

Guidance on Establishing Health Monitoring Panels for Laboratory Mice to Reflect Contemporary Pathogen Prevalence

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Abbreviations and Acronyms: DCM, direct colony sampling; EDIM, epizootic diarrhea of infant mice; EDT, exhaust duct testing; HM, health monitoring; LCMV, lymphocytic choriomeningitis virus; LDV, Lactate dehydrogenase elevating virus; MAV, mouse adenovirus; MCMV, mouse cytomegalovirus; MHV, mouse hepatitis virus; MNV, murine norovirus; MPV, mouse parvovirus; MTLV, mouse thymic virus; MVM, minute virus of mice; PVM, pneumonia virus of mice; RCHPV-1, Rodent chaphamaparvovirus; SBS, soiled bedding sentinel; SFB, Segmented filamentous bacteria; SFSB, sentinel-free soiled bedding; TMEV, Theiler's murine encephalomyelitis virus

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Introduction

Rodent health monitoring (HM) programs are designed to detect infectious agents in rodents that have the potential to negatively impact animal health or research findings. These programs are an essential component for verifying the desired health status of a research mouse colony. While multiple factors can provide information about a colony's health status, including clinical observations, gross and microscopic pathologies, unexpected experimental results, and other factors, the term 'health monitoring program' in this review refers specifically to the routine screening/testing of laboratory mice or their environment for the presence (for example, by bacterial culture or visual identification or ectoparasites) or indicators (for example, nucleic acid or elicited antibodies) of infectious agents. Despite the importance of such programs, there is minimal consistency among institutions on how HM programs are designed, which infectious agents are included for routine testing, and the frequency for which agents are tested. The list of agents that a facility tests for and excludes can vary at both the intra- and interinstitutional levels. It is our goal to provide guidance on which agents should be included in a routine HM program (Table 1). In addition, information on designing HM programs for other situations, such as barrier facilities, quarantine areas, and incoming research biological materials, is presented in Table 2. It is important that facilities periodically evaluate the efficacy and appropriateness of their HM program as it relates to both their specific animal care

program as well as to best practices in the field of laboratory animal science. Previous publications have provided similar guidance, but many are grounded in historical data and do not provide information regarding contemporary pathogen prevalence.^{1–7}

General Considerations in the Design of an HM Program

Few have the opportunity and burden of starting from scratch when stepping into a role that oversees mouse HM and colony biosecurity. Instead, it is more common to inherit both the successes and failures of the current program. When inheriting an HM program, it is important to assess the method(s) being used to detect pathogenic agents, the agents being tested for and/or excluded, and the specialized aspects of the program that generate risk for pathogen introduction. The specific detection methods employed in an HM program (such as soiled bedding sentinels [SBS] compared with environmental HM such as exhaust dust testing or sentinel-free soiled bedding) may influence the accuracy of the testing program. Various HM methods have been extensively reviewed, and most recent changes to these methods focus on replacement of sentinel animals through the use of environmental HM due to its increased sensitivity.⁸ There may be considerations for choosing one method of HM as compared with another; however, reviewing these differences is beyond the scope of this article and is thoroughly addressed in other publications.⁹

An "exclusion list" is a list of agents that are excluded from a particular colony to achieve a specific pathogen-free (SPF) health status. This is often not the same as the 'testing or screening list or panel' as not all agents on an exclusion list may be monitored through routine testing. For example, K virus and mouse papillomavirus are both likely to be excluded by most modern research vivaria, but neither may be included on a routine testing panel due to their low prevalence in laboratory mice today.¹⁰ It is also

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Table 1. Recommended infectious agents for testing and exclusion in all routine HM programs (at minimum) and frequencies of monitoring for laboratory mice (*Mus musculus*)

