

Chimpanzees in Biomedical and Behavioral Research

Assessing the Necessity

CHIMPANZEES IN BIOMEDICAL AND BEHAVIORAL RESEARCH

ASSESSING THE NECESSITY

INSTITUTE OF MEDICINE AND NATIONAL RESEARCH COUNCIL OF THE NATIONAL ACADEMIES

For many years, experiments using chimpanzees have been instrumental in advancing scientific knowledge and have led to new medicines to prevent and treat life-threatening and debilitating diseases. However, recent advances in alternate research tools, including cell-based technologies and other animal models, have rendered chimpanzees largely unnecessary as research subjects.

Over the past decade, the National Institutes of Health (NIH) has financed the largest amount of federal research involving chimpanzees. A 2010 announcement that the NIH intended to consolidate chimpanzee colonies, saving an estimated \$2 million annually, generated significant feedback from the public, state officials, and members of Congress, and raised questions about the necessity for chimpanzees in biomedical and behavioral research.

At the request of the NIH and in response to congressional inquiry, the Institute of Medicine, in collaboration with the National Research Council, conducted an in-depth analysis of the scientific necessity of chimpanzees for NIH-funded biomedical and behavioral research.

A committee evaluated ongoing biomedical research to determine whether chimpanzees are necessary for research discoveries and to gauge the safety and efficacy of new medicines. In addition, the committee was asked to explore contemporary and anticipated behavioral research questions to determine if chimpanzees are necessary for progress in understanding social, neurological, and behavioral factors that influence the development, prevention, or treatment of disease. The committee was asked to describe chimpanzees' unique attributes in order to determine when to use chimpanzees in biomedical and behavioral research.

The committee's report, *Chimpanzees in Biomedical and Behavioral Research: Assessing the Necessity*, does not endorse an outright ban on chim-

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panzee research. Rather, it establishes a set of uniform, though restrictive, criteria to guide current and future research use of chimpanzees to treat, prevent or control public health challenges.

Applying Guiding Principles

The committee's conclusions were heavily influenced by advances in non-chimpanzee models, such as genetically modified mice, clinical trials involving human volunteers, studies that can be done in an artificial environment outside of the living body, and technologies that leverage computer software or computer simulations.

Each NIH-supported center where chimpanzee research is performed has its own procedures to evaluate requests to use chimpanzees in studies. In the absence of uniform criteria, the committee developed three principles to assess research on chimpanzees.

1. The knowledge gained must be necessary to advance the public's health;
2. There must be no other research model by which the knowledge could be obtained, and the research cannot be ethically performed on human subjects; and
3. The animals used in the proposed research must be maintained either in ethologically appropriate physical and social environments or in natural habitats.

These principles were used to develop criteria to guide the use of chimpanzees in biomedical and behavioral research (see Box).

Past Use Fails to Predict Future Necessity of Chimpanzee Research

To illustrate how the committee's criteria could be applied to existing research using chimpanzees, various case studies were examined, including:

- 1. Monoclonal Antibodies:** For more than a decade, researchers have relied upon chimpanzees to produce and test monoclonal anti-

BOX: Criteria to Guide the Assessment of the Necessity of Chimpanzee Use in Research

Biomedical Research Criteria:

The use of chimpanzees in biomedical research is limited to those studies that meet the following three criteria:

1. There is no other suitable model available, such as in vitro, non-human in vivo, or other models, for the research in question, and
2. The research in question cannot be performed ethically on human subjects, and
3. Forgoing the use of chimpanzees for the research in question will significantly slow or prevent important advancements to prevent, control and/or treat life-threatening or debilitating conditions.

Animals used in the proposed research must either be maintained in ethologically appropriate physical and social environments or in natural habitats. Biomedical research utilizing existing samples is exempt from these criteria.

Comparative Genomics and Behavioral Research Criteria:

The use of chimpanzees in comparative genomics and behavioral research is limited to those studies that meet the following two criteria:

1. Studies provide otherwise unattainable insight into comparative genomics, normal and abnormal behavior, mental health, emotion, or cognition, and
2. All experiments are performed on acquiescent animals, using techniques that are minimally invasive, and in a manner that minimizes pain and distress.

Animals used in the proposed research must either be maintained in ethologically appropriate physical and social environments or in natural habitats. Comparative genomics and behavioral research utilizing existing samples are exempt from these criteria.

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bodies—which bind to a specific location on a molecule, permitting, for instance, precise targeting and neutralization of viruses and bacteria. New methods, such as recombinant technologies, can replace the chimpanzee in these efforts. While laboratories adopt these alternate approaches, therapies in development may require continued use of chimpanzees to avoid stalling progress and delaying patients' access to needed treatments. These cases should be assessed to ensure that they meet the criteria outlined in this report, and NIH should continue to support the development of and access to alternatives.

2. Hepatitis C: More than 3.2 million Americans are chronically infected with hepatitis C virus (HCV), and HCV infection has become the most common cause of liver failure and transplantation. Only chimpanzees and humans are susceptible to HCV infection, and no other suitable animal models exist to test a prophylactic, or preventive, vaccine.

The committee did not reach consensus on whether chimpanzees are necessary to the development of a preventive HCV vaccine or how much use of chimpanzees would accelerate or improve this work. The committee agreed that it would be possible and ethical to test a prophylactic vaccine in humans without prior testing in chimpanzees, provided it was first shown to be safe in other animals. However, the committee was split on whether use of chimpanzees is required to rule out can-

didate products with lesser potential before costly and time-consuming human clinical trials or whether such testing would provide otherwise unattainable information on the safety of candidate vaccines.

Research to develop a therapeutic vaccine for people already infected with HCV to boost their immune systems' ability to clear the virus, and antiviral drugs for patients with chronic HCV infection can be performed without use of chimpanzees.

3. Cognition: Humans use “joint attention,” a communication style that combines gestures with speech, to alert others about an object of interest, such as pointing at and cheering on a baseball player. Researchers wondered whether the same areas of chimpanzees' complex brains are used during joint attention as is the case for humans. They gave chimpanzees a drink containing a radioisotope, and placed a favored food out of reach. PET scans of the chimpanzees' brains provided the first direct evidence that regions of the brain used by chimpanzees in joint attention communication were similar to that in humans. The committee concluded that the techniques used in such research were comparable to those experienced by chimpanzees in a complete veterinary exam. Because of chimpanzees' unique contribution to insight into human communication, the small number of animals involved, and the temporary removal of research chimpanzees from their social groups, this study could meet all of the committee's criteria.



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Conclusion

Of the many animals used in research, the chimpanzee's genetic proximity to humans and the resulting biological and behavioral characteristics make it a uniquely valuable species for certain types of research, but also raise distinct ethical issues. The committee's considerations were suffused with an awareness of the moral cost of such research, which resulted in the heightened justification the committee required to support the necessity of chimpanzee research in specific areas of research it assessed.

The committee concludes that while the chimpanzee has been a valuable animal model in the past, most current biomedical research use of chimpanzees is not necessary. Notable exceptions include prophylactic HCV vaccine development, short-term continued use for monoclonal antibody research, comparative genomics research, and behavioral research. Overall, the committee notes that the present trajectory of scientific research indicates a decreasing need for the use of chimpanzees due to the emergence of non-chimpanzee models. The committee recognizes how disruptive an immediate outright ban would be, affecting animal care and potentially causing unacceptable losses to the public's health. What's more, chimpanzees may prove uniquely important to unraveling the mystery of diseases that are unknown today. While the committee was not asked to provide guidance on implementation, it encourages the NIH to establish an independent oversight committee with broad medical expertise to apply the new criteria in research that might include chimpanzees. 

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