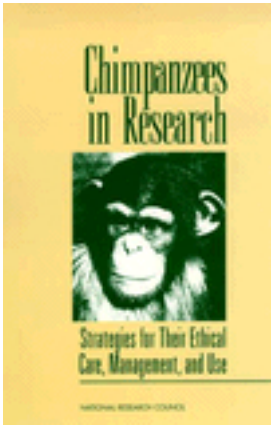

Chimpanzees in Research: Strategies for Their Ethical Care, Management, and Use

Committee on Long-Term Care of Chimpanzees, Institute for Laboratory Animal Research, Commission on Life Sciences, National Research Council

ISBN: 0-309-59115-5, 108 pages, 6 x 9, (1997)

CHIMPANZEES IN RESEARCH

STRATEGIESFOR THEIR ETHICAL CARE, MANAGEMENT, AND USE

COMMITTEE ON LONG-TERM CARE OF CHIMPANZEES
INSTITUTE FOR LABORATORY ANIMAL RESEARCH
COMMISSION ON LIFE SCIENCES
NATIONAL RESEARCH COUNCIL

NATIONAL ACADEMY PRESS
WASHINGTON, D.C. 1997

NATIONAL ACADEMY PRESS 2101 Constitution Avenue, NW Washington, DC 20418

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This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, National Academy of Engineering, and Institute of Medicine.

This study was supported under contract NO1-OD-4-2139, T.O. 17, from the National Institutes of Health. Core support is provided to the Institute of Laboratory Animal Resources by the Comparative Medicine Program, National Center for Research Resources, through grant 5P40R-R0137; by the National Science Foundation through grant BIR-9024967; by the US Army Medical Research and Development Command, which serves as the lead agency for combined US Department of Defense funding, also received from the Human Systems Division of the US Air Force Systems Command, Armed Forces Radiobiology Research Institute, Uniformed Services University of the Health Sciences, and US Naval Medical Research and Development Command, through grant DAMD17-93-J-3016; and by research project grant RC-1-34 from the American Cancer Society.

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Cover photograph by Susanna Berdecio, Primate Foundation of Arizona

Additional copies of this report are available from the Institute for Laboratory Animal Research, 2101 Constitution Avenue, N.W., Washington, D.C. 20418.

Printed in the United States of America.

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COMMISSION ON LIFE SCIENCES

PREFACE

The use of chimpanzees (*Pan troglodytes*) in biomedical research has led to numerous medical advances, including the development of a vaccine for hepatitis B virus. In 1986, chimpanzees were thought to constitute the critical model for understanding the human immunodeficiency virus, and a breeding program was established to provide animals for the study of this virus. The breeding program was very successful, and the combination of an increase in chimpanzee numbers and less-extensive research use than was expected has created a surplus of chimpanzees and a substantial management problem. Although chimpanzees are available for research, there are also pressures not to use them, such as the high cost of housing and maintenance and their endangered status in the wild. Their close genetic relationship to humans, which makes them the appropriate surrogate for human-health research, also creates serious concerns about the ethics of their use by scientists and the public. The US federal government now owns or supports some 900-1000 chimpanzees at a cost of approximately $7.3 million per year, but government investigators pay "use fees" for using animals in government research. Each of those issues contributes to the cost to investigators and the complexity of using chimpanzees in research.

The cost, ownership, and complex genetic management requirements of chimpanzees so greatly affect US policy regarding the use of chimpanzees in research that in 1994 the National Institutes of Health (NIH) requested advice from the National Research Council on

- The size of the breeding colony required to support the need.
- Issues of ownership, long-term care, and use in research.
- Mechanisms by which nongovernment organizations could assist in achieving appropriate goals and solutions for the long-term care of chimpanzees.

To address these issues, the National Research Council appointed a committee of experts. The committee convened four public meetings and communicated with chimpanzee-colony directors and behaviorists in each of the six major chimpanzee facilities and with the administrators and scientists who use chimpanzees in research. The public meetings provided opportunities for scientists, members of the public, and representatives of animal-protection societies to voice their concerns. One of the meetings was held in the form of a seminar at the joint meeting of the American Society of Primatologists and the International Primatological Society and was attended by many of the world's leading chimpanzee biologists and conservationists. Brief questionnaires were also sent to all grantees listed in the NIH Computer Retrieval of Information on Scientific Projects (CRISP) database who use chimpanzees in research. The public meetings and questionnaires all yielded information that was used in the preparation of this report.

The committee was faced with conflicting scientific, financial, and ethical situations. Euthanasia and cost were the chief contentious issues and led to a minority opinion (see Appendix A). The committee, like the public, found it difficult to agree on a single approach that embraces both euthanasia and cost. Euthanasia is common in veterinary medicine to alleviate uncontrollable suffering and for population control, but it is not easy to decide when it is acceptable for chimpanzees. Nor is it easy to address the expenditure of public funds for the "retirement" of chimpanzees that perhaps have never been used in government research, although they were bred for this purpose. The committee provides recommendations on these and other issues, but putting the recommendations into practice will require as much diligence and soul-searching as the committee itself used in developing the recommendations.

Presenting the population numbers and costs clearly and unambiguously has been a difficult task. It is largely because of the difficulty of accounting

for sizes of the various subpopulations of chimpanzees (such as, those used in infectious research, available for research, and not needed for research) and the funding to support the research and the not-needed-for-research populations that the National Research Council was asked to prepare these recommendations. Great care has been used in collecting accurate information, but different sources of the same information often differed because of overlapping distributions. For example, surveys of chimpanzee facilities of the numbers of animals available for research and the number posing a public health threat, revealed 360 and 260, respectively (table 3.2). However, when asked just about the numbers of animals posing a public health threat they report 350. One *might* conclude from this that there are 360 animals available for research and 350 posing a public health threat, but to do so would double-count some animals. The difference is due to the fact that in the former case some of the animals posing a threat are also available for research. Such overlap exists in every subpopulation. The numbers presented in the text and tables are accurate to the best of the committee's ability. When the numbers are approximate or the populations overlap, they are so labeled. With this in mind, careful reading of the text in conjunction with the tables should yield an accurate picture, but, it is because of the difficulty in understanding these issues that the report addresses a need for an autonomous, high-level management and oversight structure with funding from increased appropriations to avoid reducing support for biomedical research.

We believe that our recommendations are sound, justifiable, cost-effective —although not inexpensive—and ethically responsible. We anticipate that they will meet with the approval of scientists, chimpanzee-colony directors, animal protectionists, the public, and members of Congress. We also strongly believe that NIH must work hard to achieve that breadth of approval.

This report would not have been possible without the information and advice provided by those who wrote to and met with the committee. All the chimpanzee-colony directors participated in conference calls and responded to questionnaires, for which the committee is most grateful. The NIH Interagency Animal Models Committee was helpful and frank in assisting the committee; its breadth of experience and its records were invaluable. The committee appreciated the opportunity to tour and have discussions

with the staff of the Southwest Foundation for Biomedical Research and the University of Texas M.D. Anderson Cancer Center Science Park.

Equally important were the people who came to the public meetings or wrote to the committee because they cared. They came or wrote to share their concerns for chimpanzees and to seek assurance of their appropriate long-term care. Members of humane, protectionist, and anti-vivisectionist groups came to public meetings and gave testimony of their sincerity in seeking partnerships with the government for the long-term care of chimpanzees no longer needed in research. Among these were Nancy Blaney, American Society for the Prevention of Cruelty to Animals; Peggy Cunniff, Donald J. Barnes, and Claire Haggarty, National Anti-Vivisection Society; Tina Nelson, American Anti-Vivisection Society; Alan Berger, Animal Protection Institute; Holly Hazard, Doris Day Animal League; Anne Kleiman, In Defense of Animals, People for the Ethical Treatment of Animals, and the New England Anti-Vivisection Society; Carole Noon, International Primate Protection League; Valerie Stanley, Animal Legal Defense Fund; Martin Stephens, Humane Society of the United States; and Christine Stevens, Animal Welfare Institute. We are indeed grateful to the reception and informative tours provided to members of the committee by Wally Swett, Primarily Primates, and Martine Colette, Wildlife Waystation. The committee was saddened by the death of Michael McGehee during the course of this study. He was a strong spokesman for the National Chimpanzee Sanctuary Task Force, and the committee members appreciated the time that he took to inform them of the task force and for his dedication on behalf of chimpanzees. We thank all for their time and for their expressions of concern for this unique species. They are strong allies of the goals of this report and should be consulted in the implementation of its recommendations.

Naming people who assisted the committee risks errors of omission, yet some must be acknowledged. The work in the field by Jane Goodall and others has greatly assisted in the understanding of appropriate captive management and housing of chimpanzees. Their work contributes substantially both to the well-being of chimpanzees in captivity and to our recommendations. We appreciate the time and thoughtfulness of Donald Buford, Jane Goodall Foundation; Joseph Erwin; William I. Gay; Travis Griffin, Coulston Foundation; and Barbara Orlans, Kennedy Institute of

Ethics. We also thank three staff behaviorists from chimpanzee colonies who briefed the committee on the physical and social structures of captive facilities that contribute to well-being: Mollie Bloomsmith, University of Texas M.D. Anderson Cancer Research Center; Linda Brent, Southwest Foundation for Biomedical Research; and Sue Howell, Primate Foundation of Arizona. Finally, we wish to acknowledge Lilly-Marlene Russow's contribution. Her thoughtful assertiveness stimulated discussion and resolution of difficult ethical issues. Her choice of wording throughout the text attests to her commitment to the animals and to her profession. We thank her.

We also want to acknowledge the contribution of the many individuals who agreed to review our work. Their labor improved the quality of the report. Readers who detect errors of omission or commission in this report are encouraged to send their suggestions to the Institute for Laboratory Animal Research, National Academy of Sciences, 2101 Constitution Ave., NW, Washington, DC 20418.

The committee extends its appreciation to the sponsor of this report; to Norman Grossblatt for editing the manuscript; to Carol Rozmiarek and Cheryl Mitchell for their skillful support at each of the committee's meetings and for coordinating the great flow of information to and from committee members; and to Tania Williams for her skillful assistance in the coordination and planning of two meetings. The committee reserves special thanks for Thomas Wolfle, expressed by the following quotation: "Working with Dr. Wolfle has been an enriching experience for the committee. His insistence on continuous progress toward the resolution of the complex issues facing the committee was always tempered by patience, professionalism, and the warmth of his genuine and unassuming personality. The ability of the committee to reach consensus was due, in no small part, to his unusual skill in bringing people of diverse backgrounds together for a common purpose. We are grateful for his guidance."

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CONTENTS

CHIMPANZEES IN RESEARCH STRATEGIES FOR THEIR ETHICAL CARE, MANAGEMENT, AND USE

EXECUTIVE SUMMARY

Chimpanzees in biomedical and behavioral research constitute a national resource that has been valuable in addressing national health needs. Facilities that house chimpanzees owned and supported by the National Institutes of Health (NIH) have successfully met the research requirements of the scientific community. The captive chimpanzee population in the United States has grown substantially, particularly over the last decade. That growth is due primarily to the success of the NIH-sponsored Chimpanzee Breeding and Research Program, which achieved the birth numbers thought necessary to meet the projected needs of biomedical research. However, the expected level of use of the chimpanzee model in biomedical research did not materialize, and that has created a complex problem that threatens both the availability of chimpanzees for research in the future and the infrastructure required to ensure the well-being of captive chimpanzees used in biomedical research.

Because the present system is fragmented, it is impossible to formulate an accurate overview of the size and nature of the chimpanzee population. But, if the chimpanzee is to continue to be used in biomedical research responsibly, effectively, and cost-effectively, we must be able to oversee, track, and coordinate the maintenance and use of chimpanzees and to control the size of the population. To assess the long-range situation and to develop, implement, and monitor the application of policies for the proper use and care of chimpanzees, an authoritative, centralized oversight structure is imperative. Once it is in place, it will be possible to refine and implement this report's recommendations, which are summarized here.

The existing chimpanzee population is more than adequate to meet research needs for at least five years. Moreover, increasing the number of chimpanzees maintained in the major NIH-supported biomedical chimpanzee facilities would risk eroding the quality of their care as a result of overcrowding, pressure on limited resources, and contamination of breeding and other research-naive animals by those used in infectious-disease studies. Therefore,

(1) A breeding moratorium should be imposed for at least five years (1997-2001).

Such a moratorium, necessary to prevent additional strain on the system, will not itself create more housing space or improve the housing of many animals now in the research population, but it will reduce operating costs by about 15% from present costs by year five. Decisions about acceptable means of population maintenance and control in a setting of scarce resources are inordinately complex and involve both scientific and ethical questions; there are no simple solutions.

The committee has been made aware that both the NIH National Center for Research Resources (NCRR) and the Interagency Animal Models Committee have orally communicated to breeding colony managers and researchers that euthanasia as a means of population control is not desirable. The committee agrees with those groups and with members of the public with whom these issues were discussed and recommends that this position be formalized and communicated to all government-supported chimpanzee managers and researchers. Therefore,

(2) Euthanasia should not be endorsed as a general means of population control.

The committee fully recognizes the implications of that recommendation in regard to lifetime funding for all animals and the need for additional space and facilities for an aging population, the third fundamental issue addressed in this report. There are about 1,500 US biomedical chimpanzees. The committee examined in detail the trend of reduced use of the chimpanzee model in biomedical research. Chapter 2 discusses this topic by first reviewing the past use of chimpanzees

and their major contributions to the understanding and alleviation of human health problems. New developments in biomedical research and threats to society from emerging and re-emerging infectious microorganisms are expected to contribute to future demands for chimpanzees. However, several barriers prevent or reduce the use of the chimpanzee model. One expressed by scientists is that the chimpanzee is not now a good research model, for three reasons: the availability of government-supported chimpanzees is not well advertised, use fees for nongovernment animals are often over $50,000 per animal, and government protocol-review procedures inhibit the use of chimpanzees in NIH-sponsored research and by commercial institutions. Because the importance of chimpanzees in biomedical science has been amply demonstrated—for example, in the development of vaccines for hepatitis B—and equally important uses in the future are likely,

(3) A core population of approximately 1,000 chimpanzees should be assured lifetime support by the federal government, and ownership of these animals should be transferred to the government.

Government ownership of animals used in federally-funded studies will be critical for ensuring the long-term care of this important biomedical resource. The scientists' concerns will be addressed by reducing the cost of using chimpanzees (through elimination of use fees), thereby increasing the opportunity to improve understanding of the chimpanzee's biology and behavior, which is essential for its proper characterization as a research model. Government ownership, as detailed in chapter 5, should be carefully designed to sustain a captive population, provide animals for research, and protect human health through the provision of lifetime care, *in existing biomedical chimpanzee facilities*, of animals thought to constitute a human health hazard.

To facilitate developing its recommendations, the committee divided the chimpanzee population into five components: the present breeding population supported by NCRR, animals now on research protocols, animals available for research (both naive and those used in prior studies), animals used in previous government-sponsored research that are no longer needed for research and pose a risk to human health, and animals that are no longer needed for research or breeding and pose no

risk to human health. Each component presents unique opportunities and problems and is more fully addressed in chapter 2.

Not all of the initial core population recommended for government ownership is likely to be needed, and options should be sought for nongovernment support of animals that are no longer needed for research and breeding and are not thought to constitute a human health hazard. Cost savings and more effective use of the current overcrowded facilities could be achieved by transferring such animals to appropriate public (nongovernment) sanctuaries. That would save money by reducing the number of animals for which long-term maintenance is required in research facilities and reducing the requirements for expansion of current facilities. Properly designed, such sanctuary facilities should provide lower-cost maintenance of the animals than is possible in existing research facilities. Therefore,

(4)The concept of sanctuaries capable of providing for the long-term care and well-being of chimpanzees that are no longer needed for research and breeding should become an integral component of the strategic plan to achieve the best and most cost-effective solutions to the current dilemma.

The most obvious deficiency in present population management is the absence of a central coordinating program responsible for balancing the need to advance scientific knowledge relevant to human health with the short-term and long-term needs of the chimpanzee population. Rather, there is a system driven by fragmented approaches that primarily react to immediate needs. The committee believes that many of the scientific and ethical problems addressed in this report are a consequence of the general lack of coordination. Therefore,

(5)A single multiagency organizational unit, the Chimpanzee Management Program (ChiMP), should be established within the office of the director of the National Institutes of Health, or as described below, and be given direct administrative and fiscal responsibility for government-owned animals that are considered necessary to meet current and long-term national needs.

ChiMP should be an autonomous body with sole responsibility and

authority for coordinating the management and use of a US-government-owned population of chimpanzees for use in biomedical research by any government agency or department, irrespective of whether an investigator is employed by the government, receives research funding from a government source, or represents private enterprise. The committee believes that ChiMP, housed within the office of the Director of NIH (or a suitable alternative that has the autonomy, infrastructure, and expertise to manage the program), should serve as the leader of a consortium of government agencies that would include the Centers for Disease Control and Prevention, the Food and Drug Administration, and the Department of Defense, all of which need chimpanzees to fulfill their missions. Substantial cost savings will be achieved if participating agencies pool existing resources allocated to chimpanzees and jointly develop procurement plans for the long-term care of government-owned animals. Because the animals constitute a national resource that benefits all of society, they should not have to compete for funds for their long-term care with other entities that need resources that are already overextended for current and future biomedical research. The committee urges that the ChiMP office encourage and assist in efforts now being led by private initiatives and animal-protection organizations to develop sanctuary facilities for chimpanzees that are no longer needed for research or breeding.

The committee views development of a centralized management structure as the only rational vehicle for implementing its recommendations. It also recognizes that the breadth of expertise needed for oversight of the chimpanzee resource is not likely to exist in a single office or agency. Therefore,

(6)An appropriate advisory council of nongovernment experts should be created as a chartered committee for the purpose of establishing policies of ChiMP and for monitoring the short-term and long-term implications of the foregoing recommendations, including implications for research use, breeding-colony size, demography, genetics, and long-term care.

