

NIH POLICY MANUAL

3043-1 - Introduction of Rodents and Rodent Products

Issuing Office: ORS/DVR (301) 496-2527

Release Date: 1/10/06

1. **Explanation of Material Transmitted:** This chapter describes procedures to be followed when rodents and rodent products originating from sources other than those approved by the NIH Rodent Import Officer are introduced into NIH facilities. Procedures have been revised to endorse the NIH initiative to facilitate rodent movement onto the NIH campus and to reflect changes in accountability for preventing the introduction of infected rodents and rodent products into the NIH.

2. **Filing Instructions:**

Remove: NIH Manual Chapter 3043-1, dated 8/17/04

Insert: NIH Manual Chapter 3043-1, dated 1/10/06

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A. Purpose: This Policy Manual establishes procedures designed to prevent the introduction of infected rodents and rodent products into the National Institutes of Health (NIH) that could: adversely affect the health of rodents used in research; directly or indirectly interfere with research; pose a health hazard to personnel.

B. Background: The conduct of a vigorous research program necessitates the movement of animals and their tissues from animal colony to animal colony and between laboratories. This movement creates the possibility of introducing into new environments agents that are pathogenic to either animals or humans. Examples of the latter include lymphocytic choriomeningitis virus (LCMV) and the hantaviruses, which can have serious implications for human health. Hantaviruses infect wild rodents and have been detected in laboratory rats in Europe and Asia, and in wild mice (*Mus musculus*) in Europe and the United States; humans who come into contact with infected animals can become ill and occasionally die.

Federal regulations pertaining to the movement of laboratory rodents or their products relate mainly to organisms causing diseases in humans or domestic poultry or livestock. It is important for the NIH to supplement these regulations

with policies that protect intramural animal colonies and scientific and support staff who come into contact with rodents or rodent products.

C. Applicability: The policies and procedures in this chapter apply when rodents and rodent products are introduced into NIH facilities from sources other than those approved through the Division of Veterinary Resources (DVR), Office of Research Services (ORS). In addition to applying to all facilities located on the NIH Bethesda campus, any off-campus facility covered under the Association for the Assessment and Accreditation of Laboratory Animal Care's (AAALAC)-file number 000777, is subject to this policy.

D. Policy This policy is designed to protect NIH animal facilities from accidental contamination with zoonotic agents and rodent infectious agents that pose a substantial risk to the NIH mission. Rodents or rodent products from a non-approved source shall not be introduced into NIH animal facilities without prior written approval of the applicable Institute or Center's (IC) Scientific Director or a delegate thereof (i.e., the IC Rodent Import Officer (IC RIO)); the Facility Veterinarian for the facility where the animals are to be housed; and knowledge of the DVR Director, or delegate thereof (i.e., the NIH Rodent Import Officer (NIH RIO)). Similarly, rodents from a non-approved source shall not be introduced into an NIH laboratory without the approval of the applicable Scientific Director or the IC RIO. Rodent products from non-approved sources destined only for NIH laboratories for in vitro use, require the approval of the applicable Lab/Branch Chief. (See Appendix 1)

Approval to introduce rodents or rodent products for in-vivo use, and infected with a zoonotic agent, is obtained by the IC RIO (in coordination with the NIH RIO and the Quarantine Permit Service Office in the Division of Occupational Health and Safety).

E. References:

1. Animal Welfare Act (7 U.S.C. 2131 et. seq.), as amended, and implementing regulations at 9 C.F.R., Part 1, et. seq.
2. 9 C.F.R., Part 93
3. Public Health Service Act, Sections 361-369 (42 U.S.C. 264-272), as amended and its implementing regulations at 42 C.F.R. Parts 71 and 72
4. PHS Policy on Humane Care and Use of Laboratory Animals, 2002
5. NIH Manual Chapter [3040-2](#), Animal Care and Use in the Intramural Program

6. USDA Guidelines for Importation, #1103

7. National Research Council Guide for the Care and Use of Laboratory Animals, 1996

F. Definitions:

1. **Alternative Quarantine Site (AQS)** A quarantine site, other than the DVR operated Rodent Quarantine/Rederivation Facilities at the NIH Animal Center (NIHAC) and in building 14E on the NIH Campus, Bethesda, that is operated by an IC and approved by the NIH RIO.

2. **Animal Program Director (APD)** A veterinarian who receives delegated program authority from the IC Director or IC Scientific Director for all activities involving animals in the IC.

3. **APD's Committee** An NIH committee that consists of the APD from each IC.

4. **Application** Refers to the "Application for Permit to Introduce Rodents and Rodent Products," [NIH Form 2369-1](#) (Appendix 2). The issued permit is valid for a six (6) month period.

5. **Approved Source** A source of rodents or rodent products which has a contract with the DVR or another program within the NIH to supply genetically-defined, specific pathogen-free animals to NIH investigators. These contracts characteristically require barrier production practices, genetic management and monitoring, microbiologic standards and health surveillance equal to that outlined in the DVR-held NIH Animal Procurement Contract, shipment in a manner to assure maintenance of health status, and at least one site visit during the contract period involving at least one disinterested (non-sponsoring IC) party to ensure the availability of high-quality animals suitable for NIH research. The NIH Rodent Import Officer maintains a list of sources that meet the Approved Source criteria. Proposals for additions to the Approved Source list are evaluated and approved by the Rodent Import Advisory Subcommittee.

6. **Domestic Source** A source of rodents or rodent products located within the United States. In all cases, the source must provide evidence that their colonies test free of mouse poxvirus and lymphocytic choriomeningitis virus (LCMV). Wild caught rodents or colonies founded with wild caught stock must also test free of hantaviruses and *Salmonella sp.*

7. **Facility Veterinarian** A veterinarian who has direct or delegated responsibility for the management of the animals in the facility.

