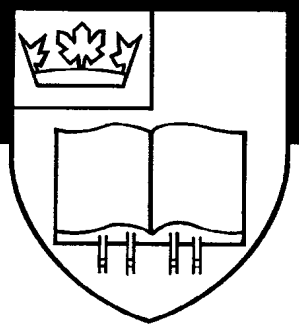
Recommendations for the Disposition of the Health Canada Primate Colony

An Expert Panel Report
prepared at the request of

The Royal Society of Canada

for
Health Canada



"studiis eodem diversis nitimur"
"different paths, one vision"

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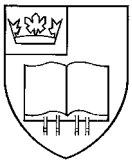

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Expert Panel on the Non-Human Primate Colony

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November 20, 1997

Dear Dr. Haynes:

I am pleased to enclose a copy of the report "Recommendations for the Disposition of the Health Canada Primate Colony" prepared by the Expert Panel on the Health Canada Primate Colony established by the Royal Society of Canada Committee on Expert Panels in response to a request from Health Canada. Our report addresses questions posed by Health Canada in Terms of Reference agreed upon by the Expert Panel. These Terms of Reference asked the Expert Panel for its considered opinion on the public policy need for a Canadian non-human primate breeding colony, and in light of the assessment of this need to make recommendations for the disposition of the existing Health Canada primate colony.

The enclosed report responds to this request by carrying out an assessment of the current trends in Canadian research use requiring this species of monkey (*macaca fascicularis)*, the value of the species to the conduct of research critical to Canadian interests, and the value of the current Health Canada facility at Tunney's Pasture. The report evaluates various options for disposition of the colony in light of this assessment, and in light of considerations governing the ethical treatment of animals. The various options considered were those specifically suggested by Health Canada as well as others suggested by groups and individuals who responded to the Expert Panel's public invitation for submissions.

I am happy to inform you that the enclosed report represents a full consensus of opinion among the members of the Expert Panel, who represent a wide range of disciplines and perspectives. This is a tribute to the RSC Committee on Expert Panels, which selected a group of individuals with extraordinary abilities to work at complex and divisive issues in a collegial and collaborative manner. It is also, of course, a tribute to the Panel members themselves, who made my work as Chair an easy task.

The work of this Expert Panel was, as you know, carried out under severe limits of time. It required efficient coordination of our research, discussion and writing, most of which had to be carried out by means of electronic communication. We were able to obtain the needed information and to produce this report on time thanks to the experienced coordination by Dr. William Leiss, Chair of the Committee on Expert Panels, the administrative efficiency of Ms. Sandy Jackson, the Project Administrator for the RSC, and the tireless competence of Ms. Holly Mitchell, Executive Assistant to the Panel, who managed the complex logistics of this exercise skillfully and with good humour.

I trust that you will convey the report to Health Canada. I hope that it will find our recommendations of value in the critical decisions it faces with respect to the primate colony.

Yours sincerely,

Conrad G. Brunk
Chair, RSC Expert Panel on the Health Canada Primate Colony

Prefatory Note

In June 1997 Health Canada's Health Protection Branch approached the Royal Society of Canada with a request to commission an expert panel on the future of the non-human primate colony at Tunney's Pasture. The Society agreed to do so, and the Committee on Expert Panels undertook the task of screening and selecting for panel service the individuals whose names now appear as the authors of this Report.

The report entitled "Recommendations for the Disposition of the Health Canada Primate Colony" represents a consensus of the views of all of the panelists whose names appear on the title page. The Committee wishes to thank the panel members and panel chair, the peer reviewers, and the panel staff for completing this very important report within a short period of time.

The Society has a formal and published set of procedures, adopted in October 1996, which sets out how expert panel processes are conducted, including the process of selecting panelists. Interested persons may obtain a copy of those procedures from the Society; the Committee on Expert Panels will also respond to specific questions about its procedures and how they were implemented in any particular case.

The Terms of Reference for the expert panel on the non-human primate colony are reproduced elsewhere in this Report. As set out in our procedures, the terms are first proposed by the study sponsor, in this case Health Canada, and accepted provisionally by the Committee. After the panel is appointed, the terms of reference are reviewed jointly by the panelists and the sponsor; the panelists must formally indicate their acceptance of a final terms of reference before their work can proceed, and those are the terms reproduced in this Report.

The panel first submits a draft of its final report in confidence to the Committee, which arranges for another set of experts to do a peer review of the draft. The peer reviewer comments are sent to the panel, and the Committee takes responsibility for ensuring that the panelists have addressed satisfactorily the peer reviewer comments.

The panel's report is released to the public without any prior review and comment by the study sponsor. This arm's-length relationship with the study sponsor is one of the most important aspects of the Society's expert panel process.

Inquiries about the expert panel process may be addressed to the Chair, Committee on Expert Panels, Royal Society of Canada.

William Leiss,
Chair, Committee on Expert Panels

on behalf of the Committee members for this Panel:

Professor Christopher Garrett, F.R.S., F.R.S.C., University of Victoria
Dr. F. Kenneth Hare, C.C., F.R.S.C., Oakville, Ontario
Dr. Earle Nestmann, CanTox

November 20, 1997

TABLE OF CONTENTS

RECOMMENDATIONS FOR THE DISPOSITION OF THE HEALTH CANADA PRIMATE COLONY

An Expert Panel Report Prepared at the Request of
THE ROYAL SOCIETY OF CANADA
for Health Canada

November 20, 1997

EXECUTIVE SUMMARY

This Report is a response to Health Canada's request to the Royal Society of Canada that an Expert Panel be assembled by the Society to advise the Department on the future of the cynomolgus macaque monkey colony maintained at its Tunney's Pasture facilities in Ottawa. The Terms of Reference asked the Expert Panel to assess the public policy need for a Canadian non-human primate breeding colony and, in light of this assessment, to propose a preferred course of action for the disposition of the colony.

The Terms of Reference asked the Panel to "present the pros and cons of maintaining the existing monkey breeding colony" and specified that the Panel should consider, in addition to the central question of the welfare of the animals, the following aspects:

- The value of the Health Canada monkey colony in supporting research in the health effects of disease and disease prevention, especially in the university, private sector and other government organizations.
- The responsibility of the Government of Canada for the maintenance of the colony in light of public policy interests in research and development, health protection, and health security. This includes consideration of the costs and benefits to future Canadian research and development of maintaining the monkey colony, and the importance of maintaining security of supply within Canada for future Canadian research needs.

- Whether there are ways other than the current arrangement for the maintenance of the colony (e.g., management by universities, the private sector, a consortium of interested parties, or foreign suppliers) to maintain security of supply for Canadian research.

The Expert Panel considered all of these issues during the course of its investigations, which included its own collection of data as well as a general public invitation to interested parties to make submissions on these questions to the Panel. The Report addresses the issues in the following manner:

- **Section I:** The Panel interprets and clarifies the Terms of Reference. The Panel interprets the Terms of Reference to require the consideration of options not specifically mentioned, the development of an explicit ethical framework with which to assess the options, and to include recommendations for the "research colony" as well as the "breeding colony."

- **Section II:** The Panel considers the historical and current role played by the Health Canada primate colony in Canadian health research, including the current patterns in usage of non-human primates. With the ending of the duplicate vaccine testing program and the research projects carried on within the Animal Resources Division, internal demand in Health Canada will drop to zero. The available Canadian usage data indicates a pattern of decreasing use and probable decreasing future demand for the macaque as a research model.

- **Section III:** The Panel provides a profile of the cynomolgus macaque species in order to develop an understanding of the ethical and welfare implications of maintaining this particular species of animal in captivity and using it for research purposes. This species is a behaviourally and emotionally complex animal which requires a fairly rich environment to provide adequately for its well-being.

- **Section IV:** The Panel assesses the Tunney's Pasture primate facility from the point of view of its adequacy as a research and breeding facility, and from the point of view of the research value of the animals. The Panel finds that the facility is a "world-class" facility in many respects for the conduct of research with non-human primates and that the animals housed there constitute one of the most valuable macaque colonies to be found in the world. However, the Panel also reviews

criticisms of the current facilities from the point of view of animal welfare and finds some aspects to be in need of significant improvement.

- **Section V:** The Panel addresses the question of current and future health research needs with which Canada should be concerned, and in which the cynomolgus macaque monkey is an essential or important research model. The Panel identifies a number of areas of critically important health research in which the macaque monkey is a vital component and cites reasons why Canada should be involved in this research.

- **Section VI:** The Panel lays out the ethical assumptions and principles which guided its assessment of the various options for disposition of the animals. The Panel identified as the object of its ethical concern the potential impact upon the welfare of, not only the animals in the breeding colony, but also other animals which might potentially be used as replacements for research in Canada or elsewhere. The Panel assumes for the purposes of this Report the ethical acceptability of limited and strictly controlled research use of the macaque monkey. However, it cites several principles governing the responsibility of animal breeders, owners, and researchers towards these animals. The Panel argues that general euthanasia as a method of population reduction or control for financial reasons is ethically unacceptable.

- **Section VII:** The Panel identifies and evaluates the various options for the disposition of the colony which have been suggested to Health Canada and to the Expert Panel directly. The economic, political, and ethical considerations that work in favour of each option, as well as those that work against it are laid out by the Panel. The options considered are:
  - Sanctuary of the animals, both domestic and foreign
  - General euthanasia of the entire colony
  - Maintaining the status quo at Tunney's Pasture
  - Sale of the breeding colony to other research centres
  - Take-over by a new Canadian university/industry/government consortium
  - Employee take-over proposal

- **Section VIII:** The Panel outlines the conclusions reached on the basis of its analyses of the previous sections and its evaluation of the various options. The Panel reached the following conclusions:

1. The possibility that Canada might be faced in the future with a major health crisis posed by the onset of a new or re-emergent highly infectious disease or some other challenge to human health and well-being is not to be dismissed lightly. The macaque colony at Tunney's Pasture could play an essential role in the research that might be needed to meet such challenges. The loss of the colony would constitute an irreversible loss of the capacity to respond to these challenges should they arise, and could expose Canadian society to substantial health risks in the future.
2. These potential health security challenges may not provide sufficient ethical justification for the holding of animals in restrictive captive conditions. If the financial resources, either public or private, are not available to carry on significantly beneficial health research requiring non-human primates, the animals should be retired from those restrictive conditions into "sanctuary" conditions.
3. There currently exist important health research challenges of the kind outlined in Section V of this Report. However, there is not currently in Canada the level of health research funding or activity in areas requiring the macaque model that would make the establishment of an independent, or jointly funded, primate research centre feasible.
4. Only a major government initiative in support of such research can rationalize, either economically or ethically, the continuation of such a large primate breeding colony in Canada, even in cooperation with the private sector. Absent such a major public commitment to this research, immediate steps should be taken to begin the closing of the colony.
5. Whether or not there is funding for primate research in the future, Health Canada retains an ongoing ethical responsibility to dispose of the colony in a way that guarantees the protection of the animal's welfare, whether as a breeding colony for research purposes or as a sanctuary for animals permanently retired from research. The Panel does not believe

that any of the options for off-loading financial responsibility for the current breeding colony are feasible or ethically acceptable, e.g.,

B. The sale of the colony on the open market, which would abandon responsibility for the welfare of the animals and, by flooding the market, would not bring their normal market value as Specific Pathogen Free (SPF) animals and could lead to the encouragement of unnecessary use of animals in scientific research.

C. The privatization of the colony, which is not judged to be financially feasible.

D. The establishment of a government/university/industry consortium, for which there does not appear to be sufficient financial or other support, absent a commitment of major government funding.

E. The continuation of the status quo, which is unacceptable insofar as the breeding colony is larger than current research demands justify, and because of inadequate housing conditions for a portion of the population.

F. The wholesale euthanasia of the colony, which is ethically unacceptable.

Thus, Health Canada retains a financial obligation for one of two options:

- Placing the entire primate colony into sanctuary conditions, either in the current facility or elsewhere, discontinuing all breeding, and caring for the animals until the end of their natural life-spans, OR
- Establishing funding for a health research initiative which rationalizes the responsible research use of a portion of the current breeding colony, and makes the facility and research funding available to Canadian researchers.

- *On the basis of these conclusions the Expert Panel makes the following recommendations with respect to the breeding colony:*

Preferred Option: Maintain Canadian Health Research Capacity with Reduced-Size Monkey Colony

1. The Government of Canada should allocate funding for a health research grant program in areas of strategic health needs.

2. Part of this funding initiative should provide for the transformation of the Tunney's Pasture primate colony into a Canadian Primate Research Centre.
3. An immediate program to reduce the population of the primate colony to numbers necessary for actual Canadian research needs should be instituted.
4. The transfer of all animals in excess of those needed for research into permanent sanctuary in a renovated part of the Tunney's Pasture facility.

Secondary Option: Phase Out of Entire Breeding Colony and Sanctuary of Remaining Animals

If the Government of Canada does not undertake the establishment of some type of health research grant initiative requiring the macaque model such as that suggested for the Preferred Option, then the Panel recommends that Health Canada take immediate steps to reduce the population in the breeding colony to zero. This should be done by:

1. An immediate end to all further breeding.
2. Placing the entire colony into acceptable sanctuary conditions in Canada, to be maintained there for the natural life span of the animals.
3. Maintaining the sanctuary open to Canadian researchers wishing to conduct purely observational, non-invasive research, and permitting regular monitoring by CCAC and other competent organizations concerned with the welfare of the animals.
4. Permitting, only as an alternative to further imports of animals into Canada for research purposes, the sale of some animals to CCAC sanctioned Canadian investigators conducting bona fide research with their own sources of funding.

Section IX: The Expert Panel was also charged with responsibility to make a recommendation on the disposition of the Health Canada non-human primates at Tunney's Pasture currently part of research projects which are slated for termination under financial cutbacks. The Panel chose to make separate recommendations for these 148 animals because of considerations unique to their situation and the research projects of which they are a part.

If the funding of these projects is not restored, the Panel recommends the following course of action:

1. For as long as the research projects continue under the supervision of the researchers, any humane euthanasia of the animals required by the research protocol for the collection of valid scientific data or the prevention of suffering to the animal should be carried out in the time frame and the manner specified by the research protocol.
2. When the research projects are discontinued, the animals (unless infected with transmissible viruses) should be retired into permanent sanctuary. Since some of these animals have been subjected to toxins or other stresses which may lead to the early deterioration of their health, they, like any animal in sanctuary, should be humanely euthanized at the most appropriate time for the prevention of irreversible suffering.

