

Recommendations for experimental mice entering MMPC institutions

(see accompanying Powerpoint schematic)

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Introduction – There is a body of literature to support the notion that rodent viruses and bacteria have the capacity to alter phenotypes. A partial list of publications supporting this notion is noted below (1-16). Hence, two reasons to assure the health and pathogen status of shipped experimental mice is to a) assure data integrity for the obesity/diabetes phenotypes being studied and b) maintain the health standards of receiving institutions.

A brief survey (see below; Summary of Survey of National Mouse Metabolic Phenotyping Centers Quarantine Procedures 2010) reveals varying quarantine procedures and time periods (some lengthy) but no MMPC or other phenotyping cores contacted attributed institutional pathogen outbreaks to entering MMPC animals. However, it is in the interest of the receiving MMPC institution to have a relatively short quarantine period so mice can be studied as soon after receipt as possible to avoid ageing effects and to avoid extra per diem costs while mice are held in quarantine. The program outlined below is recommended as a minimal approach resulting in an accelerated quarantine period (3-4 weeks) yet still minimizing the risks of pathogens being introduced into the receiving MMPC.

- Review of health reports - Veterinary staff at receiving MMPC institution reviews health reports of sending institution to determine whether rodents from sending institution meet MMPC institutional requirements (1) We are recommending that experimental mice be free of the following organisms (minimally) *Ectromelia virus*, *Lymphocytic choriomeningitis virus*, *Mouse hepatitis virus*, *Mouse parvovirus*, *Minute virus of mice*, *Mouse rotavirus*, *Mycoplasma pulmonis*, *Pneumonia virus of mice*, *Reovirus*, *Sendai virus*, *Theiler's virus (GD-7)*, *fur mites* and *pinworms* in order to ensure data integrity for obesity/diabetes phenotypes. Assurance of negativity for additional agents may be required by the receiving MMPC institution.

- How mice are transported – Receiving MMPC will carefully inspect the transport container on arrival of the mice. If there is a break in the filter, the individual MMPC will decide the fate of these animals. Choices include diverting these animals to the regular quarantine procedure of the institution or euthanasia of the animals. It is strongly recommended that high quality shipping crates be used to decrease the risk of compromise of the crate and exposure of animals to pathogens.
- Experimental mice - Experimental mice will go into the Quarantine Room of MMPC institution (2a); at entry and again 14 days after mice arrive (3a), fecal samples are collected from 50% of mice shipped and fecal samples from up to 6 mice may be pooled, and are submitted to a diagnostic laboratory for comprehensive fecal PCR testing for prevalent agents found in the US*. *This will presumably identify early on mice that may be shedding organisms and would be the 'most risk' to the receiving institution; the later time point will detect organisms that may have been acquired during shipment.*
- Surplus mice - At the same time, Surplus mice from the same colony and housed in the same room as the experimental mice are shipped along with the experimental mice and enter Quarantine (2b). Surplus mice should ideally be 2 younger (4-6 wks) and 2 older (3-6 mos) female mice; preferably wild-type or heterozygote littermates that are presumably immunocompetent mice and can act as '*sentinel mice*'. Surplus mice should be exposed to dirty bedding from the transport container and also dirty bedding from the experimental mice during the 14 day period.
- Evaluation of Surplus mice - These mice are necropsied 14 days after arrival (3b) with serology done for pathogens per the usual Quarantine panel for the receiving institution. This serology panel should minimally exclude *Ectromelia virus*, *Lymphocytic choriomeningitis virus*, *Mouse hepatitis virus*, *Mouse parvovirus*, *Minute virus of mice*, *Mouse rotavirus*, *Mycoplasma pulmonis*, *Pneumonia virus of mice*, *Reovirus*, *Sendai virus*, *Theiler's virus* (GD-7). Surplus mice are also evaluated for fur mites by pelage examination, pinworms by direct examination of cecum and proximal colon contents, and splenic tissue PCR for Mouse parvovirus. *These mice serve as further assurance that experimental mice are free of excluded organisms.*
- Assurance for exclusion of mites. Assurance that mice entering the MMPC institution are free of mites will be accomplished by doing a check for mites 3 times. Experimental mice will be examined 2X for ectoparasites via fur pluck/tape test once on entry and again at 14 days later. Surplus mice will have pelage exam done at necropsy representing a 3rd check for ectoparasites.
- Movement of mice out of Quarantine into MMPC facilities - If all results from experimental and surplus mice are negative, experimental mice can be moved into the general colony and studies can begin. Total time in Quarantine will be **approximately 3 – 4 weeks** depending upon turn-around time for laboratory tests and any confirmations that have to be made. Any positive tests will be confirmed and if confirmed, the mice will be euthanized minimizing pathogen risks to the receiving MMPC. *It should also be noted that movement of mice for analysis into MMPC institutions is a 'one way trip'; it is not recommended that mice be shipped back to sending institutions.*

- Access to mice while in Quarantine - Generally, mice are not worked on while in Quarantine since this is considered a high risk room. This may not apply if the MMPC has their own designated room/s.

**mouse comprehensive PCR fecal panel*

Agents excluded by MMPC – MPV-1, MPV-2, MPV-3, MVM, MHV, TMEV, EDIM, *Syphacia obvelata*, *Aspiculuris tetraptera*. Some institutions may want assurance that mice are also free of *Helicobacter* spp. and MNV. approximate cost \$270.00x2=\$540.

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Summary of Survey of National Mouse Metabolic Phenotyping Centers (MMPC) Quarantine Procedures 2010 - KW

MMPC Generalities

- Core facilities are located within institutional rodent housing areas
- Imported mice with clean rodent health surveillance data go into quarantine, or are rederived
- Home institution mice do not need undergo quarantine
- Home institution mice can go back and forth between vivaria; imported mice cannot
- Most cores exclude all pathogens listed on “Minimum testing requirements” MMPC web page (as per individual core’s home websites); one institution allows Murine Norovirus suspect animals into facilities

Comments

- Institution with longest quarantine has separate equipment and housing for imported and home institution mice
- Number of institutional mice that go back to vivaria not tracked
- No MMPC or other phenotyping cores can attribute an institutional outbreak from imported mice in the past two years

Observations from other institutions (3 institutions)

- Mice from non SPF vivaria stay in the non SPF vivarium or quarantine; are manipulated towards the end of the week, euthanized and the equipment sanitized; one way trip for all imaged animals (imaging core; non SPF mice are anesthetized imaged in a plexiglass container to minimize contact with equipment)
- Institutional mice from SPF vivaria are accepted; all other mice are rederived; one way trip for all animals (behavioral core)
- Institution with several cores (cardiovascular, metabolic, irradiation, behavioral) that are in or near vivaria has no quarantine requirements; institutional mice can come and go; imported mice must have a current health report and the core they are going to determines how “clean” the health report needs to be; imported mice can be shipped back to home institution with the caveat health status may have changed while at core