parturition in the bitch, the birth of puppies.

WORKPLACE HAZARDOUS MATERIALS INFORMATION SYSTEM (WHMIS) – A federal system to provide information on hazardous materials used in the workplace, it concentrates on three key elements; labels, material safety data sheets, legislation and employee education.

ZOONOSIS – A disease of animals that may under natural conditions be secondarily transmitted to humans.

* Excerpted from: 1) Dictionary of farm animal behaviour. Hurnik, J.F., Webster, A.B. and Siegel, P.B., eds. University of Guelph 1985; 2) Glossary of terms relevant to farm animal behaviour and welfare. In: Farm animal behaviour and welfare. Fraser, A.F. and Broom, D.M., eds., Ballière Tindall, London 1990: 385-391.