

OUTLOOK

RESEARCH MODELS • LABORATORY ANIMAL DIAGNOSTICS •
TRANSGENIC SERVICES • SURGICAL SERVICES • GENETIC TESTING



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PROTECTING YOUR COLONY'S HEALTH STATUS

Keeping pathogens out of animal colonies, while letting in food, water, and other supplies, is a common challenge for both animal researchers and vendors. Health complications that result in clinical diseases and pathological changes can have devastating effects on research results and cost investigators time and money. At Charles River Laboratories, we implement strict biosecurity and surveillance programs to protect the health profiles of our colonies. We utilize our diagnostic laboratory to monitor our commercial colonies, and offer quarantine for client colonies through our Transgenic Services division.

The Importance of Biosecurity and Surveillance

Charles River's diagnostic laboratory advocates good biosecurity as the best, if not only, way to help prevent the spread of infectious agents. Biosecurity practices prevent a pathogen from spreading to a susceptible host. Different pathogens can be spread via different routes (vertical, airborne, direct, and fomite/vector transmission), and an effective biosecurity program works to eliminate or reduce all possible modes of transmission. Therefore, your biosecurity program should include practices that address each route of transmission—such as irradiation of bedding and food to prevent fomite transmission or maintaining directional work flow within an animal facility to prevent airborne transmission from one colony to another.

A biosecurity program alone is not enough to assure that pathogens are being excluded from your colony. Biosecurity must be complimented with surveillance. Routine colony testing will either show that animals are of the expected health status or provide the information necessary to make informed colony-management decisions. Because infections that interfere with research are often subclinical, surveillance should include microbiologic laboratory methods, in addition to serological monitoring, to detect inapparent infections. The same methods should be used to identify specific etiologic agents, because disease signs are often not enough to identify an organism. Methodologies may include:

- Gross and microscopic examination of animal specimens
- Cultural and *in vivo* isolation and biochemical identification of organisms
- Serology for detection of specific antibodies formed in response to infection (ELISA, IFA)
- Infectious agent detection via molecular-based techniques (PCR)


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Varieties of sentinel animals are available through our Research Models division.

The Role of Sentinel Animals in Surveillance

Key to effective surveillance are species-specific sentinel animal programs to help detect pathogens. When designing a sentinel program, investigators should consider animal number, age, sex, and placement and plan how frequently they want to test animals. Typically sentinel animals are from the same species and sometimes the same line. For example, we monitor our commercial colonies with retired breeder sentinels from our production colonies, provided that they are susceptible hosts of the agents in question. Sometimes it is appropriate to use sentinel animals of a different species than that of the colony. For example, mice are good sentinels for guinea pig colonies. Guinea pigs infected with human parainfluenzavirus strains may test positive for Sendai virus, due to cross-reacting antibodies. Mice are not susceptible to the human parainfluenzavirus strains. As a result, tests for Sendai virus in mice are more specific and positive results are more reliable.

Sentinels should be housed in a way that maximizes their exposure to any microorganisms present in the colony. Exposure to soiled bedding is usually, but not always, a sufficient means of pathogenic transmission. Some pathogenic agents are transmitted via airborne particles (i.e., cilia-associated respiratory bacillus and Sendai) or through direct contact (i.e., fur mites). For client quarantine services, our Transgenic Services group exposes sentinels both directly to colony animals and indirectly to soiled bedding.

Selecting sentinel animals of various ages, sexes and, if applicable, strains from different areas within the holding or breeding room can yield results different than random sampling, because some infections and positive assay results can have an age- or strain-dependent distribution. A good surveillance program must take into account the fact that different animals have varying responses to different pathogens and diagnostic methods. For example, with serology the animals must be able to mount an antibody response to infection to be useful. Since serum antibodies in immunocompetent hosts can take two to three weeks to reach detectable levels, we recommend that sentinels be kept in a colony for at least one month. Also, enteric protozoa are readily observed in weanlings but not in other rodents, while adult pinworms are more often found in adolescent mice than in weanlings. There are also strain-specific susceptibilities to certain pathogens that should be considered.

