

NIH POLICY MANUAL

3044-1 – Nonhuman Primate Quarantine

Issuing Office: OD/OM/ORS/DVR (301) 402-9862

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1. Explanation of Material Transmitted:

This chapter updates NIH policies and procedures for quarantine of nonhuman primates to be used in the NIH Intramural Research Program. Revisions to this chapter include changes in operational policies and procedures, incorporation of former Appendices 1-3 into the main text of the chapter and updates Records Retention and Disposal language.

2. Filing Instructions:

Remove: NIH Manual 3044-1 dated 10/06/03

Insert: NIH Manual 3044-1 dated 4/8/2008

PLEASE NOTE: For information on:

- Content of this chapter, contact the issuing office listed above.
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A. Purpose

This chapter updates, based on changes in operational policies, the responsibilities and procedures for the quarantine of nonhuman primates received from facilities outside of the NIH and for research use within the NIH Intramural Research Program.

B. Background

The Division of Veterinary Resources (DVR), Office of Research Services (ORS) contributes to the advancement of NIH research through the application of laboratory animal sciences by providing consultative and collaborative interaction with NIH intramural researchers in the provision of professional and technical support services related to the care and use of animals. Support services include the provision and care of research animals and providing disease control and diagnostic services. Nonhuman primates are quarantined in Building 103 of the NIH Animal Center (NIHAC), NIH Primate Quarantine Facility (NPQF) located in Poolesville, Maryland. The NIH-managed animal facilities operated outside of Maryland may quarantine nonhuman primates at their facilities.

C. Policy

DVR and each NIH Institute and Center (IC) that uses nonhuman primates shall be responsible within its respective area for ensuring compliance with the procedures outlined in this policy. This policy applies to all NIH operated animal programs. The NIH-managed programs operated outside the State of Maryland may quarantine and necropsy nonhuman primates at their facilities, but they must adopt procedures consistent with this policy. Agencies that lease space from NIH operated animal programs must comply with this policy.

D. References

1. 9 CFR 1.1 Subchapter A, Animal Welfare.
http://a257.g.akamaitech.net/7/257/2422/14mar20010800/edocket.access.gpo.gov/cfr_2003/pdf/9cfr1.1.pdf
2. Center for Disease Control and Prevention (CDC). Oct., 1991. Update: Nonhuman primate importation: modified special permit requirements for importation and quarantine of nonhuman primates. MMWR.
<http://www.cdc.gov/MMWR/preview/mmwrhtml/00015309.htm>

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3. NIH Manual Chapter 3044-2, Protection of NIH Personnel Who Work with Nonhuman Primates.
<http://www1.od.nih.gov/oma/manualchapters/intramural/3044-2/>
4. The Guide for the Care and Use of Laboratory Animals. National Research Council (NRC) 1996, 58-60. <http://www.nap.edu/readingroom/books/labrats/>
5. "Guidelines for the Prevention and Control of Tuberculosis in Nonhuman Primates in the NIH Intramural Program" NIH ARAC Guidelines 2007.
<http://oacu.od.nih.gov/ARAC/TBPrevCont.pdf>
6. NIH Manual Chapter 1743, "Keeping and Destroying Records," Appendix 1, NIH Records Control Schedule:
<http://www1.od.nih.gov/oma/manualchapters/management/1743/>
7. 42 CFR 71.53. <http://www.cdc.gov/ncidod/dq/pdf/42cfr71.pdf>

E. Procedures**1. Procurement**

To place an order or to otherwise have nonhuman primates quarantined at the NIHAC, the IC Animal Program Director (IC APD) or designee shall submit a completed form NIH 79-3 (Rev. 10/90) [NIH Centralized Animal Order Request](#) or equivalent to their IC and/or the administrative officer for review and approval. The form will then be submitted to the DVR Facility Management Branch, located in Building 103. A copy of an approved Animal Study Proposal will also be provided or on be on file with the DVR Facility Management Branch.

The specifications of the animals to be procured must be completely and accurately described. The procurement of nonhuman primates must also comply with USDA regulations and CDC requirements. (See D. References #1 and #2) DVR will contact the IC APD if additional information is required or the request is incomplete or not approved.

Whenever possible, nonhuman primates shall be obtained from domestic source breeding and conditioning programs, shall be obtained from sources that hold a Public Health Service Animal Welfare Assurance and/or are accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC), International. When appropriate DVR staff will make site visits to suppliers to evaluate their ability to meet NIH requirements.