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I. INTRODUCTION

This Report is provided in response to Health Canada's request to the Royal Society of Canada that an Expert Panel be assembled by the Society to advise the Department on a series of questions regarding the future of the cynomolgus macaque monkey colony maintained at its Tunney's Pasture facilities in Ottawa. The questions were laid out in provisional Terms of Reference provided to the Royal Society of Canada. These Terms of Reference were refined and clarified to the satisfaction of Health Canada and the Expert Panel at the first meeting of the Panel in July, 1997. The Royal Society agreed to submit the Report of the Expert Panel to Health Canada by November 30, 1997.

Terms Of Reference

The Terms of Reference for the Expert Panel were stated as follows:

An Expert Panel to Assess the Public Policy Need for a Canadian Non-Human Primate Breeding Colony has been convened to examine the need to continue the colony that has been developed at Health Canada.

This examination will present the pros and cons of maintaining the existing monkey breeding colony and, while considering the welfare of the animals, will include, but not be limited to, consideration of the following aspects:

1. *In what way(s) is the nature of the monkey colony at Health Canada unique, valuable and necessary in that it provides the only such facility in Canada to support the examination of the health effects of disease and disease prevention? In as much as the Health Canada present and foreseeable needs for non-human primate research are minimal, this consideration should focus on the needs in the university, private sector and other government organizations.*
2. *Taking into account the assessment of need from a Canadian public policy perspective, including research and development, health protection, and health security, what is the appropriate responsibility of the Government of Canada for the maintenance of the colony?*

- *What would be the costs and benefits (short-term and long-term) to on-going and future Canadian research and development of maintaining the monkey colony?*
- *How important is security of supply to future Canadian needs and can these needs be guaranteed from other international sources?*

3. *Could the identified needs be met and responsibility be discharged in ways other than the current arrangement for the maintenance of this colony, for example:*

- *could such a colony be effectively managed by universities, the private sector, or a consortium of interested parties?*
- *are there facilities elsewhere in the world that would be able to provide primates suitable for use within the framework of scientific health studies in Canada and are these facilities likely to be maintained in a manner that would ensure they will remain a reliable source of primates in the future?*

Interpretation Of The Terms Of Reference

- The Expert Panel and Health Canada officials agreed that these Terms of Reference should be interpreted broadly rather than narrowly and technically. This was important in several respects. First, it was agreed that the Expert Panel should investigate the options explicitly referred to in the Terms of Reference, but should not limit itself only to those options. For example, there were requests made directly and indirectly to the Expert Panel by various intervenor groups and individuals that it consider the option of retiring the animals in the colony from invasive research to "sanctuary" conditions, as well as the option of euthanasia. The Expert Panel included both these options in its assessment.
- Secondly, the Expert Panel interpreted the references to considerations for animal welfare in the Terms of Reference to mean that the question of the ethical treatment of the animals should be a critical component of the assessment of all options for the disposition of the primate colony. For this reason the Expert Panel felt it necessary to lay out explicitly a set of guiding ethical principles for the treatment of animals [Section VI], especially of non-human primates like the cynomolgus macaque monkey, and to assess each potential option

in light of these considerations as well as considerations of health security and economic feasibility.

- Thirdly, after an initial period of uncertainty Health Canada officials clarified for the Expert Panel their expectation that reference to the "breeding colony" in the Terms of Reference be interpreted as denoting all the non-human primates in the Health Canada facility, including those animals currently involved in research protocols as well as those in the breeding program. Since the animals currently involved in research are under special conditions relating to the requirements of their respective research protocols, the Expert Panel decided to approach the question of their ultimate disposition independently from that of the animals in the breeding program. The recommendations for the animals in the research program are given in the concluding section of the Report. For purposes of clarity, however, these two groups of animals will be referred to in this Report as the "Research Colony" and the "Breeding Colony".
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- **Panel Procedures**
- The members of the Expert Panel were appointed by the Royal Society of Canada Committee on Expert Panels in July, 1997. On July 14, the RSC issued a press release announcing the establishment of the Expert Panel. The press release included the provisional Terms of Reference and solicited written comments and suggestions from all interested parties in Canada. Although the press release called for these interventions to be submitted to the Royal Society by August 31, the Expert Panel became aware that many potential intervenor groups received information about the process too late to meet this deadline and agreed to receive submissions right up the beginning of its meeting on September 25-26, 1997.
- The Expert Panel convened its first meeting in Ottawa on July 28-30. During these three days the Panel met with officials from Health Canada to revise and clarify the provisional Terms of Reference, to outline the research tasks that needed to be carried out in order to address the questions put to the Panel, and to assign these research tasks to

Panel members. On July 30, the Panel members took a 3-hour tour of the Health Canada primate facility at Tunney's Pasture, conducted by Dr. Pierre Thibert, Chief of the Animal Resource Division. The Panel toured the entire primate facility, observing the animals in both the research and breeding colonies as well as the research labs. The Panel Chair, accompanied by one Panel member who had been unable to join the original tour of facility, revisited the facility on September 25.

- During the period between its first meeting in July and the meeting in late September, the Expert Panel received and studied submissions from over forty intervenor organizations and individuals. These are listed in ***Appendix I*** at the end of this Report. These represented a wide spectrum of interests relating to non-human primates and a wide range of viewpoints with respect to the disposition of the Health Canada primate colony. These submissions were sent to all members of the Panel and were thoroughly assessed and discussed by means of electronic mail communication. The Expert Panel is indebted to many of these intervenor groups for providing excellent background materials on many of the issues with which it had to grapple in reaching its conclusions. A number of the intervenors representing the welfare interests of the animals were especially helpful in providing well-researched data on the psychological and behavioural characteristics and needs of the cynomolgus macaque species, as well as the welfare considerations in the current housing conditions and the various options for the disposition of these animals. The Panel also received important information on the value of these animals for Canadian research from university research centres and individual researchers in Canada. The Expert Panel wishes to express its deep gratitude for the very significant assistance provided by the intervenors in this process.

After review of all the submissions from intervenors, and the conduct of independent research by each of the members, the Panel convened a second two-day meeting on September 25. At this meeting the members reviewed the submissions and its own research data. It also discussed, and reached consensus on, the ethical principles the members were prepared to adopt as the framework for assessing the various options A systematic assessment of the

research data as well as the Ethical Framework led the Panel to a consensus on the recommendations contained in this Report.

The first draft of this Report was sent out to an anonymous group of six Peer Reviewers selected by the Royal Society Committee on Expert Panels. The Panel received extensive comments from the Peer Reviewers, including many helpful suggestions for changes and amplification of various parts of the Report. In addition, two independent Peer Monitors advised the Expert Panel on which of the suggestions from the Peer Reviewers were critical and required incorporation into the Report or a response. The Expert Panel found the suggestions from both the Peer Reviewers and Peer Monitors to be extremely valuable in most instances. The incorporation of these suggestions into the Report strengthened it significantly.

II. ROLE OF THE HEALTH CANADA PRIMATE COLONY IN CANADIAN RESEARCH

Background

The concept of the Health Canada Primate Colony began in 1979 when the Federal Cabinet authorized Treasury Board to review the need for the establishment of a breeding centre for non-human primates, primarily to satisfy the needs of Health Canada for a polio-vaccine testing program as required under the Food and Drug Act. The other stated objective for the establishment of this colony was to "provide a nucleus for a full scale Canada breeding program should off-shore supply dry up."

The colony was actually established in 1983 with the importation of 1000 animals from the Philippines and within one year 406 births were recorded. Subsequent production figures ranged from 159-333 births/year (average = 256 births/year from 1985-1994). Approximately 15% to 80% of the domestic births (colony born - Animal Resources Division) during this period were utilized by the Bureau of Biologics for the polio vaccine testing program. The remaining animals used for research during this period were imported, wild caught (feral). It is noteworthy that all of the animals assigned to research projects during a 6-year period (1988-1994) were obtained from domestic production with no contribution from feral populations.

The primary usage of the breeding colony within Health Canada was for the polio vaccine testing program, with an average annual use of 120 animals. The population of the colony has ranged from a high of 1500 animals to a low of 726 (early 1997). As of 1997-98, program policy changes eliminate the need for Health Canada to conduct duplicate testing of polio vaccines tested by the manufacturer. This has reduced the Department's requirement for non-human primates in testing polio vaccines to zero for the foreseeable future.

Animal Resources Division (ARD) of the Health Protection Branch (HPB) of Health Canada is responsible for maintaining the Primate Colony. The budget of the ARD has fallen from $2.5 million in 1995-96 to $0.2 million in 1997-98. A further reduction of $0.5 million in

1998-99 by Program Review II leaves the ARD with a negative $0.3 million.[1] These budgetary cutbacks have placed in jeopardy the whole breeding and research program of ARD, not only the non-human primate colony.

In light of the bleak financial outlook for the ARD, the Program Management Board of the Health Protection Branch called for an internal review of the Division to address the future role and use of experimental animals in supporting HPB programs, and to develop options for alternate funding and program delivery. The report of this internal review group was submitted in June, 1997. Among its specific recommendations were the following two concerning the primate breeding colony:

- To determine a market value for the monkey colony as a commercial operation, and,
- To seek a national consensus on the requirement of the monkey colony for national health security needs.

The Internal Review Report concluded that the internal requirements for the cynomolgus model could not justify the maintenance of the breeding colony, and it went on to suggest that options be explored to find other options for preserving the valuable primate colony within Canada. Several of the options considered by this Expert Panel were proposed in this Internal Review Report.

Patterns of Use of the Health Canada Non-Human Primates

In addition to the use of cynomolgus monkeys from the colony for vaccine testing, Health Canada's own staff researchers have carried out a number of research projects over the years. Among the most recent of these have been projects on topics such as, "Dioxin In Pathophysiology Of Endometriosis In Cynomolgus Monkeys," "Macaque Model For SIV/HIV AIDS Vaccine Development", "Behavioural Effects Of Aging In Lead Exposed Monkeys; Behavioural Effects Of Postnatal PCB Exposure In Monkeys; And Trace Elements," "Toxicity

[1] However, more recent announcements by the Minister of Health have suggested that some of these budget cuts may be reviewed in the future.

Of Toxaphene In The Cynomolgus Monkey," and "Bone Lead Remobilization In Non-Human Primates Following Menopause." Health Canada has announced the termination of the current projects due to lack of funding, despite the fact that many of them are in midstream. This will result in the loss of a great deal of research data from years of work with the animals. A number of the distinguished researchers who have been working with the animals will be leaving the employ of Health Canada within the coming months.

HPB documentation provided to the Expert Panel indicates that the allocation of cynomolgus macaques to research and testing projects in Health Canada has decreased in recent years, from a high of 210 in 1989-90, 157 in 1995-96, to a low of 3 in 1996-97. The documentation also confirms that the projected need for cynomolgus monkeys within Health Canada itself in 1998 will drop to zero. This suggests that, unless there is a greatly expanded extramural Canadian research market for the animals, the continuation of the colony at its present rate of breeding is economically unfeasible, as well as pointless from the point of view of policy.

The Animal Resources Division attempted to take up this slack by increasing its sales of animals to other Canadian researchers and recovering at least part of its costs. ARD has sold animals over the years to Canadian universities and industries. Among the former were the following universities: British Columbia, Western Ontario, Waterloo, Manitoba, McGill, Toronto, Laval, Alberta, and Calgary.

Data provided by ARD show that the rate of transfer to external researchers has increased from an average of approximately 20 animals per year to 98 animals in 1995-96 and 142 animals in 1996-97. This recent increase in the transfer rate has not made the breeding colony at its current size financially viable on a cost-recovery basis. Over the period from 1985 to 1997, a total of 464 monkeys were provided to users. Of this total 227 were not useable for the breeding colony and were provided at less than market price. The remainder were sold at commercial or higher prices in order not to compete unfairly with the private sector.

During the past several years the breeding program has been actively continued, despite

the cuts in funding to the colony and the clear and repeated indications that it would not be able to continue as a Health Canada program. In most years the number of surviving births exceeded the total number of animals being used internally and externally. This has contributed to the continuing problem of over-crowding in the facility and the consequent animal welfare concerns that have been raised (see below).

Canada-Wide Research With Non-Human Primates

The Expert Panel did not find it easy to obtain reliable and accurate data on the actual numbers of non-human primates used in Canadian research and testing. The best data are those collected by the Canadian Council on Animal Care on the basis of the reporting from those institutions under its jurisdiction. The Canadian Council on Animal Care has altered its system of collecting data several times over the past few years in order to better achieve its own objectives, hence it is difficult to have direct comparisons over a series of years. However, the total numbers in its reports are accurate. Any use of non-human primates outside of CCAC's purview, of course, would not be included in their data. Cynomolgus monkey and other non-human primate usage in Canada are indicated in the following Table of CCAC data.

Animal Utilization Survey Data - (Non Human Primates)

Year		Univ/Colleges/ Hospitals	Govt.	Commercial	Others	Total
1989*	All					2100
1991*	All					2800
1993*	All					1900
1994	Cynomolgus	178	222	729		1129
	Others	217	27	172		419
	Total (all)					1548
1995	Cynomolgus	84	359	291	0	734
	Others	231	20	383	11	645
	Total (all)					1379
1996**	Cynomolgus	156		1237		1393

	Others	342		150		492
	Total (all)	498		1387		1885

*For the years 1989 through 1993 only total numbers with no categorization were collected.
**The data collection system was changed in 1996 to categorize usage by type of work rather than by type of institution. Numbers categorized by institution therefore are estimates.

It should be noted that such data lists animals actively used for research, teaching or testing. It does not include those held in the breeding colony. Secondly, animals used may be long-term animals; i.e., they are not necessarily euthanized and can be used over a number of years and hence can re-appear in utilization data for a number of years. Also, the same animal may be used in different studies during its lifetime. There is variation in usage from one year to another. Therefore this data does not provide an accurate accounting of the actual number of animals used in research.

