TRANS-NIH MOUSE INITIATIVES

NIH Statement on Sharing and Distributing Mouse Resources

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I. NIH Statement on Sharing and Distributing Mouse Resources

The National Institutes of Health (NIH) supports and encourages the timely sharing and distribution of mouse resources generated using NIH funding so that other researchers can benefit from these resources. Sharing and distributing mouse resources promotes many goals of the NIH research endeavor, allowing scientists to expedite the translation of research results into knowledge, products, and procedures to improve human health. This statement applies to NIH intramural investigators as well as to extramural scientists funded by extramural grants, cooperative agreements, and contracts.

The term "mouse resources" includes genetically modified mice, inbred mouse strains, mutagenesis protocols, as well as DNA vectors and murine embryonic stem cells used in the production of knockout mice. Genetically modified mice are mice in which mutations have been induced by chemicals, irradiation, and transgenesis (e.g., knockouts and injection of DNA into blastocysts), in addition to mice that have had spontaneously occurring mutations.

There are many reasons to share mouse resources generated using NIH funds. Sharing reinforces open scientific inquiry, encourages diversity of analysis and opinion, promotes research, and allows testing of new or alternative methods for analysis and replication of results. Sharing enables the exploration of topics not envisioned by the initial investigators. By avoiding the duplication of very expensive efforts to generate mouse models with genetic changes, the NIH is able to support more investigators than it could do if these useful mouse models had to be generated in duplicate by more than one NIH grant applicant.

There are two ways to make genetically modified mouse strains available to the research community after publication in a peer-reviewed journal. The investigator can respond to requests from other laboratories to provide access to a genetically modified mouse strain. Alternatively, the mouse strain can be placed in a mutant mouse repository, such as those maintained by The Jackson Laboratory (http://www.jax.org) or the Mutant Mouse Regional Resource Centers (MMRRC) supported by the National Center for Research Resources (http://www.mmrrc.org).

II. General Considerations for the Submission of Mutant Mice to a Repository

Please note that repositories selected by a PI and/or his/her institution should be using distribution policies consistent with NIH policies for the distribution of any NIH-funded research resources.

A. Responsibilities of Donating Investigator (DI) or mutant mouse strain submitter

1. The DI shall provide PCR assay protocols/primers, tissue, DNA or related research tools to the repository for PCR assay and genotyping of the mutant mouse strain.

2. The DI shall provide a current health certificate for the submitted mutant mouse strain from their institution. The Health Status of the strain may not affect the acceptance status of the strain; it is solely to assist the repository with managing the risk of contamination of their facilities.

B. Mouse transfer and shipping to a repository (or requesting investigator)

1. Each repository has developed its own shipping and receiving policies. Therefore, the DI will contact the specific repository and obtain instructions for the shipping and transfer of the mutant mouse strain. If shipping between institutions is arranged, representatives from the Laboratory Animal Care (or Medicine) units will need to establish contact.

2. In general, the following guidelines can be used for mouse transfer and shipping:

    a. For mutant mouse strains submitted to a repository, the DI is encouraged to provide as many mice as possible (e.g., 10 females & 6 males, 5-12 weeks of age recommended minimum).

    b. Generally, the DI assumes all shipping costs. In the case of shipping of mice to a requesting investigator from a DI, the requesting investigator assumes all shipping costs.

    c. Upon receipt of the mutant mice, the repository confirms receipt with DI. Alternatively, the requesting investigator confirms receipt of the mice with the DI.

d. Examples of requested information may include: Health status certificate, backcross information, genotype, genotype assay protocol, husbandry protocol if non-standard, founder# if Tg, and other information which may be necessary to maintain the strain.

III. Example of Mouse Sharing Plan

Following the characterization and peer-reviewed publication of the transgenic mouse strain generated, mice will be freely distributed to investigators at academic institutions wanting mice for non-commercial research. Individual requests for shipment of mice generated by this program project funding to AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care International) accredited institutions will be honored. The recipient investigators would provide written assurance and evidence that the animals will be used solely in accord with their local IACAC review; that animals will not be further distributed by the recipient without consent of our-Program; that animals will not be used for commercial purposes.