8. **Minimum Health Standard** Mouse poxvirus (aka Ectromelia), lymphocytic

choriomeningitis virus (LCMV), the hantaviruses and *Salmonella sp.* are excluded from NIH rodent colonies except when used in an approved research protocol. All rodents or rodent products accepted into an NIH facility must be shown to present minimal risk for introducing these agents as outlined in the Domestic and Non-domestic Source definitions. The sending facility must provide assurance and/or evidence that annual testing for the specified agents is performed throughout their facility, or it must be demonstrated (serology or PCR) that the specific animals to be shipped are **likely** free of these agents. Additional health standards may be set at the animal facility level. Investigators may not move rodents or rodent products between animal facilities without first contacting the Facility Veterinarian for approval.

9. **NIH Facility** Any building, structure, laboratory or other facility, whether or not animals are housed or used there, associated with the NIH intramural research program. This includes any facility on the Bethesda, Maryland, campus, the NIHAC, off-campus leased facilities and other sites where intramural research is performed.

10. **Non-domestic Source** A source of rodents or rodent products originating outside of the United States. The source must demonstrate that their colonies test free of all Minimum Health Standard excluded agents.

11. **Non-approved Source** A source of rodents or rodent products that does not meet the definition of an approved source.

12. **Quarantine** Refers to holding and testing of animals at a DVR operated Rodent Quarantine/ Rederivation Facility for the purpose of this policy.

13. **Quarantine Permit Service Office (QPSO)** An office in the Division of Occupational Health and Safety (DOHS) that assists investigators in obtaining permits that may be required when importing/exporting animals, animal products, etiologic agents, or vectors of human or animal disease (Building 13/3K04, (301) 496-3353). Permits must be obtained from the QPSO in coordination with the IC RIO and the NIH RIO.

14. **Rodent** A mammal of the order Rodentia, including but not limited to mice, rats, guinea pigs, and hamsters.

15. **Rodent Import Officer, NIH (NIH RIO)** A veterinarian appointed by the Director of the DVR, ORS, with delegated responsibility for activities defined in this policy and for overseeing activities at the DVR operated Rodent Quarantine/Rederivation Facilities.

16. **Rodent Import Officer, Institute/Center (IC RIO)** A veterinarian, the APD of an IC and/or their designee, with responsibility for import activities

defined in this policy within their IC.

17. Rodent Import Advisory Subcommittee (RIAS) A committee appointed by the APDs to serve in an advisory capacity to the NIH RIO in periodic reviews of this policy. The NIH RIO may seek the counsel of the RIAS in reviewing applications for AQSs, waivers, Approved Source status, and to settle disputes involving this policy.

18. Rodent Products Any rodent tissue or derivative, including but not limited to antibodies (polyclonal or monoclonal), body fluids, proteins, or cells, unless contained in commercially available test kits, when these reagents have been produced or processed in a manner that will exclude or inactivate all pathogenic agents.

19. Waiver Under the conditions outlined in section J, a waiver of quarantine for a particular shipment of rodents may be obtained, or a waiver of the import permit may be granted for a particular source.

G. Responsibilities:

1. Director, DVR, ORS. Implements those aspects of this policy relating to the DVR and the NIH RIO.

2. The Facility Veterinarian may: 1) approve the animals for entry into their animal facility; 2) require the animals to be quarantined with further testing, 3) reject the animals for entry into their facility; or, 4) require more information before making a decision. In the first two cases, the Facility Veterinarian approves the import and forwards the application to the NIH RIO. In the latter two cases, the Facility Veterinarian returns the application to the submitting IC RIO. After animals have completed quarantine, including testing and approved release by the NIH RIO, the Facility Veterinarian determines if the animals can enter the facility.

3. IC RIO:

(a) assists the principal investigator/applicant in securing approvals, permits, transportation, etc., related to the introduction of rodents or rodent products into an animal facility or laboratory. The above includes obtaining health monitoring and husbandry information for review by the Facility Veterinarian;

(b) reviews and approves or disapproves applications for introduction of rodents or rodent products from non-approved sources into NIH IC animal facilities, under their purview, based on the supportive evidence for absence of LCMV, ectromelia virus and hantaviruses. Forwards to the facility veterinarian applications for introduction of rodents or rodent products from non-approved

sources into animal facilities;

(c) reviews and approves or disapproves applications for introduction of rodents from non-approved sources into laboratories of an IC; and

(d) provides oversight for AQSs within their IC to ensure quarantine of animals until such time that data can be generated to verify that they are free of LCMV, ectromelia virus and hantaviruses (as applicable).

4. IC Scientific Director. Ensures compliance with this policy by intramural staff within his/her IC.

5. Laboratory/Branch Chiefs' reviews and approves or disapproves the introduction of rodent products, not destined for in vivo studies into the laboratory by a principal investigator under his or her supervision after assessing the zoonotic potential of the material and determining if testing is required prior to importation and use.

6. NIH/ORS/DVR RIO.

(a) reviews applications for introduction of rodents or rodent products from non-approved sources into NIH animal facilities for compliance with this policy. May suspend an approved permit within 24 hours, pending further discussion with the IC RIO, if it is determined that a high risk decision was made.

(b) assigns and applies a Rodent Import Permit number to each application received. Provides a copy of the numbered permit to both the IC RIO and the Facility Veterinarian.

(c) coordinates use of the DVR Rodent Quarantine at NIHAC and 14E/104; sets testing requirements for and releases animals from quarantine once testing demonstrates the rodents meet the minimum health standard.

(d) maintains a file (paper or electronic) of IC RIO approved Rodent Import Permits and the supportive health information.

(e) provides guidance on this policy to IC RIOs and Facility Veterinarians.