The CCAC data show a pattern of diminishing usage of the cynomolgus monkeys in Canada over the years since 1989 until 1996, when a record high of 1393 animals were reported. The Panel investigated the basis for this unexpected break in the trend of diminishing usage. It found that the 1996 number largely was due to a significant importation of non-SPF animals by one Canadian research company to perform contracted toxicological research for a non-Canadian company. The Panel has no reason to believe that this is indicative of any change in the overall trend to decrease the use of this species in Canadian research. It is impossible to predict whether or not this kind of contracted research will become a regular commercial activity in Canada in the future, or, even if it does, whether it would rely upon its own foreign supply of animals. Thus, the Panel concludes that the 1996 statistic is an anomaly that should not be read as suggesting any significant change in the long-term trend toward diminishing demand for cynomolgus macaques as research animals in Canada. It also must be pointed out that such privately contracted toxicological research does not represent a potential market for animals with the highly valuable SPF status of the Health Canada cynomolgus colony. The prices which this non-SPF animal market would bear are substantially below that which would sustain the Health Canada colony on a cost-recovery basis.

It is clear that projecting future usage is very difficult. Obviously the number used by the HPB laboratories will be zero for polio vaccine testing according to current plans, and if Health Canada goes ahead with announced plans to discontinue staff research projects involving monkeys, its own internal research use will approach zero as well. Some non-human primates will continue to be used for research and/or testing by universities, hospitals and by industry; however, the numbers required are probably impossible to predict. While the Panel received some letters from university researchers indicating their desire for continued availability of SPF animals from the Health Canada colony, these researchers could not predict their long term funding, and hence, their usage. Industry will continue to require non-human primates for testing and the numbers used for this testing show considerable yearly variation, although the general trend appears to be in the direction of diminishing use. While the drastic cuts in the Department's funding of health research make it difficult to rationalize maintenance of the Health Canada breeding colony for its own use, it is impossible to make reliable predictions about the future demand from external sources.

Cynomolgus monkeys, like all non-human primates, are expensive laboratory animals. The cost of maintaining the current colony of under 1000 animals is approaching $900,000 annually. Health Canada has spent nearly $11,500,000 on the non-human primate breeding program since 1983. The ARD recently obtained quotations from several American companies on the costs of purchasing 130 animals annually (approximately the number currently being bred in the colony). The prices quoted ranged from $2500 to $4000 (US) per animal, with the total transfer costs amounting to over a half million dollars (US) per year. Further, the suppliers indicated that orders for such a large quantity of animals would require them to import the animals from their countries of origin (presumably wild caught animals or animals bred in unregulated "monkey farms") and to hold them in quarantine in order to determine their disease status. This gives a good indication of the high value of the Health Canada colony macaques in a market requiring SPF animals. It would be a mistake, however, to conclude that the Health Canada macaques have this value in the actual Canadian market

today or in the foreseeable future. This is likely the reason why Health Canada has been unable to market its animals to Canadian researchers on a competitive basis as a cost recovery measure. The CCAC data on cynomolgus macaque usage in 1996, quoted above, does not establish the existence of a market for SPF animals of this high value.

III.PROFILE OF THE CYNOMOLGUS MACAQUE MONKEY[2]

Background

The cynomolgus macaque (*Macaca fascicularis - subspecies fusca*) is one of four to six macaque species studied in the lab and to a varying degree in the field. Of these species the rhesus macaque (*M. mulatta*) is, by far, the most studied; other species that have been studied include the bonnet monkey *(M. radiata*), the pig-tailed macaque (*M. nemestrina*), the Japanese monkey (*M. fuscata*) and the Barbary Ape (*M. sylvanus*). Taken together, the data acquired from the studies of these species provide the framework of knowledge to construct a profile for the needs of the cynomolgus monkey in an artificial environment.

The macaque species share many social and behavioural (and presumably emotional and cognitive) traits. They are typically a multimale-multifemale society. Adult females usually outnumber the males because the younger males form bachelor groups and randomly move in and out of the mixed sex groups. Group size varies; for the cynomolgus macaque, group size ranges from 6-58, and for rhesus monkeys, group size may range from 5-100. Differences in group size are attributed to differences in predation risk, and larger groups may have larger home ranges. Density appears to range from 0.7 to 1.3 monkeys per hectare (approximately 2.5 acres). They live in a variety of environments. The cynomolgus monkeys most commonly inhabit the forest since they are largely arboreal.

A dominance hierarchy is common to most macaque species and is particularly well characterized among the males. A matrilineal hierarchy has also been observed in both the

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[2] Information for this section is taken from the following sources: Clarke, A.S. and Lindburg, D.G. (1993) Behavioral contrasts between male cynomolgus and lion-tailed macaques. American Journal of Primatology 29:49-59. Sugardjito, J., van Schaik, C.P., van Noordwijk, M.A., and Mitrasetia, T. (1989) Population status of the simeulue monkey (*Macaca fascicularis fusca*). American Journal of Primatology 17:197-207. van Schaik, C.P. and van Noordwijk, M.A. (1985) Evolutionary effect of the absence of felids on the social organization of the macaques on the island of *Simeulue (Macaca fascicularis fusca*, Miller 1903). Folia primatol. 44:138-147.

cynomolgus and rhesus macaques in both wild and domestic colonies. Fighting usually occurs more commonly in domestic colonies than it does in wild groups.

Psychological research contrasting rhesus, cynomolgus and bonnet macaques suggests some species differences. When presented with novel objects rhesus were the most active, bonnets the most passive and least disturbed, and cynomolgus the most disturbed. In another study contrasting lion-tailed (*M. silenus*) and cynomolgus macaques, the latter were less curious toward their environment and less willing to manipulate their environment, compared to lion-tails. Both species are arboreal and each has a preference for perches, the cynomolgus preferred perches at the mid-level and the lion-tails at the highest levels in the cages. In terms of social behavior, cynomolgus macaques show a fair amount of tolerance between males, whereas lion-tail males tend to be aggressive toward each other. The cynomolgus monkey is more 'easy going' than the both the Barbary Ape and Japanese macaque. Thus, different macaque species appear to have different psychological characteristics, relating to boldness, aggressiveness, manipulativeness, responsiveness, etc.

Recent studies at Monkey Jungle, Florida, a 10-acre natural "sanctuary" for macaques, have shown several interesting features of this species which have not been reported.[3] For example, the cynomolgus monkey is capable of primitive tool use (i.e., rubbing sticks and other material, such as scrap metal, together to make noise). Also, the female actively seeks out her male of choice for mating, rather than being a passive partner. These observations suggest that the cynomolgus macaque may have significantly more cognitive, manipulative and intellectual capacity than previously reported. Furthermore, recognition of these behaviors must be considered in designing housing facilities.

Housing Requirements

[3] This information is based upon personal communication with Dr. Anne Zeller, an anthropologist at the University of Waterloo, who has conducted extensive observational research with macaque monkeys, both in native or "wild" conditions, and in captive sanctuaries such as Monkey Jungle in Florida. The Expert Panel is grateful to Dr. Zeller for her contributions to this report.

The design of the housing facility should give top priority to the behavioral, social, emotional and cognitive traits of the species, in this case the cynomolgus monkey. Social companionship is essential. In order to reduce stress, the animals should have some degree of predictability and control of their environment. Thus, the group should be stable in terms of group composition (i.e., do not put strangers together) and feeding patterns. Ideally, in an outdoor facility ground cover and foliage at different heights should provide visual privacy and opportunities for escape from skirmishes.

Other considerations for group housing should include daily activity. In the wild cynomolgus monkeys spend about half of their time feeding, a quarter of their time resting and a quarter of their time traveling. Feeding areas strategically located in various areas of the sanctuary should create some similarities to the natural conditions, and it would reduce group size, at any given feeding station. Since cynomolgus monkeys do not share food readily, fighting would be reduced. Perches at various heights should also create opportunities for locomotion and privacy, particularly for close family members (i.e., mothers and offspring).

IV.ASSESSMENT OF THE TUNNEY'S PASTURE FACILITY AND THE MACAQUE COLONY

Facility

Members of the Panel visited the primate facilities on two occasions. The Banting facility is approximately 15 years old and is, from a research point of view, considered state-of-the-art for primate housing and disease/toxics control. The original design included features for Biocontainment Safety Level (BSL) which controls the majority of viral diseases that may infect primates and makes this a unique resource for primate studies. In addition, it provides the essential safety features for research on environmental toxicants that are of significance to Canada. The facility is in excellent condition overall and appears to have had excellent care and maintenance over the years.

The supporting resources for the colony are sufficient for routine procedures of animal care and colony management as well as general research support, and include a surgical suite(s), x-ray facilities, medical diagnostic/treatment rooms, clinical chemistry/hematology laboratories and pathology rooms.

The entire facility includes a variety of rooms which maximize different housing conditions, and are essential to both the research and breeding programs. Currently, the research colony contains 148 cynomolgus monkeys involved in AIDS-related research, heavy metal toxicology, and toxaphene research. The breeding colony of 788 cynomolgus monkeys includes 271 adult females, 42 adult males, 190 weanling males, 198 weanling females, and 87 infant animals. Since there are 45 pregnant females that will give birth within the next three months, the total population of the breeding colony will reach 833 animals by the end of 1997.

The majority of the primates in the colony are housed in social groups of varying sizes and ages. The separate groups include adult females and their newborn offspring; adolescent and adult females only; adolescent males; and, in a few instances adult females and a single adult male. This last form of housing (multiple females and single male) was commonly used until recently when the need for producing additional animals was reduced.

A smaller number of animals are maintained in individual cages, either for research purposes, or for the health or social conditions of individual animals. For example, individually-housed animals include geriatric animals and males removed from breeding groups. All 148 animals in the research colony are housed individually for research purposes. In the breeding colony there are approximately 36 adult males housed individually in small cages and approximately 200 adult females housed in pairs in small cages with 53 young progeny. It is these animals in the small cages, especially the individually housed males, which have been the object of a great deal of ethical concern and public criticism.

All of the cages, especially those housing social groups, contain various forms of Ôsocial enrichment' devices, ranging from a few small toys in individual cages to swings, perches, climbing chains, and ladders, among other things, in the group housing cages. The level of environmental enrichment provided to the colony in group housing is equal to, or greater than, that available in other contemporary colonies. However, Panel members also observed that some single cages in both the research and breeding colonies had solid steel side panels which prevented animals from having visual contact with their neighbours. These cages are often in banks of four placed two by two, even though there is adequate space in the research rooms for caging to be placed in banks of two with space separation and wire grill or mesh to facilitate visual contact. In the research areas the banks of cages could be placed on opposite walls to facilitate visual contact.

Protocols, or Standard Operating Procedures (SOPÕs) for all colony activities are in place and routinely followed by Health Protection Branch staff (i.e., formation of groups of various compositions - numbers, age, sex). All of these SOP's were approved by the HPB Animal Care Committee and have been available for Canadian Council on Animal Care review, including the research protocols, which indicate the appropriate endpoints (e.g., euthanasia) for the animals. The individual animal rooms and cages are kept in very sanitary conditions according to specific SOPÕs for animal care and housing. The Panel observed one practice that detracted from beneficial husbandry practices -- the use of wood product bedding in which

peanuts and other ÔtreatsÕ were occasionally added to provide behavioural enrichment (foraging for food), with the increased risk that food and feces get mixed.

The overall health of the colony appeared to be excellent as judged by appearance, hair coat, body weight (no obese or thin animals), and social interactions. For example, the hierarchy of the different groups appeared to be well-defined and there was little evidence of stress. However, the Panel members noted several isolated instances of apparent stress/depression in individually caged adults, as well as illness/diarrhea, particularly in recently weaned infants. The annual ÔspontaneousÕ mortality rate for the colony is estimated to be about 1%, which is excellent and somewhat better than cynomolgus monkey colonies elsewhere. The high-quality indoor housing and care of the animals is also a factor in the low death rate.

Overall, the facility is truly unique to Canada, and to the North American continent, where only a few such facilities exist even today. In this respect, Canada has been a leader internationally in developing a state-of-the-art facility; only in recent years have other countries taken a similar initiative in developing these types of facilities. These does not mean that there are not serious deficiencies, as noted in the next section.

Criticisms of the Facility

There have been obvious problems surrounding housing conditions since the inception of the colony. The basic problem is the lack of sufficient space to house such a large number of animals under acceptable conditions. Until 1995, Health Canada contracted with the University of Waterloo to house a substantial number of juvenile animals in group housing arrangements. When this contract ended, these animals were all returned to Tunney's Pasture, intensifying the over-crowding problem. There have been a number of recommendations to increase the housing space at Tunney's Pasture, followed by announcements of plans to proceed. However, the plans never were actualized because of the lack of funding. While progress has been slow, there have been some improvements, with some expansion of group housing.

The slow pace of housing improvements has led to considerable negative publicity in

the media and regular, strong criticisms from organizations such as the Canadian Federation of Humane Societies (CFHS) and Animal Alliance of Canada. They have repeatedly pointed out the problems of metal caging, lack of group housing for many animals, lack of social stimulation, and lack of windows permitting natural light. Over the years a number of organizations, including the CFHS, the Canadian Veterinary Medical Association and a group of three members of parliament (including two veterinarians) have visited the facility. All visitors agreed that the animals were receiving good veterinary care and appeared to be healthy. But all or most have commented negatively on the crowded housing conditions and lack of accepted standards of socialization for all animals.

The Canadian Council on Animal Care (CCAC) has visited the primate colony on a number of occasions since its beginning. These include regular visits (every 3 years) and special visits to follow-up the progress on significant recommendations about housing problems. (This represents the normal CCAC practise of monitoring institutions that use animals for teaching, research and testing). During the regular visit in 1984 the recommendations included:

•that immediate steps be taken to provide additional space for the non-human primates from the breeding facility.

•that appropriate cage density be maintained for all species; failing provision of additional caging, numbers of animals should be reduced.