Requests for mice from for-profit corporations to use the mice commercially will be negotiated by our institution's technology transfer office. All licensing shall be subject to distribution pursuant to my institution's policies and procedures on royalty income. The technology transfer office will report any invention disclosure submitted to them to the appropriate Federal Agency.

In addition, all of the transgenic mice generated will be deposited in the Mutant Mouse Regional Resource Centers (MMRRC) www.mmrrc.org/ system. MMRRC cryopreserves embryos and distributes the frozen embryos to biomedical researchers. The MMRRC is a collaborative effort, funded by grants from the National Center for Research Resources (NCRR), NIH.

To facilitate sharing and distribution of the transgenic/knockout mice and associated resources developed under this grant, mice will be maintained in a specific pathogen free facility. This facility will maintain the mice free of the following microorganisms and pathogens (e.g., pinworms, mouse hepatitis virus(MHV), Sendai virus, mycoplasma, mites, etc.) Should the transgenic/knockout mice become infected with any of these microorganisms, the mice will be rederived through embryo transfer.

"Other Research Resources" generated with funds from this grant will include DNA constructs, etc. These resources, as available, would also be freely distributed upon request to qualified academic investigators for non-commercial research.

My institution and I will adhere to the NIH Grants Policy on Sharing of Unique Research Resources including the "Sharing of Biomedical Research Resources: Principles and Guidelines for

Recipients of NIH Grants and Contracts" issued in December, 1999. (http://ott.od.nih.gov/NewPages/Rtguide_final.html). Specifically, material transfers would be made with no more restrictive terms than in the Simple Letter Agreement or the UBMTA and without reach through requirements. Should any intellectual property arise which requires a patent, we would ensure that the technology remains widely available to the research community in accordance with the NIH Principles and Guidelines document.

Sincerely,

Principal Investigtor(s)

And

Authorized Institutional Official

IV. Partial List of Mouse Repositories and Databases

- The Trans-NIH Mouse Initiative Mouse Resource website (lists some repositories, as well as other mouse related resources): http://www.nih.gov/science/models/mouse/resources/index.html

- The Jackson Laboratory, Bar Harbor, Maine: www.jax.org

- Mutant Mouse Regional Resource Centers (MMRRC): www.mmrrc.org
  Generally, the MMRRC will accept mice free-of-charge, however, there may be a fee to cover costs associated when frequency of requests or production of mice is low.

- Mouse Models of Human Cancer Consortium (MMHCC):
  http://web.ncifcrf.gov/researchresources/mmhcc/default.asp.

- NIAID Mouse Exchange Program: http://www.niaid.nih.gov/reposit/taconic.htm

- NCI Laboratory Animal Production Program:
  http://resresources.nci.nih.gov/database.cfm?id=404

- Mouse Genome Database Project (MGD): http://www.informatics.jax.org

- Mouse Gene Expression Database Project (GXD):
  http://www.informatics.jax.org/mgihome/GXD/aboutGXD.shtml

- TBASE: http://tbase.jax.org/

- ORNL Mutant Mouse Database: http://bio.lsd.ornl.gov/mouse/

- Tennessee Mouse Genome Consortium: http://tnmouse.org/

- Database of Gene Knockouts in Mice that Affect Nervous System Phenotypes and Function Index: http://165.112.78.65/KOS/KOSearch.taf?function=form

- MRC Mammalian Genetics Unit & UK Mouse Genome Centre, Harwell, UK: http://www.mgu.har.mrc.ac.uk/

- BioMedNet Mouse Knockout Database: http://research.bmn.com/mkmd

V. Frequently Asked Questions (FAQs) and Answers

V.a. Definition and Policy

Q1: What is the definition of the term "mouse resources"?

