

NIH Policy Manual

3044-1 - Nonhuman Primate Quarantine

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Release Date: 2/23/2017 ?

Transmittal Notice

- 1. Explanation of Material Transmitted:** This chapter updates NIH policies and procedures for the quarantine of nonhuman primates (NHPs) to be used in the NIH Intramural Research Program. Revisions to this chapter include expansion on procedures and updates to the reference section and Appendix 1: *Simian Virus Screening Profiles*.
- 2. Filing Instructions:**

Remove: NIH Manual 3044-1, dated 02/08/2012.

Insert: NIH Manual 3044-1, dated 02/23/2017.

PLEASE NOTE: For information on:

- Content of this chapter, contact the issuing office listed above.
- NIH Policy Manual, contact the Division of Management Support, OMA on 301-496-4606, or enter this URL: <https://oma.od.nih.gov/DMS/Pages/Manual-Chapters.aspx>

A. Purpose

This chapter updates the responsibilities and procedures for the quarantine of Nonhuman primates (NHPs) received from facilities other than NIH managed and/or operated within the NIH Intramural Research Program.

B. Scope

This policy applies to all NIH animal programs. The Division of Veterinary Resources (DVR), Office of Scientific Resources (SR), Office of Research Services (ORS), and each NIH Institute and Center (IC) that utilize NHPs will be responsible for ensuring compliance with the procedures outlined in this policy. Additionally, other agencies that lease space from NIH must comply with this policy.

The NIH-managed programs operating outside the State of Maryland may quarantine and necropsy NHPs at their facilities, but they must adopt procedures consistent with those outlined in this policy.

C. Background

The DVR 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. NHPs are quarantined in the NIH DVR-managed/operated Primate Quarantine Facility (NPQF) at the NIH Animal Center (NIHAC) located in Poolesville, Maryland or NIH IC-managed/operated quarantine facilities. The NIH-managed animal facilities operating outside of Maryland, may quarantine NHPs at their facilities.

D. Policy

1. Procurement

To place an order or to otherwise have NHPs quarantined at the NIHAC, the IC Animal Program Director (IC APD) or designee will submit a completed [NIH and NCI Centralized Animal Order Request Form NIH 79-3 \(Rel. 03/2000\)](#) to the person in their IC designated to review and approve the procurement. (Note: This person varies by IC and is usually the Facilities Manager or the Administrative Officer.) The form will then be submitted to the DVR NHP procurement officer or IC procurement officer for IC-managed/operated quarantine facilities. A copy of an approved Animal Study Proposal (ASP) for the animals will be provided to or be on file with the DVR Facility Management Branch or IC office for IC-managed/operated quarantine facilities.

The specifications of the animals to be procured must be specifically and accurately described. The procurement of NHPs must also comply with the [United States Department of Agriculture \(USDA\) regulations](#) and the [Centers for Disease Control and Prevention \(CDC\) requirements](#) referenced above. DVR will contact the IC APD if additional information is required or if the request is incomplete or not approved.

When available, NHPs will be obtained from domestic sources with breeding and conditioning programs. If the specification of the animal(s) required for the research cannot be met from a domestic breeding program, imported animals may be procured. (Refer to the next paragraph for the procurement requirements.)

Animals are preferentially selected from vendors that have been successful applicants, and that have been screened through the NHP procurement process, where preference is given to sources that hold a Public Health Service Animal Welfare Assurance and accreditation by AAALAC International (AAALAC). Non-approved sources will be considered only with significant scientific justification as to the necessity of this source; and will include a review of the procurement request by the IC ACUC and the DVR Director if the request is for animals that would be quarantined at the NPQF or

the IC APD for animals that would be quarantined at an IC-managed/operated quarantine facility.

1. Entry Requirements

All NHPs shall have a history of negative Tuberculin Skin Tests (TSTs). For animals coming to NIH from outside sources, one negative TST must be documented within 30 days prior to shipment. For animals transported between NIH facilities, a negative TST within six (6) months of transport is acceptable, but at the discretion of the receiving facility veterinarian. The supplier will provide complete copies of all procured animals' health records, including the origin and date of birth, if known.

Unless waived by the IC APD or their designee, NHPs shall not have been the subject of a previous scientific experiment. Additionally, unless waived by the IC APD or their designee, macaques will be polymerase chain reaction (PCR) negative and seronegative for Simian Retrovirus (SRV), herpes B virus (Cercopithecine herpesvirus 1), Simian Immunodeficiency Virus (SIV) and Simian T-Cell Leukemia Virus (STLV-1). Evidence of freedom from other pathogens may also be requested by the IC APD or the Facility Veterinarian, at the NPQF. Animals should not be accepted from registered importers who have experienced reportable diseases or significant losses (>10%) of animals within the last calendar year.