The summary and conclusions to that visit included among "very serious concerns" "the apparent lack of positive planning for the expanding primate colony, including provision for the normal social development of replacement breeding animals." Three years later (April 1987) the report noted that some improvements had been made (e.g., group housing for young primates) but older animals were being confined for long term studies in cages which were judged to be too small, and social enrichment and exercise programs for these animals were deemed deficient. This was followed by an unscheduled visit in September 1987, the report from which indicated that the recommendations made by the previous panel were being addressed but "room densities are high." The 1990 report included several "serious"

recommendations (serious and major recommendations require an action plan response within three months). Among these were the following:

- That, within three months, the housing of the adult, male cynomolgus and rhesus macaques, on the fourth floor of the Sir Frederick Banting Research Centre, be improved to provide for exercise and cage enrichment, or the animals humanely disposed of.
- That the large male NHP housed on the fourth floor of the SFBRC [Banting Research Centre] be provided with adequately-sized primary cages, and that in-cage enrichment be investigated and implemented.
- That, within six months, the long-term non-human primates housed on the second floor of the Sir Frederick Banting Research Centre, be afforded increased access to exercise; and that necessary measures be taken to either pair-house these animals in larger cages, or investigate and implement alternative caging or in some other way provide for their psychological well-being.

And among its "regular" recommendations:

- That research be undertaken to assess the usefulness of exercise cages and new types of group housing, e.g. double vertical cages (juvenile macaque housing rooms, Animal Breeding Building, second floor). That further action be taken to improve their environment and increase their schedule of exercise.

The report included among its commendations the following:

- That the Animal Resources Division's attempts to group-house juvenile NHP's and enrich their environment be commended.

The 1993 report recommended "that the HPB proceed quickly with the proposed plan for instituting group housing of primates on the 1st floor of the Animal Breeding Building," "That more exercise space be provided to the primate breeding colony on the 2nd floor," and "That environmental enrichment strategies be provided for all animals cage-housed in the primate colony."

The most recent visit occurred in 1996 and recommendations for improvement included:

•That the rationales for maintaining each of the breeding colonies at the Health Protection Branch be fully reviewed and that, if any of the breeding colonies are maintained, the number of animals bred be in proportion to the numbers required, and,

•That, if a decision is made to retain the non-human primate breeding colony, such animals be loose-housed in a “harem-breeding” setting.

The report indicated that there had been significant improvements since the 1993 report but some significant questions obviously remained. Clearly, the Canadian Council on Animal Care has had significant concerns over this facility during the past decade.

Based upon its own visits to the facility the Expert Panel believes that the concerns expressed by the CCAC, and echoed by other informed organizations, are well-founded. It appears that the facility has been breeding more animals than can be justified by the research demands in Health Canada, and perhaps even in Canada generally, and more than can be accommodated adequately by the facility in its current state. The group housing arrangements which have been introduced over the years appear to be working well in providing a reasonably enriched physical and social environment for the animals. However, there are too many animals individually and pair-housed long-term in cages too small to allow for proper exercise and social interaction. This kind of housing may be acceptable for short periods of time for health reasons or the requirements of research protocols, but not as a normal means of long-term housing.

Staff

The primate colony staff is led by an experienced veterinarian, Pierre Thibert, and colony manager, Bill Pierce. Both have been active in the development and management of the colony for many years and have acquired considerable expertise as well as an excellent reputation among their colleagues. During the PanelÕs visits to the colony they were informative and provided both historical and current perspectives concerning the research projects, medical care, breeding practices, social and biologic aspects of long-term breeding, and environmental enrichment.

The entire veterinary, animal care, and clinical/surgical support staff in the primate facility appear to be outstanding. They demonstrated their dedication to both animal care and the conduct of research. The entire staff has extensive experience in handling animals according to specific research needs and colony management protocols. All of them expressed concerns for the well-being of the entire colony. In summary, the Panel was unanimous in their opinion of the very high level of colony care provided by the staff.

Research Value Of The Health Canada Primate Colony

The most distinctive feature of the monkey colony is that it is Specific Pathogen Free (SPF) for a select group of simian viruses capable of having an adverse effect on research outcomes. The Biocontainment Safety Level (BSL 2 & 3) facility protects the colony from becoming infected by these or other agents from outside sources. The specific pathogens that are absent include Herpes B, Simian T-lymphotropic virus (STLV), Ebola, Simian immunodeficiency virus (SIV) and simian retroviruses (SRV), Type D (SRV -1, -2, and -5).

The negative status of the colony for SRV, which is endemic in many macaque colonies, is very important because it may induce immunosuppression followed by morbidity and mortality. The negative status for SRV is particularly important in viral studies, especially SIV/HIV. Herpes B virus is of great occupational health importance since human infection by this virus is almost always fatal. STLV is endemic in many populations of captive macaques and is associated with neoplastic disease in baboons and African Green monkeys. In macaques it rarely causes clinical disease but is capable of interfering with virology studies. Although the negative status for Ebola is also important, acute infections with this viral agent in non-human primates are typically lethal, thus minimizing the risk of transmission to humans.

Naturally occurring infections of SIV in macaques are rare, but once introduced into a colony, particularly under conditions of group housing, SIV has been shown to be transmissible through biting and scratching in stump-tailed macaques (*M. arctoides*). Furthermore, SIV appears to be transmitted naturally through sexual contact in sooty mangabeys (*Cercocebus torquatus atys*), the species of origin of several SIV strains. Thus

SIV, and the immunodeficiency disease it can cause, can be spread in macaques by body fluid contact, just as HIV is spread in humans. SIV is not endemic in Asian monkeys (e.g., cynomolgus); thus, its presence in a cynomolgus monkey colony would indicate prior direct or indirect exposure to African species. This would be an unlikely occurrence since different primate species and infected animals are not housed together with uninfected animals in this or other biomedical research facilities. (At one time mixed species housing was not uncommon.) In summary, the negative status of Herpes B virus provides assurance that colony personnel will not be infected with this virus. This alone distinguishes this colony from most macaque colonies in the world. The negative status for SRV, STLV and, to some extent SIV, establishes the colony as a very suitable choice for research in infectious diseases and vaccine development.

The original decision to breed the cynomolgus monkey instead of the more commonly used rhesus monkey has both advantages and disadvantages. The advantages are its smaller size which is very important for testing a new product when production costs are very expensive and the absence of a breeding season which allows for reproductive studies to be done throughout the year rather than within a breeding season of 5-6 months. A disadvantage is that the cynomolgus monkey originates from tropical countries (southeast Asia) and is unable to thrive outdoors (except for summers) in Canada. This is a liability if these animals should be placed into a Canadian based “sanctuary”.

Although domestic production occurred during a 12-year (1983-1994) period, the genetic history (parentage) of the colony is known for only two generations (generation is defined as a 4-year period based on time from birth to sexual maturation of the female). The genetic history for two, rather than the expected three, generations during this period of time may be attributed to two factors. One, start-up time is required to establish a breeding colony (production of F_1 offspring from F_o feral animals); and two, there was extensive utilization of the colony for research (see above) which limited the availability of animals for breeding purposes.

Summary

TunneyÕs Pasture primate facility is a unique and valuable resource for breeding and maintaining SPF primates which can be used in a variety of research projects, particularly those involving infectious diseases. It is important to recognize that the breeding, maintaining and research use of this colony must be done in the same facility to maintain the SPF conditions. Replicating a facility of this caliber elsewhere in Canada would not be economically feasible and cannot be justified on the basis of current use in research. The excellent health status of the colony is a tribute to a dedicated veterinary and animal care staff.

If the facility is to continue to function as a breeding and or research colony, there are changes which need to be made to enhance animal well-being. Individual caging for the long term housing of animals, except where this is absolutely essential for research purposes or for the health and well-being of individual animals, should be replaced with forms of group housing which provide an enriched environment for compatible animals (e.g., improved lighting and provision of more opportunities for exercise and social interaction). Where individual cages are necessary, they should be modified and/or repositioned to permit visual and auditory contact between animals.

Since only limited anthropological and behavioral studies of the cynomolgus monkey have been done, TunneyÕs Pasture provides an excellent opportunity for such studies. Such research would not only enhance our present limited knowledge of this species but would also contribute to providing the most suitable environment under all housing conditions in the facility.

In the future, if TunneyÕs Pasture were to be used as a sanctuary, certain modifications would be required to provide the full benefit of a natural setting, i.e., social and physical conditions. This could involve an outdoor arboreal enclosure, possibly adjoining the existing facility. Such an expanded facility could also enhance the opportunities for observational research.

I.

HEALTH RESEARCH REQUIRING THE MACAQUE AS A PREFERRED MODEL

Infectious Disease Research

AIDS

New drugs and therapeutic regimens for AIDS have offered substantial improvement in the quality of life of many North Americans and Europeans. Unfortunately these drugs are costly and the current regimens are complicated, often resulting in serious problems with patient compliance and the development of HIV resistance with long-term administration of drugs. There is no evidence available to indicate a substantial reduction in the level of transmission of HIV in the higher risk groups. Consequently, in the near-term, this will result in escalating public health costs to cover an increasingly large number of individuals infected with HIV. Thus, current drug therapies can only be viewed as a stopgap measure until an effective vaccine can be developed and employed to prevent new infections, not only in Canada, but particularly in less developed countries of the world.

Triple chemotherapy drug regimens have significantly changed the prognosis of many AIDS patients by reducing virus load to undetectable levels. However, these treatments have undesirable side-effects, it is not clear how long the beneficial effects can be sustained, and developing countries cannot afford the cost of such a therapy. In addition, the virus rapidly reappears when the treatment is interrupted. Thus, the development of an HIV vaccine remains the only long-term strategy to address the most formidable challenge faced today by the scientific and medical communities, and has been identified by United Nations agencies, through UNAIDS, as a worldwide health care priority.

Studies in AIDS vaccine research have been greatly advanced in the past few years by the availability and use of several species of macaques. Vaccine studies have been conducted with various macaque species, in particular rhesus, cynomolgus, and pigtailed macaques. The choice of macaque species is usually dependent on the type of virus stock being used and the laboratory experience with a particular species, with all of these species capable of exhibiting

symptoms and disease manifestations of AIDS. The virus stocks can vary from pathogenic SIV or attenuated SIV to chimeric SHIV (Simian-Human Immunodeficiency Virus - SIV core with HIV envelope) with variable pathogenicity dependent on macaque adaptation. Rhesus macaques have been extensively used for AIDS research in the United States, and cynomolgus macaques have been used both in Europe and the U.S., as well as Canada. Although specific vaccine products usually have not been compared directly, the preclinical HIV vaccine experiments have been largely equivalent in these macaque species and HIV vaccine products are often observed to be substantially less immunogenic than in small rodents. These studies have served to eliminate some products from further study. The experience in macaques and other non-human primates (baboons or chimpanzees) has been much more predictable of human responses than immunogenicity in rodent species. Large scale studies of HIV vaccine efficacy only are appropriate in human populations where the route of virus transmission and the actual risk of exposure to HIV would be a more appropriate setting for determining the usefulness of a candidate vaccine.

Canadian research scientists at Health Canada and collaborating institutions are well placed to contribute critical information to the design and development of an effective AIDS vaccine. AIDS vaccine research needs to incorporate multiple strategies including: design and development of new vectors to deliver the vaccine; approaches to induce effective cellular immunity; adjuvants to enhance specific components of the immune response and incorporation of new technologies for immunization with synthetic or genetic material. Canadian scientists are highly qualified, if appropriate financial support is available, to evaluate components of the human and non-human primate immune response that might be appropriate for HIV vaccines.

There is already a core expertise in Canada. A broad base of academic and clinical scientists are involved in AIDS research, an SIV model has been developed at the HPB to test attenuated SIV vaccines in macaques, chimeric SHIV strains have been used to evaluate responses to HIV envelope, and a Canadian clinical trial network has been established. Canada-based private industry is also involved in a large HIV vaccine program. Another area

of strength is the international involvement that the Canadian International Development Agency has established with countries in Africa and East Asia, in terms of AIDS education, prevention and epidemiological studies.

The development of an efficacious AIDS vaccine will require:

1.a reliable animal model to understand the mechanisms of protection against infection and disease. In this regard, the SIV model in SPF macaques has been established at the primate centre in Ottawa. HPB researchers have successfully tested the protective ability of candidate attenuated SIV vaccines in this model. The availability of state-of-the-art BSL3 facilities make it possible to test other live attenuated vaccines and hybrid SHIV in the future and to perform live virus challenges.

2.the availability of various macaque species to assess the safety and immunogenicity of all types of HIV vaccines currently being developed, such as live-recombinant vaccines, genetically engineered non-infectious HIV-like particles, DNA vaccines, sub-unit vaccines and lipopeptide-based vaccines. Such testing is not only indispensable for evaluating the respective merits of candidate vaccines but is also likely to be requested by regulatory agencies as a prerequisite to future clinical trials.

3.the use of non-human primates to establish a model for mucosal immunization.

•The primate centre in Ottawa with its SPF monkeys, BSL3 facilities and expertise in the SIV field would offer Canadian investigators the animal resources critical for HIV research and, thus, could become the central component of a national AIDS vaccine initiative.

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Cardiovascular Diseases

Recent advances in the understanding of the link between arteriosclerosis research and infection with Chlamydia presents possibilities for the development and utilization of a non-human primate model for important cardiovascular research to prevent the debilitating effects of heart attacks and stroke. These consequences of what is now recognized as a common infectious disease severely impact the quality of life in aging adult North Americans.

Chlamydia pneumoniae is a common human pathogen. The bacteria is morphologically, genetically, and antigenically distinct from other Chlamydia species. So far, it appears to consist of a single strain. The organism has been shown to be responsible for community-acquired pneumonia along with Streptococcus pneumoniae and Mycoplasma pneumoniae and to facilitate the occurrence of severe secondary Streptococcus pneumoniae infections. Bacterial pneumonia is a major cause of morbidity and mortality in institutionalized or immunocompromised elderly persons. Chlamydia pneumoniae also causes upper respiratory tract diseases, including bronchitis and sinusitis.

More recently, the discovery of an association of atherosclerosis with Chlamydia pneumoniae has raised considerable interest in the scientific community. Cardiovascular diseases represent the second most important cause of death after cancer. There are several epidemiological studies showing a correlation between previous or current chlamydia pneumoniae infection and heart attacks, and coronary and carotid artery diseases. Moreover, the organism has been detected in atheromas and fatty streaks of the aorta, coronaries, carotid and peripheral arteries. Viable bacteria were recovered from the coronaries and carotid artery. Furthermore, it has been demonstrated that infection with C. pneumoniae can induce histopathological changes typical of atherosclerosis in rabbits. Taken together, these results indicate that it is highly probable that the organism can cause atherosclerosis in humans, although the epidemiological relevance of chlamydial atherosclerosis remains to be unambiguously demonstrated.

