
University of Pennsylvania School of Medicine
Policy and Procedure Manual

MANAGEMENT OF MPV-INFECTED ROOMS/SUITES IN SOM BARRIER ANIMAL FACILITIES

RESEARCH ADMINISTRATION

Policy Number: RA-ANML-008

Date Approved: 4/11/12

I. PURPOSE

To establish guidelines for the management of a barrier animal room/suite that is confirmed to contain mice infected with mouse parvovirus (MPV).

II. RATIONALE

MPV causes a persistent, potentially life-long infection of the mouse although it does not cause morbidity or pathology (gross or microscopic) in any mice studied thus far, including neonates and immunodeficient mice. The virus is transmitted via the fecal-oral route and is extremely hardy in the environment. *In vivo* infection alters the host response to tumor cells and modulates T cell effector functions. It has also been shown to induce autoimmune responses under certain circumstances. Although not explicitly demonstrated for MPV, many rodent parvoviruses are oncolytic and/or interfere with animal models of diabetes. Given the large immunology, cancer biology and diabetes programs at the University of Pennsylvania, an exclusion policy is warranted. Most institutions in the United States exclude MPV from some or all of their vivaria.

III. POLICY STATEMENT

A policy for the management of a barrier animal room/suite that is confirmed to contain mice that are infected with MPV is essential to minimize the risk of rodent infectious disease transmission in the School of Medicine (SOM) rodent housing facilities. This policy serves as the official SOM position for the management of a barrier animal room/suite that is confirmed to contain mice infected with MPV.

IV. WHO SHOULD KNOW THIS POLICY?

- Executive Vice Dean and Chief Scientific Officer and Staff
- Assistant Dean for Animal Research
- School of Medicine Animal Research Committee (SOMARC)
- Associate Dean of Research, School of Veterinary Medicine
- Faculty and research lab personnel engaged in animal research

- University Laboratory Animal Resources (ULAR) Staff
- IACUC Chair and Staff

V. POLICY AND PROCEDURES

Detection of Virus Infection and Notification

1. The detection of MPV infection within SOM animal facilities may occur by several means including, but not limited to:
 - Notification by an external entity of a shipment of infected mice
 - Diagnostic results from individual mice within a colony room
 - The results of diagnostic tests performed on sentinel mice within a colony room
2. ULAR Diagnostic Services will provide phone and/or email notification of a presumptive MPV infection in an existing barrier colony to the SOMARC Chair immediately (within 24 hours) upon receipt of initial results or notification. In this regard, it is expected that ULAR will maintain a rigorous sentinel program to detect MPV that will involve quarterly serologic testing and annual PCR testing of mesenteric lymph nodes (MLNs) from sentinel mice housed in barrier facilities. Spleen tissue will be collected from all barrier-housed sentinel mice on a quarterly basis and stored frozen (-80C) in the event serologic testing is positive and triggers the need for PCR testing. The SOM-ARC Chair will also be notified immediately (within 24 hours) following confirmation of the initial preliminary detection of MPV by serology and/or PCR.
3. An email notification from ULAR, the Associate Director of Diagnostic Services & Rodent Quality Assurance, will be sent to the SOM-ARC, which includes the Chair of the User Group from the facility involved, within 24 hours of confirmed infection. ULAR will also notify the Associate Dean for Research at the School of Veterinary Medicine. The Associate Director of ULAR Diagnostic Services will send a general announcement via the Polaris email list to all Principal Investigators and their research staff who house animals in the affected facility. A meeting of facility research staff will be held as soon as possible and no later than one week after confirming infection, at which time ULAR Diagnostic Services will present a comprehensive Outbreak Management Plan (OMP). The OMP may be revised based on the results of each testing phase. As a part of all OMPs, ULAR Diagnostic Services will review re-locations for prior three months from affected room(s) to other barrier rooms.

Management of Infected Rooms

1. ULAR Diagnostic Services will place the MPV-infected room on quarantine immediately (within 24 hours) upon confirmation in accordance with Policy Number RA-ANML-002: Quarantine of Rodents Due to Infectious Disease Outbreak in School of Medicine Animal Facilities.
2. Prior to the announcement of quarantine to research staff, ULAR Diagnostic Services will contact the facility manager and/or supervisor to request that the room/suite locks be changed. ULAR Diagnostic Services will send an e-mail to the Polaris user group list and all faculty (as well as their lab contacts)

who have mice in the affected room/suite/facility at the same time the room/suite/facility is placed on quarantine. That e-mail will request that recipients communicate to their on-campus collaborators that an MPV outbreak has been detected. Within one week of confirming infection, ULAR Diagnostic Services will hold a meeting with all faculty (and their lab staff) who have animals in the affected room/suite to present and discuss a comprehensive Outbreak Management Plan (OMP).