A1: The term "mouse resources" includes genetically modified mice, inbred mouse strains, mutagenesis protocols, as well as DNA vectors and murine embryonic stem cells used in the production of knockout mice. Genetically modified mice are mice in which mutations have been induced by chemicals, irradiation, and transgenesis (e.g.., knockouts and injection of DNA into blastocysts), in addition to mice that have had spontaneously occurring mutations.

Q2: What is NIH policy regarding the distribution and sharing of mutant mouse strains created with NIH funds?

A2: The NIH expects mouse resources generated with the aid of NIH funding to be timely distributed and shared with the scientific community. Investigators submitting an NIH application must include a concise plan addressing the timely distribution of mouse resources, unless the proposed research will not generate such resources.

Q3: To whom does this policy apply?

A3: This statement applies to extramural investigators funded by NIH extramural grants, cooperative agreements, and contracts, including SBIR and STTR grants. This statement also applies to NIH intramural investigators supported by NIH intramural funds.

Q4: Is this a new policy?

A4: This statement is an extension of NIH Grants Policy, [NIH Grants Policy Statement (http://grants.nih.gov/grants/policy/nihgps_2001/) and Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources: Final Notice, December 1999 (http://ott.od.nih.gov/NewPages/RTguide_final.html)].

V.b. Impact of Sharing of Mouse Resources on Research Practices

Q5: My colleagues and I spent considerable time, energy, and resources on generating and characterizing the mouse resources we created. We want to maximize the fruits of our labor. Can we delay sharing until publication so other experiments can be performed and manuscripts prepared?

A5: NIH recognizes that the investigators who generated the mouse resources have a legitimate interest in benefiting from their investment of time and effort. However, unnecessary delay of publication and prolonged exclusive use of the mice are not in the best interests of the research community or the public health. Therefore, not sharing mice for a prolonged period will generally not be considered an acceptable plan. Furthermore, it may not be in your best interest as an investigator. If your publication is delayed, other investigators may publish papers first and receive credit for the same mutant mouse that you and your colleague have generated and have been characterizing. You may wish to maximize your productivity and the impact of your work by engaging in collaborations before and after publication describing the mutant mouse. By publishing in a timely manner, you and your colleagues will likely be able to publish your work in a high-impact journal, which will benefit the research community, as well as your career and the careers of your colleagues.

Q6: Can I require investigators using my mouse resources to add my name to the papers they publish?

A6: No. You may only require them to do so if you are involved in collaboration with them and contribute intellectually to the paper. This type of stipulation hinders open scientific inquiry and generates potential conflicts of interest. Investigators using the mutant mouse may find results that directly contradict your results. However, it is appropriate for you to be acknowledged as the source of research resources upon which the manuscript is based.

Q7: Is there a requirement for citation or acknowledgement of the investigators who generated the mouse resources in papers based on research that used the mouse?

A7: It is appropriate to acknowledge the source of the mutant mouse upon which the manuscript is based. This follows best practices for scientific publication. Journals usually have an

acknowledgement section. Before submitting a paper, you should read and consult the editorial policies of the journal.

Q8: If I made a knockout mouse or a transgenic mouse, can I distribute only the DNA vectors?

A8: Sharing the mice, sperm, and/or embryos may be the most efficient and effective means of meeting the best interests of the scientific community and of furthering research. Providing vectors used in the generation of transgenic or knockout mice may be an efficient and effective distribution alternative for furthering research in some cases. This situation would be acceptable, if you can show that the person requesting the mutant mouse can: 1) make the mouse from the reagents given; 2) make the same allele as the mouse you made; 3) make the mouse at a cost that is equal to or less than the cost to breed and ship the mice or breed the mice from cryopreserved sperm or embryos; and 4) generate the number of mice equal to or greater than the number of mice that could be generated from cyropreserved sperm or embryos in the same period of time. In any event, NIH expects you to make the mice available to the scientific community as well as reagents such as vectors and cell lines used to generate the mutant mouse strains.

Q9: Can I patent my mouse resources to protect my intellectual property rights and the property rights of my institution?