The need for combined centralization of management and oversight is so obvious that the last two recommendations of the Committee on

the Long-Term Care of Chimpanzees represent platforms for carrying out its core recommendations. If the committee's recommendations are followed, biomedical and behavioral research using chimpanzees can continue to thrive in a productive, ethically responsible, and cost-effective manner. If, however, the current lack of long-range planning and coordination continues, the combination of excess captive chimpanzees in the US biomedical population and lack of facilities and resources to care for increasing numbers adequately will soon become an insurmountable problem of enormous complexity, cost, and ethical concern. Lacking the ability to relocate their animals to acceptable alternative facilities, colony managers will be forced to reduce population numbers through euthanasia. The likelihood of this "train wreck" scenario must be considered in light of the broader issues surrounding the well-being of chimpanzees. 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 option.

1

INTRODUCTION

Chimpanzees, because of their close evolutionary relationship to humans, are attractive models for physiological, biomedical, and behavioral studies. For example, they have participated in such important developments in the category of "national needs" as the development of vaccines against hepatitis B and in early aerospace programs. A current census maintained by the International Species Information System (ISIS) indicates that of about 2,500 known captive chimpanzees globally, about 1,500 are housed in six biomedical institutions in the United States. In 1986, the National Institutes of Health (NIH) launched a breeding and research program at five institutions for several basic reasons: a perceived need for these animals for AIDS research, concerns about the potential for sustaining future generations of breeding chimpanzees, and concerns about the ability to provide sufficient animals to meet other national needs. The effort met production goals, and an initial breeding population of 315 animals has produced 394 live births. Of these offspring, 331 were alive in February 1997 (176 of which remain in the NIH breeding program). The combination of an increase in chimpanzee numbers and smaller than expected use of chimpanzees in research, has created a substantial management problem that jeopardizes both the chimpanzee model for research (because of their high cost) and their quality of care in research facilities (because of reduced funding). All animals that constitute the research and breeding pool now owned or supported by NIH require provisions not only for the short term, but also for long-term maintenance, regardless of their use in research. However, the funding required for long-term maintenance of a sizable population of chimpanzees

is considerable. Concerned with the burgeoning population of chimpanzees, the stress that the additional animals have created on available facilities, and issues associated with long-term care of captive chimpanzees, NIH asked the National Research Council to study these and related problems. Captive chimpanzees are behaviorally complex and have an average life span of 25 yr for males and 34 yr for females (maximal life spans are 55 yr and 65 yr for males and females, respectively), and their long-term management presents formidable challenges.

The challenges are not simply scientific or financial. The form and substance of this report reflect the fact that questions of science and questions of ethics are often inextricably blended. The very feature that can make the use of chimpanzees critical in biomedical research also entails unique moral questions. On the one hand, chimpanzees constitute a vital scientific resource for research on critical issues of human health, and proposals for their long-term care must not undermine the availability of adequate numbers of them for such research. On the other hand, the complexity of the ethical and scientific challenges follows from the fact that chimpanzees are our closest genetic relative in the animal kingdom. These two factors—scientific use and close genetic relative—cannot be divorced; one cannot appeal to one and ignore the other.

The dilemma of why or whether chimpanzees ought to occupy a special niche in moral deliberations relative to their experimental use cannot be reduced to an either-or situation. It is not simply a question of whether the chimpanzee is "just" another animal or otherwise equal in all respects to a human being. We believe that relevant differences between chimpanzees and humans justify the use of chimpanzees in research that would not be sanctioned if it were proposed to use human subjects. However, the close phylogenetic relationship to humans and complex psychological and social character of chimpanzees that make them more similar to humans than other laboratory animals are also relevant.

The conclusions reached by the authors of this report are based on scientific, financial, and ethical reasoning. Although the scientific and financial arguments might be more understandable to many readers of the report and are sufficient justification by themselves in reaching a decision for some readers, the ethical issues are also important and should be seriously considered, in our opinion. In the traditional sense, ethics requires that decisions be based on clearly articulated core human values—concepts

of right and wrong, good and evil, taking responsibility for one's choices—that go beyond purely pragmatic or economic considerations. Portions of the committee's recommendations are based on this concept, which, through numerous discussions with members of the public and the scientific community, led to our endorsement of the premise that the similarity of chimpanzees to humans distinguishes them in substantial ways from other laboratory animals and implies a moral responsibility for the long-term care of chimpanzees that are used for our benefit in scientific research. This special status of chimpanzees is supported by the following considerations of medical science, genetics, population biology, cost, and perception.

The similarities between chimpanzees and humans that make them desirable surrogates for studying diseases and conditions of humans constitute the reason for our recommendation for their continued use in scientific research. The committee believes that chimpanzees have provided and will continue to provide important scientific contributions, but that requires a captive population of sufficient size to sustain breeding and research. Unlike many other species used in research, chimpanzees cannot be recovered quickly if the population is disbanded or allowed to be reduced below a critical size. That is true for several reasons: their listing as endangered in the wild by the US Endangered Species Act and their listing in Appendix I of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) make importation from the wild impossible; their long generation time of about 10-yr makes recovery of a population time-consuming, expensive, and unresponsive to research demands; and recovery from cryopreservation of chimpanzee embryos or gametes is not yet possible. The need to maintain a healthy population is an important aspect of our responsibility for the care and well-being of chimpanzees used for scientific research.

We believe that our responsibility for the long-term care of chimpanzees is greater than that for other laboratory animals. Chimpanzees are genetically very similar to humans (Morin and others 1994). The special connection of chimpanzees to humans has been reinforced by decades of watching the rich repertoire of chimpanzee social, maternal, and tool-using behavior on television and at zoos; the public therefore expects a high level of respect for the animals. Our view is that this special status of chimpanzees implies a moral responsibility for appropriate long-term

care of chimpanzees used in scientific research. Therefore, recommendations are provided for their life-time care. This view definitely has financial consequences, and the committee recognizes such a position is not embraced by everyone.

The issue that perhaps best articulates the result of the committee's ethical position and the other major recommendations of the report is the manner in which the animals are treated after they are no longer needed for research or breeding. If these animals are euthanized on completion of their usefulness to the research enterprise, many of the expensive and complex issues discussed in the report will not exist. Because of the considerations reviewed above, the committee could not agree to euthanasia for population control. One member of the committee provides a thoughtful counter argument (see Appendix A).

We believe that responsibilities for the long-term care of chimpanzees are shared by both the scientific community and society in general. The issues associated with long-term care are intertwined: We cannot say that "this" is purely the responsibility of scientists and "that" is the sole responsibility of society. Societal needs warranted the past research with chimpanzees and will demand future research on emerging disease threats. These considerations must be appreciated if the committee's task is to be understood in its proper social context.

These considerations must be appreciated if the committee's task is to be understood in its proper social context. The National Research Council asked the committee to:

- Gather information from the biomedical institutions where chimpanzees are housed, from scientists at large, from animal welfare organizations, and from the general public.
- Prepare ethically and scientifically balanced cost-effective recommendations for a strategy for long-term care of chimpanzees in biomedical and behavioral research.
- Provide recommendations that strive to ensure a population adequate for research needs to enhance public health while promoting chimpanzee conservation and well-being.
- Address issues of policy, including relevant aspects of animal welfare, ethics, and public-private interactions, and recommend whether, or under what conditions, euthanasia is an acceptable means

of population control and whether government-owned animals might be transferred to private sanctuary facilities.

- Recommend funding mechanisms for long-term care facilities (government and nongovernment).
- Identify types of studies using animals not actively involved in research that would be beneficial to the public health, aid in conservation of the species, and be acceptable to managers of sanctuaries who receive funds from public donations.

On the basis of the charge and the committee's findings, this report provides recommendations pertinent to six interrelated questions:

- What are the current and future needs for chimpanzees in research?
- How will research needs affect the breeding population?
- How should the current and future populations be housed and managed?
- What are the estimated costs of high-quality long-term care of the chimpanzee population?
- Can the federal government, industry, and the public work together toward solutions?
- How can quality in both research and long-term care be kept at the highest possible levels?

The principles that the committee developed to guide its recommendations are as follows:

An adequate population must be maintained because chimpanzees constitute an important resource that can be used to protect the national health against emerging infectious diseases and a useful model for many kinds of biomedical and behavioral research, including research to develop vaccines and therapies for major human diseases. There is a critical need for long-term policies for proper care, housing, and management of captive chimpanzees—policies that would ensure the well-being of this population beyond the immediate future.

The body of this report consists of five chapters. Following is a brief overview of the content of these chapters.

Chapter 2, "Research Needs," analyzes the needs for chimpanzees in biomedical and behavioral research. This chapter is based on discussions among members of the committee and with scientists, directors of the government-supported chimpanzee facilities, and members of the public; surveys of the chimpanzee facilities; and literature reviews. It concludes that chimpanzees have made and should continue to make substantial contributions to biomedical research. The chapter summarizes some of these contributions and includes estimates of future requirements for chimpanzees based on the number used in recent studies related to important viral diseases.

Chapter 3, "Long-Term Care," recommends standards for ensuring the well-being of chimpanzees in long-term housing, divides the US chimpanzee population into six groups, and offers specific recommendations for each group. A brief description of types of successful and unsuccessful housing is followed by recommendations. A section on euthanasia provides a discussion of the pros and cons of this procedure relative to chimpanzees.

Chapter 4, "Genetics, Cost, and Demography," discusses the genetic management of the US biomedical chimpanzee population and the current and expected costs of caring for the various groups of chimpanzees. Recommendations are provided regarding inbreeding and the desired size and demography of breeding colonies to sustain the population for future research. Two models are presented that discuss the costs, options, efficiencies, and liabilities associated with each of two possible management options. The two models estimate the numbers of animals needed in the breeding colony and not needed for breeding. Associated costs of the subpopulations in the models are provided to assist in management decisions. Record-keeping is discussed as an essential element of the genetic management of these colonies, and the role of cryopreservation is addressed.

Chapter 5, "Centralization of Research Chimpanzee Management and Development of a National Chimpanzee Resource," describes the rationale and a mechanism for centralizing all aspects of managing the chimpanzee population with the goal of ensuring its cost-effective maintenance and use. Ways to implement the recommendations, provide financial support, and establish continued oversight of all facets of the chimpanzee resource are discussed in the context of federally funded colonies and privately owned (nongovernment) sanctuaries.

2

RESEARCH NEEDS

Chimpanzees have been used in biomedical research to gain an understanding of various diseases that result in substantial morbidity and mortality. The value of chimpanzees in studies designed to make it possible to prevent or treat diseases is due in large part to their genetic similarity to humans. In the case of some infectious diseases, such as hepatitis B, chimpanzees are the only nonhuman species that can be infected with the causative microorganism. Furthermore, some important therapies for diseases not caused by microorganisms have been developed only because they were evaluated in chimpanzees when other species proved to be unsuitable or provided suboptimal results. Because situations like these are likely to arise in the future, chimpanzees should continue to be available for research protocols that benefit human health and well-being. Furthermore, the possibility of a national emergency due to a new infectious agent that presents a major hazard to human health and for which no obvious prophylaxis or therapy is available is a compelling reason to maintain a population of chimpanzees for biomedical research.

VALUE OF PAST STUDIES WITH CHIMPANZEES

An important perspective on future research needs for chimpanzees can be gained from an evaluation of the results of previous studies. Over the last 20 years, chimpanzees have been used as experimental models of humans in several research fields, including infectious disease, reproduction, language, and behavior. The contributions with the greatest effect

on human health have come from infectious-disease research that focused on the development of vaccines and new classes of therapeutic agents. Instances in which the use of chimpanzees was considered either critical or a prerequisite to introducing an agent into humans include development and safety testing of vaccines for hepatitis B virus (HBV) and identification of the hepatitis C virus (HCV) both of which had enormous benefit to humankind; and development of novel inhibitors of neutrophil elastase. Those and other examples warrant additional discussion to emphasize the value of chimpanzees as an experimental model of human health problems.

INFECTIOUS DISEASE

Experimental infection of chimpanzees as animal models in biomedical research has involved such diverse microorganisms as mycoplasma species, the filarial nematode Onchocerca volvulus, numerous viruses, and unconventional agents associated with subacute degenerative diseases of the central nervous system (such as spongiform encephalopathies, including kuru and Creutzfeldt-Jakob disease). Major contributions to human health have resulted from the use of chimpanzees in studies to control transmission of and disease induced by the hepatitis viruses, respiratory syncytial virus, and human immunodeficiency virus (HIV).

Early research on HBV was hindered by the inability to propagate it in tissue culture. Because chimpanzees are the only nonhuman primates susceptible to infection with HBV, they were critical to the development of a vaccine by providing a source of virus and viral antigens and by making it possible to evaluate the safety and the effectiveness of candidate vaccines. The benefits of HBV vaccination to humanity can be characterized as not only controlling an important disease but also presenting a potential approach to controlling the transmission of disease from mother to child, thereby eliminating a major problem for mankind, particularly in Asia, but also in the United States. Even though hepatitis B is relatively rare in the United States, the major vaccine-recommending bodies, including the American Academy of Pediatrics and the Immunization Practices Advisory Committee, now recommend universal hepatitis B vaccination of newborns. This is important because about 75% of

newborns who acquire it from their mothers become chronic carriers, which provides the potential for lifelong transmission of the disease, lifelong carriage of the virus in an active replicating form, and an increase by a factor of 200 in the relative risk of developing hepatocellular carcinoma, compared with a noninfected person. The latter possibility makes this the first vaccine against a form of cancer. That enormous long-term benefit to humanity represents the harvest that we will continue to reap from the research on hepatitis B that was carried out in chimpanzees.

Although the exact number of chimpanzees used in the successful development of a vaccine against HBV is not known, institutions reporting past exposures of chimpanzees to specific agents indicate that 195 animals that they now house, including those also exposed to HCV and HIV, participated in hepatitis virus research (Table 2.1). That number substantially underestimates the total used, because of normal attrition and the fact that many chimpanzees housed at New York University's Laboratory of Experimental Medicine and Surgery in Primates (LEMSIP) were not counted but are known to have been used in HBV studies.

Infection of chimpanzees with the hepatitis A, C, and delta viruses also provided important models for gaining an understanding of disease. HCV virus is a bloodborne pathogen that can establish a chronic infection and lead to cirrhosis or hepatocellular carcinoma. It is rapidly evolving, and already 1-2% of people in the United States are infected (Purcell 1994). Using molecular biological techniques and plasma samples from a chimpanzee chronically infected with HCV, previously called non-A, non-B (NANB) hepatitis virus, Choo and others (1989, 1990) successfully identified the causative agent of the infection. That would not have been possible without the clearly documented titration and transmission studies that were performed in chimpanzees. A successful vaccine for hepatitis C remains elusive because of the extensive genetic diversity of the virus. Chimpanzees continue to be important in the search for a solution to this problem (Lemon and Thomas 1997).

Respiratory syncytial virus (RSV) is an RNA virus that causes annual epidemics of upper and lower respiratory disease, primarily in infants and young children; some of these infections can be life-threatening. Only the chimpanzee develops disease symptoms comparable with those observed in infected humans, particularly the more-severe lower respiratory infections.

As with the hepatitis viruses, that fact has made the use of chimpanzees critical for evaluating RSV vaccine efficacy. A temperature-sensitive, attenuated RSV mutant has been used in vaccine trials, and chimpanzees were required for two reasons: to determine whether the attenuated viruses revert to wild-type and thereby cause disease, and to determine whether antibodies induced by immunization will enhance disease on exposure to infection with wild-type RSV.

TABLE 2.1 Chimpanzees Exposed to All Hepatitis Viruses and HIV at Six Research Facilities[a]

Facility	Infectious Exposures[b] to Hepatitis Viruses	Noninfectious Exposures to Viruses	Infectious Exposures to HIV Only	Infectious Exposures to Both Hepatitis and HIV	Total
A	4	3	20	72	99
B	16	2	34	1	53
C	0	31	0	0	31
D	22	7	43	15	87
E	6	2	0	0	8
F	14	0	13	0	27
Total	62	45	110	88	305

[a] These data were compiled from ISIS data of June 1996 and a survey by this committee in July 1996.
[b] To hepatitis and immunodeficiency viruses. Not included are 57 known infectious exposures to kuru, Creutzfeldt-Jakob, and malaria. Other infectious and noninfectious exposures are likely to have occurred.

As with HBV and HCV, the only animal species initially tested that could be infected with AIDS-patient material, or with the virus itself after it was isolated, was the chimpanzee (Francis and others 1984; Gajdusek and others 1985). This primate species remains the only one (except humans) that can be persistently infected with multiple HIV-1 strains by both intravenous and mucosal routes. That chimpanzees can be infected with HIV strains representing different subtypes is critical because of the unprecedented genetic diversity of strains circulating worldwide (WHO Network for HIV Isolation and Characterization 1994). That diversity (and data obtained in studies with chimpanzees) indicates that a vaccine based on only one HIV subtype will have limited protective value, so it

will be necessary to test different combinations of antigens to identify the ones that together induce the broadest cross-reactivity. This is even more important in light of the high costs associated with the current successful advances in the treatment of AIDS; these costs will limit their use not only in the United States, but especially in poorer nations. Thus, the formulation of clinically effective, inexpensive vaccines is likely to be the best long-term solution to this global problem.

Although only one of about 200 chimpanzees infected with HIV-1 has so far succumbed to an AIDS-like disease, several animals that have been infected for a long time exhibit decreased CD4:CD8 lymphocyte ratios. Virus isolated from the chimpanzee that died of AIDS elicited a rapid decline in $CD4^+$ cells in all of three chimpanzees experimentally infected with this HIV variant (Fultz unpublished data; Novembre and others 1997). Thorough evaluation of immune responses and virus-host interactions in these infected animals, compared with chimpanzees infected with other, less pathogenic isolates, might provide new insights into HIV pathogenesis. In addition, chimpanzees have been and will continue to be important in studies to develop HIV vaccines and to evaluate their immunogenicity and protective efficacy against infection.

Although HIV infection of chimpanzees has not been an ideal model of disease, at least 198 chimpanzees have been used to date in HIV-related studies; this number reflects only HIV-1-infected animals now held at various institutions, excluding animals exposed at LEMSIP of which the committee has no knowledge (Table 2.1).