(f) evaluates and approves proposals for import permit waivers. Approved Import Permit Waivers will be reviewed annually and renewed triennially.

(g) maintains an electronic list of Approved Sources and Approved Import Permit Waivers.

(h) reviews and approves Alternative Quarantine Site applications; maintains an

electronic list of approved sites.

7. Principal Investigator/Applicant.

(a) initiates rodent import application(s) for approval of shipments from non-approved sources for:

(1) rodents and rodent products into NIH laboratories or animal facilities

(2) rodent products to be introduced into NIH animals

(b) initiates any additional permits/applications which may be required, such as United States Department of Agriculture permits, when necessary (refer to Section K).

H. Procedures for Introduction of Rodents: (See Appendix 1 for flowchart of procedures.) The introduction of rodents from non-approved sources requires submission and approval of [NIH Form 2369-1](#), "Application for Permit to Introduce Rodents and Rodent Products" (Appendix 2). In situations where quarantine is likely, applications should be submitted at least 60 calendar days prior to the anticipated date of entry into an NIH animal facility to allow time for diagnostic testing. Procedures for submission and approval are as follows:

1. The principal investigator must complete their sections of form 2369-1 and submit the application to their IC RIO. The IC RIO reviews health information for compliance with the minimum health standard, then approves the import or submits the application to the Facility Veterinarian for the facility in which the animals are to be housed.

2. In addition to meeting the minimum health standard, animals destined for an NIH animal facility must also meet the health requirements of the receiving facility. The Facility Veterinarian reviews the health information submitted for compliance with their facility's requirements and on approval, forwards the application to the NIH RIO who assigns it an import number, provides a copy to the IC RIO and the Facility Veterinarian, and files the application.

3. In most cases, imports from non-domestic, non-approved sources will require quarantine and health assessment at a NIH-approved quarantine location. A waiver of quarantine may be obtained on a case-by-case basis, through the NIH RIO.

4. Animals to be quarantined will be housed at the DVR Rodent Quarantine Facility at NIHAC or 14E/104, or at an approved AQS. The NIH RIO will: (1) specify the minimum criteria for release from quarantine; (2) review all test results; and (3) approve release of animals. The quarantine site will provide copies of all results from tests performed during quarantine to the sponsoring

Facility Veterinarian and/or the IC RIO, and the NIH RIO prior to release.

5. If rodents are destined for a laboratory where no contact with other animals is planned and no materials from the rodents will be introduced into rodents or used in materials destined for introduction into rodents or other animals, then the application can be approved by the IC RIO. The IC RIO must ensure that the imported animals represent a low risk to both personnel and animal colonies for LCMV, ectromelia virus and hantaviruses (as applicable). The approved application is forwarded to the NIH RIO who assigns it an import number, provides a copy to the IC RIO, and files the application.

I. Procedures for Introduction of Rodent Products: For in vivo use, the introduction of rodent products into NIH laboratories or into animal facilities also requires the submission and approval of an application NIH Form 2369-1. In vitro use of rodent products requires permission from the principal investigator's laboratory or branch chief, as described below:

1. Procedure for Introduction of Rodent Products into Animals.

(a) The principal investigator must complete and submit an application through their IC RIO to the Facility Veterinarian in charge of the facility in which the products are to be used. This applies to all rodent products from non-approved sources. Routinely, Polymerase Chain Reaction (PCR) or Mouse Antibody Production (MAP)/Rat Antibody Production (RAP) /Hamster Antibody Production (HAP) testing is required to ensure products are free from LCMV, ectromelia virus, hantaviruses (as applicable) and other agents as required by the receiving facilities. In rare situations (e.g. highly purified proteins), with the concurrence of the IC RIO and the receiving Facility Veterinarian, products may be approved for import without testing. Embryos should be collected and rederived in accordance with the latest edition of the Manual of the International Embryo Transfer Society as modified for rodents. (Appendix 4)

(b) The IC RIO or Facility Veterinarian approves and forwards a copy of the application to the NIH RIO, who reviews the application, assigns it an import number, provides a copy to the IC RIO and Facility Veterinarian, and files the application.

2. Procedure for Introduction of Rodent Products into an NIH Laboratory.

If rodent products will not be introduced into, or come in contact with live animals, an NIH rodent import permit is not required. The QPSO should be consulted to determine if a USDA permit is required (for reasons stated below). It is the responsibility of the principal investigator's laboratory or branch chief to assess the zoonotic potential of the material and determine if testing is required prior to importation and use. Assistance in making this determination is

available from the NIH Biosafety Officer, DOHS. (301) 496-2960.

J. Waivers:

1. Of Quarantine.

Quarantine of rodents introduced to the NIH campus from non-approved domestic sources, may be waived based on health and husbandry information provided by the sending facility, showing that the animals originate from colonies routinely tested and shown to be free of mouse poxvirus and LCMV. Alternatively, immune competent animals to be shipped may be tested prior to shipment. Before signing the application, the IC RIO must inform the NIH RIO if there is an increased risk of hantavirus infection. Waivers are not available for shipments of wild rodents. These rodents must be quarantined and shown to meet the NIH minimum health standard.

2. Of Import Permit.

Domestic non-approved animal sources and non-domestic commercial entities may request Approved Import Permit Waiver status, from the NIH RIO through an IC RIO, by providing:

- (a) a statement that their program is committed to meeting the NIH minimum health standard within their facilities, they are taking measures to exclude the agents from their colonies, and have tested their colonies for the applicable agents in the last year.
- (b) a description of the facility(s) to be covered by the waiver.
- (c) a description of the husbandry, health surveillance program at the facility(s), etc, and
- (d) written assurance that the institution will, within 24 hours, notify the NIH RIO (of positive test results for a NIH Minimum Health Standard excluded agent) and the sponsoring IC RIO (of any changes in their facility health status).