A9: Yes. You and your institution may choose to retain title to subject inventions such as a mutant mouse developed under federal funding under the provision of the Bayh-Dole Act and incur all the costs and expenses of filing patents on this technology. However, such a research resource must still be made reasonably available and accessible to the research community in accordance with the NIH Grants Policy Statement (http://grants.nih.gov/grants/policy/nihgps_2001/), including the NIH Research Tools Policy (http://ott.od.nih.gov/NewPages/RTguide_final.html). If a Determination of Exceptional Circumstances (DEC) is announced before a grant or contract is awarded, you may not patent a technology covered under the approved DEC.

Q10: Could patenting of mice interfere with the distribution of mutant mice to the scientific community?

A10: Patenting of mice could possibly interfere with the distribution of mutant mice to the scientific community if such patents are enforced inappropriately. However, the NIH Research Tools Policy

provides guidance on the appropriate implementation and use of intellectual property. This policy also provides for reasonable availability and accessibility of such resources to effectively further the research enterprise (http://ott.od.nih.gov/NewPages/RTguide_final.html).

Q11: What types of agreements are acceptable under NIH policy?

A11: Most transfers to not-for-profit entities should be implemented under terms no more restrictive than the Uniform Biological Materials Transfer Agreement (UBMTA) (http://ott.od.nih.gov/newpages/UBMTA.pdf). In particular, recipients are expected to use the Simple Letter Agreement provided at http://ott.od.nih.gov/NewPages/RTguide_final.html, or another document with no more restrictive terms, to readily transfer unpatented tools developed with NIH funds to other recipients for use in NIH-funded projects. If the materials are patented or licensed to an exclusive provider, other arrangements may be used, but commercialization option rights, royalty reach-through, or product reach-through rights back to the provider are inappropriate. Similarly, when for-profit entities are seeking access to NIH-funded tools for internal use, recipients should ensure that the tools are transferred with the fewest encumbrances possible. The Simple Letter Agreement may be expanded for use in transferring tools to for-profit entities, or simple internal use license agreements with execution or annual use fees may be appropriate. [http://ott.od.nih.gov/NewPages/RTguide_final.html] There may be additional issues regarding genetically modified mice. Therefore, you should confer with your organization's technology transfer office and sponsored research program office to transfer such mice. Your transfer agreement may also need to address issues of animal custody, care, and use under all applicable Federal laws, including but not limited to the Animal Welfare Act.

Q12: If I receive funding from both the NIH and a biotechnology company and the company's sharing policy conflicts with the NIH, which policy should I follow?

A12: Organizations receiving funding from the NIH must have policies and procedures in place to ensure that any agreements entered into with third parties are consistent with the terms and conditions of their NIH funding award, including the provision of intellectual property rights to the NIH, and that third parties are informed of the NIH requirements [see the NIH Grants Policy Statement for guidance (http://grants.nih.gov/grants/policy/policy.htm)]. Therefore, to remain in compliance with the NIH award, you will need to revise any third-party agreements that are

inconsistent with the terms and conditions of an NIH award. For guidance, see "Developing Sponsored Research Agreements: Considerations for Recipients of NIH Research Grants and Contracts" (http://ott.od.nih.gov/newpages/text-com.htm) and "Intellectual Property Reporting for NIH Grantees That Also Have Involvement with the Veterans Administration" (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-033.html).

Q13: Can I charge money to investigators requesting mouse resources?

A13: Yes, you can charge for shipping and distributing the mouse resource so long as the mouse resource remains reasonably available and accessible to the research community. For additional information, see section II of this document, under "General considerations for submission of mutant mice to a repository." You should also confer with your technology transfer office and/or office of sponsored programs for guidance.

Q14: I don't want to share my mutant mice and reagents used to make the mice. Can I be forced to do so?

A14: Sharing of research resources is a very important NIH policy. NIH requires that you include a plan for sharing mice in your application and the quality of that plan can affect the institute's decision to make an award.