	Quarterly	Annually
Lymphocytic choriomeningitis virus (LCMV)		X
Mouse hepatitis virus (MHV)	X	
Mouse rotavirus (EDIM)	X	
Mouse adenovirus types 1 and 2 (MAV-1 & 2)		X
Minute virus of mice (MVM)	X	
Mouse parvovirus (MPV)	X	
Pneumonia virus of mice (PVM)		X
Reovirus		X
Theiler murine encephalomyelitis virus (TMEV)	X	
Fur mites (<i>Myobia</i> , <i>Myocoptes</i> , <i>Radfordia</i>)	X	
Pinworms (<i>Aspiculuris</i> , <i>Syphacia</i>)	X	

likely that a testing list may include agents that are not excluded but rather monitored. For example, murine norovirus (MNV) may not be excluded in some colonies of mice, but its presence may be monitored as part of a routine testing panel to provide information for institutional knowledge or to serve as a positive process control for routine screening if there is known prevalence in the colony. Most institutions agree that rodent pathogens which generate animal health concern or which may impact research reproducibility require exclusion. Due to the historical significance

Table 2. Recommended infectious agents to consider for exclusion based on risk of situation for laboratory mice (*Mus musculus*) in addition to those listed in Table 1

Establishing or maintaining a barrier facility for immunocompromised mice
Rodent chaphamaparvovirus (RCHPV-1)
<i>Chlamydia muridarum</i>
<i>Corynebacterium bovis</i>
<i>Helicobacter</i> spp.
<i>Pneumocystis murina</i>
Risk of wild rodents and pests & International imports
Hantavirus
Lymphocytic choriomeningitis virus (LCMV)
Mouse cytomegalovirus (MCMV)
Mouse thymic virus (MTLV)
Murine norovirus (MNV)
Sendai virus
<i>Helicobacter</i> spp.
<i>Ornithonyssus bacoti</i>
Use of biological materials
Lactate dehydrogenase-elevating virus (LDV)
Mouse cytomegalovirus (MCMV)
Polyoma virus
<i>Corynebacterium bovis</i>
<i>Mycoplasma pulmonis</i>

Agents under "Establishing or maintaining a barrier facility for immunocompromised mice" should be tested based on risk assessment and at the program's discretion. Agents under "Risk of wild rodents and pests & International imports" should be tested upon vermin incursion and mouse import, respectively. Agents under "Use of biological materials" should be tested before the materials are introduced in animals.

of these agents, severity on research outcomes, and the difficulty in eliminating them once reintroduced, they form the foundation of almost all exclusions lists. These agents include mouse parvovirus (MPV), minute virus of mice (MVM), and mouse rotavirus (epizootic diarrhea of infant mice [EDIM]), among others. Conversely, opportunistic and nonpathogenic agents tend to be permitted and/or monitored in general colonies with exclusion practices only in place when warranted for immune-specific or experimental needs. While the former presents pathogens that unambiguously should be included on all exclusion lists, the latter creates nebulous and individualized situations destined to be inconsistent across institutions.

There are various program features that may warrant testing for different agents; thus, having several customized and preset panels may be useful. For example, in addition to a panel for the routine HM program, it may be helpful to have different panels for quarantine areas or barrier facilities. Barrier facilities are defined as a systematic and comprehensive animal housing program that is designed and managed to protect the colony animals in a room, suite, or facility from unwanted pathogen introduction from the outside.^{11,12} Suggested testing panels for various situations are readily available from commercial diagnostic laboratories and may be an instructive starting point for further customization. This allows for a more extensive panel to be used when there is a greater chance of adventitious pathogen contamination, such as during importation/quarantine, administration of biological materials to rodents, or following a pest incursion. After resolution of these events, a more limited panel can be used to perform routine HM as the risk of adventitious pathogen incursion has subsided. The use of refined panels, as compared with using a larger panel to screen all animals, will help alleviate costs and minimize unnecessary testing for rare or inconsequential agents.

