

**UNIVERSITY OF CALIFORNIA SAN DIEGO
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE**

Policy and Guidelines for the Use of Rodents in Research

In the interest of creating a research environment which minimizes, wherever possible, the introduction of rodent diseases into animal colonies, the following policies are in effect. All personnel working with rodents are required to be knowledgeable of these policies as a condition of working on animal research protocols involving rats and mice. Since the introduction of rodent pathogens can have significant and catastrophic consequences for research using these species, investigators should assure that all of their employees who work or come into contact with these species at UCSD follow these policies.

There has been explosive acceleration of the use of specialized rodent models at UCSD in the past several years. This has resulted in many requests for the acquisition of animals from outside research facilities, all of which pose new and complex risks for disease introduction. Many of these valuable animals are microbiologically contaminated or have intentionally altered immune systems; in other cases the degree of immune-competency is undetermined.

The purpose of this communication is to reiterate many general precautions as well as to provide a practical context for expectations about disease control in research rodents.

Background

Rodent pathogens include a wide range of viruses, bacteria, protozoa and ecto- and endoparasites which may be difficult and expensive to eradicate after they become established. The complex multi-site research environment at UCSD, with many "open" animal facilities, increases the risk of contamination of rodent populations.

Notwithstanding the use of newer microisolator caging systems in most areas, the risk of colony contamination still is significant, as many rodents leave the housing unit, travel to an investigator's work-site and then return to be housed in the animal facility. The risk factors for introducing new pathogens (and exporting them to other UCSD sites) are directly related to the degree of freedom of animal movement between animal facilities and laboratories.

Transmission of pathogens occurs in different ways; some organisms are very labile and can only remain viable for short periods outside of the host animal. Others, however, such as eggs from pinworms, are very hardy and easily transported on clothing, shoes, hair and other surfaces, remaining infective for long periods in the environment. Whether a disease organism infects a host depends on immune status (general health, immature immune systems in pups, e.g.) and the conditions and dose of exposure.

Disease transmission can occur at many points in the animal use process. To reduce the likelihood of contamination through new acquisitions, only selected commercial vendors are "approved" for use. For many years it has been the policy of the University to require the purchase of research animals through the [Animal Acquisitions](#) office. Not all laboratory animals from commercial sources are totally pathogen free, and some organisms previously regarded as acceptable biota of rodents are becoming known to interfere with the immune response and other physiological systems in rodent research models. Furthermore, the use of immune-compromised rodents and transgenics of unknown immune competency create additional risk of pathogen contamination, resulting in clinical and sub-clinical disease.

While it is impractical and even undesirable, to maintain gnotobiotic (germ-free) animals for most research applications, it is important to exclude, limit or at least define most known pathogens and to prevent cross-contamination between populations of animals. Some pathogens do not cause obvious clinical disease, but can become cryptic research variables and affect the outcome of a study. Literature is available on examples of this type from the veterinary staff of the Animal Care Program and reprints have been regularly posted on the Animal Research News bulletin boards at the entrances to animal facilities.

In many large research institutes it is not uncommon for periodic incidents to occur that constitute a

disease "break." The purpose of the sampling done in the rodent housing areas on campus is to screen for a panel of common pathogens to measure the success of efforts to exclude and contain various undesirable organisms. All users of rodents in research have an obligation to have a fundamental knowledge of the existence of rodent pathogens and of the measures that can be taken to reduce the possibility that animal subjects will be affected by them. This advisory notice is intended to address this topic and expand that understanding.

Highly Controlled Facilities

In certain strictly controlled facilities, where research space has been designed into the vivarium itself, animals are not permitted to return back to the colony if they are physically removed nor should animals be transferred between investigators or populations within the facility without veterinary authorization. The obvious purposes of these restrictions are to preclude the introduction and transfer of pathogens between animals. Strictly controlled facilities may have other design features that segregate animal, personnel and equipment traffic using a "clean" and "soiled" traffic pattern. Additional measures include strict adherence to clothing changing protocols, showering of personnel to remove surface contaminants from skin and hair and sterilization of bedding, feed and equipment by autoclaving.

"Barrier" facilities are operated with the strictest set of criteria for animal acquisition, movement and husbandry; they also require significant modifications of staff work behavior and result in higher operating costs.

Conventional Facilities

In "conventional facilities," which are the more standard vivaria, the nature of building design, work practices and freedom of personnel and animal movement inherently increase the probability that colonies could become contaminated with rodent pathogens. Animals are frequently removed to areas outside the vivarium where the investigator becomes wholly responsible for limiting the risk of contamination. Animals may be transported through common hallways where the exposure to rodent pathogens can occur. Animals may become contaminated within an investigator's laboratory from secondary feral rodent contact or by primary and secondary personnel themselves, who may keep rodent pets or transfer organisms from their residences, garages, streets or endless locations.