XENOBIOTICS

Chimpanzees have been used as a final step in the evaluation of new therapeutic agents before their administration to humans. Evaluation of xenobiotics is generally brief and presents little or no potential hazard to the well-being of the chimpanzee. However, such studies can be essential in justifying the introduction of a xenobiotic to humans. A specific example is the development of novel inhibitors of the enzyme elastase, which is present at high concentrations in human neutrophils and has been implicated in tissue destruction associated with inflammatory diseases, such as those of the upper respiratory tract, including cystic fibrosis, bronchiectasis,

and emphysema. The inhibitors are much less potent in lower species, only by using chimpanzees was it possible to validate their use in human trials (Mumford and others 1995), where its remarkable potency was confirmed.

FUTURE NEEDS FOR CHIMPANZEES

Chimpanzees have not been a universally satisfactory model for human diseases. The reason (given the close genetic relationship of chimpanzees to humans) is not clear, but one reason is probably the lack of research in basic biology and medicine in chimpanzees. The cost of using chimpanzees has prevented research on all but high-visibility diseases such as AIDS and hepatitis B research. Their contribution to hepatitis B is direct and substantial; to AIDS research it is still unknown. In sum, the committee concluded that the chimpanzees have contributed to human health research and would likely do so in the future and that without sustaining a small "core population" it is unlikely that there will ever be another captive US research population. The committee's approach to these problems is to recommend a central management structure (ChiMP, see chapter 5) that can vigorously manage the population to reduce the number in research and breeding, reduce the cost, and encourage basic research. Given the unpredictable nature of emerging threats to human health, it is not possible to predict the total requirement for chimpanzees in the future. Table 2.2 shows some projected future needs, as indicated by a limited survey of investigators at NIH and elsewhere, and includes emerging health threats to mankind that could best be met by research with chimpanzees. If, as exemplified by experience with HIV and hepatitis, some of the emerging threats will involve long periods of disease latency or chronicity that will require commitment of multiple chimpanzees over periods of years. Tables 2.2 and 2.3 provide some guidance as to the numbers of chimpanzees that are required to meet such needs. Chapter 4 provides two models by which to meet the needs. The tables do not take into account needs for chimpanzees that individual investigators or organizations were not prepared to disclose. Thus, chimpanzees will be required in the future for continuation of the research discussed above and to address problems associated with aging and unforeseen health conditions.

TABLE 2.2 Projected Future Needs for Chimpanzees in Biomedical Research (Government Only)

Subject of Research	Type of Animal	Number per Year	Duration (yr)
RSV	Infant	18-24	3
Hepatitis C	Less than 25 kg	10	Several
HIV			
DNA vaccination	HIV-infected	6	1
Attenuated vaccines	HIV-infected	5	Several
Vaccine efficacy	HIV-infected, naive	6-9	Several
Malaria	Splenectomized	2-3	Several
Pharmacokinetics and pharmacodynamics of xenobiotics	Various	20	Indefinite
Behavioral[a]	Various	?	Indefinite
Emerging diseases	Various	?	Indefinite
Other (such as aging)	Various	?	Indefinite

[a] Chimpanzees for use in behavioral studies are available mostly in breeding colonies.

KNOWN INFECTIOUS AGENTS

The future use of chimpanzees will be critical in ensuring progress in controlling diseases associated with a number of specific agents that have been identified. The most efficient way to prevent infectious disease is prophylactic vaccination. Because of the complexity of the immune system and the diversity of virus-host interactions, there is no suitable substitute for a live animal in the testing of vaccine efficacy. We present here four important examples of such need for chimpanzees.

HEPATITIS

Even though a vaccine for HBV is in wide use and much progress has been made in developing an effective HCV vaccine, additional work is required for the latter (Lemon and Thomas 1997). In addition to HCV, the former NANB hepatitis viruses are known to include an enterically transmitted virus, designated hepatitis E, which has been transmitted to

TABLE 2.3 Some Present Uses of Chimpanzees in Biomedical Research[a]

Housing Institution	Subject of Research	Government or Nongovernment	Number and Type of Animals
A	Antiviral vaccines	Nongovernment	99 in study under confidentiality agreement
	Hepatitis B	Government	Not available
	Pharmacokinetics, immunogenicity, and bioavailability	Nongovernment	Not available
B	Breeding and behavior	Government	78, mixed age and sex
C	Hepatitis C and delta	Nongovernment	16 naive
D	RSV	Government	27 RSV-antibodynegative juveniles
	Hepatitis C	Government	7, mixed age and sex
	Hepatitis A	Government	26, mixed age and sex
	Malaria	Government	6 adults
	HIV	Government	3 adults
	Behavior	Government	85, mixed age and sex
E	Behavior	Government	10: 5 young in nursery and 5 adults
	Behavior in context of breeding	Government	40, mixed age and sex
	Onchocerca volvulus	Government	5, adult
	Malaria	Government	2, splenectomized
	Immunity to tumorassociated mucin	Government	22, naive to antigen
	Reproduction	Government	8, sexually mature
	Cognition	Government	30, mixed age and sex
	Behavior	Government	6, mixed age and sex
	Behavior	Government	24, mixed age and sex
	Obesity and diabetes	Government	25, mixed age and sex

[a] Data based on survey of chimpanzee colony directors in July 1996.

cynomolgus macaques, as well as to chimpanzees. Because there is evidence that more hepatitis viruses exist, and most hepatitis viruses grow poorly or not at all in tissue culture, chimpanzees will probably continue to be an important resource in efforts to control this diverse group of viruses.

Conceivably, the number of chimpanzees required for safety and efficacy testing of vaccines for several such viruses will be comparable with that for the development of HBV vaccines.

RSV

RSV is an RNA virus for which subunit vaccines are being tested in chimpanzees. However, a major problem is associated with the use of chimpanzees for RSV studies: like humans, chimpanzees become naturally infected with this virus when very young. Unless enough RSV-negative older animals are available, this research probably will require a recurring supply of animals less than about 3-yr-old. It is projected that 18-24 infant or older RSV-seronegative chimpanzees per year will be needed for at least the next 3 yr for studies with live attenuated vaccines. The use of young animals and the associated breeding would be obviated by screening all animals, particularly the older ones, for RSV seropositivity.

HIV

Substantially reducing the transmission of HIV worldwide requires two approaches: behavioral modification and vaccination. Given the urgency to develop a vaccine effective against all known subtypes of HIV, which now number nine, the continued use of chimpanzees will be required. Most studies with the HIV-chimpanzee model have used subtype B strains. Although HIV-1 subtype A and E strains have also been shown to infect chimpanzees, the latter by both intravenous and mucosal routes (Barre-Sinoussi and others 1997), HIV-naive chimpanzees also will be required to determine whether HIV strains representing the other subtypes are infectious in this species. Furthermore, transmission occurs by both parenteral and mucosal (vaginal-cervical and rectal) routes, and

it will be necessary to use additional animals to demonstrate infection by each route. If controlled vaccine-efficacy trials are conducted in chimpanzees, challenge stocks of each HIV subtype first must be titrated in vivo to identify minimal chimpanzee infectious doses by the various routes; and chimpanzees will be required as naive control animals in vaccine-efficacy trials. It is projected that two groups of chimpanzees will be important for future HIV research sponsored by NIH: about six to nine HIV-naive chimpanzees per year will be required for vaccine studies, and at least five HIV-infected chimpanzees per year will be used as surrogates for chimpanzees immunized with attenuated vaccines. Given the uses foreseen here—testing the infectivity of non-subtype-B HIV, establishing mucosal-challenge models, and serving as naive controls—as well as evaluating the pathogenesis of the HIV-1 isolated from the chimpanzee that succumbed to AIDS, the requirement could be 11-14 chimpanzees per year. If alternative models, such as transgenic mice that express both the primary and secondary receptors for HIV or infection of macaques with chimeric simian immunodeficiency virus SIV/HIV (SHIV), are validated, the numbers required will decrease. However, transgenic mice are unlikely to replace chimpanzees in HIV vaccine studies, and although the SHIV-macaque model might provide preliminary data for novel vaccine strategies, the macaque models have inherent limitations in that the infecting virus expresses only a subset of HIV antigens. Moreover, new targets for therapeutic intervention, such as coreceptors for HIV, might trigger new avenues of research with chimpanzees.

MALARIA

Malaria presents a major threat to world health. Recent publications indicate that the chimpanzee is uniquely susceptible to infection with the Plasmodium ovale strain of the parasite (Morris and others 1996; Thomas and others 1994). From 1983 to 1995, 28 chimpanzees were used to study various aspects of infection with P. ovale (Morris and others 1996). Although chimpanzees might not be used for evaluation of antimalarial vaccines, there will be a continuing need for them in malaria research, primarily for the production of antigens for immunization purposes.

EMERGING INFECTIOUS AGENTS

Scientists, physicians, and public-health officials knowledgeable about infectious diseases accept the validity of the assumption that sometime in the future, new or old microbial pathogens will present major threats to the population. That idea was examined by a panel of experts convened by the Institute of Medicine (Lederberg and others 1992). In 1995, the Centers for Disease Control and Prevention began publishing a new journal, Emerging Infectious Diseases, dedicated solely to identifying and analyzing new and re-emerging infectious diseases around the world. The emerging or re-emerging infections have the potential not only to reach epidemic proportions in their country of origin, but also to become global pandemics, as was demonstrated recently by HIV infection (Quinn 1994). In an increasingly open and extensively traveled globe, the extent to which infectious agents can be transported rapidly around the world is almost unlimited.

The list of emergent microorganisms that have caused substantial morbidity and mortality in the last few decades is long; the best known is HIV. AIDS was first recognized in the early 1980s in the United States, and HIV, a retrovirus, was later identified as its etiologic agent. However, by the time HIV was identified, it had already been disseminated from the African continent, its place of origin, into defined populations, such as homosexuals, injecting drug-abusers, and hemophiliacs (Anderson and others 1991; Curran and others 1985; Quinn 1994). Multiple factors, most of which resulted from human activities, contributed to both the emergence and the spread of HIV. Those factors included urbanization and movement of segments of the population from rural African villages to expanding cities; changes in lifestyle and sexual behavior, including increased prostitution in African cities and high-risk sexual behavior in the homosexual population; increased illicit drug use; increased international travel between all continents; and medical technology, for example, blood transfusions and immunosuppressive regimens associated with tissue transplantation.

We cannot predict what infectious disease will emerge next or when, but because the factors that contributed to the HIV pandemic will continue, new ones are inevitable. During the last 20 years, new etiologic

agents of major emergent infectious diseases have been identified at the rate of one per year (Satcher 1995). Furthermore, it is highly probable that most factors associated with the emergence or re-emergence of infectious diseases—whether their origin is viral, bacterial, protozoan, or fungal—will persist or new ones will arise (Morse 1995). Likewise, just as the chimpanzee is the only nonhuman animal that HIV and some hepatitis viruses infect, other unknown pathogens might also exhibit this property. Thus, it is critical that the captive chimpanzee population be maintained in sufficient numbers to meet a potential public-health emergency. Because experimental infection with one pathogen does not necessarily preclude use of an animal in infectious disease studies with an unrelated pathogen, many of the chimpanzees now being used in hepatitis, RSV, and HIV research could meet a future need. However, because we cannot predict when a new infectious agent will emerge or the nature of that agent, naive chimpanzees also must be held in reserve. Chapter 4 discusses possible strategies by which to address recurring national emergencies and continuing need for small numbers of chimpanzees.

OTHER RESEARCH

In addition to their use and value in biomedical research on infectious diseases, chimpanzees have provided and will continue to provide important information in existing fields—such as behavior, language, reproduction, and development of therapeutic agents—and in new fields, such as correction of inherited diseases in utero. Furthermore, as the average age of the US population rises, this will also occur in the captive chimpanzee population because of reduced breeding, making them obvious subjects for research related to medical problems of the elderly.

Behavioral research is usually performed with chimpanzees in social groups or of defined ages, such as nursery-reared infants. Thus, depending on specific requirements, future needs for these projects can be met by existing chimpanzee populations, such as the breeding colonies. Potential groups of animals for behavioral studies include those designated for uses specified above, those in breeding pools, and those housed in sanctuaries. In this context, it will be important for the Chimpanzee Management Program (ChiMP) office proposed in chapter 5 to publicize the

availability of a pool of chimpanzees for new fields of research, such as those discussed above.

There will probably be a requirement for a substantial number of chimpanzees in pivotal studies of novel xenobiotics that have potential therapeutic benefit to humans. Of particular importance are studies to define mechanisms of action or efficacy when sensitivity of the molecular target of a novel agent is similar in chimpanzees and humans but different in other species. Pharmacokinetics of drugs are known to vary greatly across species, but in this respect chimpanzees and humans are similar most of the time. In the past, critical decisions on the choice of specific agents from among groups of novel therapeutic agents were made on that basis. In general, studies of novel xenobiotics are of short duration, and any compromise of the well-being of the animals is minimized by prior extensive toxicologic evaluation in other species.

MAXIMIZING THE AVAILABILITY OF CHIMPANZEES

Chimpanzees are often used in research protocols that do not preclude their later use in unrelated research protocols. To illustrate, most chimpanzees in HIV studies were used previously in hepatitis research; in fact, their prior exposure to hepatitis virus was generally considered a prerequisite for entry into an HIV study. As indicated above, young chimpanzees in RSV studies can be used later in studies with other infectious agents or for breeding. All animals, irrespective of prior research use, would be candidates for aging studies. Moreover, it would be appropriate to draw chimpanzees from a long-term care facility into short-term research protocols that have no zoonotic potential. Currently, because of the costs of using them, chimpanzees are used primarily for studies of diseases of major human-health importance. The committee encourages ethically justifiable, IACUC-approved research with a broader perspective, such as benefits to chimpanzee well-being, basic scientific knowledge, and aging. For-profit organizations, particularly pharmaceutical companies, use chimpanzees in research and product development. In general, although the chimpanzees are housed at private facilities, including those which are part of the NIH Chimpanzee Breeding and Research Program, they are generally not the animals that are supported by NIH

funds. For-profit organizations maintain, but do not own, chimpanzees housed at the existing research facilities. The preference for using privately owned, rather than government-owned, animals is the combined result of delays encountered in complying with administrative requirements and the expectation that proprietary information would have to be disclosed. To secure the use of government-owned chimpanzees by for-profit organizations, procedures should be streamlined to eliminate redundant aspects of the process, such as review and approval of protocols by more than one committee. Furthermore, the protection of proprietary aspects of a study should be guaranteed. Encouraging and soliciting the use of government-owned chimpanzees by for-profit organizations to generate supplemental income for their support should be a responsibility of the ChiMP office (see chapter 5).

Animals determined to be no longer needed for research and transferred to a long-term care facility might be used in some kinds of research. See "Research" discussion under "Special Considerations in Chapter 3.

TERMINAL STUDIES

Although acute terminal studies with chimpanzees have been rare, they are justified in some circumstances. If such studies are proposed, they should be carefully reviewed for scientific qualification. If they are approved, they should be designed so that the maximal amount of information will be obtained, ideally benefiting more than one field of research. No obvious paradigms for such use are known. In the context of infectious diseases, it is possible that inoculation of chimpanzees with an agent could elicit disease that culminates in death. That was the original expectation when chimpanzees were infected with HIV; such experiments are justified when society is faced with new epidemics. However, care should be taken that terminal studies do not become a de facto form of euthanasia for population control.

CONCLUSIONS AND RECOMMENDATIONS

The use of chimpanzees in biomedical research has resulted in major

advances in maintenance of human health and in development of vaccines and new therapeutic approaches to disease. In several instances, success was based on the sustained availability of large populations of chimpanzees suitable for research for 10 years or more. Specific examples discussed in this chapter include the successful development of an HBV vaccine and similar efforts related to HIV and HCV. Obvious future threats to human health will be infectious agents that potentially could emerge or re-emerge anywhere and spread around the world with the help of social and behavioral patterns and routine international travel. Chimpanzees are used in diverse fields of biomedical research, primarily because of physiological characteristics resulting from their phylogenetic proximity to humans. The uses listed in this "snapshot in time" do not provide a complete picture of the needs for a captive population of chimpanzees ready for emerging global challenges to the health and well-being of mankind. In planning for future requirements for chimpanzees in biomedical research, the predictions cannot be restricted to a single year, but rather must anticipate demands for at least 5-yr in advance, as illustrated by the paradigms for HBV and HIV in which several hundred animals were used over 10-year periods. In planning for the future, one must take into account that both previously used animals and research-naive animals might meet requirements for specific studies and that the duration of studies can vary from days to years. It is therefore impossible to predict the long-term demands for chimpanzees from current usage. Hence, there is a need for a well-informed group to assess the demographics of the captive chimpanzee population continuously.

On the basis of those considerations, a review of past use of chimpanzees, and the status of the current captive population, the committee offers the following conclusions and recommendations.

- The present chimpanzee population is sufficient in overall number, and a moratorium on breeding, effective until the year 2001, should be formalized in writing. Future needs and policies on breeding should be continuously assessed, preferably by an appropriately constituted advisory council working in concert with the ChiMP office proposed in chapter 5. In this continuing assessment of needs, projections should be for periods of a decade or more (the time required for full implementation of research programs on hepatitis and HIV).

- Chimpanzees suitable for biomedical research but held in facilities intended to provide long-term care and housing should be made available for research protocols, if needed, to maximize their utility and to contribute to the financial base required for their long-term support. In addition to emergency situations associated with new infectious disease epidemics, the older chimpanzees should be valuable for aging research.
- To promote the use of government-owned chimpanzees by for-profit organizations, procedures to obtain access to the animals should be streamlined to minimize delays in initiating studies and to eliminate requirements for full disclosure of proprietary information.
- Acute terminal studies involving chimpanzees are justified under some circumstances and, when possible, should be designed as collaborative efforts to yield the maximal amount of information with the potential to benefit more than one field of research. The ChiMP office, in consultation with colony directors and investigators, should identify candidate animals for such protocols.

3

LONG-TERM CARE

Long-term housing for chimpanzees should meet high standards for quality of care and should be cost effective. The following housing and management criteria were developed with that goal in mind after the committee visited and viewed photographs of facilities (including sanctuaries), met with facility directors and several chimpanzee behaviorists, reviewed publications on wild chimpanzee behavior, and reviewed information provided during public sessions. The results of the information-gathering process are reported in the section "Housing Standards and Behavioral Well-Being."