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2. Entry Requirements

All nonhuman primates shall have a history of negative tuberculin skin tests (TSTs). At least three TSTs shall be performed, not less than two weeks apart, and one of the tests within 30 days prior to shipment. The Chief, NPQF at the request of the IC APD or their designee may decrease the number of TSTs to two tests, performed not less than two weeks apart and one of the tests within 30 days prior to shipment, for animals obtained from NIH-owned, closed colonies. The supplier shall provide a complete copy of all procured animals' health records, including the origin and date of birth, if known.

Unless waived by the IC APD or their designee, nonhuman primates shall not have been subjected to experimental use. Additionally, unless waived by the IC APD or their designee, macaques shall be culture or PCR negative and seronegative for SRV-1 and SRV-2, and seronegative for B virus, SIV and STL V-1. Evidence of freedom from other pathogens may also be requested by the IC APD or by the Chief, NPQF. Animals should not be accepted from registered importers who are experiencing reportable diseases (See Section E. Procedures #5 Reportable Diseases) or significant losses of animals.

All nonhuman primates shall be checked upon arrival to ensure they meet the order requirements. Animals judged healthy, based on a review of their health records, a physical examination, and subsequent laboratory and TST tests, shall be accepted. Animals judged to be unacceptable shall be returned to the supplier, euthanized or treated in accordance with USDA regulations (See section D. References #1) after the Chief, NPQF consults with the involved IC APD and the supplier.

Nonhuman primates released to non-NIH facilities may not be returned to NIH facilities without a full quarantine unless waived by the Chief, NPQF in consultation with the IC APD or their designee.

Nonhuman primates will be vaccinated against rubeola virus using Attenuvax (Merck & Co., Inc.) or equivalent. Vaccination may be waived by the IC APD or designee or approved Animal Study Proposal if supported by a scientific justification.

3. Quarantine Requirements

a. Quarantine and Stabilization

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Quarantine and stabilization shall be conducted in a manner that complies with The Guide for the Care and Use of Laboratory Animals, National Research Council (See D. References #4). It shall provide sufficient time for acclimation, evaluation of animal health, and expression of diseases. Animals are normally individually housed during quarantine. A variance may be approved by the Chief, NPQF for pair housing.

Offspring born to animals already in existing NIH colonies are exempt from these quarantine procedures provided that the mothers are not in quarantine at the time of the birth.

Groups of nonhuman primates in quarantine shall be maintained separately from other nonhuman primates. Cohorts should be separated by source, geographic origin, date of arrival, and presumptive health status. If different nonhuman primate groups are maintained in the same room, the quarantine period shall begin on the date the last group was placed in the room. Involved investigators and IC APDs shall be notified before cohorts are combined.

Ninety calendar days is the standard length of quarantine for newly acquired African Green monkeys, macaques and chimpanzees. Sixty calendar days is the standard for baboons, patas monkeys, and New World primates. The history of the quarantined animals and the source may be considered when any variation in the length of quarantine is being determined.

Extension of quarantine may be appropriate for nonhuman primates with incomplete histories and cohorts that develop disease during quarantine. Quarantine shall be reinstated, or the affected nonhuman primates euthanized when diseases that pose a threat to the nonhuman primate colony or to humans are detected.

Procedures shall include a TST using a USDA licensed and approved mammalian tuberculin administered 14 days apart in alternate eyelids. New World species, patas monkeys and baboons must have a minimum of three consecutive negative results. Macaques and African Greens must have five consecutive negative results. For quarantined chimpanzees, the last two TSTs shall be administered a month apart.

Test sites shall be examined 24, 48, and 72 hours after administration of mammalian tuberculin. The TST results must be recorded using the California scoring system. Refer to the Guidelines for the Prevention and Control of

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Tuberculosis in Nonhuman Primates in the NIH Intramural Program, (See Section D. Reference #5) for monitoring procedures, husbandry practices and procedures for handling tuberculous nonhuman primates and continued testing of cohorts. Weights shall be recorded with the TSTs.

Quarantined nonhuman primates shall have CBC, chemistry, and virus profiles (See Appendix 1) submitted to an appropriate reference laboratory within the first 35 days of quarantine. Virus profiles will be at the discretion of the IC APD, but if animals are not tested, then post-quarantine holding will reflect the unknown viral status. The attending veterinarian may perform other diagnostic procedures when indicated. Those animals harboring pathogens shall be rejected or treated after consultation with the involved IC APD or designee and the supplier.

