Wild rats and mice can harbor a variety of potential zoonotic organisms. In theory someone working in a facility with rodents could possibly be exposed to any zoonotic disease agent affecting wild rodents. In practice, however, these conditions are rare. Modern lab animal facilities, including UCSF, pay particular attention to vermin control, thereby reducing the likelihood of infection of laboratory rodents from their wild counterparts. There is, however, always the potential for an exposure to occur. Below is a brief discussion of a few of the diseases known to be transmitted from rodents to humans.

**Viral Organisms**

*Lymphocytic choriomeningitis* (LCM) is an arenavirus, which is most commonly associated with hamsters, but also infects mice. Wild mice are the reservoir of infection to laboratory and pet rodents.

LCM is one of the viruses that have been eliminated from most vendors through breeding and viral screening of their colonies. However, experimentally transplanted tumors that have not been properly screened are still a potential source of infection to mice.

Transmission of LCM occurs via contact with infected tissues (including tumors). Aerosolization of feces and urine from infected animals, as well as aerosolization of infected tissue or tumor material, can cause disease in humans. The disease in people manifests itself as flu-like symptoms, ranging from mild to severe.

*Hantavirus Infection* - Hantaviruses occur among wild rodent population. Although rats and mice have been implicated in foreign outbreaks of the disease, wild deer mice were the cause of an outbreak in the American Southwest in 1993.

Rodents shed the virus in their respiratory secretions, saliva, urine and feces. Transmission occurs via inhalation of infectious aerosols – brief exposures of even 5 minutes have resulted in human infection. As with other viruses, hantaviruses can be accidentally brought into the laboratory environment in infected tumor lines.

(Continued on page 3, See Health Risks)
There are large gaps of knowledge in how to define, quantify and alleviate pain. A textbook definition of pain perception is: Nerve impulses, activated by noxious stimuli, reach the central nervous system, and are processed to effect voluntary biological and/or behavioral changes. This definition is not meant to include certain reflexes, which may be activated by noxious stimuli yet are not perceived in the cerebral cortex as painful. The definition of stress can be similar, but with the word ‘potentially’ added in front of the word ‘noxious’. The definition of well-being, which is often used to mean the absence of pain and stress, is even more vague. For research using animals, pain control must be an integral part of experimental design.

Unintended pain is occasionally unavoidable in research procedures. The USDA and PHS require the appropriate use of anesthetic, analgesic, or tranquilizing drugs to relieve unnecessary pain or distress, but leave the specifics to the “professional judgement” of the scientist and attending veterinarian. Objective standards for the appraisal of pain in animals are few. Limited relevant experimental data currently make experienced observation with appropriate anthropomorphic reference the most practical methods for clinically evaluating pain.

A pain detection threshold can be established as the lowest intensity of stimulus that is perceived as painful or that induces a response. The pain tolerance threshold refers to the maximum intensity of experimental pain that an individual will tolerate. (Some have defined suffering as inescapable pain or distress that exceeds the pain tolerance threshold.) However, experimental animal data on thresholds have been based on acute pain, not “chronic” pain that might be experienced by, for instance, cancer models. It is important to remember that variations in the anatomy, physiology, previous experience, and information processing of different individuals and species will affect the intensity of stimulus perceived. As more standards for assessing pain in laboratory animals are established it is likely there will be more restrictions on painful research.

The USDA requires an annual animal activity report on the numbers, species and the invasiveness of research procedures (see http://www.els.ucsf.edu/ora/car/apply/instr.htm#P1_5 ). The most serious category is unrelieved pain or distress; experiments which involve painful stimuli in conscious animals without analgesics. An example would be research on the subject of pain or new anesthetics where it is necessary to produce pain in order to carry out the study. The consideration of pain, however, is not confined to those investigators performing traumatic procedures.

When evaluating the degree of discomfort that can be expected during the course of an experiment, the UCSF protocol review process uses a modification of Swedish guidelines which rank procedures in category A, B or C based on the level of pain induced, C being the most painful. The scrutiny of review increases with the level of pain. Because the concept of pain is so subjective, often in the protocol review process the projected level of pain must be reevaluated by the reviewers. A function of LARC veterinarians is to assist investigators and research personnel in evaluating and recommending the appropriate use of analgesics and anesthetics.

A modification of pain is effected by the use of various agents. The use of analgesics is required both post-operatively and whenever pain or distress is apparent in a research or teaching animal. Analgesics for laboratory animals in the postoperative period should be usually continued for 48-72 hours. Narcotic analgesics appear to be most effective for acute post-operative pain. While such drugs may not be necessary after every surgical procedure, the basic rule should be to assume the animal needs effective analgesia. Injectable analgesics administered as part of a balanced anesthetic technique or 15-20 minutes prior to anesthetic recovery are usually the most effective.

Tranquilizing drugs can be used to reduce stress in order to make handling easier. While these drugs may not change the pain perception of the animal, they can alter the animal’s response to its pain.

Can anesthetics and analgesics interfere with experimental results? The answer is sometimes; experimental design should treat analgesics and anesthetics as necessary fixed variables in the analysis of results. In those research proposals that require unalleviated pain or distress, strong scientific justification must be integral to the protocol; extra scrutiny by the reviewers will occur and should be anticipated.