Long-term care facilities must be designed with awareness that many chimpanzees will spend most of their natural lives there—which might span several decades. Design considerations often dictate much of the operating cost of the facility. Those issues are discussed in the subsection "Housing Models."

Provisions for the special behavioral, cognitive, social, and emotional needs of chimpanzees are crucial to their well-being. That is a basic assumption woven into the recommendations of this report and is specifically addressed in the subsection "Provisions for Behavioral Well-Being."

Euthanasia received extensive consideration in the development of this report. Discussions and recommendations of euthanasia of debilitated and sick animals, of animals in nonrecovery scientific protocols, and as a strategy for population control of animals no longer useful for research or breeding are provided in the section "Euthanasia."

Definitions for categorizing chimpanzees into subpopulations according

to history and present status are presented in this chapter. Recommendations for the specific housing and management requirements and related special issues were developed for each of these subpopulations. Because the issue of long-term care of chimpanzees is of concern to many, these recommendations are intended to provide guidance for all chimpanzee holding facilities, including facilities that are government-funded (nationally and internationally), private for-profit and nonprofit research institutions, private sanctuaries, zoos, and performing acts that use chimpanzees. The definitions and recommendations are presented in the section "Chimpanzee Population Subgroups: Definitions and Recommendations."

Transfer of ownership to another entity requires consideration of issues related to animal welfare, public health, and fiscal responsibility; and these issues are discussed in the section "Ownership Transfer."

HOUSING STANDARDS AND BEHAVIORAL WELL-BEING

Animals from government-sponsored long-term care facilities are supplied to biomedical research, and the majority of support for chimpanzees in these facilities for research and breeding comes from the federal government and the biomedical industry. Nongovernment sanctuaries normally receive the majority of their funding from public donations, although funding partnerships with the government might receive future consideration. Sanctuary animals require less intensive management than animals in research facilities, and therefore entail lower costs of daily care. Animals in non-government-operated sanctuaries would not be used in medical research, although it is recommended they be used in behavioral research to increase understanding of optimal housing, management, and captive behavior. See also "Special Considerations" in this chapter.

"Long-term" refers to any housing circumstance that exceeds six mo. Long-term facilities include both research facilities and sanctuaries. This definition is thought to be especially applicable for animals in biomedical research that might require some time in relative social isolation. Social isolation beyond 6 mo deprives infants and juveniles,

still in their formative years, of the time needed for learning and the development of skills that will be needed the remainder of their lives. Also, socialized adults isolated for more than six mo can develop behavioral abnormalities that will require intervention during and after the nonsocial period. Thus, being in restrictive housing for more than six mo could require extensive, expensive socialization or resocialization (Fritz 1986, 1989; Fritz and Fritz, 1979).

Innovative sanctuary concepts and developmental plans are encouraged. These should include less-intensive management, lower costs, and high quality of life for animals no longer needed for research or breeding. We are not aware of long-term success in managing groups of more than 20 captive chimpanzees outside research facilities, but thoughtful, humane approaches might be found that will work and that will reduce housing and management costs.

Long-term care facilities exist in different forms, but some previously used models are not recommended, such as water-moated areas and free-ranging islands. Some island and free-ranging projects have been successful in rehabilitating chimpanzees (Bourne 1977, Hannah and McGrew 1991, Pfeiffer and Koebner 1978), but they have not been acceptable with respect to chimpanzee death or loss rates (Hannah and McGrew 1991). Animals released to islands must be provisioned with food and water. If provisioners can reach the islands, so can the general public, and that increases the risk of disease in the animals and the risk of injury to the general public. Native or transplanted trees in such habitats would likely be denuded, so artificial shade and climbing structures would have to be provided (Pfeiffer and Koebner 1978). Providing medical care to the animals is at best difficult and at worst impossible. Chimpanzees do not swim, and thus risk drowning in moats or offshore water (T. Butler, personal communication, van Hooff 1967). Reintroduction of chimpanzees into wild populations of chimpanzees might pose a risk of disease in both groups—the wild population would not have immunity to pathogens from captive animals, and the formerly captive animals would have lower immunity to pathogens tolerated by the wild population. Ex-captive animals would not likely compete successfully with wild animals for food and shelter. Free-ranging or island housing for ex-research chimpanzees would place them in a "survival of the fittest" situation, and so is not recommended.

Some chimpanzees entering long-term care facilities will have had little or no social contact and therefore no opportunity to acquire the social experience necessary for compatible group living (Fritz 1986, 1989; Fritz and Fritz 1979); they should be considered asocial animals. They might require resocialization or group-formation facilities, which could be separate or incorporated into a long-term housing facility. In any case, the situation must be acknowledged and documented, and the well-being of each individual chimpanzee must be taken into consideration.

HOUSING MODELS

Chimpanzees are complex, social animals that require special housing if they are to express a full range of species-typical behaviors. Two types of housing are recommended: corrals and indoor-outdoor caging systems. All chimpanzees in long-term housing should have access to the outdoors through one or both of these models.

Corrals are areas of land enclosed by some type of barrier, such as high concrete or metal walls that connect to a section of indoor housing. The size requirements of corrals depend on the composition of the social group. Outdoor areas should provide shelter, shade, trees or artificial trees for climbing, and platforms for resting.

Indoor-outdoor caging systems provide outdoor caging that is larger than the corresponding indoor areas. Like corrals, they are connected. Outdoor caging should contain the same type of provisions as corrals, that is, climbing structures and shade. The caging is usually constructed as a building rather than an enclosed portion of land like corrals. Both models include

- Outdoor housing that would allow all chimpanzees daily access to the outside unless medical, behavioral, or research exceptions are obtained from an institutional animal care and use committee or another animal welfare oversight committee.
- Indoor housing large enough to house all animals in case of inclement weather or repairs to outside areas.
- A housing design that would permit each chimpanzee to be

observed daily and a single animal to be easily separated for medical treatment or movement to another group.

- The ability to feed animals in both the indoor and outdoor areas, which facilitates training of the animals to come inside regularly so that individual animals can be observed and provision of occupation and "travel" to outside feeding station.
- Structural and organizational complexity to provide sufficient environmental stimulation and opportunity to perform species-specific behaviors.

Existing facilities might not satisfy all those specific recommendations, but new facilities and major renovations should satisfy them in their design and existing facilities should attempt to achieve them. Cage-size recommendations for chimpanzees described in the *Guide for the Care and Use of Laboratory Animals* (NRC 1996), referred to as the Guide, apply to the inside housing component of the indoor-outdoor and corral long-term housing systems. Compliance with those recommendations should be monitored by the ChiMP office (proposed in Chapter 5).

Cost-efficient care and use of chimpanzees should consider the risk of contaminating experimentally naive animals by those involved in infectious disease studies. The routine exchange of animals among facilities adds to the risk of introducing epizootics, such as multipledrug-resistant tuberculosis. Currently, most biomedical facilities have animals that range from "clean" breeders to highly infectious "dirty" animals. Consideration should be given to housing potentially infectious and experimentally naive animals at different facilities. Breeding colonies should continue to exist at more than one location to reduce the possibility that an epizootic at one facility will seriously affect the production capability of a limited population. Dedicated centers might be established around unique abilities of the existing biomedical chimpanzee facilities, such as infectious disease research, behavioral research, or breeding. And, some might be selected as government-sponsored long-term care facilities for either infectious or clean animals; this would enable the recall of the animals for breeding or research, which is probably not in the case of publicly sponsored sanctuary facilities.

PROVISIONS FOR BEHAVIORAL WELL-BEING

Current knowledge regarding captive chimpanzee behavior suggests that well-being is most likely achieved when facilities provide for and promote a wide range of natural behaviors (NRC in press). Information regarding the nature of these behaviors and their time budgets can be gleaned from a study of the behavior of wild chimpanzees. Although time budgets generally have to be modified for captive animals, the expressions of behavior in the wild provide important insights into maintaining them in captivity. Individual and species-specific preferences must be taken into consideration in all long-term housing. Consideration of the following issues should be incorporated into the design and operation of long-term care facilities:

Daily activity percentages and travel. In the wild, adult chimpanzees spend about 10% of their waking time traveling (or generally locomoting), 20-30% resting, and most of their day—50-60%—foraging or eating (Ghiglieri 1984, Goodall 1986, Wrangham 1977). Wild chimpanzees' travel several miles per day (Goodall 1986, Wrangham 1977). Their travel includes foraging, moving from one food source to another, searching for females in estrus by males, and patrolling the perimeter of the territory (Ghiglieri 1984, Goodall 1986, Wrangham 1977). Every effort should be made to achieve activity percentages representative of wild behavior. Suggestions for increasing both travel time and distance include periodic movement of feeding stations, variation in feeding schedule, and provision of feeding-enrichment devices. In addition, a complex environment that encourages climbing or moving from one location to another should be provided. Absolute space might not be as important as compatible social partners, the complexity of the environment, and the provision of enrichment by knowledgeable caregivers. Housing should be designed to allow a chimpanzee to see beyond its immediate environment and expand the perception of space.

Above-ground areas. In the wild, female chimpanzees spend about 50-70% of their time above ground, and males spend about 35-50% above ground (Doran and Hunt 1994). Studies in captivity have also indicated that captive chimpanzees express a preference for aboveground

sites (Goff and others 1994, Traylor-Holzer and Fritz 1985). All long-term housing should incorporate climbing apparatus and resting areas above ground.

Group sizes. In the wild, group size varies considerably. A group of chimpanzees might consist of as many as 100 individuals, but several investigators have reported never seeing such a large group together at one time. Subgroups or parties range in size from one to eight individuals (Ghiglieri 1984, Goodall 1986, Sakura 1994, Wrangham 1977). Average group size in Kibale is one to three (Ghiglieri 1984). In Gombe, groups with more than six members are considered large (Goodall 1986), and parties of two to four individuals were observed in about half the observations (Goodall 1968).

All chimpanzees in long-term situations should be housed minimally in pairs and preferably in social groups of three or more compatible individuals. Long-term housing should be constructed to accommodate multiple small groups and to enhance formation of larger groups.

Individual space. To eat alone, wild chimpanzees attempt to space themselves at least an arm's length apart (Wrangham 1977). In addition, wild chimpanzees nest alone, with the exception of a mother and her infant (Goodall 1968, 1986).

SPECIAL CONSIDERATIONS

Other aspects of the care and management of chimpanzees should be considered:

Standards. Standards should be developed for sanctuaries. These standards can be less rigorous than those for research facilities, but they should ensure the well-being of animals and the health and safety of the animals and people. Sanctuaries should strive for accreditation similar to that provided by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC I). Accreditation should be based on standards developed by interested nongovernment parties in consultation with the ChiMP office (see chapter 5).

Sections of the Guide that are important to the care and well-being of chimpanzees in sanctuary situations should be consulted in the development of sanctuary standards. All sanctuaries should comply with the Animal Welfare Regulations and be inspected by the US Department of Agriculture (USDA) annually. Sanctuaries that are not required to register with USDA can request "courtesy" USDA inspections. Sanctuaries should seek active participation of informed primatologists that would help to incorporate the best knowledge of chimpanzee free-ranging biology and social dynamics.

Research. Chimpanzees in government and nongovernment long-term care facilities can continue to provide important information even when they are determined not to be needed for biomedical research. Both types of facilities should develop policies that would permit and encourage studies in various subjects, such as aging, social behavior, contraception and other birth-control strategies, husbandry, facilities design, and basic biology. Animals in government-sponsored biomedical long-term care facilities might become important for future research in infectious disease.

Personnel. There should be sufficient numbers—one animal-care technician per day for every 10-15 chimpanzees according to industry standards—of well-trained personnel to provide appropriate care to the chimpanzees 7 d per week.

Animal well-being. The goal of all chimpanzee housing and management is a high degree of well-being. To provide the necessary enriched environments, knowledge of chimpanzee behavior and of the animals' use of space and equipment is required. Long-term care facilities should have the expertise and the commitment to plan, administer, and evaluate the effectiveness of the well-being program. It is also recommended that facility staff include a trained chimpanzee behaviorist who can evaluate the well-being of individual animals and perform behavioral research and publish the results to improve the life of captive chimpanzees. Funding for such research is necessary to achieve the general goals of improved long-term care.

IDENTIFICATION. All animals should have implanted microchip identification and be tracked for life by a single agency, such as the International Species Information System (ISIS). Some microchips permit programmable encoding of life, clinical, and experimental histories, a desirable feature for this valuable population of animals.

SUBSPECIES. Common chimpanzees are considered to belong to a single species, Pan troglodytes. Recognized subspecies are P. t. troglodytes, P. t. schweinfurthi, and P. t. verus. Subspecies are not clearly distinguishable morphologically but have been discriminated on the basis of mitochondrial DNA sequence differences (Morin and others 1994). Animals in the research chimpanzee population have not been characterized for subspecies to any great extent. Demographic analyses (see Chapter 4) have provided no indication that any hybridization that might have occurred has negatively affected the population as a whole. However, characterization of subspecies would provide additional information on levels of intrapopulation variability in the research chimpanzee population.

RECORDS. Records should be maintained for each animal, and a copy should always be transferred with the animal. They should include standard information (Dyke 1993), such as lifetime identification, subspecies designation, current and past research use, reproductive status (past and present), medical and behavioral problems, and facility transfers. Even in retirement, an animal's historical records should contain important information for health care and retrospective studies. Therefore, easily retrievable records should be maintained for every animal, regardless of ownership or whether the animals are in breeding, research, or retirement. The ChiMP office (see Chapter 5) should review all historical and current records, as appropriate, in carrying out its responsibilities.

SUPPORT FACILITIES. In accordance with the Guide and the Animal Welfare Regulations, several types of support facilities are needed, including veterinary treatment and quarantine facilities, food storage, bedding storage (if used), administrative space and equipment, dry

storage, security systems, vehicles, and transfer cages. Support facilities should be appropriate for the goals of the facility.

EUTHANASIA

The committee considered several aspects of the practice of euthanasia as it applies to chimpanzees. Euthanasia has been and continues to be appropriate as a means of alleviating the suffering of individual animals, but its potential use for population control is much more complex and controversial. We discuss here some considerations for and against euthanasia, and provide some recommendations.

It is commonly agreed that if a chimpanzee's health or quality of life is seriously compromised and there are no available means to alleviate the problem, euthanasia is appropriate. The decision should be made by a veterinarian in consultation with the investigator or facility director.

Euthanasia has also long been accepted as a response to conditions that threaten the well-being of nonhuman animal populations, for example, to cull deer where their numbers exceed the carrying capacity of the population.

In statements at open public meetings with this committee, a strong sentiment was voiced that researchers are not justified in using chimpanzees without concurrent commitment for their lifetime care and that euthanasia as a means of population control is unacceptable. Many members of the public and the scientific community have called for continuing support for chimpanzees in an acceptable environment, rather than euthanizing them, even when they are no longer wanted for breeding or research. The committee fully recognizes the financial implication of this position in regard to lifetime funding for all animals and for additional space and facilities for an aging population.

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, for example, rats, dogs, or some other nonhuman primates. Simply put, killing a chimpanzee currently requires more ethical and scientific justification than killing a dog, and it should continue to do so. This argument does not suggest that chimpanzees are "the moral equivalent" of humans,

only that they are more like humans than other laboratory species might be with respect to some features relevant to the question of euthanasia.

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, and might resign. A facility that adopted such a policy could expect to lose some of its best employees. Similarly, facilities that depend on donations from the public for part of their income, or even just on the good will of their community, might expect strong negative reactions to the use of euthanasia. Those losses might well outweigh any savings that might be accrued through euthanasia.

RECOMMENDATIONS FOR THE PRACTICE OF EUTHANASIA ENDORSED BY THE COMMITTEE

The committee seriously considered the issues raised above and offers the following recommendations:

- Euthanasia should be permitted for reasons of health or quality of life of the individual, for example, terminal disease, in connection with trauma, or complications of aging. Methods should be consistent with the 1993 Report of the AVMA Panel on Euthanasia. The decision to euthanize should be left to the veterinarian in consultation with the investigator or facility director.
- The committee does not recommend euthanasia as a general means of population control (that is, to dispose of chimpanzees no longer useful for research or breeding). The committee contends that funding must be made available to maintain an appropriate level of care; otherwise, directors of chimpanzee colonies would be placed in an unacceptable position in which selective euthanasia might come to be seen as the only available means of maintaining the quality of life of the remaining research chimpanzee population.

CHIMPANZEE POPULATION SUBGROUPS: DEFINITIONS AND RECOMMENDATIONS

The biomedical chimpanzee population is not homogeneous, but is made up of subpopulations. Its management requires understanding of that fact and careful assignment of individual chimpanzees to appropriate subgroups, as defined below.

The grouping takes into account past research use and the potential for public health liability, as well as the needs of human-health research. In some instances, an individual chimpanzee can be classified nonexclusively into each of several subgroups, but research, clinical, and breeding histories can be used to identify the relevant "primary" subgroup. The long-term housing criteria and specific recommendations that follow are applicable to each of the subgroups of chimpanzees.

GROUP A: BREEDING POPULATION

This category consists of the breeders and their offspring supported by National Institutes of Health (NIH) in the National Chimpanzee Breeding and Research Program (table 3.1). The facilities in which they are housed and the associated personnel constitute a unique, irreplaceable resource. The breeding resource should remain within the present group of facilities. In addition, during the proposed breeding moratorium, it is important to maintain social groups that will promote appropriate behavioral growth and development of juveniles. Ownership of these animals should be transferred to the government, and the ChiMP office (see Chapter 5) should work with demographers, geneticists, and scientists to establish the appropriate size of the population (see also population models in Chapter 4). Alternatively, a mechanism to provide for lifetime support should be established.

GROUP B: AVAILABLE FOR RESEARCH

This category consists of chimpanzees that are available for research projects. They might or might not be research-naive, they vary from

juvenile to old, and they are recommended for ownership (or lifetime support) by the government. These animals require a controlled environment. They should remain in the present facilities, whose management understands the need to maintain standards of health required for biomedical research. There should be a greater focus on increased research use of the animals in this category, which will provide needed program income to offset maintenance costs. Investigators using chimpanzees in NIH-funded research should use animals from this category whenever possible, avoiding the payment of "use fees" and "endowments." Some animals that are now designated as belonging to this group might be determined to be no longer needed in research (see group D, below). See Table 3.2 for numbers of animals in subgroups A, B, C, and D-3.