In light of these observations, a protective vaccine against C. pneumoniae would be of considerable importance. The identification of protective antigens and the evaluation of candidate C. pneumoniae vaccines will require good animal models. The rabbit model of atherosclerosis is currently available, although not perfect. Mice have been used to study C. pneumoniae-induced pulmonary infection and more recent studies have shown an association between atherosclerosis and C. pneumoniae infection in these animals. A non-human primate model of lung infection has been described but it has not been determined whether monkeys develop atherosclerosis following infection.

The development of non-human primate models of Chlamydia pneumoniae-induced lung infection and atherosclerosis would be of considerable value in understanding the role of the pathogen in human pneumonia and cardiovascular diseases. These models will also be indispensable for testing any candidate vaccine. The primate colony could thus play a central role in helping establish these models and making them available to Canadian investigators interested in the development of C. pneumoniae vaccines that will require a sustained and concerted effort on the part of all researchers and research centres.

Emerging Infections

The recognition that the developed world is not isolated from emerging and re-emerging infectious diseases has raised the question of the research capacity to respond and develop novel drugs and vaccines to counter these very real threats. Diseases such as tuberculosis have emerged in higher numbers and/or in multivalent drug resistant forms that threaten individuals through aerosolized exposure. Bacterial enteric diseases have demonstrated evidence of genetic evolution to more virulent forms in response to indiscriminate and extensive use of broad spectrum antibiotics. Many of the microbial species that infect humans do not infect rodents or do not cause the same disease sequelae in non-primate species. Thus, scientific research in these areas critical to human health often require experimentation in non-human primates as well as human subjects.

Aging Research

Aging primates, especially macaques, have been shown to be excellent models for geriatric research which is directly applicable to humans. The main areas of aging research that are being initiated in the macaque model include the following: neurodegenerative diseases (Alzheimer's and Parkinson's disease), osteoporosis and menopause. Animals used in these studies are naturally aged (>/=19 years) or have been surgically (ovariectomy) or chemically (neurotoxins) altered to mimic a specific aspect of the aging process.

Neurodegenerative Disease

Cognitive deficits associated with various forms of progressive dementia arise from adverse effects of aging on specific types of brain neurons (e.g., degeneration of forebrain cholinergic responsive neurons in Alzheimer's disease and depletion of dopamine sensitive neurons in Parkinson's disease). Macaque models with selective neural degeneration have been developed for both of these disorders that can be utilized for functional, pharmacological, and therapeutic studies with direct impact on human well being. For example, imaging systems have been developed to assess the degenerative neurons in the living brain (e.g., positron emission tomography [PET]) and computerized testing systems have been developed to analyze cognitive performance (i.e., perception, learning and memory) that can only be achieved in primates.

Novel techniques have also been used to study various aspects of naturally occurring neurodegeneration. One of the most promising, in terms of therapeutic potential, is the experimental delivery of nerve growth factors (NGF) by gene transfer to aged rhesus monkeys to induce neuronal growth. Transplantation of fetal neurons into the mature brain (hippocampus region) is another innovative technique that is being developed in the macaque model to combat the adverse effects of aging on brain function.

Menopause and Osteoporosis Research

Menopause, a natural phenomenon for middle-aged women, is characterized by cessation of ovarian activity, disrupted sleep patterns, night sweats, osteoporosis and enhanced cardiovascular dysfunction. Many of these menopausal symptoms, which reflect changes in brain function related to age and/or ovarian function, can be studied in naturally aged or experimentally altered female macaques. Primary methods of inducing menopause to study these physiological effects involve eradication of ovarian function by ovariectomy or irradiation, essentially parallel to the treatments encountered in women faced with cancer therapy. One of the most relevant uses of ovariectomized macaques is the interventional study and careful morphometric assessment (in the spine, hip and wrist) of the progression of osteoporosis and the potential of therapies (bisphosphonate or Zoledronate administration)

designed to alleviate this debilitating condition, which affects hundreds of thousands of otherwise healthy aging women in North America.

Additional studies in naturally aged female monkeys include characterizing the changes in plasma hormone levels (growth hormone [GH] and luteinizing hormone [LH]), evaluating the prevalence and immune correlates of endometriosis, examining nutritional factors that contribute to age-related osteoporosis, and using magnetic resonance imaging (MRI) to define some of the neurological changes that accompany menopause. Future areas of research may include age-related changes associated with development of diabetes and vision impairment that might be uniquely studied in non-human primate species.

Behavioural and Social Science Research

Non-invasive behavioural and social science research, conducted in social non-human primate groupings could provide a useful adjunct to more complex epidemiological and behavioural research conducted in human subjects. Behavioural research, particularly in infants and adolescents might guide us to better strategies for positive developmental cues in human youth.

There is a great deal to be learned about the complex behaviour and psychology of the cynomolgus macaques in order to understand the impacts of different types of captive environments on the individual animals and their social structures. In the opinion of the Expert Panel, it is unfortunate that the Tunney's Pasture facility has not been made more openly available to Canadian researchers involved in this kind of observational research.

Consequences of Canadian Research Dependency on Foreign Supply

It can be argued that non-human primate supplies from the wild and possibly from breeding suppliers in the United States can be obtained for important future research, providing future costs can be met. However, there is no assurance that non-human primates captured from the wild will be equivalent in health status or encounter less distress than those specifically bred in laboratory colony environments. In fact, it is highly likely that animals

supplied from the wild are likely to encounter substantially greater stress from capture, removal from the wild, shipping and handling en route. In particular, it can be argued that Health Canada maintenance of a minimal breeding colony, under the highest standards of animal care, for important Canadian research priorities, is of immeasurable value and far more ethical.

There is a potential threat of external supplies of primates being cut off as a result of export embargo (rhesus monkeys from India as an example) and the tenuous air transport of primates. This is why France and the USA created national breeding programs. These countries, which have a larger research and pharmaceutical community, are prepared to some extent for a loss of access to external supplies.

The threat exists since there are international constraints on air carriers to prohibit primate transportation as a result of public pressure put on governments, and potential embargoes linked to concerns similar to those which arose after the Ebola virus scare. Both Canadian and Air Canada air lines officially refuse to transport monkeys.

Conclusions

Each of these areas of research could be considered important health research projects which, if undertaken, could justify maintenance of the Health Canada primate colony. None of these projects appear feasible unless funded by a major Canadian government commitment to affect adequate maintenance and research efforts at Health Canada.

If it is decided that non-human primate research will be discontinued at Tunney's Pasture, it must be recognized that Canadian research will either be deleting options to pursue this research entirely or will be substantially limiting research in these health areas as well as important ongoing research areas. In the area of emerging diseases, this may be of particular concern with regard to the health security and national health protection, independent of studies conducted in the United States or in other developed nations of the world. These concerns reach beyond the general concerns of a potential failure to maintain a strong competitive position in global health research and development of health research in areas of

particular interest to Canadians. In the AIDS crisis, Canadian responsibility to contribute to developing an AIDS vaccine for developing nations of the world should be carefully examined before being dismissed out of hand because of an inconvenient problem with the management and maintenance of a macaque colony.

I.

ETHICAL FRAMEWORK GUIDING THE PANEL'S ASSESSMENT

The Panel identified the questions with which we were presented in the Terms of Reference as profoundly ethical: that is, they were questions related to the ethical balance of our society's commitment to the protection of human health and the advancement of knowledge, and its obligations to protect the welfare of non-human primates. The context of our deliberations was set by Health Canada's decision to end funding of the primate colony. This accentuates a third question of public ethics – the appropriate use and distribution of scarce social resources.

The submissions received by the Panel clearly reflected the centrality of these considerations. While various intervenors placed different weights upon these basic values, nearly all of them identified one or more as important. Thus, it was incumbent upon the Panel to articulate the Ethical Framework within which it resolved these sometimes competing values. We did this by means of a number of principles we believed to be widely reflective of Canadian values, and which the Panel members judged to withstand critical ethical scrutiny. We do not claim that these are the foundational principles of a full animal welfare ethic. They are, however, mid-level, non-foundational principles chosen for their relevance to our mandate and for their broad acceptability to people operating from a variety of different philosophical positions on the moral standing of animals and their use in research.

Principles

•Principle One: Conditional Justification for Animal Research

It was the Panel's judgment that highly intelligent and socially/emotionally developed animals such as cynomolgus macaques may be utilized ethically only in research that is scientifically valid and which has reasonable promise of significant health benefits for human beings or other higher primates, provided that there are strict limitations on the levels of

suffering and distress imposed upon the animal. This question of the disposition of the primate colony clearly required that the Panel take a position for or against this fundamental principle.

The Panel judged that, while there is a lively and productive debate on this issue in Canadian society, this principle reflects the ethical view that is currently most widely accepted, and which is clearly reflected in current public policy. This is evidenced by the support provided by various research councils to biomedical researchers using these animals in Canada, by the current standards of care articulated by the Canadian Council on Animal Care, which oversees all publicly funded animal research in Canada, and by the fact that the primate colony is a publicly funded facility.

Most of the submissions received by the Panel endorsed this position either implicitly or explicitly, although there were different interpretations of how the principle should be applied to the disposition of this particular primate colony. Most intervenors agreed that there are potential human health concerns of sufficient gravity to justify the controlled use of animals like the cynomolgus macaque in research. Some, however, raised questions about the scientific value of animal models for understanding most of these concerns. Panel members agree that this is a serious scientific question, and that great care must be exercised by the scientific community to ensure the appropriateness and value of the animal model, especially when using non-human primates.

The Panel endorses fully the "Three R's" of animal research ethics, especially in the case of non-human primates such as the cynomolgus macaque.

"Reduce": The use of such animals in research should be reduced to the minimum levels required for obtaining legitimate research results.

"Replace": Wherever possible, animal models should be replaced with other research models that do not involve the use of whole animals. There is an ethical obligation to develop these alternative research models. Scientists normally use non-human primate models only when they are scientifically the single or the most appropriate model. The costs and difficulties of working with such models work strongly against their use if other models can be used to answer the scientific question.

"Refine": Research methods involving the use of live animals should be refined in ways that minimize the infliction of physical or psychological suffering and distress. In the case of socially and psychologically complex animals like the long-tailed macaque this includes an ethical obligation to maintain the animals in conditions which permit the maximum social and psychological flourishing of the animals consistent with scientific requirements of the research.

The "Three R's" imply that only animal use which is necessary to obtain significantly beneficial research results can justify the constraints and impositions involved in the restricted housing and physical interventions required by this research. Thus, it is ethically questionable to breed and maintain non-human primates in numbers that exceed those required for legitimate research. In the Panel's judgment, it is not ethical to hold non-human primates in the restrictive conditions of most research facilities if there is not a sufficient demand for, and funding of, the kind of research which justifies their use.

•Principle Two: Standards of Animal Welfare

The Panel accepted as a *minimum* benchmark for ethical standards of care for non-human primates in research the guidelines set out by the Canadian Council on Animal Care (CCAC). Since the CCAC is the official body recognized by the research granting councils of the Canadian government, the Panel did not deem it appropriate to substitute its own judgments about animal care standards. The Panel also recognized that the CCAC is the appropriate body to maintain the accountability of those who house and utilize research animals in Canada. For this reason, the Panel was reluctant to recommend any option for the disposition of the breeding colony which removed the animals from the protection either of the CCAC or a comparable system of animal welfare protection.

•Principle Three: Responsibility

A widely accepted principle of animal welfare ethics across our society (applicable to domestic pets and agricultural animals as well as research animals) holds that those who

produce and/or purchase animals for their use or enjoyment incur a serious obligation to make adequate provision for the appropriate care of these animals. Animals ought not be bred and then abandoned or euthanized simply because the original interests and commitments (financial or otherwise) wane. This obligation increases in importance the more highly developed, socially, emotionally and intellectually, the animal species. It is, therefore, especially incumbent in the case of non-human primates.

This has important implications for Health Canada's continuing responsibility for the primate colony it created in 1983.

•Principle Four: Euthanasia of Non-Human Primates

In general euthanasia of animals is recognized as an acceptable practice under the following three general conditions:

1.When necessary for the prevention of pain, suffering or distress of individual animals.

2.When the humane death of the animal is necessary to obtain research objectives.

3.When used as a means of population control (e.g., the culling of wild animals which overpopulate their natural environments).

With respect to higher order animals, particularly non-human primates like the cynomolgus macaque, condition 1 applies with the same force as to lower animals. Indeed, there are good reasons for holding that there is a moral obligation to euthanize animals who suffer intense pain or distress. However, when considering non-human primates with the advanced social and psychological capacities characteristic of the cynomolgus macaque, euthanasia under condition 2 is justified only by the promise of significant research benefits.

Condition 3 is especially problematic when dealing with animals with the psychological and social capacities of the cynomolgus macaque, especially those kept in the artificially produced and managed environment of a research or breeding colony. The Expert Panel does not believe that the wholesale euthanasia of a cynomolgus macaque colony is an ethical means of solving a problem of over-population (especially if due to excess breeding), or the problem

posed by a decision to stop the funding of the research requiring their use. In the Panel's view, the decision to purchase and breed the animals in this colony created a responsibility to care for them to the end of their normal life span.

The US Committee on Long-Term Care of Chimpanzees, formed by the National Research Council to solve a similar over-population problem among research chimpanzees in US research centres, reached a similar conclusion in rejecting the euthanasia option. While we do not assume that cynomolgus macaque monkeys have a moral status equal to that of the higher primates like the chimpanzee, we do believe that there are many similarities in their developmental status that warrant similar consideration. The NRC Committee argued that "researchers are not justified in using chimpanzees without concurrent commitment for their lifetime care," and thus, "euthanasia as a means of population control is unacceptable."[4] The Committee also stated:

> The phylogenetic status and psychological complexity of chimpanzees indicate that they should be accorded a special status with regard to euthanasia that might not apply to other research animals… There are practical, as well as theoretical, reasons to reject euthanasia as a general policy. Some of the best and most caring members of the support staff, such as veterinarians and technicians would, for personal and emotional reasons, find it impossible to function effectively in an atmosphere in which euthanasia is a general policy….[5]

The NRC Committee concluded that the prospect of managing the excess research population of chimpanzees in the United States by means of wholesale euthanasia was a "train wreck" scenario. "In the final analysis, it is difficult to conceive that our society would accept a system that deteriorated to the point where euthanasia of chimpanzees became the best or only humane solution."[6]

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[4] "Chimpanzees in Research: Strategies for Their Ethical Care, Management, and Use." Committee on Long-Term Care of Chimpanzees of the Institute for Laboratory Animal Research, Commission on Life Sciences, National Research Council. Washington, DC: National Academy Press, 1997.