The Scientific Review Group (SRG) may comment on your sharing plan during the peer review of your application. If your application is selected for an award, NIH program staff will review and ask you to address and resolve any concerns about the sharing plan (as well as any other issues raised in the review). These issues must be resolved before making any award. If your application is funded, you will be expected to share mice according to the sharing plan consistent with NIH policy. Failure to comply with your sharing plan may be carefully considered in future funding decisions for you and your institution.

Q15: What can I do if I believe an investigator is refusing my request for mutant mice?

A15: If you believe an investigator will refuse your request, you should still make the initial request. In certain cases, you should make your request for mice in writing. The request must contain a brief

outline of your research objectives and IACUC approval information. If the provider refuses your request, you could ask why.

If the response letter details how the investigator is making good faith efforts to abide by his/her approved sharing plans and provides a reasonable explanation as to why the mice are not yet currently available, you should try to find another source of these mice. For example, the investigator may have deposited his mice with a repository but the repository does not have sufficient stock to distribute the mice yet. On the other hand, if no letter is received or if you still do not believe the inventor of the mutant mouse strain is acting in good faith, you should speak with your NIH program officer. Also, you should confer with your own organization's technology transfer office and/or office of sponsored programs for guidance.

Q16. I am an investigator without NIH funding. What should I do if I encounter an investigator who refuses to share NIH generated mouse resources? I do not have a program officer to contact.

A16. Send a written request to the investigator specifying the objectives of your research and your IACUC approval information. If you do not receive a response or you believe the response to be inadequate, you may wish to confer with your own technology transfer office and/or office of sponsored programs for additional guidance. You may also consider conferring with a member of the Extramural Technology Transfer Policy Staff at the NIH Office of Technology Transfer. The NIH Office of Technology Transfer is the primary NIH office handling both extramural and intramural technology transfer policy matters for all of NIH.

Extramural Technology Transfer Policy Staff

NIH Office of Technology Transfer (NIH-OTT)

6011 Executive Boulevard, Suite 325

Rockville, Maryland 20852

Telephone: (301) 496-7057

Fax: (301) 402-0220

Email: NIHOTT@nih.gov

V.c. Rationale for Sharing of Mouse Resources

Q17: Why should I make my mouse resources available to the scientific community?

A17: The timely distribution of mouse resources furthers research and scientific progress without needless duplication of effort. It also enables other investigators to extend the scope of research to investigation beyond that envisioned by the creator of the mutant mouse strain. These resources afford rich opportunities for new areas of inquiry. There are more experiments to be done than can be carried out by the laboratory of a single investigator. By making mouse resources more widely available, students, post-docs, and investigators learn new methods of analysis, thus improving training. The expansion of the pool of trained investigators and the availability of mouse resources to the scientific community may lead to more rapid breakthroughs for diagnosis, prevention, and treatment of disease and improvements in public health. These goals are central to the mission of the NIH.

Q18: Is sharing and distribution of unique resources such as mouse resources with the scientific community widely accepted as good practice?

A18. Yes. Journals such as PNAS, Cell, Neuron, Immunity, The Journal of Immunology, The Journal of Neuroscience, and Science require investigators to make unique resources available so that the results can be verified and additional research promoted. Both the Society for Neuroscience, with a membership of 29,000 scientists, and FASEB, consisting of 19 societies and a membership of 66,000 scientists, have taken positions that are consonant with the NIH policy. The policy of the Society of Neuroscience is that "unique and propagatable research materials used in studies being reported must be made available to qualified scientists for bona fide research purposes" (see http://apu.sfn.org/content/AboutSfN1/Guidlines/guidelines.htm and http://apu.sfn.org/content/AboutSfN1/Guidlines/guidelines.pdf) under section 1.8 of "Guidelines: Responsible Conduct Regarding Scientific Communication," Society for Neuroscience, 1998). In 1999, a letter from David G. Kaufman, MD, PhD, FASEB President, to Barbara McGarey of the NIH Office of Technology Transfer stated that the FASEB endorsed the policy about sharing unique resources described in the document "Sharing Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts" (see http://www.faseb.org/opar/letters/1999/McGarvey.html).