For a routine HM program, it is common to test for more prevalent agents with increased frequency (for example, quarterly) as there is a greater likelihood of their presence. When testing in a specific situation, increased frequency is also recommended as this allows for more immediate and timely action if an agent is detected (for example, for the protection of the SPF status in a barrier facility). For less prevalent agents, annual or semiannual testing is more commonly performed.

Consideration of Contemporary Agent Prevalence in Mice

A recent publication by a commercial diagnostic laboratory summarized the results of murine HM performed for external clients from 2003 to 2020.¹⁰ These data support that multiple agents, once thought of as prevalent in domestic mouse colonies, are no longer prevalent and/or have been eradicated from research colonies. These include respiratory agents, such as Sendai virus and pneumonia virus of mice (PVM), which are now virtually eliminated with a prevalence $\leq 0.01\%$, and rodent coronaviruses, including mouse hepatitis virus (MHV), which now have a prevalence $< 0.3\%$. On the other hand, MNV, *Helicobacter* spp., *Rodentibacter* spp., and parasites (pinworms and fur mites) continue to have a higher prevalence ($> 5\%$). The reason for this higher prevalence is due to many factors, including a lack of cross-institutional agreement on exclusion (MNV, *Helicobacter* spp., *Rodentibacter* spp.) and the frequent exchange of mice between institutions (parasites).¹⁰ That publication¹⁰ may serve as a helpful tool for programs to begin reassessing which agents merit testing and the frequency of testing as part of a routine HM program. As an example, for agents that are now eradicated, such as PVM and *Salmonella* spp., one option is to only test for

them as part of the program's quarantine and biological materials testing panels since these areas are the main points of potential entry for pathogens. Another option is to test for these agents less frequently (annually as compared with quarterly).^{10,13} In doing so, the agents can be removed from the routine HM panel, resulting in decreased costs while ensuring that these agents are still excluded from rodent colonies. Although prevalence is a good place to start when refining an HM program, it is not the only factor to consider. Reasons for including agents of low prevalence are discussed below.

Choice of Agents and Frequency of Testing

In addition to agents that can be recommended for all HM programs regardless of institution or situation, there are various aspects of an animal care program that may warrant testing for different agents and/or testing at varying frequencies. These aspects commonly include 1) establishing or maintaining a barrier facility for immunocompromised mice, 2) consideration of new, emerging, and reemerging agents, 3) managing import, export, and quarantine programs, 4) incursions of wild rodents or other pests, 5) consideration of zoonotic agents, 6) testing of biological materials, and 7) study-related exclusions, often initiated and requested by investigators. The following sections address each of these scenarios individually.

Agents recommended for all HM programs. Despite modern advances in colony management, many agents are still common and relevant to murine research colonies today and therefore warrant frequent testing. Some of the key factors contributing to their continued presence in research mice include persistent infection or colonization of the host, tolerance of agents by some institutions, the use of untreated husbandry materials,^{14–16} pest incursions,^{17,18} and agent characteristics that promote stability and transmission. Considering both prevalence and severity of disease (and thus high research impact if present), it is strongly recommended that mouse colonies be monitored for MHV, mouse parvoviruses (MPV/MVM), Theiler's murine encephalomyelitis virus (TMEV), EDIM, pinworms, and fur mites quarterly and excluded from all programs.¹⁰ Potentially lower detectable copy numbers in addition to lower prevalence and short/nonpersistent shedding of infectious virus in immunocompetent animals (as in the case of MHV and EDIM) create an increased potential for false-negative results. Were an infection to occur within a research colony, these agents can lead to costly research-related consequences.¹⁹ Agents having lower prevalences such as MAV, reovirus, PVM, and LCMV,¹⁰ but still the potential for substantial impacts on research colonies, should be tested for annually. Although many programs continue to test for and exclude ectromelia virus (mouse poxvirus) and Sendai virus, with a 0.00% prevalence from 2016 to 2020,¹⁰ eliminating these agents from routine HM panels in well-managed programs is recommended unless individual situational factors deem it necessary.