General Work Practices

The following work practices can help to reduce the contamination potential for rodents in research, but are not all-inclusive:

1. No personnel working with research rodents should keep related species as pets.
2. All research personnel should wear clean clothing to work which is less likely to have been in contact with feral rodents.
3. All personnel should endeavor to keep their personal residences, yards, garages, etc. free from rodents.
4. Frequent changing of lab coats and other protective clothing should be made a habit.
5. Association with other personnel who work with rodent populations should consider possibilities of transfer of organisms by contact with their clothing or shared equipment.
6. When rodents enter a laboratory, designated work spaces should be used which can be disinfected after use.
7. Handling procedures should be designed to minimize cross-contamination. All cages should be opened within an operating change station or biosafety cabinet, if available. Open cages of animals may not be placed on the floor at any time. Rodents must be contained within a cage or other approved container at all times. They may not be left loose to run through the change station or sink.
8. All equipment and instrumentation which can be decontaminated should be regularly cleaned.
9. Researchers should insist that general housekeeping and floor disinfection be attended to.
10. Conditions that contribute to contamination - social traffic, keeping feral rodent attractants such as food - should not be permitted in the animal laboratory.

11. All transport carts should be disinfected regularly - and in particular prior to re-entering an animal facility.
12. Animals are not allowed to be kept over 12 hours outside of the laboratory without the express permission of the IACUC.
13. When an animal is removed from the vivarium, the cage must be tagged or labeled with the PI name, Protocol #, the time and date of removal, and the name of the person responsible for the animal while out of the vivarium.
14. All soiled cages and water bottles should be promptly returned to the "soiled" area of the vivarium for washing.
15. When visits may be made to other research facilities with animals, consideration should be given to the possibility that pathogens could return on one's clothing or person.
16. All instances of feral rodent activity in University buildings should be reported to maintenance personnel to assure that control/eradication measures are attended to promptly.
17. Do not visit animal facilities or areas unnecessarily or invite non-essential traffic to locations where animals are present.
18. Remember that all biological materials which have been passaged in rodent systems have the potential to carry disease pedestrians to live animals. Cell cultures and other such biologicals should be tested to assure their freedom from rodent pathogens prior to their introduction into rodents.

Animal Acquisitions

All animals must come from controlled sources! Animals are not to be transferred between colonies or between vivarium without the written permission of the Animal Care Program. Animals are not to be given, exchanged or borrowed from other investigators or projects. The general policy for acquisition of animals from non-vendor sources follows:

- o *From Other UCSD Colonies*
No animals are permitted to be moved between colonies or vivaria without the written consent of the Animal Care Program, even if the animals belong to the SAME investigator. A facility/colony transfer request form is available from ACP by calling campus extension 20083. The signature of the responsible husbandry supervisor on the transfer form will now be required along with veterinary authorization.
- o *From Other Institutions*
Procedures have long been in place for the acquisition of animals from non-vendor sources. For request forms and instructions, contact the Animal Care Program. An adequate colony history and credible testing data are necessary to properly assess the risk from other facilities' animals. Where unfavorable, questionable or incomplete information is provided, it is our policy to err conservatively and not permit the acquisition. Such acquisition history gathering may involve significant staff time, phone and fax expenses; investigators may be recharged for these costs if warranted.
- o *Quarantine*
The quarantine (period of isolation, observation and testing to detect disease) and testing of acquisitions may be required. Limited space for this activity may delay shipment and evaluation. Investigators may be required to arrange a period of pre-quarantine isolation at the sending institution prior to UCSD quarantine, according to circumstances. Quarantine charges are higher than conventional husbandry; all special costs, including testing and labor will be recharged. Quarantine animals are to be held in isolation and not to be contacted by researchers. Nor will breeding of animals be permitted during the quarantine period since this perpetuates the potential of disease transmission among immune-deficient neonates. The length of quarantine is determined on a case by case basis, but in no instance is less than six weeks, according to the pathogens suspected.

Summary

While it is nearly impossible to totally preclude the entry of rodent pathogens in many research settings, regular precautions can and should be taken to reduce the risk of contamination. Most of the risk can only be controlled by the voluntary, informed behavior of all personnel who come in contact or proximity to research rodents. The costs to the quality of research, as well as the costs of eradicating problems when introduced, should motivate all parties to take the extra precautions that are prudent, and assure that their colleagues do likewise. It is often impossible to determine the exact source of contamination which may occur and to assign the resulting costs to the party at fault. Most of the expenses for diagnosis and control become collectively borne by all rodent users through per diem and other recharges.