After an initial acclimation period of 14 days, investigators may request that Animal Study Proposal approved procedures such as feeding of special diets and blood collections can be performed. These procedures must be approved by the Chief, NPQF. Nonhuman primates will receive a behavior assessment during routine quarantine.

After a quarantined group of nonhuman primates has completed the last tuberculin test with all negative results, seronegative or unknown animals shall be vaccinated against rubeola virus (Attenuvax - Merck & Co., Inc., or equivalent) unless the IC APD or designee or approved Animal Study Proposal requires rubeola naive animals with scientific justification. Such animals shall be quarantined separately with appropriate quarantine measures to guard against exposure to rubeola.

b. Necropsy

All nonhuman primates that die for any reason including euthanasia will be necropsied by the Pathology Section, Diagnostic and Research Services Branch, DVR, ORS. If there is a need, for research reasons, to have a nonhuman primate necropsied at a collaborating institution, a complete necropsy is to be performed by a veterinary pathologist and a copy of the findings are to be sent to the Chief, Pathology Section, Diagnostic and Research Services Branch, DVR, ORS located at 28A Service Road West, Room 115, Bethesda, MD 20892-5230. These necropsies may be performed by other qualified veterinarians at NIH operated facilities that are outside the State of Maryland, including but not limited to NIAID Rocky Mountain Laboratories in Montana and the NIEHS Research Triangle Park, North Carolina.

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c. Tuberculosis Treatment and Isolation

Animals confirmed positive for *M. tuberculosis* complex disease should be immediately euthanized after consultation between the IC APD and the Chief, NPQF. The euthanasia of a tuberculous nonhuman primate can be delayed if the animal is of great value to a research project and can be isolated to minimize the spread of tubercle bacilli to other nonhuman primates and humans. If euthanasia is delayed for the purpose of continuing a research study or for treatment, then the Director, Division of Occupational Health and Safety (DOHS), ORS and the owning IC's APD and Animal Care and Use Committee will be notified. The DOHS will review and approve the containment requirements for the animal. Normally, nonhuman primates shall not be treated for *M. tuberculosis* complex disease. If an animal is treated, an Animal Study Proposal approved by the user IC's Animal Care and Use Committee and the Institutional Biosafety Committee is also required. A multiple drug regimen based on the most current practice standard must be used and the treatment must be for a period of at least 6 months.

d. Husbandry

Only designated facility personnel shall be permitted in quarantine rooms. Personnel shall comply with NIH Manual Chapter 3044-2, Protection of NIH Personnel Who Work with Nonhuman Primates (See D. References #3), and applicable guidelines for the prevention and control of tuberculosis in nonhuman primates at the NIH.

e. Enrichment

Nonhuman primates shall be provided toys, novel food treats, and visual contact during quarantine in compliance with USDA regulations (See D. References #1). They shall not be group housed during quarantine unless a waiver has been issued by the Chief, NPQF.

4. Variance to Standard Quarantine**a. Variance**

The Chief, NPQF and the IC APD may agree to modify quarantine when the circumstances support it and if the IC APD requests a variance. If the Chief, NPQF denies the request, or if the Chief, NPQF and the IC APD cannot agree on

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the terms of the NIH policy variance, then the IC APD may refer the matter to the Director, DVR, ORS. Normally, a variance to quarantine is only issued for conducting quarantine in a location other than at the NPQF.

b. Waivers

Quarantine shall not be waived.

5. Reportable Diseases

Registered importers must maintain records on each shipment of imported nonhuman primates received. Registered importers must notify the Center for Disease Control and Prevention (CDC), Division of Global Migration and Quarantine by phone at (404) 498-1600 within 24 hours of the occurrence of any illness in nonhuman primates that is suspected of being yellow fever, monkeypox, or hemorrhagic fever (Marburg/Ebola). In addition, if mortality for a shipment exceeds five percent, the importer must immediately report the circumstances, including cause(s) of death to CDC. Requirements for the importation of nonhuman primates are established by Federal regulation, 42 CFR 71.53.

