Chimpanzee Research Use Form Guidance

Project Summary/Abstract, Specific Aims, and Public Health Relevance

A project summary or abstract summarizes the proposed research activity. It should be a self-contained description of the project and should contain a statement of objectives and methods to be employed. It should be informative to other persons working in the same or related fields and insofar as possible understandable to a scientifically or technically literate lay reader.

Specific aims provides the research with the broad, long-term objectives and the goal of the specific research proposed, for example, to test a stated hypothesis, create a novel design, solve a specific problem, challenge an existing paradigm or clinical practice, address a critical barrier to progress in the field, or develop new technology.

Public health relevance describes the relevance of this research to public health. In this section, be succinct and use plain language that can be understood by a general, lay audience.

Exemption Determination

The following types of research involving chimpanzees or chimpanzee biomaterials are exempt from CRUP consideration:

- The use of any biomaterials, including pathological specimens, collected and/or stored prior to submission of the research application, proposal, or protocol, as part of a research project that has undergone CRUP consideration and subsequent NIH approval, or as part of regular veterinary (health) examinations; (Exempt under this criteria include research projects using samples or other biomaterials collected and/or stored as part of research projects that were previously approved by the NIH as part of consideration by the Council of Councils and the Working Group on the Use of Chimpanzees in NIH-Supported Research.)
- Other observational or non-interventional studies, such as behavioral observations in the wild that do not result in contact or otherwise interfere with the chimpanzees being observed; or (This includes noninvasive collection of samples from captive chimpanzees in a manner that does not result in contact or otherwise interfere with the chimpanzees during the collection.)
- Noninvasive collection of samples from the wild in a manner that does not result in contact or otherwise interfere with the chimpanzees during the collection." (Examples include collection of fecal samples from the wild.)

Option A: Exempt from CRUP Consideration

If the organization believes the entire research project meets the criteria above, select this option and provide sufficient detail about the proposed research to allow NIH to verify this designation. It the agency agrees with your designation, then the proposed research need not be considered by the CRUP

Option B: Subject to CRUP Consideration

If the proposed research in whole or in part, does not meet the exempt criteria above, select this option and fill out the CRU Justification tab for consideration by the CRUP.

Benefits Chimpanzees or Humans

Indicate if the proposed research is primarily for the benefit of chimpanzees or humans.

If Chimpanzees

Explain in the space provided how the research is in the best interest of chimpanzees AND addresses the mission of the NIH.

For defining animal well-being, the NIH refers applicants and offerors and the CRUP to an overview of this topic in the National Research Council's publication: *Recognition and Alleviation of Distress in Laboratory Animals*. Refer to page 17, 'Implications for Animal Welfare'. In addition, the World Organization for Animal Health (OIE) in its Terrestrial Animal Health Code provides a concise definition of animal welfare in Chapter 7.1., Introduction to the Recommendations for Animal Welfare, Article 7.1.1.

The response must also indicate how the research addresses the mission of the NIH. If applicable, the CRUP may consider the argument that research that assures the continued well-being and availability of the chimpanzee animal model could meet NIH's mission.

Item 1 – Not Ethical with Humans

Explain why the research in question cannot be performed ethically on human subjects with the prospect of achieving comparable results.

The CRUP is asked to consider whether the research can be performed ethically on human subjects. It is not asked to consider the ethics of involving chimpanzees in the research protocol or whether the research is "more ethical" in chimpanzees than in humans. The applicant's or offeror's task is to explain why the research cannot be done ethically on human subjects.

The IOM Report provides a discussion titled "*Assessing Whether the Research Can Be Performed on Human Subjects*" on page 32 and then applies these criteria to chimpanzee research in the pages that follow. The CRUP may use this resource in considering the applicant's or offeror's response.

Studies in comparative genomics that propose the use of chimpanzees will be considered. The conclusions and recommendations of the IOM Report (page 4-5) acknowledge that using the chimpanzee may be necessary because of the genetic proximity of chimpanzees to humans.

Additionally, the CRUP may consider the following questions as they discuss the applicant's or offeror's response. Applicants or offerors may wish to address some, or all of these questions or address other considerations in their response.

Potential Research Harms to Humans

1. Has the research or similar research been conducted in consenting human subjects previously?
2. What are the anticipated side effects or adverse effects of the research or investigational agent?
3. Based on what is known about the experimental methods, could the anticipated harms to human subjects (e.g., side effects) be considered acceptable?
4. Based on what is known about the experimental methods or the investigational agent, could the likelihood of unknown harms of the research be low enough to make the research acceptable in human subjects?
5. Does the experimental method rely on challenge studies (e.g., prophylactic HCV vaccine studies), such that large numbers of human subjects would need to be exposed to assess immunity?