Approved Import Permit Waivers are reviewed annually and renewed every three years by the NIH RIO. Annually, the sponsoring IC RIO must provide assurance that conditions under which the waiver was originally granted still exist and the colonies have been tested in the last year for applicable agents. A waiver of the import permit requirement does not constitute a waiver from quarantine or isolation requirements deemed necessary by a NIH veterinarian in charge of the facility where the animals will be housed or used.

K. Quarantine Permit Service Office (QPSO): Several agencies of the United States Government regulate and require permits for the importation, shipment,

or exportation of certain animals, animal products, or etiologic agents or vectors of human or animal diseases. Investigators must work with their IC RIO to determine whether an import permit other than a 2369-1, covered by this policy, is required. The IC RIO will coordinate with the NIH RIO and the QPSO to come to a decision regarding the need for additional permits. The QPSO will provide investigators with assistance and appropriate application forms to import, export, or transport regulated materials or animals. Import and Export Permits are also available on-line. The website is:
<http://www.nih.gov/od/ors/ds/qpso.html>.

1. The QPSO must be notified at (301) 496-3353, and a USDA permit obtained, if transgenic rodents, carrying receptors which enable those rodents to develop productive infection with human pathogens, are imported into the United States or transported within the United States by NIH investigators.

2. The USDA Animal and Plant Health Inspection Service (APHIS) has statutory authority to regulate the importation of any animal-derived material or biological material that has been in contact with material of animal origin. Thus, USDA permits are required for the importation of monoclonal antibodies, hybridoma cell lines, cell cultures, and other biologic materials that have been in contact with material of animal origin, such as fetal bovine serum. USDA permit forms and information are available on-line. The website is:
www.aphis.usda.gov/forms/index.html#VS16.

3. The Department of Health and Human Services (DHHS) is responsible for regulations involving the importation into the United States or distribution after importation, of any etiologic agent or any arthropod or other animal host or vector of human disease (NIH Manual Chapter [1340-1](#), Permits for Import or Export of Biological Materials, and 42 C.F.R. Parts 71 and 72). A DHHS permit must be obtained for importation and/or distribution of these materials. The Chief, QPSO, or his/her designee, is authorized to issue DHHS import permits.

4. Finally, the United States Fish and Wildlife Service (USFWS), United States Department of Interior, is responsible for regulations involving the prevention and control of wildlife diseases, and the importation of wildlife or products derived from threatened or endangered wildlife species (50 C.F.R. Parts 13 and 14). Permits for designated port exemptions are issued through the QPSO.

L. Additional Information: For further information on this policy, contact the NIH RIO at (301) 496-2527 or the applicable IC RIO. For additional information on the importation or transportation of any etiologic agent or host or vector of human or animal diseases, or the importation of wildlife, contact DOHS at (301) 496-3353.

M. 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, Appendix 1, "NIH Records Control Schedule," Item 3000-C-6.

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 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, NIH staff conducting official reviews or investigations, and the Office of Inspector General may request access to or copies of the e-mail messages. E-mail messages must also be provided to Congressional oversight committees if requested and are subject 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 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.

N. Management Controls: The purpose of this manual issuance is to establish procedures designed to prevent the introduction of infected rodents and rodent products into the NIH which could adversely affect the health of rodents used in research, directly or indirectly interfere with research, or pose a health hazard to personnel.

1. Office Responsible for Reviewing Management Controls Relative to this Chapter (Issuing Office): ORS/DVR (301) 496-2527

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

3. Method of Review: Alternative Review; NIH RIO in consultation with the RIAS, and final approval by the NIH Animal Research Advisory Committee.

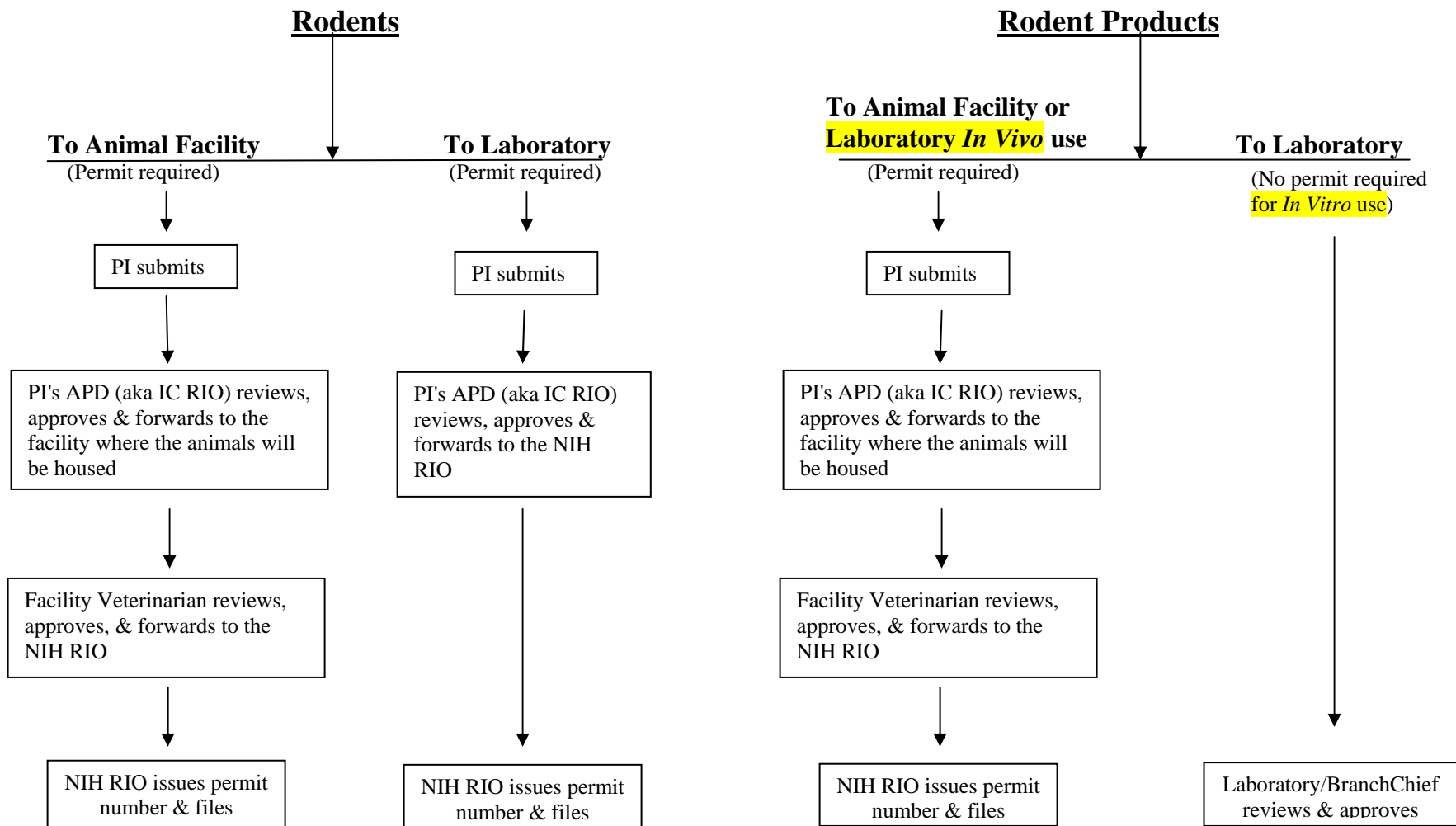
In addition, every three years an internal control review will be conducted by ORS/DVR to determine if the IC's are in compliance with the policies in the chapter. This review should include testing and look at all movement of a statistical sample of animals into NIH for the prior three years to see if the rules were properly followed and to determine if any corrective actions are required. At the same time, a risk assessment should be performed to ensure that controls are in place and are working properly.