Establishing or maintaining a barrier facility for immunocompromised mice. Often, a need develops for maintaining certain mouse colonies at a higher-level health status than the population of mice in a general colony. The development of a barrier room, suite, or facility presents a special opportunity to exclude adventitious agents that may influence specific research studies, protect vulnerable (for example, immunocompromised) or founder populations, maximize distribution options to facilities with differing exclusion lists, or to demonstrate a higher level of rigor for the sake of reproducibility. Barrier practices mitigate the introduction of agents from other lower-level health status colonies that are sometimes housed adjacent to barrier spaces.

As such, barrier facilities commonly house immunocompromised populations in which opportunistic agents should be monitored and/or excluded. Most programs do not exclude opportunistic bacteria as part of their routine HM program and instead reserve such monitoring for colonies under this higher-level health status. In addition to previously listed agents recommended for all HM programs, commonly excluded agents for immunocompromised animals may include rodent chaphamaparvovirus (RCHPV-1), *Chlamydia muridarum*, *Corynebacterium bovis*, *Helicobacter* spp., and *Pneumocystis murina*. Perhaps the most notable pathogen for this group is *C. bovis*. The introduction of *C. bovis* can be devastating, as it is easily transmitted among vulnerable mouse populations and readily contaminates the animal facility environment, which aids in infection perpetuation within a facility.²⁰ A fungal pathogen of note is *P. murina*, as it is ubiquitous, transmitted by aerosolization, and commonly found in immunocompetent or immunovague mouse populations. Although its reported prevalence is relatively low (<0.2%),¹⁰ this may be an underrepresentation due to unreliable sampling and testing methods (that is, SBS)⁹ and low frequency of screening among institutions. In the most vulnerable immunodeficient populations (such as NSG mice), *P. murina* can cause debilitating chronic progressive pneumonia. Lastly, the relatively new RCHPV-1 has been shown to cause nephropathy and tubulointerstitial fibrosis in immunocompromised mice, prompting its consideration for exclusion from these colonies as well.^{21,22} Overall, the extent of exclusion within a barrier facility will depend on the program goals. As the number of excluded agents increases, there is an increase in surveillance costs and often a decrease in staff access and available sources of mice that can enter the facility. To protect this higher-level health status within a facility, we recommend testing for these agents based on risk assessment and at the program's discretion.

New, emerging, and reemerging agents. With the application of high-throughput genetic sequencing technologies, there is likely to be an increase in the number and rate of identification of agents that may be classified as opportunistic, pathogenic, or pests. Once identified, the influences on prevalence of these new, emerging, and reemerging agents will be multifactorial with emphasis placed on organism-specific transmissibility and vivarium-specific biosecurity practices. Noteworthy new, emerging, and reemerging agents include RCHPV-1,²² also referred to as mouse kidney parvovirus or murine chapparvovirus, which was identified in 2018; the published discovery of murine astrovirus 2 (MuAstV2) in 2020;²³ the emergence of *Bordetella pseudohinzii* between 2008 and 2016;^{24,25} and the reemergence of *C. muridarum* in 2022 after first being identified in the 1930s.²⁶ The published prevalence of these agents based on samples submitted to international diagnostic laboratories are 10%,²⁷ "rare,"²⁸ 0.46%,¹⁰ and 16%,²⁶ respectively. The variability of prevalence of these contemporary agents demonstrates that agents that may be discovered in the future should not automatically be considered ubiquitous despite the lack of prior knowledge and unavailability of diagnostic testing.