Benefits (direct and indirect)

1. Have the potential benefits to the direct human subjects been considered?
2. Have the psychological benefits to the human subject been considered?

Consent

1. Could a human subject understand the research implications and harms and provide informed consent?
2. Are there psychological benefits from participating as a research subject that could compensate for the burden/stress on human subjects?
3. In the case of certain vulnerable populations for which consent is not possible (e.g., children), could assent be provided in cases where risk is low and/or there is significant chance for benefit?

Item 2 – Alternate Models

Explain why other suitable models are not available (such as in vitro, nonhuman in vivo, or other models).

Alternative animal models (e.g., mice, rats, hamsters, guinea pigs, and other nonhuman primates), culture cell and tissue model and nonvital models may increasingly replace the use of chimpanzees as these alternative models become more scientific valid and available. The continued advancement of the alternative models raises the scientific bar for justifying the use of chimpanzees in research. The applicant or offeror must provide a thorough explanation of why other models cannot meet the research need. In the IOM Report (beginning on p. 35), the committee provided specific criteria for deselecting other suitable models for certain types of research. The CRUP may use this resource in considering the applicant's or offeror's response.

Item 3 – Forgoing Chimpanzee Use

Explain why forgoing the use of chimpanzees for the research in question will significantly slow or prevent important advancements in genomics; evolutionary theory; human behavioral, cognition, or emotions research; or important advances in the prevention or treatment of life-threatening or debilitating human conditions.

NIH understands that other, suitable animal models may be available for certain diseases and conditions currently studied in chimpanzees. However, the agency also recognizes that suitable alternative models may not yet be fully available or sufficiently validated to study other diseases and conditions and using such models may not provide valid scientific results or may significantly slow the pace of progress in achieving the aims of the research. NIH understands that certain, alternative animal models may be deselected if foregoing the use of chimpanzees will significantly slow or prevent important advancements to treat potentially life threatening conditions. The IOM Report provides a discussion titled "*Assessing Advancements to Treat Potentially Life-Threatening or Debilitating Conditions*" and "*Assessing the Objectives of the Project*" on pages 32-34 and then applies these criteria to certain types of research summarized in the following pages under the subtitle "Criteria 3: Impact of Forgoing Chimpanzee Use". The CRUP may use this resource in considering the applicant's or offeror's response.

Item 4 – Limit Burden

Explain how the physical, psychological, and emotional burdens on the chimpanzees will be limited by:

- minimizing the number of chimpanzees used, the duration of the experiment and the discomfort of the procedures, and
- performing the work on acquiescent chimpanzees that have been trained to present for blood draws or anesthesia or to participate in the research and can do so voluntarily.

Limit Burden addresses the extent to which severity and duration of potential harm to chimpanzees will be limited. For additional information, the NIH refers the applicants and offerors to relevant discussions in the *Guide for the Care and Use of Laboratory Animals* (NRC 2011), especially "The Three Rs" approach (Replacement, Refinement, and Reduction) to laboratory animal research beginning on page 4, and the discussion of "*Experimental and Humane Endpoints*" beginning on page 27.

Item 5 – Benefit vs. Burden

Explain how the remaining physical, psychological, and emotional burdens on the chimpanzees are outweighed by the possible benefits to humankind and to science.

Applicants and offerors should address the knowledge the research study is designed to generate and the likelihood that this information will lead to 1) an improvement in human health, or 2) otherwise contribute substantially to science. Doing so may be particularly challenging for basic science research, such as genomic or evolutionary research, whose aim may be to produce general knowledge with unclear, predictable value to public health. For this reason, applicants and offerors may wish to focus

the benefits of basic research on whether the research will lead to otherwise unattainable insight (see Forgoing Chimpanzee Use item above).

For more information, the NIH refers the applicant or offeror and the CRUP to the relevant discussions in the *Guide for the Care and Use of Laboratory Animals* (NRC 2011), especially "The Three Rs" approach (Replacement, Refinement, and Reduction) to laboratory animal research beginning on page 4.

Item 6 – Number of Chimpanzees

Demonstrate that the number of chimpanzees proposed is statistically or scientifically justified

The applicant or offeror must show that the number of chimpanzees proposed for a study is sufficient to yield meaningful results. Mathematical calculations, often described as statistical power analyses, are commonly used to ensure that studies include enough test subjects to provide confidence that the observed results would not have occurred by chance. However, the NIH wishes to prevent the use of more chimpanzees than are needed for a study. The NIH is willing to consider applications, proposals, and protocols for research that request to use fewer chimpanzees than the statistically justified number if doing so can appropriately meet the scientific need.