The Intramural Program must make annual reports to both the United States Department of Agriculture and the NIH Office of Extramural Research (OER), Office of Laboratory Animal Welfare (OLAW). These agencies have regulatory

and administrative authority over the NIH IRP Animal Care and Use program. Per DHHS Policy, instances of significant noncompliance are required to be reported to OLAW. Instances of significant noncompliance will also be reported to the appropriate IC Animal Program Director and the NIH Animal Research Advisory Committee. In addition, the AAALAC International performs triennial peer review site visits to all NIH components that use animals in their IRP programs.

4. **Review Reports are sent to:** Associate Director for Research Services, Associate Director of Scientific Resources, Office of Research Services and Deputy Director for Management.

Introduction of Rodents or Rodent Products from Non-Approved Sources



Application for Permit to Introduce Rodents and Rodent Products

*See NIH Manual 3043-1 for complete instructions.
Use additional sheets if more space is needed.*

1. Request Permit To (<i>check one</i>) <input type="checkbox"/> Introduce from within U.S. <input type="checkbox"/> Import into U.S.	2. Permit is for: <input type="checkbox"/> Rodents <input type="checkbox"/> Rodent Products/Embryo
4. From (<i>Name, address, E-mail address, phone no. and fax no. of facility</i>)	

3a. To (<i>Name of requester</i>)	3b. Institute/Laboratory	5. Genus and Species, Common Name(s), Correct Nomenclature, Color, Strain/Stock or Description of Rodent Product	
3c. NIH Address (<i>Bldg./Rm.</i>)	3d. E-mail address		
3e. Phone No.	3f. FAX No.		
6a. Have these animals been injected/manipulated?		6b. Location currently housed Building: _____ Room: _____	
7. Number of Animals to be Received Male: _____ Female: _____ Age range: _____		8. Approximate Date of Arrival	9. Approved Animal Study Proposal No.
10a. Medical History of the Originating Colony or Tissue			

10b. Current Location or Source of the Colony or Tissue

10c. What diseases or parasites are known to be present in the originating colony?

11. Has colony or tissue been checked for Ectromelia (mouse pox), Lymphocytic Choriomeningitis (LCM) virus, and hantavirus (<i>if applicable</i>)? <input type="checkbox"/> Yes <input type="checkbox"/> No	12. Can these animals mount an antibody response? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	
13. Name, title, E-mail address, phone no., and FAX no. of sending institution's facility veterinarian or designee	14a. Final Location where animals or tissue will be housed and/or used 14b. Is this location listed in the approved ASP? <input type="checkbox"/> Yes <input type="checkbox"/> No 14c. Quarantine location	15. Special requirements for handling animals or tissue during the quarantine period <input type="checkbox"/> Rederivation by IETS Standards (modified) <input type="checkbox"/> Waiver of Quarantine <input type="checkbox"/> Quarantine at: _____ <input type="checkbox"/> DO NOT BLEED <input type="checkbox"/> Breed during quarantine <input type="checkbox"/> Other: _____

<i>I certify that these animals or tissues will be used in accordance with all restrictions and precautions as may be specified in the permit.</i>	16. Requester's Name	19. Signature	22. Date Signed
	17. IC Animal Program Director's Name	20. Signature	23. Date Signed
	18. Facility Veterinarian's Name	21. Signature	24. Date Signed

25. Quarantine Requirements

Permit to Introduce Rodents or Rodent Products

1. Permit Number	
2. Remarks	3. Quarantine location
4. Signature of DVR Rodent Import Officer or designee	5. Date Issued

Appendix 3 - Guidelines for the Importation of Rodents from Unapproved Sources into DVR Operated Rodent Quarantine Sites

Guidelines for the Importation of Rodents from Unapproved Sources into DVR Operated Rodent Quarantine Sites

I. Introduction

These guidelines are to assist NIH veterinarians in understanding the procedures for the importation of rodents from unapproved sources, assist them in obtaining information from the facility of origin regarding the health status of the rodents to be imported, and instruct them in requesting a waiver to the NIH rodent quarantine policy.