All NHPs will be checked upon arrival at the NPQF to ensure that they meet the specifications of the order. Animals judged to be healthy, based on a review of their health records, a physical examination, and subsequent laboratory and TST tests, will be accepted. Animals judged to be unacceptable will be returned to the supplier, euthanized or treated in accordance with [USDA regulations](#), after the Facility Veterinarian, at the NPQF consults with the involved IC APD and the supplier.

1. Quarantine Requirements

a. Quarantine and Stabilization

Quarantine and stabilization will be conducted in a manner that complies with the current [Guide for the Care and Use of Laboratory Animals, National Research Council \(Guide\)](#) and will provide sufficient time for acclimation, evaluation of animal health, and expression of diseases. Animals will be assessed before and after arrival for compatibility of social housing. Animals will be preferentially housed in pairs or groups, in accordance with the Guide, unless scientific justification otherwise is provided.

Groups of NHPs in quarantine should be maintained separately from other NHPs. Cohorts in quarantine should be separated by source, geographic origin, date of

arrival, and presumptive health status. If different NHP groups are maintained in the same animal room, the quarantine period commences on the date the last group was placed in the room. IC APDs and the investigators on the ASP will be notified before cohorts are combined.

Ninety (90) calendar days is the standard length of quarantine for primates where any part of the cohort has arrived in the U.S. within one calendar year of arrival at NIH. Sixty (60) days is the standard length of quarantine for primates that have resided in domestic colonies for more than one year prior to arrival at NIH. If diseases that pose a threat to the NIH NHP colony or to humans are detected within a cohort, quarantine will be reinstated for the cohort and/or the affected NHPs will be euthanized for diagnostic necropsy. The travel and medical histories and the source of the animals under quarantine will be considered when the length of quarantine is being determined. Extension of quarantine may be appropriate for NHPs with incomplete travel or medical histories, and for cohorts that exhibit disease during quarantine. If diseases that pose a threat to the NIH NHP colony or to humans are detected within a cohort, quarantine will be reinstated for the cohort and/or the affected NHPs will be euthanized for diagnostic necropsy.

Quarantine will include a TST using a USDA licensed and approved mammalian old tuberculin administered in alternate eyelids every two (2) weeks. Body weights will be recorded with the TSTs. New World species, patas monkeys and baboons must have a minimum of three (3) consecutive negative results within the entire cohort. Macaques and African Greens must have a minimum of four (4) consecutive negative results within the entire cohort. Test sites will be examined 24, 48, and 72 hours after administration of mammalian old tuberculin. The TST results must be recorded per the DVR Quarantine of NHPs SOP or IC-specific requirements for NHPs housed in IC-managed/operated quarantine facilities. For NHPs demonstrating suspect or positive reactions on TST, or determined to be infected with tuberculosis, refer to the [Guidelines for the Prevention and Control of Tuberculosis in Nonhuman Primates in the NIH Intramural Program](#) for monitoring procedures, husbandry practices and procedures, and continued testing of cohorts.

NHPs under quarantine will have viral profile testing (See Appendix 1) submitted to an appropriate reference laboratory within the first 35 days of quarantine. Animals not receiving virus profiles during quarantine will be handled as infected with the specific viruses listed in Appendix 1 upon release from quarantine, and will be housed accordingly. The clinical veterinarian may perform other diagnostic procedures as indicated/appropriate. Those animals harboring pathogens will be treated or rejected by the Facility Veterinarian, at the NPQF, after consultation with the involved IC APD or designee, and the supplier.

After an initial acclimation period of 14 days, investigators may request that approved Animal Study Proposal (ASP) procedures, such as, feeding of special diets and blood collections, are performed. These procedures must be approved by

the Facility Veterinarian, at the NPQF. NHPs will receive a behavior assessment during routine quarantine.

b.Necropsy

All NHPs that are euthanized or die for any reason during quarantine will have diagnostic necropsy performed by the Pathology Section, Diagnostic and Research Services Branch (DRSB), DVR, SR, ORS, or by other qualified veterinary pathologists or veterinarians using standard accepted necropsy procedures. Animals under quarantine in IC-managed/operated quarantine facilities or NIH-operated facilities outside the state of Maryland, including but not limited to the National Institute of Allergy and Infectious Diseases (NIAID) Rocky Mountain Laboratories in Montana, and the National Institute of Environmental Health Sciences (NIEHS) Research Triangle Park in North Carolina, may have the necropsy performed by other qualified veterinary pathologists or veterinarians using procedures consistent with those of the DRSB, DVR, SR, ORS.

c.Tuberculosis Treatment and Isolation

Animals confirmed positive for *Mycobacterium tuberculosis*

(*M. tuberculosis*) complex disease should be immediately euthanized after consultation between the IC APD and the Facility Veterinarian, at the NPQF. The euthanasia of a tuberculosis-positive NHP may be delayed if the animal is of great value to a research project and can be isolated to minimize the spread of disease to humans and other NHPs. **If euthanasia is delayed**, then the Director of the, Division of Occupational Health and Safety (DOHS), SR, ORS, the IC APD and the investigator's IC Animal Care and Use Committee (ACUC) must be notified. The DOHS Director must review and approve the containment requirements for the animal.