TABLE 3.1 NIH Breeding-Colony Age Distribution

Age	Males	Females	Total
Birth–30 d	1	2	3
31 d–12 m	7	8	15
13 m–3 y	29	35	64
4–6 yr	41	42	83
7– yr	27	48	75
10–15 yr	30	58	88
16–20 yr	13	20	33
21–30 yr	40	84	124
>31 yr	16	37	53
Total	204	334	538

GROUP C: CURRENTLY IN RESEARCH PROTOCOLS

This category consists of chimpanzees that are in research protocols. These animals need to remain in a controlled environment with knowledgeable management, biocontainment facilities, and trained personnel. When assigned to research projects lasting longer than six mo, the

animals should have access to the outside and have social and tactile contact with other chimpanzees, unless an exception has been obtained consistent with the needs of research protocols. Some biocontainment research facilities do not comply with the standards for long-term care established by this committee. Funding is required to improve facilities and provide new alternative group housing that will satisfy appropriate biohazard precautions while meeting long-term housing guidelines. It is recommended that government agencies and commercial organizations that have used or plan to use chimpanzees cooperate in meeting those funding needs. Congress should provide sufficient funding to the affected agencies to ensure that their biomedical-research programs are not harmed because of their contributing funds for such facilities and housing. Estimates of funding required must be developed by ChiMP after an assessment of the health status of all animals and the number of animals to be housed in each long-term care housing type has been determined.

Some animals are suitable and available for infectious disease research, but are not being used, for at least two reasons: some holding and breeding facilities do not have appropriate housing for this type of research, and some research facilities do not have suitable housing for large chimpanzees being studied. A moratorium in breeding is called for but can be adhered to only if investigators find alternatives for two-to four-yr-old animals for respiratory syncytial virus (RSV) research. The ChiMP office should seek assurance from Public Health Service (PHS) investigators that only young animals are suitable for RSV research and that use is based on scientific grounds, rather than on convenience or caging limitations. Older animals might be suitable if screened and found negative for RSV. Existing facilities that can support the use of larger and stronger chimpanzees should be better used, or caging for infectious disease research should be modified to allow the work to be conducted on older juvenile and adult animals.

GROUP D: NOT NEEDED FOR RESEARCH OR BREEDING

This category consists of chimpanzees that are no longer needed for research projects or breeding. The committee divided this into three subgroups as listed below:

1. *Chimpanzees That are Not Needed for Breeding and That Have Not Been and Will Never Be Used for Research.* This subgroup has the greatest potential for ownership transfer to private long-term care facilities, such as sanctuaries, zoos, and private compounds. Transfer of these animals has the potential to provide financial benefits to the government and improvement in the quality of life of the animals. This subgroup includes animals from group A that are not needed for breeding.
2. *Chimpanzees That Have Been Used in at Least One Research Protocol and That Pose No Public Health Threat.* Some chimpanzees used in infectious disease or other studies can be placed in the public sector or returned to the breeding population. Under appropriate housing conditions, management, and staff protection, these animals could be considered to pose no disease threat to humans. However, staff should be appropriately immunized, medically monitored, and experienced in the care and handling of potentially infected chimpanzees. The health status of these animals should be evaluated regularly. If private funding is available and the criteria stated above are met, these animals could be removed from PHS-supported colonies and their ownership transferred to a nongovernment institution. The government should be aware of possible liability due to zoonotic disease transmission to humans after the animals are transferred to long-term care facilities. Chimpanzees assigned to this subgroup could include animals that are not hepatitis B carriers; animals that were immunized with a potential vaccine that did not stimulate the immune system and that therefore were not challenged with an infectious agent; animals that are HIV-seropositive from a vaccine but were not challenged; and animals from the breeding program used for RSV research.
3. *Chimpanzees That Have Been Used in at Least One Research Protocol, Are No Longer Needed, and Might Pose a Public Health Threat*. Some of these animals have been used in infectious disease studies and are viremic with the inoculated virus. Others are seropositive for infectious agents and have uncertain public-health status. The animals in this subgroup could remain at their present facilities or be housed at a specifically designated government-supported centralized facility that has appropriate housing and manpower experienced in handling infected chimpanzees. These animals should be government-owned. If such animals are moved to a privately owned and operated

facility, that facility must be able to contain these animals according to procedures recommended by the Centers for Disease Control and Prevention (CDC).

The sizes of the subgroups discussed above and their costs are provided in Table 3.2. Another accounting of the approximately 1,500 chimpanzees in the research population is provided in Chapter 5. Although the accountings subdivide the population differently and are based on different information provided to the committee, the totals are similar and provide the basis for the committee's recommendation that the government own or provide lifetime support for approximately 1,000 animals.

OWNERSHIP TRANSFER

The federal government should accept ownership or provide lifetime care for chimpanzees from the above groups (see also Chapter 5). Government ownership or lifetime support is thought to be an essential early step in implementing these recommendations. However, some animals for which government ownership or support is recommended are no longer needed for research or breeding. The government should identify those animals and seek to transfer them to long-term care facilities.

If any chimpanzees are transferred to nongovernment, long-term care facilities, it would assist in reducing overcrowding in existing facilities. However, reproduction, long-term financial stability, expertise in care, and elimination of risk to public health must all be addressed. Thus, the committee offers the following recommendations. Before transfer, the government should

- Ensure that all chimpanzees to be transferred are permanently incapable of reproduction, for example, because of vasectomy or tubal ligation.
- Provide complete health and research-use histories for each animal. Any animal missing documentation for any period of research use should not be transferred to the public sector until its complete research history is made available.
- Perform appropriate screening of each animal as further

assurance of little or no possibility of a public health threat. NIH and other agencies initiating new activities or renewing existing ones with the research chimpanzee facilities should identify this need at the earliest opportunity.

TABLE 3.2 Current Estimates of Chimpanzees in Six Colonies by Subgroup and Cost

Subgroups	Current Number	Current Annual Cost at $20 per day
A. Breeders and offspring[a]	573	$4,182,900
B. Available for research[b]	549	$4,007,700
C. Currently on research protocols[b]	360	$2,628,000
Subtotal	1,482	$10,818,600
D-1. Breeding colony and offspring not needed for breeding or research—candidates for sanctuaries[c]	?	(included in above categories)
D-2. Used in research but not posing public health threat—candidates for sanctuaries[c]	?	(included in above categories)
D-3. Used in research and posing a public health threat—candidates for nonsanctuary long-term care[d]	260	$1,898,000
Subtotal	1,742	
Adjusted for double count in several categories	<248>	
Total	1,494	$10,906,200

[a] Category A consists of 325 animals of mixed ages from the initial 1986 NIH breeding program, 121 offspring ranging in age from infancy to 10-yr, and 127 offspring produced and available for research but currently supported by NIH under the breeding program. The 573 figure includes 35 animals from an institution not supported under the NIH breeding program.

[b] As reported to ISIS in survey dated September 1996.

[c] Unknown. See projections for number of animals not needed for breeding in Chapter 4.

[d] As reported to the committee by the six major institutions holding chimpanzees primarily for hepatitis B virus and HIV protocols. It is likely that an additional 100 to 150 animals have been used in hepatitis C virus, malaria, kuru, and Creutzfeldt-Jakob and other infectious protocols. See Chapter 2.

- Agree to provide immediate assistance, advice, and housing if any animal transferred to the public sector later develops signs of illness resulting from previous exposure that might pose a public health threat.
- Ensure fiscal-management expertise and long-term financial stability and strength of the recipient.
- Implant in each animal a microchip that contains the animal's unique identification number (assigned by ISIS). Any important research history could also be encoded at this time.

Before transfer, the proposed recipient should

- Provide evidence of expertise in captive chimpanzee biology, husbandry, and veterinary care.
- Provide evidence of ability to meet or exceed the long-term care recommendations in this report.
- Provide written documentation of the proposed use of the individual animals, including public viewing of the animals, and noninvasive or nonmanipulative research.
- Provide demonstration of fiscal responsibility.
- Agree to report required information to a national tracking system, as designated by the ChiMP office.
- Agree to maintain detailed health records and to contact the ChiMP office immediately if there is any question of a public health threat, and agree to abide by the decision of the ChiMP office to eliminate such a threat—even if euthanasia is determined to be warranted.
- Agree to adhere to the euthanasia policy endorsed in this report.
- Agree to adhere to a personnel health policy, as outlined by the ChiMP office, which would include appropriate immunization of staff.
- Agree to notify the ChiMP office of any potential later ownership transfer or loan or lease of individual animals and agree to make reasonable efforts to ensure that any subsequent owner will also abide by all of the agreements required for transfer of ownership. This is recommended as a means of tracking public health threats from an animal transferred out of biomedical facilities.

CONCLUSIONS

- Euthanasia of chimpanzees should be permitted for reasons of health or quality of life. Euthanasia is not recommended as a general means of population control.
- With the assistance of colony managers and investigators, the ChiMP office should classify all animals in supported facilities in the categories defined here. When they have been classified, strategic management of the entire population will become possible.
- Long-term management programs as defined herein, including sanctuaries, should meet or exceed all recommendations in this report.
- Funding will be required to bring current facilities into compliance with the guidelines in this report. Long-term savings can be expected, depending on the success of transferring animals to the nongovernment sector and increasing efficiency by centralizing management.

4

DEMOGRAPHY, COST, AND GENETIC MATERIAL

Chimpanzees have been important animals in many biomedical and behavioral research programs, as outlined in chapter 2. Because of restrictions against importation of these animals from the wild, research needs for chimpanzees have been met by captive breeding colonies since the Convention on International Trade of Endangered Species of Wild Fauna and Flora (CITES) became effective in 1975.

DEMOGRAPHY

Cost-effective management of the research chimpanzee population depends on an understanding of its demography. Whether the goal is to increase, decrease, or stabilize population size, demographic analysis of history and projection of future trends is critical for sound population management. Detailed demographic analysis requires that high-quality individual records be maintained. The five breeding facilities supported by the National Institutes of Health (NIH) and the facility at the Southwest Foundation for Biomedical Research (SFBR) have excellent records available to allow evaluation of demographic management issues.

Chimpanzee population demography resembles that of human populations and hence is quite different from that of other laboratory animal models. In addition to their long life span, chimpanzees have a relatively

late onset of reproduction (7 yr for females is the youngest ever recorded in the NIH breeding program; 10-12 yr is more typical). Reproduction can be sustained by at least some individuals beyond the age of 40 yr. Chimpanzees almost always produce one offspring per pregnancy.

These life-history characteristics mean that the growth potential of chimpanzee populations is much less than that of populations of all other species used in research, but growth in captivity can be achieved. The NIH breeding program averaged 10 live births per 100 animals during the peak years of 1987-1993. The birth rate was reduced later because of a potential surplus of chimpanzees for research.

The age structure of a population is important for understanding population dynamics. The biomedical research chimpanzee population in the United States now has a generally stable age structure with captive-bred animals filling in the lower age classes as a result of the ban on importation of wild chimpanzees imposed by CITES in 1975. The NIH breeding-program population has a similar structure.

Because of the success of the breeding program during a period when relatively few animals were being used, many younger animals are now in the population. Life expectancies of animals of various age classes can be calculated from the existing records. Life-table models can be used to forecast how rapidly a population will decline as a result of the background rate of mortality under existing captive-management conditions.

The large number of animals available for research is ample for reasonable projections of research needs; hence, the recommendation of a 5-yr breeding moratorium. Thereafter, the ChiMP office can assess up-to-date research-need forecasts, the number of animals that have been moved to sanctuaries, and attrition due to natural mortality and then recommend needed changes to management.

MODELS OF BREEDING COLONY SIZE

If sanctuary options develop, the question of how many animals could be placed in sanctuaries might arise. Figures 4.1 and 4.2 provide

estimates of the size of the future breeding population for two possible scenarios of future research needs. Animals in excess of the needs of the breeding population in these models can be used in research or transferred to long-term care facilities. These animals are among the least likely chimpanzees to have been exposed to agents infectious to humans, so they might be considered for transfer to public sanctuaries.

Figures 4.1 and 4.2 show projected future population sizes and trends for two of the long-term management options discussed in this report. Other options can be modeled, but these were selected as distinct examples of future management decisions by the proposed Chimpanzee Management Program (ChiMP) office discussed in chapter 5 that would depend on the perception of future research needs and goals.

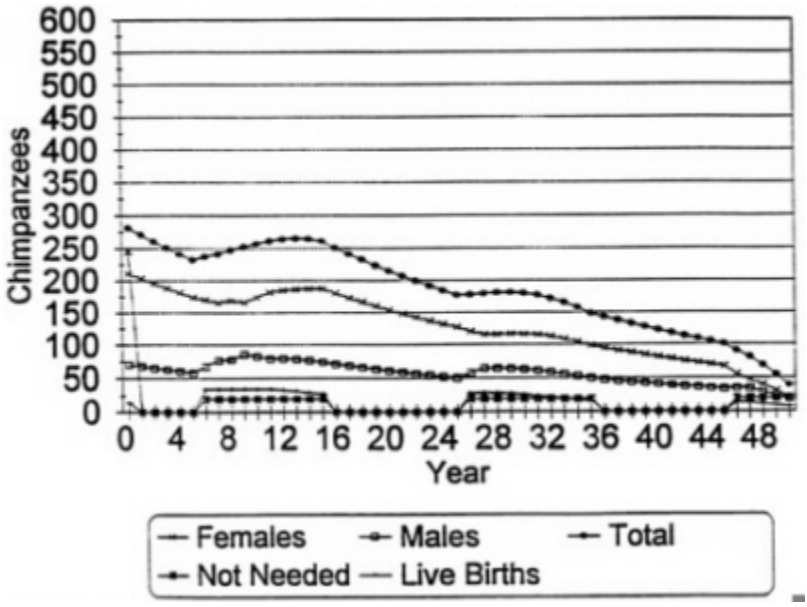

FIGURE 4.1 Ten-Year Crisis Breeding Colony Model

Figure 4.1 projects the future size of the breeding population on the basis of having to meet a national crisis every 10-yr, as discussed in chapter 2. This model begins in year 0 by removing 246 animals that are not needed for breeding from the 528 animals in the breeding program

at the end of 1996. It then provides for a 5-yr breeding moratorium in years one to five with the number of the animals in both the breeding program and those "not needed for breeding"[1] declining because of normal mortality. Breeding begins in year six and continues for 10-yr, and 20 animals per year not needed for breeding move from the breeding program. In the first two years of a 10-yr breeding period, older adults are moved from the breeding program.

Starting in the third year of a breeding period, a mixture of two-and three-year-old animals and adults is moved from the breeding program. The figure reflects a 5-yr breeding moratorium, a 10-yr breeding period, a 10-yr breeding moratorium, another 10-yr breeding period, another 10-yr breeding moratorium, and the beginning of a third 10-yr breeding period. When breeding is taking place in this model, animals older than 35 yr are moved to the "not needed for breeding" group.

Figure 4.2 projects the future size of the breeding population on the basis of a research requirement for 10 new animals per year for a period of 50 yr. This model begins in year 0 by removing 360 animals not needed for breeding from the 528 animals in the breeding program at the end of 1996. There is a breeding moratorium in years one to five, and the number of animals in the breeding program and those no longer useful to the breeding program because of old age decline because of normal mortality. Beginning in year six, breeding takes place at a steady rate to replace animals in the breeding program that have died and 10 animals per year over 35 yr are moved from the breeding program into the "not needed for breeding" group. In the first 2 yr after the moratorium, older adults are moved from the breeding program into the "not needed for breeding" group. Starting in the third year after the moratorium, a mixture of 2- and 3-yr-old animals and older animals is moved into the "not needed for breeding" group. When breeding is taking place in this model, animals older than 35 yr are moved into the "not needed for breeding" group. From chapter 2, it might be concluded that 20 young "RSV

[1] Both figures 4.1 and 4.2 model only the breeding program. In both cases, animals labeled "not needed for breeding" are available either for research or for transfer into long-term care or sanctuary facilities. Decisions on the use of these animals are to be made by the ChiMP office.

naive" animals are needed per year. This model assumes that half that need can be met with existing animals.

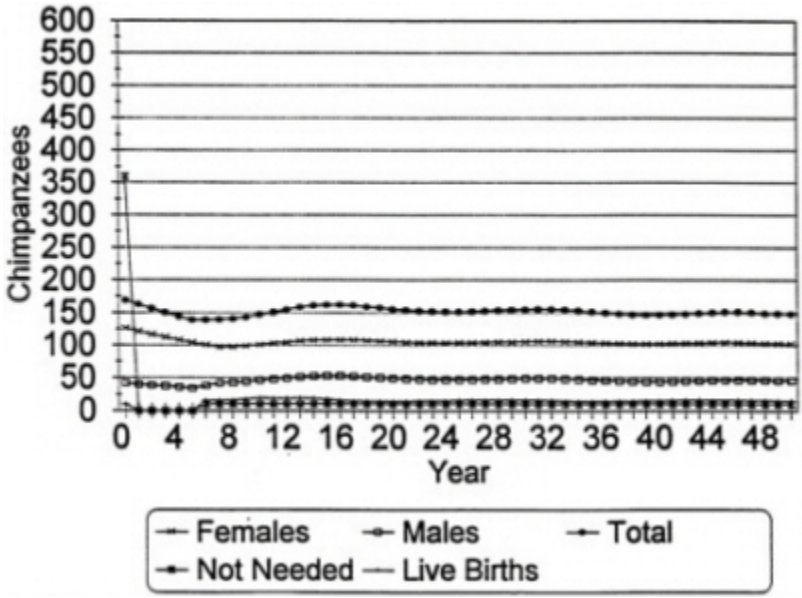

FIGURE 4.2 Stable-Production Breeding Colony Model

COSTS

Cost is a major issue in evaluating the options for long-term maintenance of and future research with chimpanzees. Chimpanzees are among the most-expensive laboratory animal models. Their large size and complex social requirements demand housing and intensive care practices that are expensive, even if minimal. Chimpanzees are also long-lived animals; the average life span of males and females is about 25 and 34 yr, respectively, and maximums of 55 and 60 yr, respectively, have been reported (Dyke and others 1995, 1996). As a result, in the absence of

euthanasia or terminal research, the cost obligations for maintaining and breeding chimpanzees are not only high, but also of long duration.