The rodent quarantine facility at the NIH Animal Center (NIHAC) is used for rodents entering the NIH from foreign countries and from colonies within the U.S. of unknown health status. The NIHAC and 14E Bethesda Rodent Quarantine/Rederivation site will be used for rodents that are known to harbor pathogens unacceptable to the facility(s) in which they are to be used. Rodents known to be infected with lymphocytic choriomeningitis virus (LCMV), ectromelia virus (mice), hantavirus or other major zoonotic rodent agents are excluded from NIH facilities. An exception for research purposes may be obtained with adequate justification. Decisions to accept rodents harboring LCMV, ectromelia or hantavirus are the responsibility of the Quarantine Permit Service Office with recommendations from the NIH Rodent Import Officer (NIH RIO). Institute Center (IC), or Facility Veterinarians are responsible for the disposition of animals harboring other infectious agents introduced into their areas.

II. Initiating The Import

An Application for Permit to Introduce Rodents and Rodent Products (NIH Form 2369-1) must be completed. It is particularly important that the name and telephone number of the veterinarian or other person responsible for animal health at the originating facility be provided. Since overseas telephone contact is often difficult and expensive, listing an e-mail address or fax number is recommended.

Attached is an Animal Health Data Request template form (Appendix 5) that NIH veterinarians may find helpful when contacting the originating facility and later when evaluating documentation of their pathogen monitoring and control program. All information acquired should be submitted to the IC RIO along with the application. The NIH RIO requires that testing for LCMV, ectromelia and hantavirus (if applicable) be conducted within the last 12 months. Rodents from

out of country going to the NIHAC quarantine should test negative for ectromelia, LCMV, and hantavirus. Rodents from out of country going to the 14E rederivation/quarantine must test negative for these three agents. See section VII, "Waiver from Quarantine" of these guidelines if an exception to the quarantine policy is desired. Note: The NIH RIO will not complete the import request form unless the Facility Veterinarian has signed it.

III. Housing at NIHAC Quarantine

Entering animals at the NIHAC will be held in standard polycarbonate cages with stainless steel bar lids without filter covers. These cages are held in a Trexler Flexible Film or semirigid isolators. Entries into and exits out of the isolators will be performed in a manner that avoids contaminating the area with pathogens that are potentially present. Isolators used to house rodents that harbor pinworms will be discarded or sanitized and stored for the future housing of known pinworm positive rodents. All animals at this site are fed a fenbendazole diet to reduce possible contamination from pinworms unless otherwise requested.

Rodents entering the 14E Bethesda Rodent Quarantine/Rederivation site are held in individually ventilated polycarbonate cages with filter covers. These cages along with stainless steel wirebar lids and water bottles are autoclaved before and after use. Personnel access to this site is restricted and cage changes or other animal manipulations are performed in a manner that avoids contaminating the area or other cages with pathogens that are potentially present. All animals at this site are fed a fenbendazole diet to reduce possible contamination from pinworms.

IV. Monitoring For Potential Pathogens (NIHAC and 14E/104)

A. Direct testing of imported animals provides the best indicator of their health status. Imported experimental animals will be tested for pathogens as shown below depending on their immunocompetency, value, and the investigator's preference. Imported animals will be bled for testing unless "Do Not Bleed" is checked in box 15 of NIH Form 2369-1.

B. Sentinel animals may be used to further substantiate the health status of imported rodents as comprehensive testing can not be performed on a live animal. Young female mice (4-6 weeks old) differentiated by coat color, ear tag or punch are placed in the cage with the quarantined animals or if this method is unacceptable the dirty bedding method will be used. The health status of the sentinels ordered will meet the health requirements outlined in the NIH-wide animal procurement contract and will ensure that no infectious agents are present that will cause harm to imported immunocompromised rodents. In most cases, sentinels will be tested after a four-week period of sentinelization. However circumstances may arise that require animals to be quarantined for a

longer time period.

Animals from the originating colony can be used as adjunct sentinels. If this method is used, at least two immunocompetent animals should be supplied in addition to the experimental animals. These animals should come from the same rack as the animals to be imported and will be bled on arrival and submitted for testing 4 weeks after arrival. In addition to these animals, sentinels from pathogen-free colonies will be used to differentiate between active shedding of pathogens versus an immune response from an earlier infection.

C. Test samples will be submitted to the Division of Veterinary Resources (DVR), Diagnostic and Research Services Branch (DRSB) throughout the quarantine period with a comprehensive necropsy performed near the end of quarantine. Additional health testing beyond that listed below may be required.

Test Animal	Test Procedures
Imported	Tape for mites, pinworms Pooled fecal for culture and parasitology Serology* Comprehensive necropsy**on extra animals
Sentinel	Comprehensive necropsy**

* If immunocompetent

** Includes gross pathology, serology, parasitology and bacteriology; specific tests performed are defined by the DVR, DRSB.

V. Release of Animals from NIHAC Quarantine

The NIH RIO offers the quarantined animals for release when test results indicate that the animals are free of LCMV, ectromelia (mice), hantavirus, and Salmonella, sp. Release from quarantine is documented using NIH Form 2369-2 'Rodent Quarantine Release' (Appendix 6). If test results indicate that the quarantined rodents have unanticipated LCMV, ectromelia, hantavirus or Salmonella, following discussions with the importing institute veterinarian, positive animals will either be relocated to an off campus site or be immediately euthanized. The isolator that housed the infected rodents will be collapsed, the outside sprayed with CLIDOX, and the isolator and all its contents placed in a heavy plastic bag and autoclaved.