Our continued use of animals in research is dependent on positive public perception of our research. We must make every reasonable effort to ensure that pain and distress are minimized in animal research subjects.

Guide for the Care and Use of Laboratory Animals, NIH. 1996.
(Health Risks, Continued)
The form of the disease in people that has been documented after laboratory animal exposure is characterized by fever, headache, muscle pain, petechiae and other hemorrhagic symptoms including anemia and gastrointestinal bleeding etc.

**Bacterial Organisms**

*Rat bite fever* - This is caused by the bite of a rat infected with the bacteria *Streptobacillus moniliformis* or * Spirillum minus* (a spirochete) which is carried in the nasopharynx of rats. People experiencing rat bite fever may develop recurrent fever, swelling at the site of the wound and arthritis.

**Enteric Pathogens** - There are several bacterial pathogens including *Salmonella* spp. and *Campylobacter* spp., that are frequently associated with diarrhea in rodents that may also cause disease in people. Transmission is via the fecal/oral route, therefore, gloves are recommended when handling rodents. In people, infection results in diarrhea or dysentery.

**Allergens**

Probably the most significant health risk to individuals working with rodents is the development of an allergy – as many as one third of personnel working directly with rodents (or other laboratory species) will develop symptoms of allergy within six months to two years of beginning work with rodents. Symptoms range from mild (sneezing, eyes and nose watering) to severe (asthma) depending on the underlying health status of the individual, the amount of exposure and the level of protective clothing worn.

Conventional and barrier rodent environments have general allergens present such as dust from bedding and animal dander. Specific rat allergy-producing exposures are associated with urine and saliva. A urine protein is implicated as the major mouse allergen.

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**CAR CORNER**

**Ten Tips for Speeding Up Approvals of Your CAR Application**

1. **Consult with a LARC veterinarian in the planning stages.** Failure to consult with the veterinarian will result in the application being held from the agenda until a consultation occurs as veterinary consultation is a federal requirement. It’s best to consult early. (See Protocol Prereview, page 1)

2. **Make sure the dosages of anesthetics and analgesics are correct and consistent** (See the LARC website [http://www.larc.ucsf.edu]). Check with the veterinarian about the proper doses and follow his advice. The most common comment in a contingent letter is that the doses are incorrect and/or inconsistent within the protocol.

3. **Make sure the animal numbers are consistent throughout the protocol.** The protocol asks for information about the numbers of animals to be used in at least five places. Often the numbers are not consistent or not clear. For example, the PI may not have made clear that more than one procedure will be performed on one animal.

4. **Make sure the background and specific aims of the study in Section E are written in non-technical, lay language, i.e., suitable for a newspaper article.** This is for two reasons: a) Not all members of the committee have the same level of scientific background; some members are nonscientists. b) If information needs to be given or released to the public about a particular study (which is something that is occurring more frequently as of late), then this section is critical for understanding the purpose of the study. It must be written in such a way that a non-scientist can understand the aims of the study. (The committee is working on developing some models for PIs to help prepare Section E.)

5. **Be sure to distinguish between sections F.1. and F.2.** That is, be sure that the justification for why live animals are needed is distinct from why the particular species or strains have been chosen for the study.

6. **Describe all procedures to be performed using animals clearly and chronologically so that the members have a clear picture of what will be done for the study.** Often the best descriptions start with a summary outline.

7. **Make sure that the Principal Investigator signs the CAR Cover Page.** Applications cannot be included on the agenda without this signature. This signature is part of the PI certification to assure that the protocol will be conducted properly.

8. **Make sure that the funding information on the CAR Cover Page is correct.** The issue of previous or pending scientific merit review is critical to the review of the study. No study can be included on an agenda for review until this issue is addressed. If federal funding has been obtained, then no additional scientific review is needed. If federal funding is pending and the investigator wishes to begin the study before funding is awarded, or if departmental funds are being used to support the study, then scientific merit review must first be obtained through the Departmental Review Committee. Or, scientific merit review may be obtained through one of the agencies on the CAR List (at [http://www.ucsf.edu/ora/car/apply/scimerit-lst.htm](http://www.ucsf.edu/ora/car/apply/scimerit-lst.htm)). (Continued on page 4, See CAR)
9. **Be complete.** Fill in every section on the CAR Cover Page. Answer all applicable questions in the applications. Applications are screened for completeness in the CAR Office and may be returned without review if they are not complete.

10. **Ask questions.** If you are not sure how to fill out a section, then please consult with one of the LARC veterinarians or call the CAR office at 476-2197.

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**SIMPLE GUIDE FOR COMPLIANCE**

It is important that Investigators comply with the requirements of the USDA. In the past, major areas of non-compliance have included:

- **Use / Presence of Expired Drugs**
  
  Please make sure you have an established mechanism to regularly (at least monthly) check for, and remove, all expired drugs or medical materials.

- **Training**
  
  Please make sure all new users have been trained before they work with animals. Call LARC at 502-7408 to schedule a class (or classes).

- **Approved Procedures**
  
  Please make sure that all authorized users read the specific protocol on which they will be working. Any change in the procedures requires CAR approval prior to their implementation.