3. One individual from the laboratory of each investigator housing mice in the affected room(s) will be identified as the only individual from that lab who will have access to the quarantined room. This individual will frequently be the laboratory manager and may assist ULAR staff in manipulation of infected mice and identification for sampling purposes. On a case-by-case basis, digital photography may be permitted if cage card information is needed by other laboratory staff who do not have access to the room(s). Manipulations of mice/cages in a quarantined room can occur only after written approval from the Associate Director, ULAR Diagnostic Services, has been sent to the investigator and the facility manager and supervisor.

Testing and Eradication

1. Phase 1 testing will begin once an initial positive test is confirmed. If the positive MPV result is based on serologic testing of a sentinel mouse, and this result is confirmed by PCR, other sentinel mice in the room will also be tested by PCR. Blood will be sampled from one mouse per cage in all cages on the side of the rack housing an MPV-positive (by PCR) sentinel mouse. If sentinel mice on multiple racks in a room test positive (by PCR), blood will be sampled from one mouse per cage on the appropriate side of all of those racks.
2. When a room is quarantined due to a confirmed MPV infection, ULAR will test sentinels in all rooms in the suite by PCR during the next round of quarterly testing.
3. If Phase 1 serology tests of one mouse from each cage on a rack identify additional MPV-positive mice, all mice in those cages will be culled. If more than 5% of the cages on a rack are positive, the rack will be de-populated by any of several methods that may include: (a) culling (euthanasia) of non-essential mice; (b) removal of essential mice via shipping to an off-campus site for holding and additional testing; (c) shipping of unique strains to an off-campus location for rederivation.
4. If Phase 1 serology tests of one mouse from each cage on a rack with a positive sentinel are negative, an additional round of serology, Phase 2, involving tests of one mouse per cage, will be performed not sooner than 6 weeks later. If all Phase 2 results are negative, a third round of serological testing, Phase 3, will be performed no sooner than 4 weeks later. If the Phase 2 and Phase 3 tests are uniformly 100% negative, this will be considered evidence of viral clearance from the population. Once a room has been released from quarantine, the Associate Director of Diagnostic Services & Rodent Quality Assurance will determine the frequency and rigor of future sentinel testing (e.g., every 6 weeks). The Associate Director will also determine when the room may return to routine quarterly sentinel testing.
5. ULAR Diagnostic Services will be responsible for these activities. Each cage and sample will be clearly identified using a system of pre-printed labels maintained by ULAR Diagnostic Services so that positive results may be traced unequivocally to specific cages.

6. Cages containing MPV-positive mice will be marked for euthanasia by ULAR staff. Principal investigators will be notified at least 24 hours prior to euthanasia.
7. All cages that contained MPV-positive animals will then be bagged for autoclaving and removed from the room(s) as soon as possible by ULAR staff. Whenever possible these events should occur within 48 hours of documenting that cages contain(ed) infected mice.
8. In accordance with the guidelines for Policy Number RA-ANML-002: Quarantine of Rodents due to Infectious Disease Outbreak in School of Medicine Animal Facilities: (a) Scientists and their staff and ULAR staff will make every effort to avoid relocating cages within quarantined rooms (shelf-to-shelf; rack-to-rack); (b) under no circumstances will cages in quarantined room(s) be moved to other rooms in the facility or any other barrier-maintained campus facility; and (c) no new arrivals of mice from approved vendors or rodents released from Levy quarantine will be approved to enter the affected room(s)/suite(s). New shipments of mice that had already been ordered prior to the quarantine will be considered on a case-by-case basis. Rather than assigning affected investigators housing space in alternate locations, they will be encouraged to use mice acutely if possible. The ULAR Procurement staff is informed of the quarantine status at the same time as the research staff and has established an SOP for informing vendors of cancelled orders.
9. Research staff having animals in the MPV-positive, quarantined room will be identified and ULAR Diagnostic Services will determine, through Polaris, whether these investigators have rodents housed in other barrier rooms/suites/facilities. "Collateral" testing will be performed as soon as possible to determine whether there has been transmission to rodents in other areas. The proportion of cages to be screened in any given room/suite/facility (identified as collateral to the affected room) will be communicated by ULAR Diagnostic Services. The use of change stations/hoods in rodent rooms has dramatically reduced the amount of transmission within and from affected rooms. For this reason, ULAR Diagnostic Services staff has been routinely testing 100% of cages in each affected or suspected room. Collateral testing may target animals belonging to investigators with positive cages in the quarantined room/suite/facility rather than testing 100% of the population. Depending on the extent and duration of the outbreak, sentinels in the facility may be periodically tested (more frequently than the quarterly schedule) as well.
10. As part of the Outbreak Management Plan, ULAR Diagnostic Services will identify any approved relocations from the affected room/suite to any other barrier room/suite/facility during the prior quarter. Any cages that are identified will be tested for MPV by serology and/or fecal (non-invasive) PCR.
11. In outbreaks involving rooms within suites (i.e., BRB or Hill Pavilion vivaria), all sentinels housed in other rooms within the suite(s) will be tested and a randomly selected subset of colony animals may be tested as well.
12. The results of all tests will be forwarded by email to the SOMARC Chair and all investigators housing mice in the affected facility on the same day that the results are available.
13. The SOMARC Chair, in consultation with the ULAR Associate Director for Diagnostic Services, will be responsible for reviewing the status of the infection and quarantine with the SOMARC. ULAR and the SOMARC will determine further actions, or modifications to the OMP required to insure infection containment and eradication.