F. Records Retention and Disposal

Records Retention and Disposal: All records (e-mail and non-e-mail) pertaining to this chapter must be retained and disposed of under the authority of the NIH Manual Chapter 1743, "Keeping and Destroying Records," Appendix 1, NIH Records Control Schedule, Section 3000 Intramural Activities, C. Veterinary Services (and any other item in 3000 that applies), Section 7000 - PART 4 Protection from Biohazards, Contaminants, Pollutants and Research Risks, A. Protection of Research Subjects, and Section 1300 Station Management (all items that apply).

NIH e-mail messages: NIH e-mail messages (messages, including attachments, that are created on the NIH computer systems or transmitted over the NIH networks) that are evidence of the activities of the agency or have informational value are considered Federal records. These records must be maintained in accordance with current NIH Records Management guidelines. Contact your IC Records Officer for additional information.

All e-mail messages are considered Government property, and if requested for a legitimate Government purpose, must be provided to the requester. Employees' supervisors, the NIH staff conducting official reviews or investigations, and the Office of Inspector General may request access to or copies of the e-mail messages.

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E-mail messages must also be provided to the Congressional Oversight Committees, if requested, and are subject to the Freedom of Information Act requests. Since most e-mail systems have back-up files that are retained for significant periods of time, e-mail messages and attachments are likely to be retrievable from a back-up file after they have been deleted from an individual's computer. The back-up files are subject to the same requests as the original messages.

G. Management Controls

(1) Office responsible for Reviewing Management controls relative to this chapter: Through this manual issuance, the Division of Veterinary Resources, Office of Research Services is responsible for ensuring that management controls are implemented and working.

(2) Frequency of Review (in years): Ongoing.

(3) Method of Review: DVR will maintain oversight and ensure effective implementation and compliance with this policy. The NIH must make annual reports through the Office of Animal Care and Use (OACU), Office of Intramural Research to the USDA and to the NIH Office of Laboratory Animal Welfare (OLAW), Office of Extramural Research which have authority to enforce compliance with regulations and policies that apply to the NIH. Per NIH policy, instances of significant noncompliance must be reported to OLAW through the OACU. In addition, the Association for Assessment and Accreditation of Laboratory Animal Care, (International) performs triennial peer review site visits of all NIH components that use animals in their intramural research programs.

(4) Review Reports are sent to: The ORS Scientific Resources Manager, the Associate Director for Research Services (ADRS) and the Deputy Director for Intramural Research. Issues of concern will be brought to the immediate attention of the ADRS.

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Appendix 1 Simian Virus Screening Profiles

The following is the current list of viral serology tests recommended to screen NIH IRP NHP colonies; the list is subject to change by the IC APD Committee:

*Asian and Mauritius Macaques(*1):*

Rhesus, Cynomolgus, Pigtailed - SIV(mac), SRV1/SRV2(*2,*3), B-virus, Rubeola, STLV-1

African Species:

Chimpanzees - HIV, Hepatitis(*4), HSV-1, HSV-2, Rubeola, VZV, EBV, RSV, SA8

Baboons - SHF, HPV-2, SIV, Rubeola

Patas - SHF, SIV, Rubeola

African Green Monkeys(*1) – SA8, SHF, SIV(agm), Rubeola

New World Primates:

Squirrel monkeys, Owl monkeys, Marmosets, Tamarins - *H. tamarinus*, *H. saimiri*, Rubeola

(*1) Filovirus testing for macaques and African Green monkeys is available if determined necessary upon consultation between the IC APD or their designee and the NPQF.

(*2) SRV5 is pathogenic to rhesus macaques of Indian origin, and is carried by cynomolgus macaques and rhesus monkeys of Chinese origin.

(*3) PCR or isolation or culture with initial serological profile is recommended. Western blots should be requested when serological results are indeterminate or positive.

(*4) Chimpanzees are susceptible to Hepatitis A, B, C, D and E.

Viruses:

SIV Simian Immunodeficiency Virus	STLV-1 Simian T-Cell Leukemia Virus
SRV Simian Retrovirus	SA8 Simian Agent 8
CMV Cytomegalovirus	EBV Epstein-Barr Virus
HVP-2 Herpesvirus papio 2	VZV Simian Varicella-Zoster Virus
HSV Herpesvirus simiae	RSV Respiratory Syncytial Virus
HSV-1 Herpesvirus simplex 1	HIV Human Immunodeficiency Virus
HSV-2 Herpesvirus simplex 2	Rubeola Measles