The Facility Veterinarian for the receiving facility must evaluate the health

status of the animals in light of that facility's policy. If the rodents have pathogens that are not acceptable at the facility they are slated to enter, the owning IC may elect to find alternative housing and eradicate the pathogen(s). If the eradication process is conducted at the NIHAC/14E, it must be accomplished within a reasonable period of time; reasonable period of time is dependent upon other demands for the use of the quarantine space. If treatment or "burn out" is used, adequate testing must be performed to assure that the pathogen(s) has been eliminated. If rederivation is used, the procedures should meet the guidelines adopted by, International Embryo Transfer Society (IETS) as modified (Appendix 4).

VI. Alternative Quarantine Site (AQS)

Rodent quarantine may be conducted at facilities other than the NIHAC. If alternative quarantine locations and procedures are to be used the NIH Rodent Import Officer must first approve them. To apply for alternative quarantine site status, an IC must provide the NIH RIO with a written outline of the procedures to be used to protect both rodent colonies and personnel from LCMV, ectromelia and hantavirus during the quarantine period. The application will include: 1) location and description of the quarantine site(s) (i.e. location, access, signage, etc.); 2) precautions taken to protect colonies and personnel (i.e. method of containment, personnel training, sanitation procedures, handling of waste, etc.); and 3) individuals accountable for the site. Unresolved issues between an IC and the NIH RIO shall be brought to the Rodent Import Advisory Subcommittee, appointed by the Animal Program Directors, for resolution.

The IC RIO will inform the AQS Facility Veterinarian of an impending import using the "Application for Permit to Introduce Rodents and Rodent Products" (NIH Form 2369-1). Prior to import, a copy of the completed form, signed by the investigator, is sent to the IC RIO. The IC RIO reviews the application for a low risk from LCMV, ectromelia and hantavirus, then signs and forwards the form to the AQS Facility Veterinarian. The AQS Facility Veterinarian reviews and approves the permit, then forwards a copy to the NIH RIO. The NIH RIO assigns a Rodent Import Permit number to the application and provides a copy of the numbered permit to both the IC RIO and the AQS Facility Veterinarian. The signed rodent import permit serves as confirmation that the IC RIO and Facility Veterinarian have been notified of the shipment. The IC RIO responsible for the alternative site shall ensure the quarantine of the animals until such time that data can be generated to verify that they are free of LCMV, ectromelia and hantavirus through testing while held within the approved AQS. Animals found positive for any of these three agents will either be relocated to an off campus site or be immediately euthanatized. With release of a shipment from quarantine, serology results must be forwarded to the NIH RIO.

VII. Waiver From Quarantine at NIHAC and 14E/104

A waiver from quarantine will be granted only if the information obtained regarding the originating facility's practices and pathogen monitoring program contains sufficient evidence to ascertain that the animals present a low infectivity risk for LCMV, ectromelia and hantavirus. When a waiver of quarantine is requested, it is particularly important that the IC RIO be provided with clear information regarding the housing, husbandry, sentinel program, and health status history of the originating facility. Suggested methods for supplying the requested information to the IC RIO are as an e-mail or fax summarizing conversations with the sending institution's facility veterinarian, as a summary letter from the sending facility, as a completed questionnaire similar to the attached template, or as actual sentinel test results. Recent test results, from the sending facility, verifying a thorough pathogen-monitoring program increases the confidence that animals to be imported are free of pathogens. In order to make a decision, the IC RIO may require additional testing or information from the sending institution. The IC RIO makes the final decision on applications for waiver based upon the information supplied relative to LCMV, ectromelia and hantavirus. Applications for waiver from quarantine should be clearly identified by checking "Waiver of Quarantine" in box 15 of the rodent import permit form.

Unresolved issues between an IC and the NIH RIO shall be brought to the Rodent Import Advisory Subcommittee for resolution.

An Animal Program Director may exempt animals from quarantine, for movement directly into a laboratory, following the procedures outlined in Section H, point 5 of [NIH Manual Chapter 3043-1](#).

Notes:

All Federal requirements for the importation of rodents must be adhered to. Copies of the current requirements can be obtained from the Quarantine Permit Service Office (QPSO), the NIH Rodent Import Officer or the following: USDA requirements-website: <http://www.aphis.usda.gov>; CDC requirements-Permit Officer, Division of Quarantine, CDC (404) 639-8108 or by referencing 42 CFR, Section 71.54.

The QPSO, in the Division of Occupational Health and Safety (301) 496-3353, or the NIH RIO (301) 496-2527 will provide assistance for the importation of rodents or rabbits from a foreign source.

Appendix 4 - Requirements for Handling Imported Mouse and Rat Embryos, Oocytes, Ovaries or Sperm

Oocytes are handled as outlined below for embryos. Ovaries or sperm received for introduction into rodents are handled in the same manner, except the washing steps are excluded.

Compile and submit information regarding the potential health status of the imported embryos as for a live rodent import.

Treat the shipping or transport vessel as contaminated on arrival at the facility; decontaminate the exterior with alcohol or Clidox. It is preferable to move the straws or tubes to a clean transport vessel (e.g. Dewar flask) on arrival, leaving the original shipper outside of the animal facility.

Consider the straw or tube that holds the embryos as contaminated and wipe down the exterior with Clidox or other approved disinfectant before use. Do not open straws or tubes where clean embryos are being transferred. If there is no dedicated area for working with potentially contaminated embryos, perform all embryo manipulations inside of a laminar flow hood that protects the environment. Discard straws and tubes as contaminated waste.

Only embryos free of gross adherent material should be washed; clean with hyaluronidase when necessary. Implant only zona pellucida-intact embryos. To confirm the zona pellucida is intact and free from adherent material, observe all surfaces of the embryos at a minimum magnification of 60X.