CLIENT QUARANTINE SERVICES

Charles River's Transgenic Services division offers state-of-the-art isolator facilities for performing quarantine of small laboratory animals (such as mice or rats). Our isolator housing system provides a biosecure environment and allows for immediate accommodation of your animals, regardless of their health status. Quarantine services are supported by our diagnostic laboratory, the world leader in its field, specializing in assays that monitor the health status of rodent colonies. Varieties of sentinel animals, commonly used in quarantine protocols, are available through our Research Models division.



Transgenic Services maintains each client's colony in a dedicated isolator.

Transgenic Services has developed a standard quarantine protocol over years of screening thousands of rodent colonies from hundreds of sources globally. If requested, we will customize the health monitoring protocol for evaluating genetically-modified animals in accordance with the attending veterinarian responsible for the investigator's colony. A customized program may include establishing a quarantine protocol that mimics one in place at the home institution. In addition, screening can be adjusted based on any history of past health issues at the source facility.

Why Use Sentinel Animals?

Transgenic Services recommends the use of sentinel animals, rather than the direct screening of colony animals, for several reasons. First, genetic manipulation may affect the immune system of transgenic and knockout animals, potentially causing false negative serological results. Secondly, transgenic and knockout animals are usually available in small quantities and euthanizing colony animals for health monitoring could potentially delay production goals. Finally, it is also possible that spread of a pathological agent throughout a colony may be impeded in the source institution through the use of micro-isolator type housing. Therefore, screening a small percentage of colony animals may result in inaccurate health monitoring results.

We often suggest using a combination of immunodeficient (homozygous nude) and immunocompetent (heterozygous nude) mice as sentinels. The immunodeficient nude mice are recommended for their sensitivity to bacterial pathogens and endoparasites, while the immunocompetent animals are recommended for the detection of viral antibodies and ectoparasites. In addition, we recommend that the sentinel mice be maintained in the same cages as the colony mice for at least part of their exposure period in order to facilitate transfer of pathogens. This step is particularly important when screening for ectoparasites.

Recommended Protocol for Quarantine of Transgenic and Knockout Rodent Colonies

We maintain each client's colony in a dedicated isolator. Four immunocompetent animals and four immunodeficient nude mice are added to the isolator for two weeks of direct contact (sentinels are co-housed with the colony animals) followed by six weeks of soiled bedding exposure. Once the exposure time has been achieved, two of the immunodeficient nude mice are submitted to our diagnostic laboratory for bacteriology, parasitology, and gross pathology screening. Two of the immunocompetent mice are submitted to the laboratory for comprehensive health assessment, which includes serology, bacteriology, parasitology, and gross pathology screening. Histopathology is performed on any tissue with gross lesions. The remaining immunodeficient nude mice and immunocompetent animals are reserved for any repeat testing, if needed, to confirm equivocal or unexpected results.



Our staff is available to discuss specialized protocols.

Customized Protocols

Quarantine and health monitoring protocols range in type and complexity. Our program is offered at many levels, allowing clients to custom design protocols depending on their individual needs and requirements. We recommend that any decisions regarding actions that may impact the health status of the colony be made in consultation with the client's institutional veterinary resources. Charles River Laboratories' professional staff is also available for consultation and recommendation to help meet your specific health monitoring needs.

Charles River Laboratories' *Outlook Newsletter* offers a single source of information about the research models and surgical, transgenic, genetic testing, and diagnostic services that impact your research. For your convenience, this publication is also available electronically. We welcome comments and suggestions about which services you would like to hear more about. Please direct comments as well as requests to be removed from the mail list to askcrl@criver.com. If you prefer to receive this newsletter electronically, please e-mail with "electronic *Outlook*" in the subject line.

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