Laboratory Animal Resources Guidelines

**Guidelines for Testing of Biological Specimens to be Implanted into Laboratory Rodents**

# **Purpose**

Many years ago, when tissues were first obtained from humans and animals for transplantation, the tissues would frequently be contaminated by other rodent pathogens (from the original host or other hosts used), or human pathogens from the original patient or passage in rodents. Tissues and biological materials may be infected with a variety of agents that may be infectious to humans or animals and potentially jeopardize the health of both or act as confounding variables on research results. Although animal tissues, such as transplantable tumors, cell lines, hybridomas, blood products and other biological materials, can be sources of pathogens that can contaminate laboratory rodents, or be infectious to humans, the incidence of contamination of these tissues has decreased significantly over the years.

Because of this, the current recommendation when **transplanting tissues or biological materials from rodents into rodents is to determine the origin and source of the biological product or tissue and if there is no known evidence of contamination, to use the material without testing.** If there is suspicion that the material has been contaminated by rodent pathogens, testing of the tissues or material should be conducted on cells, tissues and biologicals for rodent pathogens before they are injected or implanted into rodents housed in IUB animal facilities. On the other hand, **any biological materials of human origin is considered potentially contaminated by human pathogens and does not require testing but must be handled at the BS2 or ABSL2 level with universal precautions and blood-borne pathogen handling.**

1. **Scope**

These guidelines apply to:

* All mammalian cells and tissues from a rodent source;
* Mammalian cells and tissues that have been passed through rodents or rodent cells without subsequent purification; and
* Non-mammalian agents cultured in rodents or rodent cells without subsequent purification. *Non-mammalian agents cultured in rodents or rodent cells with subsequent purification do not require this testing.*

Biological specimens included under this description, but not limited to, are: embryonic stem cells, immortal cell lines, cells intended for hybridoma formation, tumor cells, cell culture media, viral or bacterial agents cultured in rodent cells or tissue, and blood products, including serum or antibodies. Cells or biological materials from ATCC should also be tested for murine viruses.

# **Responsibilities**

Biological specimens originating from rodents as described below should be determined to be free of contamination from agents of concern to rodents before use in rodents.

1. **Role of the Principal Investigator:** If the Principal Investigator (PI) suspects tissues or biological materials from rodents are contaminated with rodent pathogens, he/she is responsible for providing Laboratory Animal Resources (LAR) with suitable documentation of the specimen’s source, history of use, and any previous and current testing. Previous testing may satisfy the policy requirements, if appropriate documentation demonstrating the method, scope, and date of testing are adequate, and the specimens have not been passed through rodents or rodent cells since the most recent testing. Previous use in a rodent colony for which concurrent health surveillance reveals no infectious agents may also be adequate.
   1. If testing is required, the PI is subsequently responsible for consulting with LAR to determine which laboratory and testing methods are appropriate. Following testing, LAR is to be provided with documentation of testing results. If the specimen test results indicate that the specimen is likely free from all rodent pathogens of concern, the PI can continue to plan to use the material in transplant or xenograph studies.
   2. **Any tissues transplanted into rodents that result in contamination of the PI’s colony or other colonies in the room must abide by testing and culling recommendations made by LAR to eradicate the infection.**
2. **Role of Laboratory Animal Resources:** LAR is responsible for assessing testing methods and results as provided by the PI and determining whether specimens injected or implanted into rodents are most likely free of rodent pathogens. LAR will provide specific recommendations for approved testing methods and laboratories, assisting the PI with arranging the required testing.
3. **Role of the Institutional Animal Care and Use Committee:** The IACUC is charged with the general oversight of the Animal Care and Use Program, exercising its responsibility for the periodic review and evaluation of these guidelines.

# **Testing of Cell Lines**

1. Specimens to be implanted into **mice** should be tested for the following agents of concern:
   1. Mycoplasma spp.
   2. Sendai virus
   3. Mouse hepatitis virus (MHV)
   4. Pneumonia virus of mice
   5. Minute Virus of Mice (MVM)
   6. Mouse Parvovirus (MPV 1-5)
   7. Theiler’s murine encephalomyelitis virus (TMEV)
   8. Murine norovirus (MNV)
   9. Reovirus 3 (REO3)
   10. Mouse rotavirus
   11. Ectromelia virus
   12. Lymphocytic choriomeningitis virus
   13. Polyoma virus
   14. Lactate dehydrogenase elevating virus
   15. Mouse adenovirus (MAV1, MAV2)
   16. Mouse Cytomegalovirus (MCMV)
   17. K virus
   18. Mouse thymic virus (MTV)
   19. Hantaan virus
   20. *Corynebacterium* spp.
2. Specimens to be implanted into **rats** should be tested for the following agents of concern:
   1. *Mycoplasma* spp.
   2. Pneumonia virus of mice
   3. Kilham’s rat virus
   4. Toolan’s H1 virus
   5. Rat parvovirus (RPV)
   6. Lymphocytic choriomeningitis virus
   7. Rat cytomegalovirus
   8. Sendai virus
   9. Rat coronavirus
   10. Sialodacryoadenitis virus (SDAV)
   11. Rat minute virus
   12. Seoul virus
   13. Mouse adenovirus (MAV1, MAV2)
   14. Reovirus 3 (REO3)
   15. Rat theilovirus (RTV)

Previously, testing would have been conducted using the Mouse Antibody Production (MAP) or Rat Antibody Production (RAP) Testing. These services are available at different laboratories, including Charles River Laboratories. The methodology however required injecting the submitted sample into live mice or rats to see if the animals developed a titer to any pathogen. The process therefore took about 6-8 weeks to obtain results.

LAR now recommends polymerase chain reaction (PCR) testing of specimens. This service is available at different laboratories, including IDEXX BioAnalytics, which refers to it as Infectious Microbe PCR Amplification Test (IMPACT I). Information about testing, prices, and shipment of specimens may be located at the website:[IDEXX Bioanalytics IMPACT website](https://www.idexxbioanalytics.com/impact-pcr-0). In general these PCR tests are less expensive, turnaround time is days instead of weeks and are preferred due to less animal welfare concerns. Current costs for testing of mouse tissues at RADIL through the Mouse IMPACT 1 is $642.00 and for the Rat IMPACT V is $457.00 as of 12/18/19.

# If there are questions concerning this required testing, please contact LAR at 855-2356.