With respect to statistical justification:

- The number of chimpanzees (sample size) should be sufficient to yield high statistical power
    - Minimum of 80%
    - Preferably at least 90%
    - Power substantially higher than 90% may be undesirable, resulting in the use of too many chimpanzees (overpowered study)
- Statistical power depends on
    - Size of the treatment effect to be detected (power increases with size)
        - Size of the effect to be detected is specified by the applicant or offeror and must satisfy two criteria
            - It must be large enough to be of scientific interest
            - It must not be so large that its feasibility is questionable
    - Variation in the estimate of the treatment effect from observing response with and without treatment (power decreases with variation)
        - Variation in the estimate of the treatment effect depends on
            - Variation in the response difference with and without treatment (variation in effect estimate increases with variation in response difference)
                - Lowered by using a chimpanzee as its own control or a similar chimpanzee as control (matching)
            - Sample size (variation in effect estimate decreases with sample size, thereby increasing statistical power)

With respect to scientific justification:

To the greatest extent possible, applicants and offerors should ensure that the research is designed with sufficient statistical power to provide confirmation that observed results did not occur by chance. There,

however, may be scientifically justifiable occasions to use fewer chimpanzees (resulting in an underpowered study) or more chimpanzees (an overpowered study). Scientific proposals that seek to perform discovery research on an unknown/new disease occurring in a chimpanzee in a "case study" manner are an example of research that may involve low numbers of chimpanzees. Overpowered research may be justified if, for example, the study focuses on chimpanzee colonies. In these cases, it may be safer for the chimpanzees and caretakers and less disruptive to chimpanzee colonies to study more animals than needed.

Ethologically Appropriate Facility

Indicate the possible facility or facilities where the chimpanzee(s) will be maintained.

Indicate the facility(ies) that will be used to house the chimpanzee(s) for the duration of the experiment from this list of facilities. NIH has determined that these facilities meet, or have a satisfactory plan to meet, the characteristics of an ethologically appropriate environment.

If the facility you intend to use is not on the list, then write it in the space provided. The write-in space allows enough room to indicate multiple facilities, if appropriate. The NIH will assess whether chimpanzee facilities satisfy the characteristics of an ethologically appropriate environment.

Sample Letter for the Signature of the Signing Official for Certification and Assurance Required for Chimpanzee Research Use Form.

[Letter must be signed by the Signing Official (Authorized Organizational Representative) and be on institutional letterhead]

Date:

National Institutes of Health:

I hereby certify that the statements on the Chimpanzee Research Use Form, submitted by *[insert name of individual submitting request to NIH]*, and below, are true, complete, and accurate to the best of my knowledge.

In particular, I certify that: (check all boxes)

- ☐ When the submitter selects the "Submit" button, the system will perform a final verification check that may require the organization to respond to any areas deemed to be incomplete. After submission is successful, I will receive a "Submission Received on [Date]" verification screen showing the date and time NIH received it.
- ☐ The statements herein are true, complete, and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.
- ☐ The information provided herein is materially consistent with the research methods proposed in the grant application, contract proposal, intramural protocol, or 3rd party research protocol to which this information supports.
- ☐ I am the Signing Official with all rights, authority, and responsibilities appropriate to that role for the organization provided above. As the Signing Official, I am the individual, named by the applicant or offeror organization, who is authorized to act for the applicant or offeror and to assume the obligations imposed by applicable Federal laws, regulations, requirements, and conditions.
- ☐ The applicant or offeror gives permission for the NIH to share its contents with the CRUP and the NIH Council of Councils. In addition, the applicant or offeror gives permission for NIH staff and contractors to use the information for administrative purposes, such as reviewing materials for completeness, routing materials to the CRUP and the Council of Councils, and managing subsequent steps related to discussions of the CRUP and the Council of Councils.

If the organization indicated that the proposed research is exempt from CRUP consideration as defined herein, I understand that NIH will consider the submitted information to validate that determination. If the NIH disagrees with the organization's assessment that the research is exempt from CRUP review,

NIH will return this form to us to provide additional information about the research. I acknowledge that a form returned to the organization for this reason may delay further consideration by NIH.

If the proposed research is subject to CRUP consideration as defined herein, I understand that the information submitted through this form will be used by the CRUP and the Council of Councils to consider whether the use of chimpanzees in the proposed research satisfies interim agency policy on the use of chimpanzees in research. After the CRUP considers the Required Information, it will inform the Council of Councils of its deliberations. The Council of Councils will consider the CRUP's input and recommend to NIH whether the research satisfies the interim agency policy. The NIH will consider the Council's recommendation when making a funding decision about the research or allows the research to proceed. **There is no process to appeal the recommendation from the Council of Councils or the CRUP.**

[Name and Signature of Signing Official and Date]