NIH POLICY MANUAL

3044-1 – NONHUMAN PRIMATE QUARANTINE
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1. **Explanation of Material Transmitted:** This chapter describes NIH policies and procedures for quarantine of nonhuman primates (NHPs) for NIH operated Intramural Research Animal Programs (NIH IRP).

2. **Filing Instructions:**

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**A. Purpose:**

This policy establishes the responsibilities and procedures for the quarantine of nonhuman primates (NHPs) for NIH operated Intramural Research Animal Program (NIH IRP). The Office of Research Services (ORS), Division of Veterinary Resources (DVR) and each NIH Institute and Center (IC) that uses NHPs shall be responsible within its respective area for ensuring compliance with this policy.

**B. Scope:**

This policy applies to all NIH IRP operated animal programs. The NIH IRPs operated outside the state of Maryland may quarantine and necropsy NHPs at their facilities, but they must adopt procedures consistent with this policy. Agencies that lease space from NIH intramurally operated animal programs must comply with this policy or seek a variance from the Veterinary Medicine Service Poolesville (VMSP) as a term of the lease agreement.

**C. Facilities:**

Nonhuman primates quarantined by the DVR are quarantined at the VMSP, NIH Animal
Center (NIHAC) in Building 103. The NIH IRPs operated outside of Maryland may quarantine NHPs at their facilities.

**D. Procurement:**

These procurement procedures apply to the VMSP, NIHAC, Building 103. Similar procedures are followed at other locations.

To place an order or to otherwise have NHPs quarantined at the NIHAC, the IC Animal Program Director (APD) or designee(s) shall submit a completed NIH Centralized Animal Order Request Form (Appendix 1) or equivalent to their IC and/or the AC administrative officer for review and approval. The form will then be submitted to the Veterinary Medicine Service Poolesville (VMSP), NIHAC, Building 103. A copy of an approved Animal Study Proposal will also be provided to the VMSP.

Prior to processing the order, the VMSP will review the request. The specifications of the animals to be procured must be completely and accurately described. The procurement of nonhuman primates also must comply with USDA regulations and CDC requirements (Appendix 2, References 1, 2). The VMSP will contact the IC APD if the request is incomplete or not approved.

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

**E. Entry Requirements:**

Rhesus, Cynomolgus, and Pigtail macaques, provided under competitive contracts, shall have a history of negative tuberculin skin tests (TSTs). At least three (3) TSTs shall be performed, not less than two weeks apart, and one of the tests within 10 days prior to shipment. 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 APD or their designee, nonhuman primates provided under contract shall not have been subjected to experimental use. Additionally, macaque monkeys provided under contract shall be serologically negative and culture or PCR negative for SRV-1 and SRV-2, and seronegative for B virus, SIV and STLV-1. Evidence of freedom from other pathogens may also be requested by the APDs or by the VMSP. Animals should not be accepted from registered importers who are experiencing reportable diseases (Appendix 3) or significant losses of animals.

All NHPs shall be checked immediately upon arrival at the VMSP, NIHAC, Building 103, to ensure they meet the order requirements. Animals judged healthy, including a review of their
health records, a physical examination, and subsequent laboratory and TST tests, shall be accepted. Animals judged unacceptable shall be returned to the supplier, euthanized or treated in accordance with USDA regulations (Appendix 2, Reference 1) after the VMSP 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. Full quarantine upon re-entry may be waived by the VMSP veterinarian in consultation with the APD or their designee.

Nonhuman primates in NIH colonies will be vaccinated against rubeola virus (Attenuvax - Merck & Co., Inc., or equivalent) at six and nine months of age and tested at twelve months of age, unless the approved ASP requires rubeola naive animals. Animals that do not have a positive titer will be revaccinated.

F. Quarantine Requirements:

1. Quarantine and Stabilization:

All nonhuman primates that are introduced into animal colonies located on the NIH campus in Bethesda or the NIHAC must be quarantined in Building 103 at the NIHAC, unless a variance is approved by the Chief, VMSP. The NIH IRP APD or designee(s) must contact the VMSP to arrange quarantine or request a variance in the location or duration of quarantine.

Groups of nonhuman primates in quarantine shall be maintained separately from other NHPs. Cohorts should be separated by source, geographic origin, date of arrival, and presumptive health status. Quarantine and stabilization shall be conducted in a manner that complies with the NRC Guide (Appendix 2, Reference 4). It shall provide sufficient time for acclimation, evaluation of animal health, and expression of diseases. Animals shall be individually housed during quarantine. A variance may be approved for pair housing.

Ninety days is the standard length of quarantine for newly acquired African Green monkeys, macaques and chimpanzees. Sixty 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 NHPs with incomplete histories and cohorts that develop disease during quarantine. Quarantine shall be reinstated, or the affected NHPs euthanized when diseases that pose a threat to the NIH NHP colony or to humans are detected.

Procedures shall include a TST using a USDA licensed and approved Old Tuberculin (OT) administered 14 days apart in alternate eyelids. New World, patas monkeys and baboons must have a minimum of 3 consecutive negative results and Old World Monkeys (other than *Patas* and *Papio*) must have 5 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 OT. The TST results
may be recorded using the California scoring system; however, a written description of the TST results must be provided with the score. Refer to the guidelines for the "Prevention and Control of Tuberculosis in Nonhuman Primates in the NIH Intramural Program," (Appendix 2, Reference 5) for interpretation of TST results. Weights shall be recorded with the TSTs.