[5] *Ibid*. p. 28.

[6] *Ibid.* p. 4.

The Expert Panel members believe that similar considerations apply to the cynomolgus macaque population at Tunney's Pasture. The mass euthanasia of 1000 macaques would be unacceptable to the Canadian public, as is evidenced by the public outcry in response to the media announcement made during this Panel's deliberations that Health Canada was planning to euthanize the 115 macaques in the research colony, and the Health Minister's immediate public announcement that no euthanasia would take place in the colony until further notice.

There is an important implication of this principle for the management of research colonies. There is an ethical obligation to manage the breeding of animal research colonies in a way that maintains the population in proportion to reasonably anticipated need. With higher order animals it is inappropriate to manage away surplus numbers through a program of euthanasia, especially when the overpopulation has resulted in part from a failure to maintain breeding in proportion to reasonable prospects of need. Similar considerations apply in the case of changing priorities and budgets.

•Principle Five: Non-Displacement

As stated earlier, the Panel supports the view that Canadian policy on the research use of non-human primates should promote the "3 R's" of Reduction, Replacement and Refinement. Any disposition of the Health Canada primate colony that encouraged unnecessary research usage of non-human primates is in conflict with this principle.

So, too, would any disposition which, while removing the Health Canada monkeys from the research market, would only lead to the increased importation of animals for research from other countries where, possibly, they may be wild-captured, bred in facilities far more detrimental to their welfare than in the present colony, and exposed to the trauma and inevitable attrition of long-distance shipping. Such a disposition would serve neither the needs of Health Canada or Canadian health researchers for high quality, disease-free animals, nor the welfare of non-human primates in general. It would not necessarily reduce the total numbers of animals used in research, and could even increase the numbers held in captivity.

For example, a decision to retire all the Health Canada macaques to captive sanctuary, substituting imported animals for Canadian research and testing, is no advance for research or for animal welfare. The euthanasia of the entire Health Canada colony would have similar implications.

VII.EVALUATION OF OPTIONS FOR THE PRIMATE BREEDING COLONY

Overview

As indicated in the Introduction, the Expert Panel decided to make separate recommendations for the two groups of animals in the Health Canada primate colony – those in the breeding colony and those in the research colony. In this section the Panel lays out its recommendations for the breeding colony. Recommendations for the research colony are presented in the next section.

The Expert Panel identified and assessed a number of options for the disposition of the primate breeding colony. Some of these were specifically mentioned in the Terms of Reference. Others were mentioned by intervenor groups or by the Internal Review Report submitted to Health Canada earlier this year. Still others were identified by the Panel itself. Each of the options for the breeding and the research colonies was assessed for its scientific, economic, and public policy feasibility as well as its acceptability in terms of the Ethical Framework adopted by the Panel. The options were divided into the three broad categories: those involving some form of **sanctuary**, those involving **euthanasia** of the animals, and those involving continued **research** use of the animals.

Some of the options involve combinations of two or more of these categories, e.g., sanctuary for some of the primates and research use for others. What follows is a description of various options along with the Panel's assessment of the major considerations for and against each option. These assessments led the Panel to its consensus on the recommended options for the primate colony.

Sanctuary of the Animals

Sanctuary means the permanent retirement of animals from any form of active research involvement other than certain non-invasive, observational research. The objective of sanctuary is to reproduce as closely as possible the conditions of the natural environment in which the

animals exist in their wild state, albeit within an artificially constructed and confined space and under continued human management. "Sanctuaried" animals would be allowed to live out their normal life-spans.

It is consistent with the concept of "sanctuary" to prevent further breeding of the animals in order to reduce the colony of captive animals to zero through sterilization or other measures, even though this results in the disruption of the normal social life of the animals because of the increasing absence of younger generations in the colony. An ethically acceptable sanctuary would need to provide adequate care, shelter which allows space for free exercise, and the social interaction and environmental enrichment required for the cognitive and physical capacities of the animals, and to do so for the remainder of their natural lives. Euthanasia of animals in sanctuary would be carried out only for humane reasons germane to the welfare of the individual animals, but not for other reasons such as accelerated population reduction or cost cutting.

The sanctuary option should not be confused with return of animals to a natural, wild environment without continued human management and care. Animals such as cynomolgus macaques which have lived all or most of their lives in human-made environments would likely not be able to survive in the wild without unacceptable levels of mortality and disease. Animals raised in captivity would be subjected to predators in the wild with which they have no coping experience. The Panel did not consider the release of the Tunney's Pasture macaques into the wild to be a realistic, ethically acceptable option.

The sanctuary option was proposed recently by the U.S. National Research Council Committee on Long-Term Care of Chimpanzees for the excess animals in the chimpanzee research program supported by the US National Institutes of Health. In its Report, referred to earlier, the NIH Committee recommended sanctuary for all animals in excess of the 1000 the Committee deemed necessary for research to protect human health.[7]

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[7]"Chimpanzees in Research: Strategies for Their Ethical Care, Management, and Use." *Op. cit.*

The Panel identified two principal sanctuary options for the Health Canada breeding colony: **(1) foreign sanctuary** and **(2) domestic sanctuary** (in Canada).

A.**Foreign Sanctuary**

With this option, some or all of the macaques at Tunney's Pasture would be sent to a sanctuary in another country, which could provide the supervisory, shelter, and environmental conditions mentioned previously. The Panel investigated the possibility of one such facility in the United States, considered by many animal welfare groups and primatologists in the U.S. and Canada to be among the most reputable primate sanctuaries in that country.

We requested and received a preliminary proposal from the organization on the costs and other requirements of a transfer of the Health Canada macaques to their facility. The organization could take the animals only by purchasing additional property and building additional enclosures and facilities for its care. The costs of building this facility and maintaining the animals in it for the remainder of their natural lives are, understandably, very considerable. It would require an initial capital grant of approximately five million dollars (Cdn) for the first year ("conservative" estimate), plus a yearly maintenance fee of well over one million dollars (diminishing over the next 35 years until the death of the last animal).

Considerations in Favour of Foreign Sanctuary:

•It would be possible to use year-round outdoor housing if the animals were sent to a warmer climate, thus most closely approaching the animals' natural habitat.

•Many intervenors proposed the sanctuary option, usually with the assumption that it would involve a temperate climate not available in Canada.

Considerations Against Foreign Sanctuary:

•The option would be extremely expensive in terms of both start-up and ongoing costs. The Panel's investigation of one of the few facilities that might accommodate the colony

illustrates this. In fact, foreign sanctuary would not in any way decrease the financial burden of the primate colony upon Health Canada. Instead, it would significantly increase it. This is probably the most expensive of all the options considered by the Panel. It is significantly more expensive even than renovating the current Tunney's Pasture facility to reasonably acceptable sanctuary conditions, which would have the added advantage of keeping the money within the Canadian economy.

- From the perspective of the principle of responsibility articulated in the Ethical Framework, there are several major concerns with this option. Even with carefully constructed terms of agreement with a foreign sanctuary, the colony would be moved effectively outside Canadian animal welfare standards and the system of animal welfare accountability (CCAC). Concerns about responsibility are heightened given the relatively youthful age profile of the colony. Moreover, since the Panel is not aware of any foreign sanctuary with facilities currently adequate to provide sanctuary for the whole colony, any transfer of the colony would essentially be to a newly established, and hence unproved, facility.
- This option encounters difficulties with the Principle of Non-Displacement. It does not make sense for the entire Canadian breeding colony to be shipped to a foreign sanctuary, thus requiring Canadian researchers to import macaques into Canada for their research purposes. Macaques are often difficult and expensive to obtain from U.S. breeding colonies, forcing suppliers to obtain them from off-shore sources far more suspect from the point of view of animal welfare.
- It might be assumed that outdoor sanctuary in a foreign temperate climate is the best alternative solely from the point of view of the welfare of the animals. This may be true in principle, but when combined with the considerations of distress, dislocation (e.g., the breaking up of well-formed social units), and mortality that are inevitably part of the relocation of a large primate colony, it may not be true in practice.

A.Canadian Sanctuary

The Expert Panel felt that the option of a Canadian-based sanctuary for the animals ought not to be dismissed, even though the concept was suggested (belatedly) by only one intervenor. If one were starting from the ground up, of course, it would make little sense from either a financial or animal welfare point of view to construct a new (primarily indoor) sanctuary facility in Canada. However, the current Banting Research Centre, which houses the research colony and part of the breeding colony at Tunney's Pasture, already has the potential to be upgraded to an acceptable (though possibly not ideal) sanctuary facility, at a much lower cost than the construction of a new facility. The facility would have to be upgraded in significant respects, in particular with regard to caging and environment (as noted earlier), so that all the animals could be group housed in socially and behaviourally enriched environments. The addition of outdoor access in the summer months would be desirable, or at the very least the introduction of natural light to portions of the current facility would be essential.

The present facilities at Tunney's Pasture offer advantages as a sanctuary that may not be achieved elsewhere. First, since this colony has been housed in small groups, it is a better management practice to continue this arrangement. Second, the expertise of the staff at Tunney's Pasture, who have provided excellent care for these animals to date, is an important factor in their continued well-being. The experience at several North American primate facilities supports the view that modifications (e.g., upgrading conditions to house small groups and the provision of natural lighting) would provide an appropriate sanctuary for these animals in Canada.

Hence, with this option, some or all of the colony could be maintained at Tunney's Pasture under sanctuary conditions, which would include sterilization of the animals to achieve zero breeding and "hospice" conditions for aging animals. As indicated earlier, such sanctuary conditions would be entirely consistent with the allowance of non-invasive, observational research, and with full monitoring by the CCAC and animal welfare organizations.

Considerations in Favour of Canadian Sanctuary:

- This option clearly meets the responsibility principle since Health Canada would continue to exercise its obligation to care for the animals it has imported and bred.
- The animals would remain under the accountability system in place in Canada where they would be subject to the standards of CCAC and transparent to the scrutiny of the Canadian public.
- The animals would continue to enjoy the levels of care provided by a staff with a proven record of quality care. As noted earlier, reviews conducted by CCAC, other independent reviewers, and the Expert Panel consistently acknowledge the high quality of the personnel caring for the non-human primates at Tunney's Pasture.
- This option would retain the animals in Canada, making them available to Canadian researchers who wish to carry on purely observational, non-invasive studies of macaque monkeys.
- Many intervenors proposed sanctuary as the preferred option for the colony.

Considerations Against Canadian Sanctuary.

- There would be significant initial costs for establishing a sanctuary within Tunney's Pasture. It would require replacing all single caging (except for veterinary purposes) with group housing and "harem" housing, introduction of natural light where possible and providing a richer, more stimulating environment suitable for cynomolgus macaques (perhaps even outdoor access during summer months).
- There would be continuing costs of maintaining a sanctuary. Costs would gradually decrease to zero as the population decreased to the last animal.
- The sanctuary of the entire primate colony in Canada would, like foreign sanctuary, conflict with the non-displacement principle, especially if replacement animals would be imported into Canada for research purposes. If, however, provisions were made to retain some of the animals for research availability, this could be avoided.

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1.**Euthanasia of the Entire Primate Colony.**

Even though most of the submissions from animal welfare organizations and individuals recommended sanctuary as the preferred option, many indicated that euthanasia of the entire Health Canada primate colony was preferable to any continued research use of the animals. For the reasons laid out in the Ethical Framework, the Panel did not consider euthanasia as a means of population reduction for financial reasons to be ethically acceptable.

3. Continued Research Use of the Animals

Research options for the Health Canada primate colony involve maintaining available for research usage some or all of the animals. Such research would take place under the regulatory or other animal welfare controls of the jurisdiction in which the research would be conducted. There were strong pleas from some of the intervenors not to "waste" the valuable research resource represented by Health Canada macaque colony. As noted earlier, the SPF status of the colony (especially freedom from Herpes B) makes it one of the best sources of research macaques in North America. It was therefore incumbent upon the Expert Panel to assess the full extent of the research needs these animals could serve in Canada and elsewhere. As stated in Principle One of the Ethical Framework, the Expert Panel did not question the ethical justifiability of the cynomolgus macaque for research that is necessary to achieve significant human or animal benefit, provided that the research is conducted under strict conditions protecting the welfare of the animals, and is done in accord with the "3-R's" principle. If there are, in fact, important human or animal health benefits to be obtained from the judicious and ethical use of these animals, then the critical question for the Expert Panel was that of how to best achieve these benefits. Further, as outlined in Section V, the Panel concluded that, in addition to some of the current AIDS and toxicology research, there are additional health research imperatives for which the macaque monkey is an important, if not essential, model. The Panel considered the following research options:

A. **Maintaining the Status Quo at Tunney's Pasture**

It is instructive to consider the option of maintaining the status quo situation at Tunney's Pasture, if for no other reason than to establish a benchmark against which to assess other possible options. The "status quo" assumes that Health Canada funding to the Animal Resources Division would be continued at levels sufficient to sustain the current activities. These activities include maintenance of the current research facility, continuation of the current breeding program and "in house" research projects, as well as the provision of animals to other Canadian research centres and researchers.

Considerations in Favour of the Status Quo

•A continued supply of valuable research animals sufficient to meet current and future Canadian research needs would be guaranteed.

•A potential resource for critical research on new, highly infectious diseases or other unforeseen health crises in the future would be maintained.

•A valuable, world-class primate research facility would be retained. Abandoning such a facility would constitute a serious waste of Canadian taxpayers' money. The high costs of relocating or replicating such a facility elsewhere would be avoided.

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•Considerations Against the Status Quo

•Health Canada would continue to have the financial responsibility for maintaining the primate colony at Tunney's Pasture. The decision to discontinue the funding for the facility would have to be reversed.

•The current system of cost-recovery from users of the animals has made the animals largely inaccessible to Canadian researchers. Thus the facility is not optimally serving Canadian research needs.