The high costs of maintaining and breeding chimpanzees are reflected in the "use fees" charged to researchers. Those fees are generally used to cover the continuing costs of chimpanzee facilities, although a portion (sometimes called an "endowment") is designated for the future care of the animals in some cases (for example, Eichberg and Speck 1988). The high cost of chimpanzees for research results in diminished use, which in turn increases costs to researchers who still use them because fewer use fees are available to cover the costs of breeding and maintenance. If the chimpanzee is to remain a viable animal model for research, mechanisms for increasing the cost effectiveness of chimpanzee breeding, maintenance, and research must be developed.

The available information indicates that government funding now supports 900-1,000 chimpanzees. These animals are in several different categories, including those owned by the government (and maintained for diverse purposes, including the breeding program), non-owned animals supported in the breeding program, and diverse non-owned animals supported for various periods for research grants in science and medicine. Government has also made multimillion-dollar contributions to some facilities for long-term care of some animals, and in addition, researchers have paid use fees up to $55,000-66,000 per animal. The diversity of funding mechanisms, the different approaches used, and the absence of a central accounting summary made it impossible for the committee to determine actual expenditures by the various agencies. We recommend that the government assume ownership, or provide lifetime support, for this population of approximately 1,000 chimpanzees. The approximately 500 remaining chimpanzees in the total US research population are privately owned, not used in government research, or their owners might not be willing to transfer ownership to the government.

The present direct cost of supporting these animals is $15-30 per day; the NIH National Chimpanzee Breeding and Research Program (NCBRP) animals are at the lower end of that range and animals in infectious-disease research are at the upper end. Using $20 for direct per diem costs and 1,000 for the number supported by government, we can estimate that

the direct cost for chimpanzee support now being paid from multiple government budgets is $7,300,000 per year. Available figures indicate that the NCBRP supports more than half of the 1,000 animals (573) with about half the estimated total, or $3,608,884[2] for FY 1996.

PROJECTED BREEDING COLONY COSTS

The "crisis" model presented in figure 4.1 assumes a national crisis affecting the nation's public health will recur every 10-yr. Another aspect of this model is depicted in figure 4.3 as consisting of breeders (lower, light-colored bars) and those not needed for breeding (upper, dark-colored bars). The cost associated with this model are determined by the size of those two subgroups that begin in year 0 with a breeding colony of 282 animals, at an annual direct cost of $2,058,600, and 246 animals not needed for breeding, at an annual direct cost of $1,795,800. It remains more expensive than the stable-production model until year 35, after which it declines to only 39 animals by year 50 because of natural mortality, at an annual direct cost $284,700.

Figure 4.2 presented a model in which a low but stable birth rate is needed for many years. Another aspect of this model is depicted in figure in 4.4 as consisting of breeders (lower, light-colored bars) and those not needed for breeding (upper, dark-colored bars). The costs associated with this model are determined by the size of those two subgroups that begin in year 0 with a breeding colony of 168 animals at an annual direct cost $1,226,400. At year 50, this model projects 148 animals remaining in the breeding colony at an annual direct cost of $1,080,400.

Chimpanzees not needed for breeding might remain the responsibility of the government as "available for research," or they might be transferred to lower-cost long-term care or no-cost sanctuary facilities. Tables 4.1 and 4.2 enable determination of the cost to the government for the two models presented in figures 4.3 and 4.4. The annual cost for each model is based on the number of government-supported animals. For example, figure 4.3 shows that at year 16, 546 animals (251 breeders and

[2] Data provided by the NIH, National Center for Research Resources, Comparative Medicine Program and include research and equipment costs associated with the NCBRP awards.

295 not needed for breeding) must be supported. If those not needed for breeding are removed from government support, the cost obligation is limited to the 251 breeders.

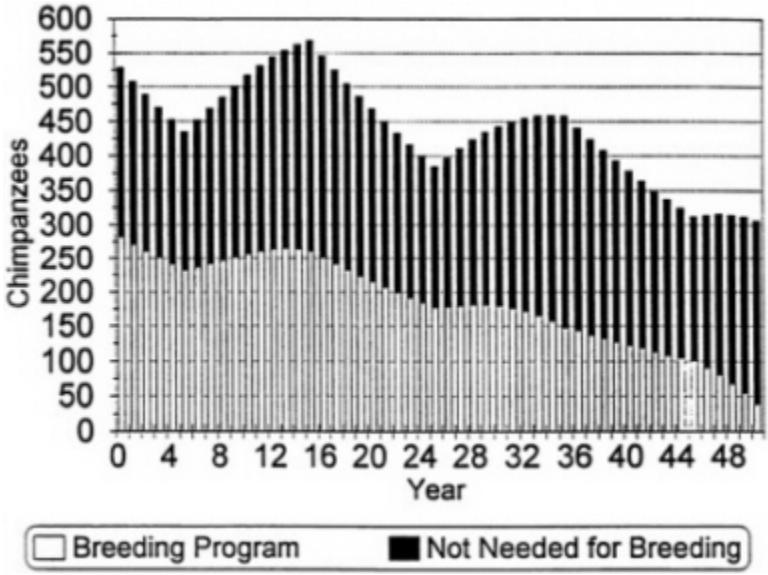

FIGURE 4.3 Crisis Model: Annual Number of Chimpanzees in Breeding and Not Needed for Breeding.

Tables 4.1 and 4.2 provide the annual direct costs, at $20 per day, for breeders and those not needed for breeding that are represented in figures 4.3 and 4.4, respectively. For example, table 4.1 shows that at year 16, the annual support for the 251 breeders in the crisis model is $1,832,300. If the government also supports the 295 animals not needed for breeding, the total government obligation is increased by $2,153,500, for a total of $3,985,800.

REDUCING COSTS THROUGH SIMPLIFYING FUNDING AND ENHANCING COORDINATION

We recommend elsewhere that the government accept ownership, or

provide a mechanism for lifetime support, of animals not owned, but now being supported by the government. We believe that a large component of the general public and the scientific community feel that society, acting through government, has responsibility for these animals. We point out that this does not increase current government animal-support annual costs—the animals are already being financially supported by the government. In fact, simplification of the support mechanisms would likely save some costs and make animals available to a wider segment of the research community for important research.

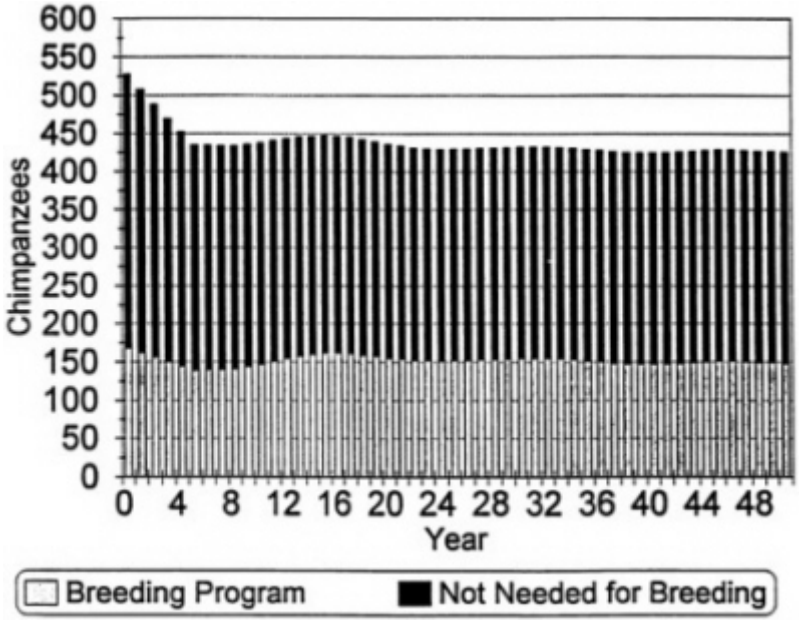

FIGURE 4.4 Stable Production Model: Annual Number of Chimpanzees in Breeding and Not Needed for Breeding.

Simplification and centralization would also allow better coordination of population management in response to perceived national needs. At present, decision-making and accountability for overall population management are too fragmented and complex to function properly.

We recommend elsewhere, on the basis of our perception of current

TABLE 4.1 Crisis Model: Annual Costs for Breeding and Not Needed for Breeding

	$20.00 per day		365 days per year		
Year	Breeding Colony	Not Needed for Breeding	Breeding Colony	Not Needed for Breeding	Require Support
0	282	246	$2,058,600	$1,795,800	528
1	271	237	$1,978,300	$1,730,100	508
2	261	228	$1,905,300	$1,664,400	489
3	251	219	$1,832,300	$1,598,700	470
4	241	211	$1,759,300	$1,540,300	452
5	232	203	$1,693,600	$1,481,900	435
6	237	215	$1,730,100	$1,569,500	452
7	242	227	$1,766,600	$1,657,100	469
8	247	238	$1,803,100	$1,737,400	485
9	252	249	$1,839,600	$1,817,700	501
10	257	260	$1,876,100	$1,898,000	517
11	261	270	$1,905,300	$1,971,000	531
12	264	280	$1,927,200	$2,044,000	544
13	265	289	$1,934,500	$2,109,700	554
14	264	298	$1,927,200	$2,175,400	562
15	261	307	$1,905,300	$2,241,100	568
16	251	295	$1,832,300	$2,153,500	546
17	241	284	$1,759,300	$2,073,200	525
18	232	273	$1,693,600	$1,992,900	505
19	223	263	$1,627,900	$1,919,900	486
20	215	253	$1,569,500	$1,846,900	468
21	207	243	$1,511,100	$1,773,900	450
22	199	234	$1,452,700	$1,708,200	433
23	191	225	$1,394,300	$1,642,500	416
24	184	216	$1,343,200	$1,576,800	400
25	177	208	$1,292,100	$1,518,400	385
26	178	220	$1,299,400	$1,606,000	398
27	179	232	$1,306,700	$1,693,600	411
28	181	243	$1,321,300	$1,773,900	424
29	181	254	$1,321,300	$1,854,200	435
30	179	264	$1,306,700	$1,927,200	443
31	176	274	$1,284,800	$2,000,200	450
32	171	284	$1,248,300	$2,073,200	455
33	165	293	$1,204,500	$2,138,900	458
34	157	302	$1,146,100	$2,204,600	459
35	148	310	$1,080,400	$2,263,000	458
36	143	298	$1,043,900	$2,175,400	441
37	137	287	$1,000,100	$2,095,100	424
38	132	276	$963,600	$2,014,800	408
39	127	266	$927,100	$1,941,800	393
40	122	256	$890,600	$1,868,800	378
41	118	246	$861,400	$1,795,800	364
42	113	237	$824,900	$1,730,100	350
43	109	228	$795,700	$1,664,400	337
44	105	219	$766,500	$1,598,700	324
45	101	211	$737,300	$1,540,300	312
46	91	223	$664,300	$1,627,900	314
47	81	235	$591,300	$1,715,500	316
48	68	246	$496,400	$1,795,800	314
49	55	257	$401,500	$1,876,100	312
50	39	267	$284,700	$1,949,100	306

TABLE 4.2 Stable Production Model: Annual Costs for Breeding and Not Needed for Breeding

	$20.00 per day		365 days per year		
Year	Breeding Colony	Not Needed for Breeding	Breeding Colony	Not Needed for Breeding	Require Support
0	168	360	$1,226,400	$2,628,000	528
1	162	348	$1,182,600	$2,525,800	508
2	156	333	$1,138,800	$2,430,900	489
3	150	320	$1,095,000	$2,336,000	470
4	144	308	$1,051,200	$2,248,400	452
5	139	298	$1,014,700	$2,160,800	435
6	140	295	$1,022,000	$2,153,500	435
7	140	294	$1,022,000	$2,148,200	434
8	141	293	$1,029,300	$2,138,900	434
9	144	292	$1,051,200	$2,131,600	436
10	147	291	$1,073,100	$2,124,300	438
11	151	290	$1,102,300	$2,117,000	441
12	155	289	$1,131,500	$2,109,700	444
13	158	288	$1,153,400	$2,102,400	446
14	160	287	$1,168,000	$2,095,100	447
15	162	286	$1,182,600	$2,087,800	448
16	162	285	$1,182,600	$2,080,500	447
17	161	284	$1,175,300	$2,073,200	445
18	159	283	$1,160,700	$2,065,900	442
19	157	282	$1,146,100	$2,058,600	439
20	155	281	$1,131,500	$2,051,300	436
21	154	280	$1,124,200	$2,044,000	434
22	152	279	$1,109,600	$2,036,700	431
23	152	278	$1,109,600	$2,029,400	430
24	151	278	$1,102,300	$2,029,400	429
25	152	278	$1,109,600	$2,029,400	430
26	152	278	$1,109,600	$2,029,400	430
27	153	278	$1,116,900	$2,029,400	431
28	153	278	$1,116,900	$2,029,400	431
29	154	278	$1,124,200	$2,029,400	432
30	155	278	$1,131,500	$2,029,400	433
31	155	278	$1,131,500	$2,029,400	433
32	155	278	$1,131,500	$2,029,400	433
33	154	278	$1,124,200	$2,029,400	432
34	153	278	$1,116,900	$2,029,400	431
35	151	278	$1,102,300	$2,029,400	429
36	150	278	$1,095,000	$2,029,400	428
37	148	278	$1,080,400	$2,029,400	426
38	147	278	$1,073,100	$2,029,400	425
39	147	278	$1,073,100	$2,029,400	425
40	147	278	$1,073,100	$2,029,400	425
41	147	278	$1,073,100	$2,029,400	425
42	148	278	$1,080,400	$2,029,400	426
43	149	278	$1,087,700	$2,029,400	427
44	150	278	$1,095,000	$2,029,400	428
45	151	278	$1,102,300	$2,029,400	429
46	151	278	$1,102,300	$2,029,400	429
47	150	278	$1,095,000	$2,029,400	428
48	149	278	$1,087,700	$2,029,400	427
49	149	278	$1,087,700	$2,029,400	427
50	148	278	$1,080,400	$2,029,400	426

research needs, that a smaller breeding and reserve population be maintained. The government-supported experiment-naive young animals and old animals released from the breeding population (to reduce its size and potentially lower the cost to the government) can be used for research, or moved to long-term care or sanctuary settings. The scientific community should be better informed about the availability of these animals for important research and about the elimination of use fees. Reduced costs to investigators through elimination of use fees should result in greater use and understanding of the chimpanzee as an animal model. Payment of use fees generally inhibits the use of chimpanzees in research. Some investigators have appealed to the present committee to recommend elimination of such fees. Use of animals that belong to a government-owned or lifetime-supported resource would accomplish that goal.

With the recommended 5-yr breeding moratorium in place, natural mortality will reduce the population size. Survival rates of chimpanzees in biomedical research facilities are better than those in the wild (Dyke and others 1995), so this will take time. An initial estimate is an annual reduction of 3%. Over five years, we would project a reduction in size of about 15%, caused by natural mortality. Applied to our estimate of $7.3 million in current support, that would reduce the annual support costs for the government-owned population by one million in constant dollars.

Dyke and others (1996) have calculated lifetime costs for various segments of the captive-chimpanzee population. The cost of supporting a single chimpanzee, at the per diem rates needed in existing facilities and aggregated over its long expected life span, is estimated at $125,000-300,000. Such large figures argue for careful population management and multiple use whenever possible. We believe that these lifetime cost calculations are an important warning about financial encumbrances in the future. We also recognize that most of society's budget decisions are made on an annual or limited-year grant basis, and that is the level at which the value and costs of research chimpanzees will be continually assessed.

SANCTUARY CONSTRUCTION

In order to evaluate the options for long-term care of chimpanzees no longer needed for research or breeding, the committee prepared

"what if" financial models of sanctuaries. The models were used to evaluate the potential cost savings that would result from the lowering of per diem costs in a purpose-built "sanctuary." The models included capital construction costs for the sanctuary, a fixed annual cost of operating and maintaining the facility, and marginal costs related to the number of chimpanzees housed. As might be expected, the models showed that the larger the number of animals moved to a sanctuary and the lower the annual marginal costs of adding one chimpanzee to the facility, the more the construction cost could be justified. For some plausible ranges of values, the models indicated net savings could be achieved from sanctuary construction.

The committee believes that funds for long-term care of chimpanzees, especially the phase when they are no longer needed for research or breeding, should not come from biomedical research budgets, and it urges that creative approaches to develop and support sanctuaries be sought. Societal obligations to chimpanzees no longer needed for research or breeding require cooperative support from federal agencies, Congress, commercial companies, and nongovernment organizations.

GENETIC MANAGEMENT

Conservation-oriented genetic management traditionally has been used to manage captive nonhuman primate colonies. That approach emphasizes preservation of genetic variability and avoidance of inbreeding as the primary goals of genetic management, with a general objective of preserving the evolutionary potential of the population (Soulé 1986, 1987). However, genetic management in the research environment does not operate with the aim of preserving a species in perpetuity for possible reintroduction into the wild. Rather, research-oriented genetic management must balance the goals of preserving the long-term viability of the population with those of specific research needs (Williams-Blangero 1993).

The pedigree is the primary source of information for genetic management. With good record-keeping and single-male breeding groups, available pedigree information is generally sufficient for most genetic management procedures. The colony pedigree can be constructed from basic record information on dam and sire for all individuals.

If multimale breeding groups are used, paternity testing might be required to resolve pedigrees. Genetic-marker analyses have resolved most paternity questions in the NCBRP population. However, even in captive colonies that use single-male breeding schemes, mistakes in pedigree assignments can occur. The need for routine pedigree verification with genetic-marker analysis has been emphasized in many genetic management schemes. The expense of fully verified pedigrees might be warranted for a long-term, large-scale chimpanzee breeding program designed to sustain research demands for multiple generations. However, if the ChiMP office does not expect a long future for chimpanzee experimentation or a substantial increase in genetic research with these animals, genetic management programs involving extensive genetic-marker analysis might not be justified.

