charles river

360 DIAGNOSTICS™

Health Monitoring of Immunodeficient Rodents in Isolators in North America and Europe

Overview/Abstract:

This white paper describes the methods Charles River uses to monitor the conditions of its isolators containing immunodeficient mouse and rat models. While the isolator environment is microbiologically controlled, it is not completely devoid of all known organisms and can continue operating normally if occasional benign mold, yeast, or nonpathogenic bacterium is found. If, however, during routine testing an undesirable organism is found Charles River will activate the appropriate protocols, which include removal of affected isolator from service and notification sent out to impacted clients.

Charles River currently maintains approximately several thousand isolators at numerous locations across North America and Europe to produce immunodeficient mice and rats. These animals, while maintained under a microbiologically controlled environment, are not axenic (i.e., they are not free of all known organisms). Moreover, while each isolator is initiated with defined flora, our policy is to continue operating individual isolators if an occasional mold, yeast, or common nonpathogenic environmental bacterium is detected.

In assessing the health and bacteriologic profiles of the isolators, it is important to understand that each individual isolator functions as a small barrier production room containing, typically, between 30 and 65 cages with open (wire) tops. Since each isolator potentially has a slightly different profile in terms of additional organisms beyond the Charles River Altered Schaedler Flora (CRASF), the discrete bacterial profile may vary between individual groups of animals.

Each isolator is cultured (isolator internal surfaces, feces, drinking water) for assessment of bacterial flora at least every six weeks. Annually, select animals from every isolator are collected and screened by serology (Assessment Plus profile), PCR on feces, respiratory samples for bacteria and fungi, microbiologic culture of respiratory and gastrointestinal systems, complete parasitology, and a full necropsy with histopathology of any lesions. Typically, immunodeficient and/or immunocompetent animals are sampled from each isolator for this intensive screening process. In all the years Charles River has produced immunodeficient animals in isolators for commercial sale, we have never detected a contamination from an organism on our VAF®/SPF profile list (Category I), even in the presence of a change in bacterial flora in an isolator. Such historical results support our approach of frequent bacterial screening augmented by annual health monitoring. Health monitoring reports are provided by Charles River on our website (http://www.criver.com/products-services/basic-research/health-reports), and are continuously updated as new results become available. These reports document the status of the composite of all the isolator colonies for that immunodeficient species, strain, or area located at a given facility.

EVERY STEP OF THE WAY

Outlined below are infectious agents categorized by the action that will be taken by Charles River if the organisms are ever detected in an isolator of immunodeficient rats and mice. Confirmation of any Category I agent would initiate an immediate notification of ALL customers that had received animals from any of the isolators in the facility. In keeping with our policy of open communication, all Charles River customers, regardless of whether or not they received isolator-reared animals, would also be notified. These organisms would result in cessation of shipment of animals from affected isolators and the immediate recycle of the affected isolator(s). Charles River considers each isolator as a microbiologic unit, and will not "test and cull" individual cages within an isolator. The circumstances involving the contamination would also be thoroughly investigated and reported to our customers in accordance with standard policies.

A finding of a Category II organism would also result in immediate recycling of the contaminated isolator. Customers receiving animals from that isolator during the period since the last negative screening will be notified. The entire customer base would not be notified, nor would customers that did not receive animals from the contaminated isolator be routinely notified.

Charles River Guidelines for the Recycling and Customer Notification of Production Isolators for Immunodeficient Rats and Mice in North America and Europe

Category/Action	Organisms				
Category I	**Mice**		**Rats**		**Mice and Rats**
Stop shipment from isolator	EDIM	ECTRO	RMV	REO	CAR bacillus
Immediate recycle	MPV	MAV	KRV	SDAV	Tyzzer's Disease
Notify **all** customers	MHV	K	RPV	MAV	*Corynebacterium kutscheri*
	MVM	POLY	H-1	ECUN	*Mycoplasma pulmonis*
	TMEV (GD-7)	MCMV	RTV	HANT	*Citrobacter rodentium* (mice)
	MNV	ECUN	SEND	LCMV	*Helicobacter hepaticus*
	SEND	HANT	PVM		*Salmonella* spp.
	PVM	LDV			*Streptobacillus moniliformis*
	REO	LCMV			Helminths
					Pathogenic protozoa
					External Parasites
Category II	**Mice and Rats**				
Stop shipment from isolator	*Pneumocystis* spp.		*Pasteurella pneumotropica*		*Pseudomonas aeruginosa*
Immediate recycle	β-hemolytic *Streptococcus spp.*		*Pasteurella multocida*		*Streptococcus pneumoniae*
Notify customers that received animals from the isolator	Coagulase-positive *Staphylococcus* spp. including *S. aureus*		*Helicobacter bilis*		*Proteus mirabilis*
	Corynebacterium bovis		All other *Helicobacter* spp.		Non-pathogenic *protozoa*
			Bordetella bronchiseptica		
			Any *Klebsiella* spp.		