•The breeding program appears currently to be producing more animals than are necessary for current or foreseeable future Canadian research needs. This is contributing to the overpopulation situation in the facility and is contrary to the ethical imperative not to hold more animals in captivity than can be justified by actual need.

•In certain respects, the current facilities at Tunney's Pasture are not acceptable from the point of view of animal welfare. The Panel judges that housing arrangements for a significant minority of the animals in the breeding colony (those in single or double caging) are unacceptable. Substantial renovation and regrouping of animals would be necessary to bring the facility up to acceptable housing standards, even if the current over-breeding situation were curtailed.

(B) Sale of the Breeding Colony to Other Research Centres

This option would involve the sale of the entire breeding colony to one or more primate research centres or to brokers who would hold and sell the monkeys to such centres. There is a high level of demand for SPF primates in the US and other countries. Thus, there would be a market for the Health Canada animals, although the introduction of such a large number of animals onto the market at once would likely diminish the price considerably. Health Canada could not reasonably expect to receive anywhere near the current market price of between $2500 and $4000 per animal.

While there is some modest demand in Canada for cynomolgus macaques, the recent pattern of usage suggests that there would likely be no Canadian bidders for the large number of animals from the colony. (As indicated earlier, actual Canadian demand for non-human primates in research was hard to determine with great precision.)

The most realistic option would be an unconditional (no strings attached) sale to the highest bidder. While it might be tempting to attach conditions to a sale (to address specific animal welfare concerns and to ensure some access to the animals by Canadian researchers), the Panel felt that this might make the animals unmarketable (or at least greatly reduce their market value) and in any case could not protect the animals from transfer to end users who were not bound by the initial conditions.

Considerations in Favour of the Sale of the Breeding Colony

•Sale of the colony (conditional or unconditional) would permit Health Canada to recover some of the costs incurred from maintaining the colony, or at a minimum, to achieve its objective of reducing expenditures on the colony to zero.

•Sale of the colony might displace at least some research primates that would be otherwise be bred, imported, or captured from the wild for research (but see caveat below concerning encouragement of overuse).

•Sale of the colony would make these animals available for potential use in important health care research (e.g., the development of an HIV vaccine). Sale outside of Canada would allow the animals to be used in countries which are currently providing much higher levels of funding for such research.

Considerations Against the Sale of the Breeding Colony

•Health Canada would be washing its hands of responsibility for the animals it purchased and bred for research purposes. There would be no direct control by Health Canada over the end uses of the animals once they are handed over to the buyer.

•Sale of the colony outside Canada (the only feasible market for such a large number of animals) could severely limit access by Canadian researchers to these animals. The animals were bred and housed at the expense of Canadian taxpayers for Canadian research needs. Canadian researchers should have first rights of access.

•Since it would not be possible for Health Canada to monitor treatment of the animals, this option raises problems with the Responsibility Principle (continued responsibility for the welfare of the animals), and might well generate substantial adverse public reaction once this is recognized.

•No intervenor group recommended this option to the Expert Panel. In fact the one notable point of strong agreement between the animal welfare organizations and Canadian researchers was that the animals should not be sold for research purposes outside Canada. The Expert Panel judged that sale of these publicly owned animals for research outside Canada would be considered politically unacceptable by the Canadian public.

•Introduction of a large supply of cynomolgus macaques onto the market at greatly reduced prices would encourage overuse of these animals in research, in violation of the "3 R's" principles.

(C) Take-over by a New Canadian University/Industry/Government Consortium

This option would involve the transfer of the breeding colony to a Canadian primate research centre, funded by a consortium of participants from the Canadian university community, private industry involved in health research, and federal and/or provincial governments. This option was recommended for further study by the Internal Review conducted by Health Canada earlier this year. The Report of this group suggested that this might be a way to expand the funding base for non-human primate research in Canada in general and for the Health Canada primate colony in particular, thus relieving the funding pressures on the latter.

Only one of the submissions to this Expert Panel advocated the consortium idea, and no university, private company or government agency came forward with any concrete proposal or offer of participation in such a consortium. Members of the Panel were of the opinion that, given the current levels and structures of public funding for research of this kind in Canada, it was not likely that Canadian universities would have the resources to commit to such a venture. Those members of the Panel with knowledge of private sector health research using non-human primates did not consider it likely that the major Canadian companies involved in this research would find the proposal attractive from a business viewpoint.

In the Panel's view, it is unlikely that a consortium could succeed without a significant government health research initiative (e.g., the development and testing of an AIDS vaccine) requiring non-human primates. This is not only because of the absence of potential partners with the resources to finance such a consortium; if the facility were to be relocated from Tunney's Pasture, the costs of creating a new facility for housing the breeding colony would be prohibitive.

Considerations in Favour of a Research Consortium

•It would provide the funding base for continuation of a Canadian health research program that required the use of the cynomolgus macaque monkey, potentially reducing the funding pressures on Health Canada.

•It could reduce the duplication of primate research facilities and use of non-human primates in Canada. This would be a more efficient use of research money and scientific expertise. It could also allow more efficient use of research animals in accord with the "3-R's" principle.

•It would promote collaboration among researchers and funding agencies and allow for a more cooperative and coherent Canadian research strategy.

•Considerations Against a Research Consortium

•The consortium would require a major expenditure of money, especially if it involved the relocation or reproduction of the current facility to a different research centre. If it remained at Tunney's Pasture, it would still require funding for a major upgrading of the facility.

•There is no evidence that the university and/or private sector has the interest or the resources to take on the burden of support for such a consortium in a way that would relieve the government of a significant portion of the financial responsibility for the primate colony. Use of non-human primates among Canadian researchers appears to be decreasing, and is expected to continue to do so, unless there is a major infusion of public money into health research requiring this model.

•The consortium idea appears feasible only under the assumption of a major government funding of health research in the primary areas that would require non-human primate models. Thus it not a feasible alternative to Health Canada's current funding problem with the primate colony.

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A.**Employee take-over proposal (at Tunney's Pasture)**

The Health Canada Internal Review also raised the possibility of turning over the operation of the Tunney's Pasture facility to a private enterprise, owned and managed by employees. The Internal Review specified certain conditions under which such an employee take-over plan would be acceptable. Among these were certain guarantees that the Government of Canada retain full access to animals needed to meet national policy objectives, that it have right of first refusal if the colony were eliminated or sold (within the first three years), and that the subsidization be consistent with Departmental policy. A group of employees of the Animal Resources Division have expressed interest in such a take-over of the colony. However, in communication to this Expert Panel a representative of the group emphasized that he considered the plan only as a last-resort alternative to the breaking up and/or loss of the colony to Canadian researchers.

The Expert Panel has seen no feasible business plan that would suggest that the commercial operation of the colony under an employee take-over plan would be economically viable. In the past few years Health Canada has attempted to operate the breeding colony on a commercial basis by costing out the production and care of individual animals and attempting to market them to researchers or charge researchers a per diem for use of the animals on a cost recovery basis. This has not been successful in freeing the colony from the need for continued government subsidy. Canadian users report that they find the per diem charges to be excessive, and find it cheaper to go elsewhere (i.e., outside Canada) for research primates. Companies in Canada regularly purchase their animals in Texas as well as in other parts of the world, and there is indication that some of these companies are moving their non-human primate research activities outside of Canada where publicly subsidized animals are available at much lower costs, or even at no cost. Given this history and the expectation of continued reduction in Canadian demand for these animals, the Expert Panel did not consider the employee take-over plan economically feasible. If the costs of the plan include the costs of upgrading the current facility to meet minimal ethical standards for housing of the animals, the economic viability of employee take-over is even further diminished.

Considerations in Favour of Employee Take-Over

•If economically feasible, the plan would retain the macaque colony in Canada and make the animals available for Canadian health research needs.

•A highly trained and competent staff would be retained in place to provide care for the animals.

Considerations Against Employee Take-Over

•There is no business plan to indicate that there is sufficient demand to make the colony commercially viable as a private enterprise.

•Given the current over-population of the colony, it is likely it would be economically necessary to conduct a large-scale sale of animals to buyers inside and outside Canada, as well as continued regular sales into foreign markets. This raises the concerns listed above about selling the colony to foreign researchers and primate centres.

•It is highly unlikely that adequate long-term care of the animals, requiring the substantial renovation of the current facility could be carried out without massive public subsidy.

•This plan removes the colony from any public policy interests, scrutiny or control, as well as accountability, especially if privatization fails.

VIII. CONCLUSIONS AND RECOMMENDATIONS

The Expert Panel's weighing of the pro's and con's of each option as outlined above led the members to a consensus on the conclusions to be drawn regarding the issues presented in the Terms of Reference. These conclusions are summarized below, followed by the recommendations which the Panel believes are most consistent with them.

CONCLUSIONS

I. Health Security of Canada in the future is an important issue. The possibility that Canada might be faced with a major health crisis posed by the onset of a new or re-emergent highly infectious disease or some other challenge to human health and well-being is not to be dismissed lightly. The cynomolgus macaque colony at Tunney's Pasture is without question a valuable national resource, which could play an essential role in the research that might be needed to meet such challenges. In the Panel's view, any action which removed this valuable resource from Canada or from access by Canadian researchers, would constitute an irreversible loss of the capacity to respond to these challenges should they arise. This could expose Canadian society to substantial health risks in the future.

II. Potential health security challenges, as important as they are, may not by themselves provide sufficient ethical justification for the holding of animals in restrictive captive conditions typical of a research facility like that at Tunney's Pasture. If the financial resources, either public or private, are not available to carry on significantly beneficial health research requiring non-human primates, the animals should be retired from those restrictive conditions into "sanctuary" conditions.

III. There currently exist important health research challenges of the kind outlined in Section V of this Report. It is not evident that either the universities or the private sector in Canada have the resources to carry on this research without significant public funding. There is not currently in Canada the levels of research activity in areas requiring the

macaque model that would make the establishment of an independent, or jointly funded, primate research centre feasible.

IV. Only a major government initiative in support of such research can rationalize, either economically or ethically, the continuation of a primate breeding colony in Canada of the size of the current breeding colony. This is true whether the colony is retained as a Health Canada facility, as a consortium with universities, hospitals and the private sector, or as an entirely privatized operation. Absent such a major public commitment to this research, immediate steps should be taken to begin the closing down of the primate breeding colony.

V. Health Canada retains an ongoing ethical responsibility for the care of the animals in the breeding colony, whether or not there is funding for primate research in the future. This responsibility stems from the original decision to develop the breeding colony and to produce the animals through a breeding program. It includes the responsibility to dispose of the colony in a way that guarantees the protection of the animal's welfare.

VI. In the Panel's view, this ethical responsibility entails an ongoing financial obligation for the animals, whether as a breeding colony for research purposes or as a sanctuary for animals permanently retired from research. This is because the Panel does not believe that any of the options for off-loading financial responsibility for the current breeding colony are either feasible or ethically acceptable. In particular, on the balance of considerations discussed in Section VII, the Panel does not find feasible or ethically acceptable:

A. The sale of the colony on the open market. There is not currently in Canada a sufficient research demand for SPF animals that would permit the sale of these animals at anywhere near their true international market value. Selling them on the international market would be to abandon responsibility for the ongoing welfare of the animals, and flooding the market with a large number of animals could encourage unnecessary research use and purchase by buyers who might

not be constrained by acceptable standards of ethical conduct governing animal use.

B.The privatization of the colony, which is not judged to be financially feasible.

C.The establishment of a government/university/industry consortium, for which there does not appear to be sufficient financial or other support, absent a commitment of major government funding.

D.The continuation of the status quo, which is unacceptable insofar as the breeding colony is larger than current research demands justify, and because of inadequate housing conditions for a portion of the population.

E.The wholesale euthanasia of the colony, which the Panel finds ethically unacceptable for the reasons outlined in Section VI.

VII.Thus, Health Canada retains a financial obligation for one of two options:

A.Placing the entire primate colony into sanctuary conditions, either in the current facility or elsewhere, discontinuing all breeding, and caring for the animals until the end of their natural life spans, OR

B.Establishing funding for a health research initiative which rationalizes the responsible research use of a portion of the current breeding colony, and makes the facility and research funding available to Canadian researchers.

RECOMMENDATIONS

Preferred Option: Maintain Canadian Health Research Capacity with Reduced-Size Monkey Colony

1.The Government of Canada should allocate funding for a health research grant program in areas of strategic health needs. These include, but are not limited to, those identified in Section V.

2.Part of this funding initiative should provide for the transformation of the Tunney's Pasture primate colony into a Canadian Primate Research Centre. This Centre should be open to all Canadian researchers to conduct collaborative health research requiring non-human

primate models, as well as researchers conducting purely observational research on cynomolgus macaques. The Centre could follow the model of the seven primate research centres in the United States – extending this very successful research infrastructure to Canada. The Centre could recover some costs by making animals available at competitive prices to external researchers working under the jurisdiction of the CCAC.

3.An immediate program to reduce the population of the primate colony to numbers necessary for actual Canadian research needs should be instituted. This means an immediate and complete cessation of all breeding, to remain in effect until the colony reaches the minimum number reasonably required to sustain Canadian research needs. Any future breeding should be resumed strictly in conformity with reasonable demand.

4.The transfer of all animals in excess of those needed for research into permanent sanctuary. The Panel members believe that it is preferable to establish a sanctuary in Canada rather than transfer animals to new, more expensive sanctuary quarters elsewhere. A portion of the Tunney's pasture facility should be renovated to meet at least minimal sanctuary conditions. Health Canada should encourage Canadian researchers to conduct non-invasive, observational research with the animals in sanctuary.

Considerations in Favour of the Panel's Preferred Option:

•Canada retains the possibility of meeting potentially serious health challenges in the future with a valuable SPF colony that could be expanded if necessary.

•Canada puts in place a research initiative which would contribute to important contemporary health research imperatives, and which would provide the ethical justification for the breeding and captivity of the animals currently in the colony.

•Canadian researchers would have a supply of animals bred in captivity, of known parentage, accustomed to human handling and free from diseases that potentially threaten both good research and the health of researchers.