Pedigree information alone will allow evaluation of founder contributions, inbreeding coefficients, and kinship coefficients between potential mating pairs or potential sample animals (Williams-Blangero and Dyke 1992). This basic level of genetic information generated from colony records permits avoidance of inbreeding, maximization of effective population size through equalization of founder contributions, and selection of unrelated experimental animals. "Pooling" and sharing of colony records so that multicolony pedigrees are available to each colony manager (as done through the International Species Information System, ISIS) will allow managers to consider genetic diversity and minimize inbreeding in their colony with reference to the pedigree of the total research chimpanzee population.

The finite size of the US research chimpanzee population indicates that inbreeding is inevitable if chimpanzee breeding is to be continued in perpetuity. That implies that genetic-management techniques should be used to avoid inbreeding and maintain genetic variability. Although high levels of inbreeding have been shown to have important consequences for colony viability (Crawford and O'Rourke 1978; Noble and others 1990; Ralls and Ballou 1982), the potential negative effects of long-term inbreeding at low levels in nonhuman primates remain to be seen. Many unrelated potential mating pairs are present in the research chimpanzee population, so inbreeding can be easily avoided for many years through selection of unrelated breeding pairs.

Genetic studies have shown that there is substantial genetic variability in the US research chimpanzee population (Williams-Blangero and

others 1993, 1994). Thus, although genetic management techniques are needed to maintain variability, intensive strategies for increasing genetic diversity (such as high rates of intercolony transfer and introduction of new animals from other nonresearch captive populations) might not be warranted.

Effective population size is the proportion of the number of breeders to the total population and is predictive of the extent of genetic variability that can be maintained in a population (Lande and Barrow-clough 1987). Captive nonhuman primate populations often have relatively low effective population sizes (for example, breeders represent 13.8% of the total population in the SFBR chimpanzee colony) [Williams-Blangero and others 1992], because of the inequitable distribution of offspring among founders, thus reflecting heavy reliance on proven breeders to produce animals. Increasing founder representation is a simple mechanism for maintaining variability and increasing effective population size (for example, Lacy 1989). The effective population size of a colony can be evaluated through computer simulation analyses of pedigree information (for example, Waples 1989).

Maintenance of heterozygosity is a common component of genetic management programs and can be evaluated through computer simulation analyses of pedigree data or directly from genetic-marker data. The emphasis on heterozygosity in conservation genetics is based on Fisher's fundamental theorem of natural selection, which predicts that the evolutionary potential for adaptation is a function of genetic variance (Allendorf and Leary 1986). The applicability of heterozygosity measures for assessing the status of captive groups is limited because heterozygosity is relatively unaffected by changes in breeding structure when the initial effective population size is greater than 20.

The rate of allelic loss is more sensitive than heterozygosity to changes in breeding structure; allelic loss is halved by doubling of the effective population size (Kimura and Ohta 1969). Allelic diversity can be used in both genetic management and some experimental protocols.

Selection of unrelated mates and equalization of founder contributions can be used in colonies to maintain genetic diversity. With due concern to avoid transmission of disease, exchange of animals between colonies can also be useful for long-term avoidance of inbreeding and maintenance of genetic diversity. Such temporary or permanent transfer

of animals between colonies for genetic-management purposes requires diligent recordkeeping within a colony and among colonies, as is currently provided for the multi-institutional NCBRP by ISIS.

FUTURE BREEDING

Current genetic management decisions must be considered in the light of long-term demographic consequences. Animals bred to meet current or projected research demands entail a substantial financial liability because of their long life span. The costs associated with the future maintenance of chimpanzee colonies should be important considerations for current genetic and demographic management (Dyke and others 1996).

As previously discussed, appropriate numbers and proportions of breeders among research animals can be evaluated with computer simulation techniques. The underlying assumptions for the demographic projections in these simulation analyses will be based on the guidelines generated by the ChiMP office. Key points to be considered include the expected number of naive research animals required per year, the expected number of previously used research animals that can be reused per year, and the appropriate age and sex structures of the experimental animal population. For example, will experimental protocols require primarily young animals, adolescent animals, or adult animals? Will males and females be equally useful? Will experimental groups require age-or sex-matched animals?

Research protocols generally assume that individual animals can be treated as independent cases. That assumption does not hold if an experimental sample contains related animals, which necessarily share a genetic background. If potentially confounding genetic relationships exist among animals, they should be well defined so that they can be explicitly considered in statistical analyses of resulting experimental data. Ignoring the nonindependence of related sample animals can lead to increased type I errors, in that sample sizes will be overestimated. Adding the restriction that sample animals be unrelated to existing protocol requirements regarding animal histories (such as experimental, reproductive, and caging backgrounds) and characteristics (such as age,

sex, weight, and health status) might substantially reduce the pool of available experimental animals in a colony. Under the perview of the ChiMP office, breeding-colony production programs should be designed to ensure availability of adequate samples for experimental protocols.

CRYOPRESERVATION OF GAMETES OR EMBRYOS

Cryopreservation of chimpanzee gametes or embryos has been suggested as a mechanism for preserving chimpanzee variability in the absence of numerous breeding colonies (Ballou 1992). However, this approach will not be inexpensive for adult female chimpanzees still would be needed in the future to serve as recipients of frozen embryos or frozen sperm.

Frozen storage of human and nonhuman primate sperm and embryos is possible (Balmaceda and others 1986; Dresser 1996; Durrant 1990; Lambert and others 1991; Pope and others 1984, 1986ab; Rall 1993; Sankai and others 1992, 1994; Summers and others 1987; Tollner and others 1990), but almost no research has been done specifically with chimpanzee gametes or embryos, except for the freezing of chimpanzee sperm (Gould and Styperek 1989).

Cryopreservation of oocytes has been accomplished in numerous species from mouse to humans and most recently in macaques (Younis and others 1996). Attempts to store oocytes with cryopreservation have resulted in live births in mice (Harp and others 1994; Schroeder and others 1990), cattle (Fuku and others 1992), and humans (Chen 1986; Van Uem and others 1987), but efficiency has been low. Problems associated with the process include damage to the subcortical microfilaments and to microtubules that control chromatin assembly and spindle formation (Parkes and Ruffing 1989), which has caused aneuploid and polyploid chromatin abnormalities in the resulting embryos or fetuses (Al-Hasani and others 1986; Kola and others 1988).

To avoid those problems, Gosden and others proposed removing slices of ovarian tissue containing follicles with oocytes of early stages, freezing them, and returning them to the ovary by transplantation. The

ovarian tissue transplantation procedure has resulted in mature oocytes that were fertilized and resulted in offspring in mice (Carroll and others 1990; Gosden 1992) and sheep (Gosden and others 1994). In primates, follicular development has been restored after cryopreservation and transplantation of ovarian tissue (Candy and others 1993); however, the fertilizability, embryo production, and normalcy of embryos or offspring are as yet untested.

RECOMMENDATIONS

- The government should anticipate initial annual expenditures of approximately $7.3 million to support approximately 1,000 chimpanzees.
- The ChiMP office should determine when breeding is to be reinitiated on the basis of projected research demand and the vitality of the population.
- The ChiMP office should determine the number of births needed to meet research needs for chimpanzees and the size and demography of the breeding population to sustain that population.
- Genetic management should be an important component of the overall management of the research chimpanzee population. Inbreeding should be avoided whenever possible. When unrelated mates are unavailable, pairs should be formed from the least-related potential mating pairs. Managers should try to equalize founder contributions in order to maintain diversity.
- High-quality recordkeeping is essential for genetic management. Pedigree records should be maintained for all animals (both living and dead) that have ever resided in a colony. The records for a given animal should include identification number, the sire's identification number, the dam's identification number, birthdate, sex, acquisition date, disposition date, and a disposition code that reflects whether the animal left the colony because of death, loan, sale, or other reasons. Guidelines for items to be included in standardized laboratory animal records at individual colonies are provided by Dyke (1993) and the Guide for the Care and Use of Laboratory Animals (NRC 1996). In addition to

recordkeeping at local facilities, a centralized source of records should be maintained for the entire US research chimpanzee population, as is currently done by ISIS.

- Given the state of the art, cryopreservation does not yet allow for a drastic reduction in or elimination of breeding colonies of chimpanzees.

5

CENTRALIZATION OF RESEARCH CHIMPANZEE MANAGEMENT AND DEVELOPMENT OF A NATIONAL CHIMPANZEE RESOURCE

Chimpanzees constitute a national resource for biomedical research that can be perpetuated only by breeding animals already in the captive population. However, there are more chimpanzees than are now needed for research, and the high cost of maintaining them makes it difficult to meet the special requirements for their care and diverts funds from research. A major concern of the committee is the fragmentation of financial support and decision-making related to the research chimpanzee population in the U.S. There is a critical need for better organization, coordination, responsibility, and oversight at a national level for this important animal model resource, which is used by various federal agencies in programs that ultimately benefit humanity—the biomedical research activities of the National Institutes of Health (NIH), the drug development programs of the pharmaceutical industry and the Food and Drug Administration (FDA), and the emerging infectious disease programs of the Centers for Disease Control and Prevention (CDC) and the Department of Defense (DOD).

The committee recommends that

- Chimpanzee breeding and research programs be centralized in a

Chimpanzee Management Program (ChiMP) and its Advisory Council, to be based in a national office, preferably in the office of the director of NIH or a suitable alternative that has the autonomy, infrastructure, and expertise to manage the program (figure 5.1).

- A single entity in a government agency (ChiMP) be assigned ownership, or lifetime care, with responsibility and authority for stewardship of this vital resource, which is to be supported by and used in partnership with other federal agencies.

This national program (designated the National Chimpanzee Resource, or NCR) consists of the ChiMP office, the ChiMP Advisory Council, and chimpanzees owned or supported by the government. ChiMP should be an autonomous body with sole responsibility and authority for coordinating the management of a US government-owned population of chimpanzees for use in biomedical research by any government agency or department, irrespective of whether an investigator is employed by the government, receives research funding from a governmental source, or represents private enterprise. Because most biomedical research with chimpanzees is supported by the NIH intramural and extramural programs, it is logical that ChiMP be housed at NIH to facilitate transfer of information between ChiMP and the intramural NIH institutes and centers and the extramural chimpanzee-using institutions. Although the office is proposed to be at NIH, it is intended that it be supported by a consortium of federal agencies that use chimpanzees in research (such as FDA, CDC, and DOD) and therefore not be subject solely to NIH operating and budgetary constraints.

Elsewhere we have recommended that scientific review of protocols in which chimpanzees are proposed to be used be conducted by the principal investigator's institution and approved by that institution's animal care and use committee (IACUC). It is therefore the intent that ChiMP not serve this function; rather, its goal should be to expedite and simplify the assignment of chimpanzees to IACUC-approved protocols. The ChiMP office would serve as a resource for information on government-sponsored chimpanzee studies and seek to avoid unnecessary duplication of research, maximize efficiency of use of the chimpanzees, and ensure the implementation of the best practices of animal care and careful attention to the welfare of the chimpanzees. Requests

for use of chimpanzees by NIH-funded investigators and those at other federal agencies and commercial organizations—such as FDA, CDC, DOD, and pharmaceutical companies—would be ranked by ChiMP on the basis of scientific merit; urgency of the public health-related problem; availability of animals with specific requirements regarding their age, sex, and past history; and preservation of the resource.

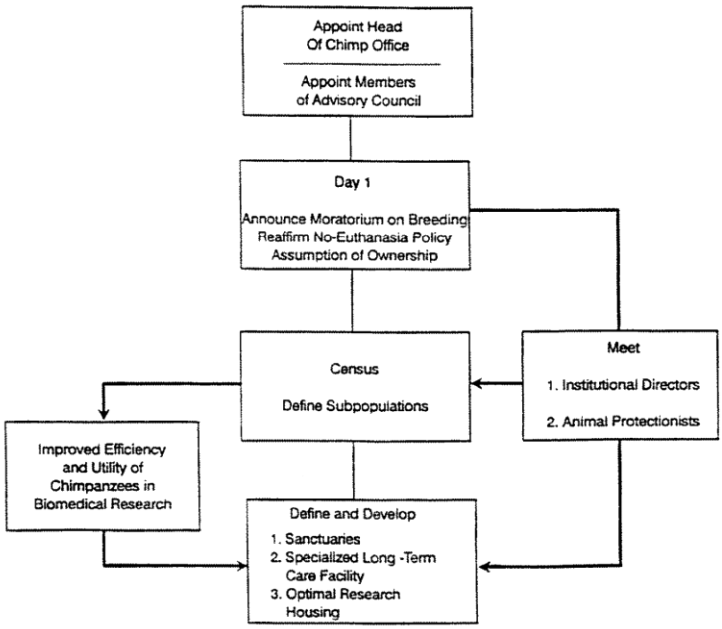

FIGURE 5.1 Comprehensive Care and Utilization of Chimpanzees in Biomedical Research—Implementation by Chimpanzee Management Office

Because of ChiMP's broad range of responsibility, it is the committee's intent that it would operate with the full backing of the leadership of the NIH and other user agencies.

About 570 research chimpanzees in the United States are owned by government agencies, and about 700 are maintained by government

entities, including those in the breeding program and in research protocols. Some 600 animals housed in biomedical facilities are owned by private and state institutions. The fragmentation of support, ownership, and management has resulted in inefficiencies and inconsistencies in the use of animals for research and in the maintenance of optimal numbers and breeding capacity.

The committee recommends that a Chimpanzee Management Program (ChiMP) be created and given direct administrative and fiscal responsibility for about 1,000 government-owned or government-supported animals, which would constitute the NCR. The NCR would be comprised of all chimpanzees judged necessary to serve critical national needs. Also, the NCR would be responsible for animals used in government-supported research that might represent a public-health threat. Monitoring the NCR would lead to more-efficient use of chimpanzees in research and facilitate strategic planning for the long-term care of chimpanzees in the breeding population, available for research, on research studies, not needed for research and breeding, and posing public health threat. Such monitoring could include surveillance for disease conditions that might threaten the NCR population as a whole. To these ends, the ChiMP office would

- Serve as responsible steward and custodian of the NCR.
- Facilitate communication between institutions housing government-owned or government-supported and privately owned chimpanzees.
- Communicate the availability of chimpanzees to appropriate scientists.
- Be well informed of the status of all chimpanzees used in biomedical and behavioral research, both government and private.
- Have budgetary authority for administering Public Health Service (PHS) and other government funds for maintaining the resource.
- Articulate the principles and objectives of breeding, demography, and long-term care to appropriate institutional animal care and use committees (IACUCs) to promote coordination with research needs.
- Establish a plan (before reinitiating breeding) for chimpanzees

no longer needed in research that adequately recognized ethical and moral obligations.

- Ensure that government-owned or government-supported chimpanzees were used in federally supported biomedical research, except when scientific factors dictate the use of animals available from other sources.
- Assign chimpanzees to approved and funded protocols.

The last responsibility requires specific attention. At present, the paperwork and time required for second-level peer review by the Interagency Animal Models Committee delay and limit the use of chimpanzees. This special second-level peer-review process was instituted because of concern that HIV-related research might rapidly deplete the available supply of research chimpanzees—a scenario that has not materialized. Active NIH control and restriction of the use of chimpanzees in research will no longer be needed and should be discontinued. Use of chimpanzees in research protocols should be approved or disapproved by IACUCs, which should apply the principles and objectives of ChiMP in their reviews. Under those circumstances, ChiMP's function would be to monitor the supply, demand, and specific uses of the chimpanzees, and to assign the most appropriate animals for specific purposes.

Elsewhere in this report, the committee recommends that use fees not apply to federally funded use of government-owned or government-supported chimpanzees. High use fees have substantially impeded the use of chimpanzees in biomedical research. The result of these recommendations would be to remove unnecessary expense, paperwork, and delay in the use of chimpanzees for important research activities.

OWNERSHIP

The fragmentation of ownership of chimpanzees and of oversight of their use in research has resulted in inefficiency and added immeasurably to the associated costs. The issue of "surplus" chimpanzees is problematic and raises both practical and ethical concerns with respect to who should be responsible for such animals. Over 500 chimpanzees

are available for research, of which at least 200 are supported by the NIH National Center for Research Resources (in addition to those dedicated to breeding) and have not been used in any infectious disease research. PHS agencies have supported both the production of additional chimpanzees at the facilities that hold PHS-supported animals available for research and the leasing of chimpanzees from non-federal-government sources. The consequence of the combination of high productivity of the breeding program and less-than-anticipated research use has resulted in a surplus of animals, which has led to overcrowding and a risk of contamination of the breeding population with infectious disease. Use of animals in some studies, such as those involving the hepatitis viruses and HIV, might result in contaminated animals that have little prospects of future financial support. To offset that possibility, payment of endowments or use fees up to $55,000-66,000 per animal have been assessed. These fees could be eliminated from federal budgets if provisions for long-term support of chimpanzees as recommended in this report were made by the federal government, thereby making the chimpanzee model more accessible to investigators and substantially increasing its use.

Centralization of management of a specified number of chimpanzees as a critical national resource for ensuring the public health must include the outright ownership or lifetime support of the animals by the federal government. Because responsibility for long-term care is a major determinant of the cost of using chimpanzees, the committee believes that at least a minimum number of government-owned and-supported animals should be maintained for research and breeding. To reduce research costs and achieve the oversight required, it is recommended that ownership or lifetime care of selected animals, including those now owned by the DOD, be transferred to NIH. Management of their long-term support and use would be the responsibility of the ChiMP office.

Many animals requiring long-term management and care are owned by the government, others are supported but not owned by the government, and some of both of these categories were used in infectious disease research in the past and pose unknown health risks to humans. This committee recommends that ChiMP assume or retain ownership

or establish a mechanism to provide lifetime support of chimpanzees.