Contingency De-Population Plan

1. If the results of testing show that there are still positive animals (evidence of a spreading infection) after Phase 2 or Phase 3 testing, the room may be depopulated and essential mice relocated to an off-campus facility or entity, as determined by the SOMARC. Essential mice are defined as unique strains that cannot be purchased or re-derived from another source, or ongoing experiments that are not possible to repeat in a reasonable time frame. Exceptions to this policy will be considered by the SOM-ARC on a case-by-case basis if Phase 2 and/or 3 results indicate that the vast majority of infected animals have been eliminated. In this instance one additional test/cull phase may be permitted.
2. The SOMARC and ULAR Diagnostic Services will jointly convene a meeting of all affected faculty to communicate the depopulation plan, including timelines, within 2-3 days of receiving results from Phase 2 or Phase 3 bleeding.
3. Investigators who have mice in a room that is scheduled for depopulation will identify cages containing essential mice for relocation and submit a request to the Assistant Dean for Animal Research and Executive Vice Dean which documents:
 - A description of all essential strains
 - Estimated number of animals per strain
 - Estimated number of required breeding and non-breeding isolators
 - Brief justification for why individual strains need to be preserved
4. The Assistant Dean, in consultation with the Executive Vice Dean, will evaluate individual faculty requests and forward decisions to the faculty within 48 hours.
5. Until such time when on-campus housing exists that will not present health risks to other rodent populations, the SOMARC will identify an external vendor. Faculty must then obtain a vendor cost estimate (a formal quote), and submit this to the Assistant Dean and the Executive Vice Dean for final approval. Faculty will work with the Office of the Executive Vice Dean to insure that appropriate Risk Management invoices are completed prior to shipment of any animals. The Office of the Executive Vice Dean will coordinate the request for reimbursement with Risk Management. The full SOM procedure for this process is included as Attachment 1.
6. Upon receipt of full SOMARC approval, ULAR will coordinate the evacuation of the infected room/suite/facility and the transfer of essential mice to another location/vendor within a timeline identified in Phase Three of the OMP. The OMP will precisely state the deadline by which all animals must be removed. After this deadline, ULAR Diagnostic Services will notify investigators that the deadline has passed and ULAR staff will be authorized to euthanize any remaining animals.
7. ULAR will schedule the room decontamination, which will occur within 1 business day of full depopulation, and will then coordinate the re-introduction of mice to the room.

Request for Exemption

- Requests for exceptions to this policy will be considered on a case-by-case basis by the SOMARC in consultation with the Director of ULAR Diagnostics and Executive Vice Dean/Chief Scientific Officer. A request for exemption can be submitted via email to somar@mail.med.upenn.edu. Any exemption to this policy must be obtained in writing from the Assistant Dean for Animal Research.

V. CONTACTS

Executive Vice Dean and Chief Scientific Officer, School of Medicine

Phone: 215.898.2874

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Director, University Laboratory Animal Resources

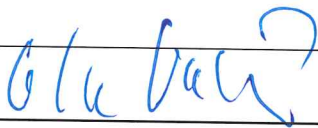
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Supersedes: NONE-New Policy	APPROVED: <u></u> Date: 4/11/12 Executive Vice Dean and Chief Scientific Officer Perelman School of Medicine
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