Many factors will determine whether new, emerging, or reemerging agents are added to routine HM panels to simply monitor for presence of agents or ultimately be added to an institution's exclusion list. Several of these factors are institutional, or even vivarium specific, and based on risk assessments. Deliberations may also occur at the national or international level, which may contribute to a collective movement toward exclusion. Two primary factors that can have a significant impact on the argument for excluding a new agent is the demonstration of adverse impacts on research outcomes and induction of clinical disease. This is demonstrated best by

the 2003 identification of MNV.²⁹ While no longer considered new or emerging, MNV remains highly prevalent in research mouse colonies despite being identified >20 y ago.^{10,30} MNV is not excluded by many research institutions because infection has limited impact on biomedical research and causes no clinical disease in most mouse strains.^{30–33} A thorough assessment of each new, emerging, or reemerging agent will be required to determine whether screening or exclusion is appropriate or prudent. This process is currently underway for RCHPV-1, *C. muridarum*, and *B. pseudohinzii*. RCHPV-1 and *C. muridarum* are both widely distributed within research mouse colonies,^{26,27} with a disproportionate clinical impact on immunodeficient mouse strains.^{21,22,34,35} In contrast, *B. pseudohinzii* causes a sub-clinical infection in immunocompetent mice with limited data on its impact on immunodeficient mice. Despite a lack of clinical signs, *B. pseudohinzii* is known to elevate inflammatory cell counts in the lungs of infected mice, foreshadowing an impact on research outcomes.^{24,36–38} Nevertheless, it could be argued that research has been successfully conducted for decades in the presence of these infections. Despite this, historical ignorance cannot be the sole rationale for continued tolerance. Rationale for continued tolerance may include high prevalence between, and within, colonies; difficulty of agent detection due to pathogen infectivity and shedding kinetics; and the significant cost and time that would be required to facilitate rederivation to eliminate these agents. Furthermore, exclusion at academic institutions may be dependent on the initial exclusion at commercial breeding facilities. For example, RCHPV-1-free mice were only recently available from most commercial vendors in 2022. In contrast, most mice from commercial vendors were found to be *C. muridarum*-free at the time of reemergence of this agent.²⁶ A collective movement will be needed within the scientific or laboratory animal science communities to add new, emerging, or reemerging agents to screening and ultimately exclusion lists at scale. Until that occurs, individual institutions will need to make risk assessments based on site-specific research programs and constraints to determine for which agents screening is conducted and those where testing is performed for exclusion.

Import, export, and quarantine. The sharing of mice between institutions remains an important consideration when developing HM programs. Unlike with vendor-supplied SPF animals, research animal facilities typically require incoming animals from other institutions to undergo quarantine and testing upon arrival as this may be a point of entry for pathogens. In some cases, to preserve a higher health status, facilities may require that mouse lines are rederived before entry, but this is associated with significant costs and operational implications. The risk associated with introducing new mice should be evaluated for each transfer. This includes a review of HM reports specific to the animals being imported, an assessment of biosecurity practices, and a thorough review of the overall HM program of the exporting facility including history of outbreaks. Additional factors to consider may include the frequency and type of HM performed (for example, SBS, direct colony sampling, sentinel-free soiled bedding, exhaust dust testing), size/layout of facility and type of caging, the immune status and previous manipulations of the animals being transferred (for example, injections with biological materials), previous outbreaks, and the potential for contamination during the transfer. As part of a quarantine program, facilities may want to screen incoming animals with a more extensive panel of agents that includes those tested for on a regular basis by the routine HM program as well as agents of low prevalence such as *Salmonella* spp., Sendai virus, mousepox, hantavirus, polyomavirus, K virus, and

mouse thymic virus (MTLV). This is because the importation of animals has high potential for introducing excluded pathogens to a facility. Screening of incoming animals may involve quarantine and testing animals directly or indirectly (that is, with environmental HM) via PCR and/or prophylactic treatment with antibiotic or antiparasitic medications.⁸

Facilities with specialized programs that regularly export mice to other institutions, such as model production or transgenic facilities/cores, may require a more extensive HM program with a larger number of agents excluded, compared with routine HM programs, to facilitate the transfer and acceptance of animals by receiving institutions without the need for further testing prior to export. Similarly, if a receiving facility has unique HM requirements, they may request that the exporting facility test the animals via direct colony sampling for specific agents (for example, hantaviruses) before exportation. These details are typically coordinated between the importing and exporting facilities as part of the transfer process.