The NHPs should not be treated for *M. tuberculosis* complex disease. For an animal to be treated, the IC ACUC must be contacted to approve the treatment. A multiple-drug regimen based on the most current practice standard must be used and the treatment must continue for a period of at least six (6) months. The animal containment requirements must be used for the duration of treatment. At the conclusion of the treatment regimen, further housing, testing, and research use of the animal will be collaboratively decided between the Facility Veterinarian, at the NPQF, the IC APD, the investigator's IC Animal Care and Use Committee (ACUC), the DVR Director, the DOHS, and the IBC.

d.Husbandry

Only designated facility personnel will be permitted in quarantine rooms. Personnel will comply with [NIH Manual Chapter 3044-2, Protection of NIH Personnel Who Work with NHPs](#), and applicable [Guidelines for the Prevention and Control of Tuberculosis in NHPs](#) at the NIH.

1. Variance to Standard Quarantine

a. Variance

The Facility Veterinarian, at the NPQF and the IC APD may agree to a variant of quarantine if the IC APD requests it, and the circumstances justify it. If the Facility Veterinarian, at the NPQF denies the request, or if the Facility Veterinarian, at the NPQF and the IC APD cannot agree on the terms, the IC APD may refer the matter to the Director, DVR, SR, ORS for further review/consideration. Usually, a variance to quarantine is only issued for performing quarantine in a location other than at the NIH Primate Quarantine Facility (NPQF) or a need for an abbreviated quarantine procedure using the DVR Quarantine of NHPs SOP.

At the discretion of the DVR Director or his/her designee, NHPs arriving from non-NIH facilities that have been through the NPQF quarantine within 1 year of arrival, may be eligible for abbreviated quarantine procedures per the DVR Quarantine of NHPs SOP. Animals in this category should have a negative TB test at the facility of origin within 30 days of shipment to NIH facilities. The DVR Director may be contacted for information regarding the details of the abbreviated quarantine procedures.

NHPs may be quarantined in IC-managed/operated quarantine facilities instead of the NPQF if the IC APD of the IC-managed/operated quarantine facility approves. NHPs arriving into IC-managed/operated quarantine facilities will be processed according to the IC-specific quarantine procedures.

b. Waivers

Quarantines will not be waived.

1. Reportable Diseases

Registered importers must maintain records on each shipment of imported NHPs 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 NHPs that is suspected of being yellow fever, monkeypox, or hemorrhagic fever (Marburg/Ebola). Additionally, if mortality for a shipment exceeds five (5) percent, the importer must immediately report the circumstances, including cause(s) of death to the CDC. Requirements for the importation of NHPs are established by [Federal Regulation, 42 CFR 71.53](#).

E. References

1. [NIH and National Cancer Institute \(NCI\) Centralized Animal Order Request Form NIH 79-3 \(Rev. 10/90. Online version released 03/13/2000\).](#)
1. [Animal Welfare Regulations. Code of Federal Regulations, Title 9, Chapter 1, Subchapter A - Animal Welfare: Parts 1-4. U.S. Department of Agriculture Regulations \(USDA\).](#)
1. [Capitanio JP et al. Considerations in the Selection and Conditioning of Old World Monkeys for Laboratory Research: Animals from Domestic Sources. ILAR J \(2006\) 47\(4\): 294-306.](#)
1. [Center for Disease Control and Prevention \(CDC\). Oct., 1991. Update: Nonhuman primate importation: modified special permit requirements for importation and quarantine of nonhuman primates. Morbidity and Mortality Weekly Report \(MMWR\).](#)
1. [Guide for the Care and Use of Laboratory Animals, 8th edition. National Research Council \(NRC\) 2010, 110-112.](#)
1. [Guidelines for the Prevention and Control of Tuberculosis in Nonhuman Primates in the NIH Intramural Program. NIH Animal Research Advisory Committee \(ARAC\) Guidelines 3/22/2017.](#)
1. [Lerche NW et al. New Approaches to Tuberculosis Surveillance in Nonhuman Primates. Institute for Laboratory Animal Research Journal \(ILAR J\) \(2008\) 49\(2\): 170-178.](#)
1. Mansfield K. "Specific Pathogen Free Nonhuman Primate Colonies" in The Laboratory Primate, Wolfe-Coote S ed. Elsevier Academic Press, London, 2005.
1. [Morton WR et al. Specific Pathogen-Free Macaques: Definition, History, and Current Production. ILAR J \(2008\) 49\(2\): 137-144.](#)
1. [NIH Policy Manual 1743, Keeping and Destroying Records.](#)
1. [NIH Policy Manual 3040-2, Animal Care and Use in the Intramural Program.](#)
1. [NIH Policy Manual 3044-2, Protection of NIH Personnel Who Work with Nonhuman Primates.](#)
1. [Nonhuman Primate Import Regulations. Code of Federal Regulations, Title 42, Chapter 1, Part 71, Section 53. United States Government Publishing Office.](#)
1. Kramer JA, Ford EW, Capuano S. 2012, Preventative Medicine in NHPs. In: Abee CR, Mansfield K, Tardiff S, Morris T, eds, Non-human Primates in Biomedical Research, Vol. 1, Biology & Management, Academic Press, pp 296-317