• Owned by NIH (excluding 99 in NIH breeding program)		341
• Owned by the US Air Force		135
• In NIH breeding program (including 99 owned by NIH)	538	
• That are breeding adults and offspring not in NIH program	35	
• That make up the total breeding population		573
• That were previously used in infectious disease protocols		350
• That are in research protocols or available for research		100
Total		1,499
• Privately owned, not expected to transfer to government		-500
• Recommended for ChiMP ownership or support		999

It is recommended that ChiMP assume ownership of life-time care of approximately 1,000 of these animals, as recommended in chapters 3 and 4. The committee derived the number 1,000 from two different calculations. In addition to the above listing, table 3.2 derives the same recommendation through categorization of population subgroups, excluding ownership. This number is thought to represent animals for which current owners would agree to transfer ownership or lifetime care to ChiMP. Approximately 500 animals distributed in all categories of the above listing are privately owned and used in nongovernment research. It is not recommended that ChiMP seek ownership of these animals. It should be noted that the figures are the best available to the committee but are not exact and that some categories overlap considerably. The data should be considered as general estimates to serve as guidance to ChiMP in managing the population. Current owners of selected animals should be provided with a one-time option to transfer ownership or responsibility for lifetime support to the government. Animals not transferred to the government under either scenario should remain the responsibility of the nongovernment owner.

A key question to be addressed by ChiMP is how many of the 1,000 animals designated for government ownership or life-time support might be removed to lower-cost facilities. On the basis of identification of the number needed for research use, the number needed for breeding to sustain this use, and the number considered to present a public health hazard, this figure can then be calculated. The determination will be based on the breeding model selected (e.g., the number of

animals needed in the breeding colony), the numbers needed for research, and the number that might present a public health threat. For example (using data from table 3.2 and breeding colony models in chapter 4):

Crisis Breeding Model	168
Now in research (e.g., "needed for research")	360
Potential public health threat	260
Total	788

Thus, 212 of the 1,000 animals might be released to public sanctuaries or other long-term care facilities. A different model with different assumptions and population sizes will have a different result. It is likely that careful review of those chimpanzees currently used in research and those considered infectious will reveal considerable overlap, and the number on active research will be considerably smaller. In addition, it should be recognized that animals considered to pose a public health threat might continue to be useful for research and be included in the number "needed for research" although they might be held in a lower-cost long-term care facility with experience in housing infectious chimpanzees and returned to research later. These details and the categorization of individual animals must be resolved by ChiMP before there can be a definitive response to the above question. If nongovernment sanctuaries become available, a substantial number of animals in each category might be designated as no longer needed for research or breeding and transferred to such facilities. Animals infected with agents that could pose a public health hazard or a risk for contamination of native chimpanzees (category D-3) require supervision by the ChiMP program and should be transferred to long-term care facilities that maintain existing NIH-supported chimpanzee colonies. They might be transferred to public facilities that have suitable experience in housing and handling such animals. The number of animals in D-3 underestimates the animals that pose a public health threat, in that it primarily includes animals used only in HIV and hepatitis infectious protocols.

In the aggregate, most of the remaining animals would serve as the breeding nucleus and research pool for use in biomedical research sponsored by the government. Other investigators, such as those in

pharmaceutical and biotechnology industries, should be encouraged to use animals from this pool at a cost determined by the ChiMP office. The additional revenues should be applied to the lifetime maintenance of animals in the NCR.

FINANCIAL SUPPORT OF THE NATIONAL CHIMPANZEE RESOURCE (NCR)

The committee recommends that ChiMP, in concert with the ChiMP Advisory Council, use this report as an aid in determining the short-term and long-term requirements for maintaining the NCR in ways that are consistent with the projected research needs and the long-term care of the animals. The costs for support of these animals can be met in part through appropriate payments from the various government agencies that support research with chimpanzees or for which maintenance of an adequate population of animals in readiness is essential. Several components of NIH, FDA, CDC, DOD and other agencies now use and fund research with chimpanzees although the responsibility for their long-term care and facilities has rested primarily with NIH. The current and long-term national need for chimpanzees in research might involve emergencies to which any agencies must respond. Therefore, the committee further recommends that

- Funding for chimpanzee facilities, maintenance, and long-term care be sought and directed to chimpanzee use jointly by NIH, DOD, FDA, and CDC.
- The agency responsible for coordinating chimpanzee budgets and procurements be NIH (or a suitable alternative that has the autonomy, infrastructure, and expertise to manage the program), which should delegate responsibility to ChiMP.

The committee foresees the need for congressional appropriations to provide full support for ChiMP, the facilities, and research to understand chimpanzee biology, management, and welfare better and emphasizes that these would be new funds—the current and future biomedical research base is already overextended. The committee does not view it

justifiable to expect the biomedical research community to bear the entire cost of the NCR when its existence is motivated by broader societal values, such as the demand for biomedical research and special ethical considerations for chimpanzees.

In the long term, one can expect that the improved coordination of the management of the entire US research chimpanzee population by the ChiMP office and its Advisory Council to result in a reduction in federal funds for supporting chimpanzees. In the short term, additional funds will be needed to maintain ChiMP and its Advisory Council, to institute ways to optimize efficiency of use of facilities and support services, and to meet housing standards recommended herein. The committee believes that these efforts will receive the support of the public, the animal protection community, and scientists who use chimpanzees in research, and it urges that the ChiMP office seek implementation of its recommendations through development of appropriate public and private partnerships.

PRIVATELY OWNED CHIMPANZEES IN BIOMEDICAL RESEARCH

Owners of privately owned research chimpanzees should be encouraged to include their animals in the ChiMP inventory because their numbers and availability will affect the demand for government-owned animals. Information on these chimpanzees should be considered in the evaluation of all requests for animals so that ChiMP can act as a clearinghouse to facilitate the most effective use of the entire US research chimpanzee population and so that ChiMP standards for care and housing can be disseminated to all chimpanzee colonies and institutions that use government-supported chimpanzees. The importance of privacy and confidentiality for industrial product development suggests that industry might prefer to use privately owned research chimpanzees as negotiated directly with holding institutions. However, requests for the use of government-owned chimpanzees by private industry should be considered and be accompanied by an appropriate use fee. Although it was suggested to the committee that private industry (e.g., pharmaceutical companies) might not contribute directly to the joint funding of the

NCR by government agencies, preferring instead to pay use fees as required for each study, the possibility should not be discounted. Privately owned animals could also be valuable to federally supported research if they fulfill requirements that cannot be met by the pool of government-owned animals; an example would be very young animals for studies with respiratory syncytial virus. As noted earlier, ChiMP must require strong scientific justification for government use of privately owned animals and be prepared for the short-term and long-term consequences related to the disposition of such animals. Even though ChiMP would not automatically become responsible for the lifetime care of these animals, it should anticipate the possibility of such responsibility if an infectious agent that poses a public-health threat is involved.

CHIMPANZEE SANCTUARIES

Sanctuaries and other long-term care facilities constitute a mechanism for removing surplus animals (defined as animals for which there is no current or projected need in research or breeding) from the core population needed to meet current and future research requirements. Sanctuaries offer an opportunity for substantially reducing costs of long-term maintenance of chimpanzees without compromising high standards of well-being. There are at least three scenarios for long-term maintenance of chimpanzees no longer needed for breeding and research: surplus animals could be permanently removed from the national resource pool and sent to sanctuaries, possibly national sanctuaries supported by a combination of congressional and private sources; they could be sent to existing private sanctuaries; and they could be maintained at US government-owned or government-supported chimpanzee facilities remodeled for cost-effective long-term housing. This committee enthusiastically supports the principal of retiring chimpanzees not needed for research or breeding to a low-cost, high-quality life. It does not recommend any of the three above alternatives over the others; each probably has a role in a strategy to enhance their welfare, and reduce the cost of maintaining them.

However, the committee strongly underscores the need for owners

to guarantee lifetime care of animals designated for retirement. Procedures for retirement of surplus animals must include a detailed evaluation of the financial stability of the sanctuary or long-term-care facility and an assessment of current or proposed animal-care programs. The ChiMP office should coordinate the transfer of all pertinent animal records between the donor and receiving facilities and oversee the legal transfer of ownership when government-owned animals are moved to sanctuaries. Creating standards for sanctuary and long-term-care facilities should be encouraged, and it should be recognized that high-quality care of chimpanzees can be achieved with standards less rigorous than those now used in biomedical facilities. The minimal standards are those of the Animal Welfare Act and those detailed in chapter 3. The committee strongly encourages the ChiMP office to be proactive in assisting with strategic planning, development, and maintenance of private sanctuaries. Careful planning and communication are needed to build a base of mutual respect in preparation for meetings with animal protectionist organizations.

THE NATIONAL CHIMPANZEE MANAGEMENT PROGRAM ADVISORY COUNCIL

In this report, the committee has assessed the present and future role of chimpanzees in biomedical and behavioral research, proposed guidelines for the long-term care of the captive-chimpanzee population with appropriate consideration of ethical and moral obligations, and recommended an operational structure that centralizes management of this national resource. The committee believes it to be an absolute necessity that appropriate and continuing oversight of such an enterprise be instituted. A national Advisory Council (AC), in concert with ChiMP, would provide continuity in the management of this valuable resource and ensure that quality care of the animals is maintained in a cost-effective and ethically acceptable manner.

CHARGE

The ChiMP AC should consist of representatives of the disciplines

discussed in this report. Its charge should be to oversee ChiMP's implementation of and adherence to this committee's recommendations, including ensuring that an adequate number of chimpanzees for use in biomedical research be maintained and housed in approved facilities where high-quality veterinary care and behavioral enrichment programs are provided as economically as possible. This charge could be facilitated by the establishment of continuing discussions with all institutions and facilities that house chimpanzees and the maintenance of a regularly updated census of animals being used or available for use in research protocols. It is hoped that non-government-supported facilities will comply voluntarily with recommendations and policies established by ChiMP and cooperate fully with ChiMP and the Advisory Council.

DUTIES

The duties of the proposed AC are in five categories: implementation, adherence, monitoring, reassessment, and recommendation. As indicated above, the first responsibility of the AC is to provide guidance to all facilities through ChiMP and ensure proper implementation of specific recommendations that are adopted. The AC should also promote a strategic plan for the use and breeding of chimpanzees and for periodic review of each facility.

Second, it should be the duty of the AC to ensure that all facilities that house government-owned or-supported chimpanzees or chimpanzees in studies supported by federal grants adhere to the policies and standards established in this report for the long-term care and use of chimpanzees in biomedical research. These policies and standards would apply to all facilities, irrespective of whether resident chimpanzees are being used for research or breeding or are "retired." To accomplish this goal, the AC should ensure an ongoing dialogue between ChiMP and all facility managers.

Third, to remain well informed about the numbers of animals both in use and available for use in research protocols, the AC should oversee the monitoring of the number of chimpanzees in each facility and the specific research in which they are or were used. Because a hierarchy of use has been established for different infectious agents (for example, chimpanzees are considered appropriate for entry into some

HIV-1 protocols only after completion of hepatitis studies), the knowledge gained through such monitoring would be important if a new infectious disease emerged that required the use of animals exposed to specific agents. Because of the need to maintain accurate census records at the national level and the fact that chimpanzees are considered an endangered species in their native habitats, a close liaison should be established with the International Species Information System (ISIS) or an equivalent. It would also be advantageous if the AC could obtain relevant demographic information from international facilities that house chimpanzees for research purposes, such as the Biomedical Primate Research Center in the Netherlands. Such information would assist in monitoring genetic diversity in the world's captive population.

Fourth, because of changing needs for chimpanzees in biomedical research, the AC should periodically reassess the recommendations made by the present committee and the initial strategic plans of ChiMP. The overall reassessment should be made at least once every two-three yr. Although we recommend that breeding of chimpanzees be stopped for the next five yr, this recommendation should be reevaluated annually to ensure that sufficient numbers will be available for up to 10-yr for continuing research programs or in case of a public health emergency. Any policy regarding euthanasia that is adopted or recommended should also be reviewed periodically.

Finally, on the basis of its periodic reassessments not only of the need for chimpanzees, but also of the plan to maintain the quality of their long-term care, the AC should advise and make new recommendations to ChiMP.

MEMBERSHIP

The AC should include persons with a wide range of expertise: colony management, veterinary medicine, reproductive biology, demography, population genetics, biomedical research, animal welfare, ethics, and chimpanzee health and behavior. The majority of AC members should not be federal employees. The AC might also include representatives of the privately supported facilities that house chimpanzees, such as members of their advisory boards. It should also include at

least one nonscientist and one member of the general public. The members of the AC should be appointed to serve for specified terms; new members should be appointed to replace others in such a way that continuity is ensured.

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APPENDIX A

MINORITY STATEMENT

BY
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A recommendation against the use of euthanasia for population control is envisioned as the philosophical basis for managing the US research chimpanzee population in the report on *Chimpanzees in Research: Strategies for Their Ethical Care, Management, and Use.* This recommendation has major financial implications which threaten the long-term viability of the research chimpanzee resource. The critical need for the continued maintenance of a national resource of chimpanzees for biomedical and behavioral research is clearly outlined in the report. The tremendous costs associated with maintaining this resource indicate that a mechanism for controlling population size is essential. Removal of animals no longer needed for breeding or research to privately funded sanctuaries is one such mechanism. The minority view is that euthanasia is also an appropriate strategy for maximizing the quality of life of the remaining population while facilitating the continued production of chimpanzees to fulfill critical needs in biomedical and behavioral research when faced with limited financial resources and lack of adequate alternative facilities.

The use of the chimpanzee as an animal model has been fundamental to many advances in human health. As outlined in chapter 2 of the document, recent developments pertaining to the control of hepatitis B were dependent in large part upon the use of chimpanzees in vaccine research. The continued threat of current and emerging infectious diseases

to public health highlights the importance of maintaining and perpetuating the chimpanzee resource in order to address critical needs in biomedical research. While the present population is sufficient to meet projected research needs over the next five years, if the resource is to be maintained in perpetuity a chimpanzee breeding program will have to be implemented in the future and will result in resumed growth of the population.

Continued breeding of chimpanzees to meet future research needs will necessarily result in further production of surplus animals (i.e., animals not needed for breeding or research programs) because of the practical inability to exactly match sex-specific production and death rates. Demographic and genetic management schemes based on projected demand should be used to minimize the size of the surplus population. However, research demand for chimpanzees is difficult to project accurately and management programs cannot be expected to completely prevent a surplus. Effective mechanisms for dealing with the current surplus animals, and the new surplus animals that will be generated if breeding for biomedical research is continued, are required.

Chimpanzees are expensive animal models, with direct cost per diem rates ranging between $15 (representing a breeding and maintenance facility with no requirements for extensive biohazard containment facilities or intensive research manipulations) and $30 (representing a facility with an active research program involving biohazardous agents). Dyke et al. (1996) have determined that the lifetime costs projected to be incurred for a single animal born in 1995 range between $113,430 and $226,860 for males depending upon the per diem rate, and between $160,860 and $321,710 for females because of their longer average life-span (Dyke et al., 1995).

These high costs apply to all chimpanzees maintained in a colony, including breeders, research animals, and surplus animals that have no potential utility for breeding or research. An alternative perspective on the costs of research with chimpanzees is given by evaluating all the colony costs that go into the production of each individual research chimpanzee. For example, the total cost of producing a naive research chimpanzee includes the costs both of maintaining that animal and of maintaining the breeders to produce the animal. This suggests that the

real cost of each research chimpanzee may be substantially higher than the individual life-time cost.

Chimpanzees are behaviorally complex, highly social animals and quality of life issues must be considered in the maintenance of these animals. Non-social housing in barren environments is considered unacceptable for chimpanzees, indicating that sufficient financial resources must be available to ensure adequate enrichment of both the social and physical environments.

The National Institutes of Health Chimpanzee Breeding and Research Program was developed to meet the national need for chimpanzees in biomedical and behavioral research. The breeding program has been highly successful, and there is now a large population of chimpanzees sufficient to meet current requests, and a perceived surplus of animals (i.e., animals with no current or projected utility for breeding or research). The financial resources for maintenance of these animals are ultimately limited and managers are faced with the choice of devoting funds to maintaining chimpanzees with no potential research value, or removing those animals from the colony and utilizing the funds for continued maintenance and production of high quality animal models to facilitate biomedical research with potential public health benefit. Even in the absence of breeding, managers with limited financial resources may have to choose between maintaining a large number of chimpanzees in minimally acceptable conditions which provide for the basic biological needs of the animals, or a smaller number of animals in more humane optimal conditions which allow for both the complex biological and social needs of this species.

Two approaches for managing surplus chimpanzees are compatible with the finite resources available and quality of life constraints. Animals may be moved to other more cost-effective sites, such as private sanctuaries or alternative housing at current facilities, providing sufficient resources are available to maintain an acceptable quality of life. It is not appropriate to use NIH funds in support of animals permanently transferred to private sanctuary housing since there is no potential return on research dollars invested in chimpanzees permanently removed from the research pool.

Alternatively, animals may be euthanized humanely as part of a responsible population management program. As outlined by Lacy

(1995) and Graham (1996) for zoo populations, euthanasia allows resources that would be used to preserve animals of limited value to be devoted to maintenance and propagation of valuable animals. In the zoo situation, animals that have already contributed substantially to the gene pool or who are old have little value in terms of species preservation goals and may be selectively culled. As Graham (1996) notes, this management approach emphasizing the targeting of resources to preservation of valuable animals, as opposed to animals with limited value for program goals, should be applicable regardless of whether or not the species is endangered. Selective euthanasia of surplus animals with no potential research or breeding value will free financial resources which can then be used to enhance animal well-being, quality, and research value in a long-term, self-sustaining research chimpanzee population resource. Just as the viability of the species rather than of individual animals is proposed as the primary motivation for management strategies in the zoo situation (Lacy, 1996; Graham, 1996), the long-term viability of the resource for addressing biomedical research needs should be the primary concern in the management of the US research chimpanzee population.

In summary, the minority view is that in the face of limited financial resources, euthanasia is an appropriate mechanism for maximizing the quality of life for the remaining chimpanzee population while facilitating the continued production of chimpanzees to fulfill critical needs in biomedical and behavioral research. It is recommended that an institution inform the NIH interagency animal models committee (or ChiMP office as recommended in this document) of intentions to euthanize chimpanzees and consider terminal collaborative research studies and/or tissue distribution in order to maximize the scientific value of each individual animal.

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