Wild rodents and pests. Preventing the introduction of wild rodents and pests is an important aspect of maintaining a research rodent animal care program free of adventitious agents. Animals that are not purpose bred for research (for example, pet shop animals, wildling mice, or wild rodents) can contain a wide array of potential pathogens.³⁹ If vermin incursions occur, or if mice from nontraditional sources are being used, additional testing of rodent colonies may be required to identify whether undesired agents were introduced and to control for any potential outbreaks. The HM panel may need to be adapted to ensure that agents commonly excluded from research rodents, but potentially present in wild rodents,¹⁸ are included in routine or temporary testing. In addition to routinely excluded agents, additional testing could include Sendai virus, hantavirus, *Salmonella* spp., *Helicobacter* spp. (*H. bilis*, *H. ganmani*, *H. mastomyrinus*, and *H. typhlonius*), mouse cytomegalovirus (MCMV), MNV, MTLV, and parasites. Outbreaks of the tropical rat mite, *Ornithonyssus bacoti*, are another common sequela to wild rodent incursions.¹⁷ As this mite is zoonotic and can cause immunologic research effects, early identification, treatment, and elimination are necessary.

Upon capture of a wild rodent, extensive testing of the animal (for example, by PCR and/or serology) should be performed. Most diagnostic laboratories will have a comprehensive panel that screens for all potential rodent agents (both historical and present) that can be used in this situation. Note, however, that some serology panels may not be compatible with wild rodents due to a lack of cross-reactivity with laboratory pathogen strains. If specific agents are detected in a captured wild rodent, these agents can be temporarily added to HM panels of potentially impacted colonies. For example, if a captured wild rodent tests positive for a previously nonmonitored agent, this agent can be added to the quarterly (or more frequent) screening of potentially affected colonies to prevent or mitigate the potential spread of infectious agent within the colony. Since many pathogenic agents can transmit through fomites (such as feed, bedding, or caging materials), enhanced environmental screening of potentially contaminated fomites may also be of benefit. Environmental HM can be readily used to identify these agents, which would not be normally detected using a SBS program.¹⁷ Facilities with a history or potential for wild rodent incursions, such as older buildings or those undergoing construction/renovation, as well as those where wild rodents are brought into the facility for research use, should consider adding *O. bacoti* and other wild rodent pathogens to their routine HM panels to promptly identify an outbreak.

Zoonoses. Excluding zoonotic agents may be prudent for occupational health and safety. Fortunately, the prevalence and risk of zoonotic agents in modern research rodent colonies remain minimal. Although a pathogen of serious consequence, detection of hantavirus in laboratory mice has not been reported in at least the last 25 y according to the data collected and presented in pertinent publications.^{2,4,10} Therefore, in a well-managed program, this pathogen may be removed from the routine HM panel. However, there is a risk of humans contracting hantavirus from wild rodents, so testing for hantavirus may be warranted with instances of wild rodent incursions. Also, since hantavirus is present worldwide, some facilities may choose to test for this pathogen when receiving animals from an international location. LCMV is also present worldwide and can result in serious illness in people with weakened immune systems. Historically, LCMV was a reported contaminant in one biological material,⁴⁰ but a recent publication reports a 0.00% prevalence in mouse serology samples and 0.02% prevalence in PCR samples from 2016 to 2020.¹⁰ Therefore, removal of this pathogen from routine HM panels may be merited, as well. Lastly, zoonotic ectoparasites such as tapeworms (for example, *Hymenolepis nana*) and mesostigmatid mites (for example, *O. bacoti*, *Liponyssoides sanguineus*, *Laelaps echidnina*) should be actively excluded from modern murine colonies. Exclusion can be achieved through effective management of imported animals and wild rodents/pests (for example, using custom HM panels), as previously discussed.