Quarantined NHPs shall have CBC, chemistry, and virus profiles (Appendix 4) submitted to an appropriate reference laboratory within the first 30 days of quarantine; the samples will be taken to assure that those animals remain serologically and culture or PCR negative for those viruses listed in Appendix 4. 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 ASP approved procedures such as feeding of special diets and blood collections be performed. These procedures must be approved by the VMSP. Nonhuman primates will receive a behavior assessment during routine quarantine.

After a quarantined group of NHPs has completed the last tuberculin test with negative results, they shall be vaccinated against rubeola virus (Attenuvax - Merck & Co., Inc., or equivalent) unless the approved ASP requires rubeola naive animals. In the case of the latter, such animals shall be quarantined separately with appropriate quarantine measures to guard against exposure to rubeola.

2. Separation by Geographic Origin and Source:

Different NHP groups (different geographic origin, source, or arrival dates) shall be quarantined separately, whenever possible. If different NHP 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 APDs shall be notified before cohorts are combined. Cohorts may be combined only to avoid delays in delivery.

3. Necropsy:

All nonhuman primates that die or are euthanized in quarantine must be necropsied.

4. Tuberculosis Treatment and Isolation:

Animals confirmed positive for *M. tuberculosis* Complex disease should be immediately euthanized after consultation between the IC APD and the VMSP. Nonhuman primates shall not be treated for *M. tuberculosis* Complex disease without an ASP approved by the user IC's Animal Care and Use Committee (ACUC) and the Institutional Biosafety Committee (IBC). Handling, transportation, housing and treatment of tuberculous NHPs must be conducted in accordance with instructions of the IBC.

5. Husbandry:
Only designated facility personnel shall be permitted in quarantine rooms. They shall comply with NIH Manual Chapter 3044-2, Protection of NIH Personnel Who Work with Nonhuman Primates (Appendix 2, Reference 3), and applicable guidelines for the prevention and control of tuberculosis in nonhuman primates in the NIH intramural program.

6. Enrichment:

NHPs shall be provided toys, novel food treats, and visual contact during quarantine in compliance with USDA regulations (Appendix 2, Reference 1). They shall not be group housed during quarantine.

G. Variance to Standard Quarantine:

1. Variance:

The VMSP and an IC APD may agree to shorten or modify quarantine, when the circumstances support it. The principal investigator, through the IC APD, must request a variance. If the VMSP denies the request, or if the VMSP and the IC APD cannot agree on the terms of the NIH policy variance, then the IC APD may refer the matter to the Director of DVR.

2. Waivers:

Quarantine shall not be waived.

H. 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 NIH Manual 1743, "Keeping and Destroying Records," Item 3000-C which covers “Veterinary Services”. Refer to the NIH Manual Chapter 1743 for specific instructions.

NIH e-mail messages. NIH e-mail messages (messages, including attachments, that are created on NIH computer systems or transmitted over 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 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, NIH staff conducting official reviews or investigations, and the Office of the Inspector General may request access to or copies of the e-mail messages.

E-mail messages must also be provided to Congressional committees if requested and are subjected to 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 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.

I. Management Controls:

The purpose of this policy manual is to establish policies and procedures for the quarantine of nonhuman primates for an NIH IRP.

(1) Office responsible for Reviewing Management controls relative to this chapter: DVR, ORS.
(2) Frequency of Review (in years): Ongoing
(3) Method of Review:

Other review: DVR will maintain oversight and ensure effective implementation and compliance with this policy. The IRPs must make annual reports through the Office of Animal Care and Use (OACU) to the USDA and the NIH Office of Laboratory Animal Welfare (OLAW), which have authority to enforce compliance with regulations and policies that apply to the NIH IRPs. 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 (AAALAC), International performs triennial peer review site visits of all NIH components that use animals in their IRP programs. All NIH IRP facilities are accredited by AAALAC.

(4) Review Reports are sent to: the Deputy Director for Intramural Research, Director of the ORS Division of Intramural Research Services and the Associate Director for Research Services, ORS (ADRS). Issues of concern will immediately be brought to the attention of the ADRS.
Appendix 1 is NIH Form 79-3 (Rev. 10/90). On line copies may be obtained at http://forms.nih.gov/adobe/animals/NH79_3.PDF
Appendix 2 - References:


Appendix 3 - 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 (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. These requirements are established by Federal regulation (Title 42, Code of Federal Regulations, Section 71.53).
Appendix 4 - 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 APD's Committee:

Asian and Mauritius Macaques(*1):

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

African Species:

Chimpanzees - HIV, Hepatitis A (*4), HSV-1, HSV-2, Rubeola, VZV, EBV, RSV, SA8
Baboons - SHF, SA8, SIV, Rubeola
Patas - SHF, SIV, Rubeola
Sooty Mangabeys - SIV(sm), Rubeola
African Green Monkeys(*1) - SHF, SIV(agt), Rubeola
Galagos - Rubella

New World Primates:

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

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

(*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 recommended. Western blots should be requested when serological results are indeterminate or positive.

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

Viruses:

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