Regulate volumes so that each wash is approximately a 100-fold dilution of the previous wash. Wash a minimum of five to ten times in sterile medium (allow sufficient time for thorough, gentle mixing in each wash). Use a new sterile micropipette each time embryos are moved from one wash to the next.

House recipient dams and offspring separate from research colonies, preferably in a quarantine facility. Perform comprehensive serologic, bacteriologic, and parasitologic testing on the resulting pups and mother before release of the offspring into general housing.

National Institutes of Health, _____

Institute Name Here

Bethesda, Maryland, U.S.A.

ANIMAL HEALTH DATA REQUEST TEMPLATE

NIH policy requires rodents to be free of lymphocytic choriomeningitis virus, mouse poxvirus, and hantavirus.

ORIGINATING FACILITY:

Originating Institution: _____

Investigator Last Name: _____ First: _____

E-mail: _____

Vivarium: _____ Vivarium Room: _____

Veterinarian's Last Name _____ First: _____

Vet Voice: _____ Fax: _____

Vet E-Mail: _____ Additional Contact(s)?: _____

COLONY DESCRIPTION:

Approximate Colony: Size In Room?: _____ Immune Status: Normal Deficient Undetermined

Breeding In Room?: YES NO

Colony Status CLOSED OPEN w/ Quarantine Required OPEN

Do Incoming Animals Come from Multiple Sources?: YES NO

SENTINEL PROGRAM:

(Please attach a letter explaining your sentinel program & known positives, or complete this section & provide a copy of the latest sentinel test results.)

Sentinel Boxes In Room: _____ Animals tested : Retired breeders Sentinels Experimental

Frequency of Monitoring?: Quarterly Semi-Annually Annually Other _____

Sentinel on Dirty Bedding YES NO (Other method of sentinel exposure _____)

Any Pathogens or Other Health Problems In Room in Previous Year?: _____

Please List Pathogens or Potential Pathogens Present in other Rodent Rooms in Same Vivaria: None Present

HUSBANDRY:

Is Husbandry Shared With Any Rooms that Contain Potential Rodent Pathogens?: NO YES

If Yes, List Organisms _____

Caging System: Conventional Microisolator Flow through Other _____

Protective Equipment: Gloves Shoe covers Hair covers Masks

Dedicated clothing Disposable clothing Change hoods Shower-in

TESTING BIOLOGICALS:

Are biologicals for use in animals routinely tested before use in your facility?: NO YES Unknown

Veterinarian: _____
(Print name) (Signature) (Date)

Please Fax the completed form to _____ at _____
Questions? Contact the Import Coordinator: E-mail: _____ or phone: (301) _____

Rodent Quarantine Release

Use prescribed by NIH Manual 3043-1

Name of NIH Investigator

These rodents or rodent tissues have been examined for evidence of the following diseases or agents. The results are indicated.

RODENTS, *Species, strain:* _____

RODENT TISSUES

1. Murine Viruses/Bacteria

Pos.	Neg.	Titer		Pos.	Neg.	Titer		Pos.	Neg.	Titer	
<input type="checkbox"/>	<input type="checkbox"/>	_____	MHV	<input type="checkbox"/>	<input type="checkbox"/>	_____	Polyoma	<input type="checkbox"/>	<input type="checkbox"/>	_____	Rat coronaviruses
<input type="checkbox"/>	<input type="checkbox"/>	_____	EDIM	<input type="checkbox"/>	<input type="checkbox"/>	_____	Sendai	<input type="checkbox"/>	<input type="checkbox"/>	_____	Hanta
<input type="checkbox"/>	<input type="checkbox"/>	_____	GDVII	<input type="checkbox"/>	<input type="checkbox"/>	_____	REO-3	<input type="checkbox"/>	<input type="checkbox"/>	_____	MCMV
<input type="checkbox"/>	<input type="checkbox"/>	_____	MPV	<input type="checkbox"/>	<input type="checkbox"/>	_____	Helicobacter	<input type="checkbox"/>	<input type="checkbox"/>	_____	Rat parvovirus
<input type="checkbox"/>	<input type="checkbox"/>	_____	MMV	<input type="checkbox"/>	<input type="checkbox"/>	_____	Mycoplasma pulmonis	<input type="checkbox"/>	<input type="checkbox"/>	_____	CARBacillus
<input type="checkbox"/>	<input type="checkbox"/>	_____	Mouse Adenovirus	<input type="checkbox"/>	<input type="checkbox"/>	_____	Ectromelia	<input type="checkbox"/>	<input type="checkbox"/>	_____	_____
<input type="checkbox"/>	<input type="checkbox"/>	_____	PVM	<input type="checkbox"/>	<input type="checkbox"/>	_____	LCM	<input type="checkbox"/>	<input type="checkbox"/>	_____	_____

2. Microbiology

Fecal Culture _____

Respiratory System:

Mycoplasma Positive Negative

Bacteria _____

Ear, middle _____

3. Parasitology

Pos. Neg.

Endoparasites (pinworms)

Ectoparasites (fur mites)

4. Pathology, Gross

5. Pathology, Histo

6. _____

Comments

Status of Rodent or Rodent Tissues

- A. These rodents or rodent tissues are released from quarantine. They may be used at NIH without further restriction. However, if unexpected illness or death occurs in these animals or animals with which they are associated, it is recommended that you contact your IC veterinarian and the DVR Rodent Import Officer.
- B. These rodents or rodent tissues were found to be infected with the agents cited above. The following restrictions apply to their holding at NIH.
- C. Due to evidence of infection noted above, these rodents or rodent tissues cannot be held or used at NIH in accordance with NIH Manual 3043-1.

Signature of DVR Rodent Import Officer or designee

Date Signed