Biological materials. The introduction of murine pathogens to a rodent colony through biological materials is a common concern for programs engaged in research that uses such materials.⁴¹ Pathogens that may be transmitted via this route include lactate dehydrogenase-elevating virus (LDV), MCMV, polyoma virus, *M. pulmonis*, and *C. bovis*. All except the latter have been shown to have nominal prevalence in murine samples analyzed by a commercial diagnostic laboratory from 2016 to 2020 (LDV <1.08%; MCMV <0.06%; polyoma <0.07%; *M. pulmonis* <0.09%).¹⁰ It is also important to consider that biological materials processed and stored decades ago may have a greater likelihood of harboring these undesirable pathogens. Since historical standards for exclusion were less stringent, and there was limited availability of PCR testing at the time for agents that are commonly excluded from research colonies today, biological materials that were produced in or passaged through historic animals may possess some of these undesirable pathogens. As is common in research, these aged samples may be retrieved from storage at any time and used in animals.⁴¹ An example is LDV which is still seen in modern facilities due to historical contamination of a basement membrane protein matrix used by researchers in solid tumor cancer research.⁴² Lastly, the introduction and dissemination of these agents will likely be devastating to animal colonies and certainly place a large financial burden on the institution for remediation and elimination. In recent times, this is particularly true for *C. bovis*, which is a relatively prevalent agent (2.93% by serology, 2.26% by PCR),¹⁰ and will clinically affect immunocompromised populations. Therefore, it is recommended that biological materials be screened for additional agents, beyond those screened for in a routine HM program, prior to use in research animals (via PCR on a portion of the biological material intended for inoculation).

Study-related exclusions. Segmented filamentous bacteria (SFB) are spore-forming, commensal bacteria that populate the ilea of mice and other species, including humans.⁴³ SFB have attracted the attention of researchers in recent years as they are involved in the maturation and function of the host gut immune

barrier.^{43,44} Currently, no commercial vendors offer mice that are guaranteed to be free of this agent; however, one case report describes the use of ampicillin-medicated water to eradicate SFB from a mouse colony.⁴⁵ At some institutions, SFB may be excluded with selected areas being maintained free of the agent using restricted or entry order policies in combination with more frequent testing or through the use of isolator housing.

Other agents that institutions may want to exclude due to their effects on study-specific research may include MNV, *Citrobacter rodentium*, *Salmonella* spp., and trichomonads (for investigators focusing on gastrointestinal or immunologic research), *Helicobacter* spp. (for investigators focusing on gastrointestinal or hepatic research), RCHPV-1 (for investigators focusing on renal research), *B. pseudohinzii*, *C. muridarum*, *Filobacterium rodentium*, and *P. murina* (for investigators focusing on pulmonary research), and *C. bovis* (for investigators focusing on cancer research).⁴⁶ While it is beyond the scope of this work to provide a comprehensive review of research or clinical impacts of each agent that would provide relevance for exclusion, readers are referred elsewhere learn more about specific agents.⁴⁷

Conclusion

As there is no universal consistency between institutions, we aim to provide guidance on establishing mouse HM programs with consideration given to common situations and contemporary agent prevalence. We recommend that programs periodically reevaluate their HM panels to include a refined list of agents, based on current prevalence data and situations specific to the institution. This refined list of agents will include opportunists, pathogens, and pests and will minimize both labor and costs associated with overtesting. Furthermore, a 'one diagnostic panel fits all' approach is becoming harder to apply to modern mouse facilities. While agent prevalence is an important factor, specialized programs and operational situations may also require custom HM panels to address the risk of introducing specific agents. New, emerging, and reemerging agents continue to appear, so keeping informed of their significance within the laboratory animal field will be prudent. Finally, a distinction should be made between the testing of mice for excluded agents and the testing (or monitoring) of mice for nonexcluded agents.

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Conflict of Interest

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