1. [Roberts JA and Andrews K. Nonhuman Primate Quarantine: Its Evolution and Practice. ILAR J \(2008\) 49\(2\): 145-156.](#)
1. [Tardiff S et al. Preparing New World Monkeys for Laboratory Research. ILAR J \(2006\) 47\(4\): 307-315.](#)

F. Definitions

See [NIH Policy Manual 3040-2. Animal Care and Use in the Intramural Program](#) for a comprehensive list of definitions related to animal care and use.

1. The NIH DVR-managed/operated Primate Quarantine Facility (NPQF)
2. Nonhuman primates (NHPs)

G. Responsibilities

See [NIH Policy Manual 3040-2. Animal Care and Use in the Intramural Program](#) for a comprehensive list of responsibilities related to animal care and use.

H. Records Retention and Disposal

All records pertaining to this chapter must be retained and disposed of under the authority of [NIH Manual 1743](#), "Keeping and Destroying Records," Appendix 1, "NIH Records Control Schedules" (as amended). These records must be maintained in accordance with current NIH Records Management and Federal guidelines. Contact your [IC Records Liaison](#) or the NIH Records Officer for additional information.

I. Internal Controls

The purpose of this manual issuance is to outline the responsibilities and procedures for the quarantine of NHPs received from facilities other than NIH and used for research within the NIH Intramural Research Program.

1. **Office responsible for Reviewing Internal Controls relative to this chapter:**
Through this manual issuance, the Division of Veterinary Resources (DVR), Office of Research Services (ORS) (for NHPs quarantined in the NPQF), and ICs (for NHPs quarantined in IC-managed/operated quarantine facilities) are responsible for ensuring that internal controls are implemented and working.
2. **Frequency of Review (in years):** Ongoing.
3. **Method of Review:** DVR (for NHPs quarantined in the NPQF) and ICs (for NHPs quarantined in IC-managed/operated quarantine facilities) 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 (OIR) to the USDA and to the NIH Office of Laboratory Animal Welfare (OLAW), Office of Extramural Research (OER) 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. Additionally, the AAALAC performs triennial peer review site visits of all NIH components that use animals in their intramural research programs.

DVR staff will make site visits to suppliers to evaluate their programs and ability to meet NIH requirements periodically (at least once for the duration of the contract period) or more frequently when there are concerns regarding animal health and/or welfare or interests of the NIH. Representatives from ICs that quarantine NHPs in IC-managed/operated quarantine facilities might make similar visits at the discretion of the IC APD.

1. **Review Reports are sent to:** The Research Services Advisor, ORS; Director of the Office of Research Services (ORS) for NHPs quarantined in the NPQF, the IC APD for NHPs quarantined in IC-managed/operated quarantine facilities; and the Deputy Director for the Office of Intramural Research (OIR). Issues of concern will be brought to the immediate attention of the ORS Director for NHPs quarantined in the NPQF or the IC APD for NHPs quarantined in IC-managed/operated quarantine facilities.

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:

Rhesus, Cynomolgus, Pigtail - SIV, SRV 1,2,3,5, STLV-1,2, B Virus, Rubeola

African Species:

Baboons - HPV-2, SIV, STLV-1, AgmCMV, EBV, SVV, Rubeola

Patas - SHF, SIV, Rubeola

African Green Monkeys – STLV-1,2, SA8, SHF, SIV, Rubeola

New World Primates:

Squirrel monkeys, Owl monkeys, Marmosets, Tamarins - Herpesvirus tamarinus, Herpesvirus saimiri, SquiCMV, Rubeola

Abbreviations:

SIV: Simian Immunodeficiency Virus

STLV: Simian T-Cell Leukemia Virus

Rubeola: Measles

SA8: Herpesvirus papionis

SVV: Simian Varicella Virus

CMV: Cytomegalovirus

SRV: Simian Retrovirus

B Virus: Cercopithecine herpesvirus 1

HVP-2: Herpesvirus papio 2

EBV: Epstein-Barr Virus

SHF: Simian Hemorrhagic Fever

Agm: African green monkey

Squi: Squirrel Monkey