Q19: Who benefits from the sharing and distribution of mouse resources?

A19: Everyone benefits, including investigators, the scientific community, and the public, from broader access and use of these important scientific resources. Restricted availability of unique research resources can impede the advancement of research and improvement of medical care. The sharing of biomaterials, data, and software in a timely manner has been an essential element in the rapid progress made in the genetic analysis of mammalian genomes. Sharing and distribution of unique resources such as mutant mice makes more effective use of resources by avoiding duplication of effort, thereby preserving resources and permitting investigators to focus on scientific questions instead of resource generation. Some of these questions and avenues of research may not have even been envisioned by the inventor of the mutant mouse. As the creator of the mutant mouse, your reputation will grow as the mutant mice are used in studies and subsequently cited in publications. Finally, should there ever be a disaster in your laboratory resulting in the destruction of your mutant mouse strain, other laboratories could have stocks that could be used to replenish your stock. In recent history, disasters such as floods at Baylor University, fires at The Jackson Laboratory, and power outages at Columbia University have occurred that have resulted in loss of valuable research resources.

V.d. How Investigators Can Share Mouse Resources

Q20: What are the different means of sharing mouse resources?

A20: You can share under your own auspices or you can deposit and distribute through a mouse repository.

Q21: The expectation that I provide thousands of mice to the scientific community upon publication seems unrealistic and puts an unnecessary burden upon my laboratory. Breeding mice isn't like growing up a plasmid. To breed mice, I will need to hire a technician and request more space in the mouse colony. Also, I need these mutant mice for my own research program and just have enough to do the experiments I proposed in my NIH research grant. How do I deal with this problem?

A21: A solution to this problem is to provide a breeding pair to a commercial vendor or to a national repository such as the NIH-funded Mutant Mouse Regional Resource Centers (MMRRC) (http://www.mmrrc.org/) that distributes mice consistent with NIH policy. (For some possible

repositories, a listing is in section IV of this document). These repositories can breed mice and cryopreserve sperm and embryos. This eliminates needless hassle and helps you to meet your obligations to distribute mutant mice strains. Your breeding efforts can be focused on your needs and those of your collaborators. Moreover, by providing your mice to a repository, you provide insurance against any mishap. Many investigators at Baylor were fortunate to have distributed their mice to other investigators and repositories before the flood in 2001. The flood destroyed their strains, but they were able to replenish their stocks. Furthermore, fires have occurred at the Jackson Laboratory and power failures have occurred at other institutions resulting in loss of mouse strains.

Q22: Suppose all of the repositories refuse to accept my mutant mouse strain. What should I do then?

A22: Repositories and vendors refuse to carry mutant mouse strains for a variety of reasons. They may believe that there will not be sufficient demand, that their capacity is currently being overtaxed, or that the stock is too difficult to maintain. It is also possible that a repository is at capacity or that they are having a problem with disease. You may (1) request money in your budget to pay for the cost of distributing mice, (2) request an administrative supplement, or (3) apply for a competitive supplement to your grant. Before submitting such a request, you should speak directly with your program officer to determine if funds are available and/or whether an institute supports supplement programs.

Q23: Because I anticipate relatively few requests for my mice, I'm planning to share under my own auspices. Nevertheless, this will cost technician time and will require special shipping equipment. How am I supposed to cover these expenses?

A23: NIH supports the sharing of research resources, and funding for distribution and sharing should be addressed in your initial application. You can request resources to share in your application, and you should include information in your plan to share in the relevant sections, such as budget, research plan, and animal subject section. If you have already received your award, you should talk with your NIH program official about the availability of supplemental funding.

Q24: I don't anticipate a very big demand for my mutant mice. I don't have the time or resources to respond to requests. What should I do?