- The Canadian taxpayers' investment in a valuable research facility would not be wasted, but would be utilized in a way that promotes collaborative health research among Canadian researchers.
- The current ethically unacceptable situation of over-breeding and over-population would be alleviated by the reduction of the colony to a size justified by research need and the sanctuary in humane conditions of animals in excess of that need.
- The ethically unacceptable practice of housing some of the non-research animals in restrictive single caging on a long-term basis would be alleviated by upgrading of the facility.
- A restructured primate facility would strike the proper balance of conflicting ethical concerns in the use of animals for health research. It makes animals available to aid in the alleviation of critical human health problems, while also placing this research in a collaborative facility that could be more transparently and publicly accountable to the appropriate reviews of animal care.
- Health Canada (and the Canadian public) retains full responsibility and control over the fate of the animals.

Considerations Against The Panel's Preferred Option:

- Health Canada would not be relieved of the financial burden of the primate colony. It is the view of the Panel Members, however, that there is no ethically acceptable and financially feasible means currently available by which Health Canada can relieve itself of responsibility for these animals.

Secondary Option: Phase Out of Entire Breeding Colony and Sanctuary of Remaining Animals

If the Government of Canada does not undertake the establishment of some type of health research grant initiative requiring the macaque model, such as that suggested for the Preferred Option, then the Panel recommends that Health Canada take immediate steps to reduce the population in the breeding colony to zero. This should be accomplished by the following means:

1.An immediate end to all further breeding through the sterilization of the (male) animals.

2.The placement of the entire colony into acceptable sanctuary conditions, to be maintained there for the natural life span of the animals. As with the Preferred Option, the Panel believes that establishing a sanctuary in the current facility, or at least in Canada, is both economically and ethically preferable to transferring the animals to a foreign sanctuary. Transfer to a foreign sanctuary raises for the Panel serious questions about loss of control over the long-term treatment and end use of the animals.

3.Maintaining the sanctuary open to Canadian researchers wishing to conduct purely observational, non-invasive research, and permitting regular monitoring by CCAC and other competent organizations concerned with the welfare of the animals.

4.While not entirely consistent with the concept of "sanctuary", the principle of non-displacement might justify the sale at competitive prices of some animals to CCAC sanctioned Canadian investigators conducting bona fide research with their own sources of funding (i.e., as an alternative to further imports of animals into Canada for research purposes).

Considerations in Favour of the Panel's Secondary Option:

•The option would prevent the ethically unacceptable breeding of animals that are not essential for actual health research activity in Canada.

•The ethically unacceptable practice of housing some of the non-research animals in restrictive single caging on a long-term basis would be alleviated by upgrading of the facility.

•All animals would be placed in humane conditions for the remainder of their lives.

•Health Canada (and the Canadian public) would retain control over, and accountability for, the fate of the animals.

Considerations Against the Panel's Secondary Option:

- Canada would lose its capability to respond quickly to serious new human health challenges in the future. It would become completely reliant upon foreign suppliers of (probably less scientifically valuable) animals.
- Potential Canadian research contributions to current significant health research needs in the areas of HIV vaccine development, cardiovascular disease, emerging infectious diseases, and geriatric problems would be foregone.
- The small number of Canadian researchers in universities, hospitals, and the private sector who may need macaque monkeys in the future would have to obtain them from non-Canadian sources.
- Health Canada would not be relieved of its financial responsibility for the maintenance of the primate colony. As stated with respect to the Preferred Option, however, there is no ethically acceptable and financially feasible means currently available by which Health Canada can relieve itself of responsibility for these animals.

IX.DISPOSITION OF THE HEALTH CANADA RESEARCH COLONY

As indicated in the Introduction, the Expert Panel clarified with Health Canada officials that the Terms of Reference included recommendations on the 148 non-human primates currently part of research protocols conducted by staff researchers at Health Canada. We have referred to these animals as the "Research Colony". These research projects have been described earlier in this Report (Sections II and IV)

It is the Panel's understanding that all funding for these research projects has been discontinued. Most of these are near the beginning, or in the middle of the data gathering process. The premature curtailment of the research programs will entail the loss of large amounts of valuable research data. This in itself constitutes a monumental waste of the animal resources involved, and raises for the Panel serious questions about the ethics of subjecting these animals to the rigours of research for little or no benefit in scientific knowledge or human health care. It also means the loss to Canada of several internationally esteemed researchers.

It is the hope of the Panel members that these research projects can be restored by a reinstatement of the funding under a commitment to a national health research initiative such as has been recommended for the maintenance of a reduced-size breeding colony.

However, if the funding of these projects is not restored, the Panel recommends the following course of action (whatever the course, the care and use of the animals must comply with Canadian Council on Animal Care Standards):

1.For as long as the research projects continue under the supervision of the researchers, any humane euthanasia of the animals required by the research protocol for the collection of valid scientific data or the prevention of suffering to the animal should be carried out in the time frame and the manner specified by the research protocol.

2.When the research projects are discontinued, the animals (unless infected with transmissible viruses) should be retired into permanent sanctuary. Since some of these animals have

been subjected to toxins or other stresses which may lead to the early deterioration of their health, they, like any animal in sanctuary, should be humanely euthanized at the most appropriate time for the prevention of irreversible suffering.

MEMBERS OF THE PANEL

Conrad G. Brunk, Chair

Conrad Grebel College, University of Waterloo

Dr. Brunk is a Professor of Philosophy at Conrad Grebel College, University of Waterloo, in Waterloo, Ontario. His areas of research and teaching include the normative aspects of science, technology and law, environmental and health risk management, and applied and professional ethics, with a specialization in the ethics of the biomedical, business and technological professions. He also a member of the Institute for Risk Research at the University of Waterloo. He is co-author of "Value Assumptions in Risk Assessment," a book exploring how moral and political values influence scientific judgments about technological risks, and author of many articles in journals and books on ethical issues in technology and professional practice, and a regular consultant to governments, industry and institutional ethics committees. He teaches courses in Conflict Resolution and is the Director of Legal Studies and Criminology at the University of Waterloo. Professor Brunk holds a PhD in Philosophy from Northwestern University.

Albert F. Clark

Department of Biochemistry, Queen's University

Dr. Clark is a member of faculty at Queen's University. He obtained his Ph.D. in Biochemistry from McGill University in 1964. Following 2 years of post-doctoral work at the Worcester Foundation for Experimental Biology in Worcester, Massachusetts he came to Kingston, Ontario as an Assistant Professor in the Department of Biochemistry at Queen's University and Clinical Chemist at Kingston General Hospital. He left the position of Clinical Chemist in 1981. From 1981 through 1997 he has been an Associate Dean (Medical Research Services) in the Faculty of Medicine, Queen's University and Director of Research at Kingston General Hospital. He holds the rank of Professor in the Departments of Biochemistry and Pathology. In 1994-95 he spent 9 months as the interim Acting Director of the Programs Branch at the Medical Research Council of Canada in Ottawa. From 1995-97 he was Acting Head of the Department of Biochemistry and in 1997 began a 5 year term as Craine Professor and Head. He has over 86 publications in the area of steroid hormones and prostate biology. He is Chair of the Queen's University Animal Care Committee and the Queen's University and Affiliated Teaching Hospitals Research Ethics Board which reviews all research protocols involving the use of human subjects. He is a member of the Board of Directors of the Canadian Council on Animal Care and chairs their Guidelines Committee.

Andrew G. Hendrickx

California Regional Primate Research Centre, University of California, Davis

Dr. Hendrickx is Professor of Cell Biology and Human Anatomy, School of Medicine, and Director, California Regional Primate Research Center, University of California, Davis. *Education*: B.S. (Biology) 1959, Concordia College, Moorhead, Minnesota; M.S. and PH. D. (Zoology), 1961 & 1963, Kansas State University, Manhattan, Kansas. *Major Research Interests*: Reproduction, Embryology and Developmental Toxicology of Primates. Current studies include mechanisms and pharmacokinetics of retinoids, developmental toxicity of TCDD and safety assessment of Vitamin A and biotech products. *Service and Honors*: Past President, Teratology Society (1987) and American Society of Primatologists (1982-84). Reproductive Endocrinology Study Section, NICHD, NIH (1986-89); Temporary Advisor - World Health Organization (WHO), Special Program for Research, Training and Education in Human Reproduction (1977-present), and WHO Toxicology Panel (1987-present); Warkany Lecturer: Teratology Society (1994); Human Embryo Research Panel, NIH (1994); Chair, Science Advisory Board, Prop. 65 Developmental and Reproductive Toxicology (DART) Identification Committee, State of California (1993-present).

Michel Klein

Pasteur Mérieux Connaught

Dr. Klein was born in Dijon (France) and received his M.D. degree from the Faculty of Medicine of Paris in 1969. He obtained a Master of Science from the University of Paris VII and his Diploma in Immunology from the Pasteur Institute. He did his post-graduate studies in immunology at New York University and in biochemistry at the University of Toronto. Dr. Klein practiced clinical immuno-haematology at the Saint-Louis Hospital (Paris) for several years. Concurrently, he began his research career as attaché, then chargé de recherches with the Institut National de la Santé et de la Recherche (INSERM) in France. He was subsequently appointed Head of the Laboratory of Immunology of the Toronto Western Hospital in 1977. He held the position of Associate Professor of Medicine and Pathology at the University of Toronto and is currently full Professor of Immunology with a cross-appointment in Biochemistry. After a sabbatical year in genetic engineering at the California Institute of Technology in 1986, Dr. Klein joined Connaught Laboratories as Director of Molecular Biology. He was then appointed Assistant Vice-President of Research in 1988 and became Vice-President of the new Connaught Centre for Biotechnology Research in 1989. Dr. Klein is currently Vice-President of Research for Pasteur Mérieux Connaught Canada. He is a member of the Research Operational Committee, of the Strategic Scientific Committee and of the Corporate Research and Development Action Committee of the corporation. He also sits on the University-Industry Committee of the Medical Research Council of Canada and is a member of the Conference Board of Canada. Dr. Klein has contributed chapters to numerous books in immunology, is the author of over three hundred scientific articles and presentations

and is an inventor on more than forty vaccine patents. He is a Chevalier of the Legion of Honour.

Bonnie J. Mathieson

Office of AIDS Research, National Institutes of Health

Dr. Mathieson, as a Health Science Administrator, currently serves as the Chair of the NIH AIDS Vaccine Coordinating Committee at the Office of AIDS Research (OAR), Office of the Director (OD), NIH, Bethesda, MD. She received her B.S. in Botany at the University of Illinois, did initial graduate studies in the Medical Microbiology at Stanford University, and received a Ph.D. in Biology from Cornell University Medical College, Sloan-Kettering Division of Graduate Studies, New York, NY. Dr. Mathieson was awarded a postdoctoral fellowship by the Cancer Research Institute, NY and was a Staff Fellow in the Laboratory of Microbial Immunity, National Institute of Allergy, Immunology, and Infectious Diseases (NIAID). From 1982-1983 she was a Member of the Basel Institute of Immunology in Switzerland, before joining the National Cancer Institute as Head of the Leukocyte Differentiation Section at Frederick, MD. Dr. Mathieson trained and performed research as an immunologist and developmental biologist working on studies of T-cell surface expression, immune effects on fertilization, early embryonic development, differentiation and lineages of T cells and NK cells, and mechanisms of cytokine activity. In 1989, Dr. Mathieson joined the Division of AIDS (DAIDS), NIAID, NIH as a Project Officer in the Vaccine Research and Development Branch, where she monitored HIV, SIV and other lentivirus basic and preclinical research related to vaccine design and delivery, with particular focus on immunology. She has published over 100 research articles and reviews and has served on editorial boards and ad hoc review groups. In 1995, Dr. Mathieson joined the OAR and served as the Executive Secretary for the Vaccine Area Review Panel for the Report of the NIH AIDS Research Program Evaluation Task Force. She currently serves and a Councilor for the Clinical Immunology Society and as a member of the Scientific Advisory Panel for the Adolescent Medicine HIV/AIDS Research Network for the National Institute of Child Health and Human Development. Dr. Mathieson's Awards include the Public Health Special Service Recognition Award for her role in the DAIDS Pediatric Initiative Group and an NIH, Public Health Service, Special Achievement Award for her work in the OAR.

Michael F. McDonald

Centre for Applied Ethics, University of British Columbia

Dr. Michael McDonald is Maurice Young Professor of Applied Ethics and the founding Director of the Centre for Applied Ethics at the University of British Columbia. He is also appointed to the Philosophy Department. Most recently, Dr. McDonald served as deputy chair of the Tri-Council Working Group on Ethics, which was mandated by the Presidents of MRC, NSERC, and SSHRC to produce a comprehensive set of standards for all research involving

humans. Dr. McDonald has also served as President of the Canadian Philosophical Association and Editor of the philosophical journal *Dialogue*. Before coming to UBC in 1990, he was a member of the University of Waterloo's Philosophy Department. Dr. McDonald's research and teaching is in health care ethics, business and professional ethics, ethical theory, and political philosophy.

APPENDIX I

SUMMARY OF SUBMISSIONS

- ***ORGANIZATION***
-
- Animal Action
- Animal Alliance of Canada
- Animal Defense League of Canada
- Animal Rights Coalition
- Canadian Centre for Alternatives to Animals in Research (U. of Ottawa)
- Canadian Council on Animal Care
- Canadian Federation of Humane Societies
- Canadians for Health Research
- CGB Publishing Ltd.
- ITR Laboratories Canada, Inc.
- Lifeforce
- McGill University - [AIDS Centre and Jewish General Hospital Institute for Medical Research]
- Ontario Society for the Prevention of Cruelty to Animals
- Primarily Primates
- Primate Products, Inc.
- Queen's University - [Dept. of Philosophy; Dept. of Obstetrics and Gynecology, and Kingston General Hospital; Neuroscience Group, Medical Research Council of Canada]
- Spirit Valley Wildlife Sanctuary
- University of Calgary - [Faculty of Medicine]
- University of Guelph - [Office of the V.P. Research]
- Université Laval - [Laboratory Animal Division]
- Université de Montréal - [Primate Behaviour Laboratory]
- Université de Québec - [Animal Resources]
- University of Toronto - [Dept.of Anthropology]
- University of Waterloo Public Interest Research Group - [Centre for Compassionate Living]
- Zoocheck Canada

NB: This list does not include submissions by HPB staff, or earlier reports. In addition, approximately 30 individuals, not representing organizations or institutions, made written submissions to the RSC Expert Panel.