



Health and Genetics SOP Updated February 16, 2016

I. Health Monitoring

The goal of the MMRRC health monitoring program is to ensure that all mice distributed are free of infectious pathogens. To that end, the following approaches are utilized:

- A. Mouse lines reanimated from cryopreserved materials are tested prior to distribution by evaluating recipient females at the time pups are weaned for the presence of antibodies to adventitious agents. Additional testing of rederived pups from each litter may be done at the discretion of the Center.
- B. If a live colony is maintained, production colonies or sentinels of those colonies are tested at regular intervals.
 - (1) For immunocompetent mouse strains, the infection status of each production colony are evaluated by a Comprehensive Profile at least four times per year (Table 1).
 - (2) For mouse strains documented to be immunocompromised, the infection status of each colony is evaluated by a Comprehensive Profile at least four times per year.
 - (3) Additional testing may be done, as needed, to meet importation requirements for non-US requesters of live MMRRC mice.
 - (4) Design of the sentinel program, with respect to mouse strains used as sentinels and whether contact or soiled bedding is used as the method of transmission, may vary depending on the specific health concerns and known infectious agent risks at each site. Each center is aware of the following: 1) certain mouse strains are optimal for detection of specific pathogens, *e.g.*, ICR or C3H mice are appropriate sentinels for detection of mouse parvovirus but C57BL/6 mice are not, and 2) direct contact is more appropriate than soiled bedding for transmission of some pathogens, *e.g.* respiratory pathogens.
- C. If positive results are obtained for any microorganism, the Center first confirms the positive result by testing of additional cohort mice. If the positive results are confirmed for any mouse colony, the Center reports the change in health status to the CC, and provides a recommendation to the CC for approval.
- D. The number of mice tested varies depending on the colony size, but are aimed at achieving a high level of confidence in detection of infectious agents. Each Center has SOPs regarding sampling size.
- E. For Centers that distribute cells and tissue, donors or colonies from which donors are obtained, are tested with a Comprehensive Screening Panel.

Table 1. Health Monitoring Profiles

Comprehensive Screening Profile
Viruses <ul style="list-style-type: none">◆ 17 viruses◆ Mouse hepatitis virus, Minute virus of mice, Mouse parvovirus, Mouse adenovirus, Murine pneumonia virus, Sendai virus, Theiler's murine encephalomyelitis virus, Mouse rotavirus (EDIM), Ectromelia virus, Lymphocytic choriomeningitis virus, Reovirus 3, Murine norovirus◆ Plus Polyoma virus, Lactate dehydrogenase elevating virus (LDEV), K virus, Hantaan and Mouse thymic virus.
Bacteria <ul style="list-style-type: none">◆ <i>Helicobacter sp.</i>, <i>Mycoplasma pulmonis</i>, <i>Pasteurella pneumotropica</i>◆ <i>CAR bacillus</i>, <i>Clostridium piliforme</i>, <i>Citrobacter rodentium</i>, culture to detect other respiratory and enteric pathogens
Parasites, Protozoa & Other <ul style="list-style-type: none">◆ Endoparasites◆ Ectoparasites◆ <i>Pneumocystis murina</i>, for immunocompromised mice

II. Genetic Monitoring

The intent of the genetic monitoring program is to ensure that all mice distributed by the MMRRC are of the appropriate genotype. When the genetic modification is known, gene-specific assays are developed and utilized for genetic testing of mouse lines to ensure that mice are of the correct genotype.

- A. To ensure that mouse lines submitted to the MMRRC are the correct line, all lines are genotyped upon arrival at the MMRRC. Genotyping of mutant alleles are performed prior to or concomitant with cryopreservation of gametes and/or embryos.
- B. For mice reanimated from cryopreserved materials, resulting mice are genotyped prior to distribution.
- C. For a mouse lines maintained as a live colony by breeding of heterozygotes, mice are genotyped as necessary to establish appropriate breeding pairs needed to maintain the line. All mice are genotyped prior to distribution.
- D. For mouse lines maintained as a live colony by breeding homozygotes, genotyping are performed annually at a minimum.

III. Phenotyping

In general, phenotyping is performed on an as needed basis at the discretion of the Center holding the line.

Centers creating congenic lines must confirm the phenotype, if possible, and document any differences in comparison with the original line.

Upon request from an investigator, additional phenotyping may be performed to assist the investigator in determining whether the mouse line may be of use in his/her studies. The determination of whether investigator-requested phenotyping are accommodated are done on a case-by-case basis.

IV. Screening of Embryonic Stem Cells for Infectious Microorganisms

The MMRRRC holds a large inventory of embryonic stem (ES) cells, e.g., Genetrap mutants. Upon request, these cells are shipped directly to requesting investigators. To prevent inadvertent transmission of infectious agents via ES cells distributed by the MMRRRC, all ES cells are screened by Mouse antibody production (MAP) or PCR-based assays for the following agents:

Mycoplasma sp.

Minute virus of mice (MVM)

Mouse parvovirus (MPV)

Cells that test positive for any of these agents will not be distributed.