A24: Some repositories, such as the MMRRC (http://www.mmrrc.org/), offer to accept strains for cryopreservation only. This maintenance level for mouse strains that are not in a significant demand by the scientific research community conserves research dollars for the repositories and allows preservation of a larger number of mouse strains.

Q25: When I share mice, am I also supposed to share associated records about mice and tools?

A25: Yes. You are expected to share any PCR assay protocols/primers, tissue, DNA, or related research tools necessary for PCR assay and genotyping of the mutant mouse strain. Distribution of other research tools related to the mutant mouse strain should also be addressed in the sharing plan. The breeding history of the mouse strains should also be disclosed. However, some of this information may already be disclosed in your publication. For additional details, please see section II under "General considerations for submission of mutant mice to a repository."

Q26: How well does the mouse need to be characterized before distribution?

A26: The amount of information needed from the provider may vary from investigator to investigator. Criteria for acceptance of mouse strains and resources vary among repositories. Steering or Coordinating Committees oversee the acceptance of mouse strains into the repositories. Information on web sites or phone conversations with representatives from the repositories may provide guidance. However, a few general rules apply: 1) The mutant strain should be of sufficient interest to the general scientific community that the strain is requested for research applications and 2) the mutant strain should have been described in a peer-reviewed scientific publication or at a scientific meeting.

Q27: How do I announce availability of mice?

A27: The best way to "advertise" the availability of a mutant mouse model is through peer-reviewed publications and national and international meetings. Additionally, submission of a mouse strain to one of the repositories will "advertise" the strain on that website, which can be searched by other researchers.

Q28: How do I find out what mice are available?

A28: You can find this information from publications and electronic databases. Also, websites of mouse repositories generally list the available mice. Please see section IV for a partial list of such repositories and databases.

Q29: If an investigator without a biosafety level 3 (BSL-3 or P3) containment facility requests a mutant strain of mice to be used in an experiment studying an infectious agent that requires a BSL-3 facility, can the creator of the mutant mouse strain refuse to provide the mutant mouse?

A29: The creator or source of mutant mice should not release animals into a situation where they cannot be assured that the mice are properly contained and maintained. Your transfer agreement document(s) should address issues of animal custody, care, and use under all applicable Federal laws, including but not limited to, the Animal Welfare Act. One useful reference is the NIH/ARAC Animal Transfer Agreement, which is available at http://oacu.od.nih.gov/ARAC/transfer.htm. Your technology transfer office, office of sponsored research programs, and/or office of animal care should be conferred with, as appropriate, for such transfers.

Q30: If an investigator without IACUC approval requests mutant mice from the creator of the mutant mouse strain, can the creator deny the request?

A30: The requestor's institution is responsible for ensuring that all requirements for animal care and housing are satisfied. However, some simple questions regarding animal care and the availability of a veterinarian responsible for the mice at the requestor's institution will clarify most issues. For guidance in formulating your information acquisition, please visit the Jackson Laboratory's Mice Orders website at [http://jaxmice.jax.org/orders/newcustomer.html] and click on New Customer Application Form (http://jaxmice.jax.org/orders/newcustomerform.pdf). Another useful reference is the NIH/ARAC Guidelines, which is available at http://oacu.od.nih.gov/ARAC.

Q31: What is my responsibility if the mutant strain of mice that I made became infected with a pathogen sometime during its generation and breeding?

A31: It is advisable that mice be bred in a specific pathogen facility (SPF). Sick mice can alter the results of experiments. It is likely that the enthusiasm of a study section, as well as the enthusiasm of NIH program staff, will be greatly dampened if a proposal is submitted that does not describe the use of a barrier facility in the derivation and breeding of mice. Should the investigator become aware

that the mice became infected during their creation and generation, the investigator should take steps to re-derive the animals. It is not necessary to start from scratch. Because national repositories routinely re-derive newly accepted mutant mouse strains, any strain deposited in a repository will be undergoing the process of re-derivation. Therefore, each strain's submission to a repository is handled on a case-by-case basis.

Terms and conditions of strains submitted to a repository need to be discussed on a case-by-case basis. For additional information, see section II of this document under "General considerations for submission of mutant mice to a repository."

Q32: How do I ship mice either to a repository or to a requesting investigator?

A32: In either case, you should talk to a representative of your Laboratory Animal Care Unit at your institution and seek guidance. These units ship and receive animals on a regular basis and will provide you with the necessary help and information. For example, the University of Florida maintains websites that provides useful information about animal shipping and policies concerning animal care (http://iacuc.ufl.edu/Guides.htm). Additionally, if you plan to submit your mutant mouse strain to a repository, you will need to contact the repository and work out shipping arrangements.

Q33: I am a foreign investigator who receives NIH funding. What are the rules regarding shipping mice to the United States?

A33: Regulations may vary from state to state within the United States. For information on importing animals into the United States, please contact the Veterinary Services office in the destination state. For information on exporting animals from the United States, please contact the Veterinary Services office in the origination state. A list of Veterinary Service offices can be found at the USDA animal regulations library website http://www.aphis.usda.gov/vs/area_offices.htm).

Permits can be found at http://www.aphis.usda.gov/vs/import_export.htm. USDA permit should be obtained if transgenic mice carrying receptors that enable them to develop productive infections with human pathogens are imported into the United States or transported within the United States.

You should also check with the Centers for Disease Control (CDC) for their current guidelines regarding importation of animals to the United States (http://www.cdc.gov/od/ohs/biosfty/imprtper.htm).

Your institution may be able to provide guidance regarding the shipment of live animals and related research resources. You should confer with applicable offices at your institution for appropriate guidance.

Q34: What are the rules for exporting mice?

A34: Exports fall under the jurisdictions of the U.S. Department of Commerce. For additional information, call (202) 501-7900 or visit their website to obtain additional contact information (http://www.commerce.gov).

V.e. Questions About the Mouse Sharing Plan

Q35: Do I need to address the sharing of unique resources such as the distribution of my mouse resources in my application?

A35: Yes. You must address the sharing of mouse resources in the sharing plan in your application. You can accomplish this in a brief description of the plan in the vertebrate animal section, which follows the research plan section. In addition to information required in that section, your plan should also discuss how you will make your mice available to the scientific community, how you will address intellectual property issues, and how you will maintain your mice under SPF conditions. An example of a sharing plan is included in section III. If you are requesting funds to distribute animals or resources, you should include this information in your budget justification.

Q36: Should I discuss my sharing plan with my institutional technology transfer office and business office?

A36: Yes. Issues surrounding the sharing plan and intellectual property are complex. Plans should be developed with individuals from your institution who have expertise in this area. These experts could be from your sponsored research office, your technology transfer office, your office of general counsel, and/or any other appropriate office of your particular institution. Such consultation should help clarify the policy of your institution regarding sharing and distribution of research resources

such as mutant mice, as well as your institution's policy regarding intellectual property and any inconsistent obligations with third parties.

Q37: In my sharing plan, should I describe how I plan to maintain my mice free of pathogens and other microorganisms?

A37: It is extremely difficult to distribute mice infected with pathogens and other microorganisms. In the methods section of your proposal, you should describe how mice are maintained free of pathogens and other microorganisms.

Q38: How will the adequacy of my sharing and distribution plan be evaluated?

A38: The Scientific Review Group (SRG) or study section may comment on the adequacy of the sharing plan. These comments will not affect the overall priority score assigned to the application. NIH program staff will review the plan when making funding recommendations.

Q39: Will I have to document sharing of resources in the yearly progress report for my continuing renewal?

A39. You should report the number of requests and number of requests fulfilled when submitting your non-competing renewal progress report. NIH Program Staff will examine this issue as one of the criteria for continuation of funding.

Q40: What should be addressed in my research resources sharing plan?

A40: Sharing plans may vary. An example of a sharing plan which has been found acceptable for a past RFA is in section III.