



## ROUTINE HEALTH MONITORING OF ISOLATOR-REARED VAF/Elite® ANIMALS

This letter is to familiarize you with the isolator-based production and health surveillance of **VAF/Elite®** mice. Charles River Research Models and Services North America produces these animals in flexible-film and semi-rigid isolators, originally developed to provide the high-level biosecurity environment required for mice lacking normal host-defense mechanisms. This is done specifically to limit the exposure to opportunistic bacteria, including bacteria commonly found in or on humans, as some of these organisms could pose unwanted variables in certain research studies.

Charles River **VAF/Elite®** animals, while maintained under a more microbiologically controlled environment, are not axenic, i.e., free of all known organisms. Moreover, while they are initiated as defined flora animals, i.e., containing only a few well-defined organisms, our policy is to continue operating individual isolators if an occasional mold, yeast, fungus 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 similarly to a separate barrier production room; each isolator contains between 30 and 75 cages. Depending upon the specifications for any given order, mice from multiple isolators may be required to fill that order, and different groups of isolators may fill repeat orders in subsequent weeks. Since each isolator may have a somewhat different profile in terms of additional organisms beyond the Charles River Altered Schaedler Flora (CRASF), the discrete bacterial profile may vary between subsequent groups of animals though still meet or exceed the stated criteria for the health profile.

Each isolator is cultured (isolator internal surfaces, feces, drinking water) for assessment of bacterial flora at least every four weeks. Every 13 weeks, serum is collected from two animals in each isolator for antibody screening for the *Mycoplasma pulmonis* and the most prevalent and historically important viruses (Tracking Profile). In addition, 4 animals from every isolator are sampled annually for parasites, gross pathologic lesions, bacterial profiles of the respiratory and gastrointestinal tracts and, on two animals, viral pathogens (Assessment Plus Profile).

Health monitoring reports are provided by Charles River on our website ([www.criver.com](http://www.criver.com)) and are continuously updated as new results become available. These documents describe the status of the composite of all the isolator colonies located on a given site. In the many years we have produced animals in isolators for commercial sale, we have never detected a contamination from an organism on our **VAF/Plus®** profile list. Moreover, only on a very few occasions have we found an isolator contaminated with any of the expanded list of bacteria which defines our **VAF/Elite®** profile, such as a coagulase-positive *Staphylococcus* or  $\beta$ -hemolytic *Streptococcus*, which are of the most common concern to our customers. When that has occurred, we have immediately recycled that isolator. Charles River considers each isolator as a microbiologic unit, and will not "test and cull" individual cages within an isolator.

The attached list of bacteria is categorized by the action that will be taken by Charles River if the organisms are ever detected in an isolator. As can be seen from the chart, the first group of organisms would initiate an immediate notification of ALL customers that had received mice 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 be cause for immediate recycle of a standard barrier production room and would clearly result in cessation of shipment of any animals from affected isolators and their immediate recycle. The circumstances involving the contamination would be thoroughly investigated and reported.

The second category of organisms would also result in immediate termination 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 will customers that did not receive mice from the contaminated isolator be routinely notified unless requested. Additional information is available through the Charles River Technical Services Department.

The remaining categories list organisms for which shipment would not be halted.

Clearly, management of a very large group of barrier production units such as isolators poses a difficult task both from a production and a health monitoring standpoint. We feel that it is important that our customers understand the conditions under which our animals are produced and how to interpret the health monitoring data we provide regarding these animals. In developing this production system, we have had to balance the level of risk to the health of the animals inherent in this production system with the amount, frequency and completeness of the information generated, as well as with the information our customers require or expect. We are committed to providing our customers with the information that they require to make animal health management decisions, and in this regard we would appreciate your comments on how we might cost effectively improve the present system. Should you require any additional information or have specific requests, please contact our Technical Services Department at 1-800-338-9680 or send an e-mail to [comments@criver.com](mailto:comments@criver.com).

Sincerely,

Charles B. Clifford, DVM, PhD  
Director, Pathology and Technical Services

CHARLES RIVER GUIDELINES FOR THE RECYCLING AND CUSTOMER NOTIFICATION  
OF PRODUCTION ISOLATORS FOR VAF ELITE® RATS AND MICE

<u>Category/Action</u>	<u>Organisms</u>		
CATEGORY I.	<u>MICE</u>	<u>RATS</u>	<u>MICE and RATS</u>
<ul style="list-style-type: none"> <li>• STOP SHIPMENT FROM ISOLATOR</li> <li>• IMMEDIATE RECYCLE</li> <li>• NOTIFY <u>ALL</u> CUSTOMERS</li> </ul>	EDIM	RMV	CAR bacillus
	MPV	KRV	Tyzzler's Disease
	MHV	RPV	<i>Corynebacterium kutscheri</i>
	MVM	H-1	<i>Mycoplasma pulmonis</i>
	TMEV (GD-7)	RTV	<i>Citrobacter rodentium</i> (mice)
	MNV	SEND	<i>Helicobacter hepaticus</i>
	SEND	PVM	<i>Salmonella</i> spp.
	PVM	REO	<i>Streptobacillus moniliformis</i>
	REO	SDAV	Helminths
	ECTRO	MAV	Pathogenic protozoa
	MAV	ECUN	External Parasites
	K	HANT	
	POLY	LCMV	
	MCMV		
	ECUN		
	HANT		
LDV			
LCMV			
MTLV			

<u>Category/Action</u>	<u>Organisms</u>
CATEGORY II.	<u>MICE and RATS</u>
<ul style="list-style-type: none"> <li>• STOP SHIPMENT</li> <li>• IMMEDIATE RECYCLE</li> <li>• NOTIFY CUSTOMERS THAT RECEIVED ANIMALS FROM THE ISOLATOR</li> <li>• PROVIDE INFORMATION TO OTHER CUSTOMERS REQUEST</li> </ul>	<i>Pasteurella pneumotropica</i> $\beta$ -hemolytic <i>Streptococcus</i> spp. Coagulase-positive <i>Staphylococcus</i> spp., including <i>S. aureus</i> <i>Klebsiella</i> spp.
	<i>Pseudomonas aeruginosa</i> <i>Proteus mirabilis</i> <i>Streptococcus pneumoniae</i> <i>Pasteurella multocida</i> <i>Pneumocystis</i> spp. (immunodeficient only) <i>Corynebacterium bovis</i> (immunodeficient only) <i>Mycoplasma</i> spp. <i>Helicobacter bilis</i> other <i>Helicobacter</i> spp. <i>Bordetella bronchiseptica</i> non-pathogenic protozoa

<u>Category/Action</u>	<u>Organisms</u>
<b>CATEGORY III.</b>	<b><u>MICE and RATS</u></b>
<ul style="list-style-type: none"> <li>• CONTINUE SHIPMENT</li> <li>• PLANNED RECYCLE</li> <li>• NO NOTIFICATION OF CUSTOMERS</li> <li>• PROVIDE INFORMATION TO CUSTOMERS ON REQUEST</li> </ul>	Coagulase-negative <i>Staphylococcus</i> spp. Non-β-hemolytic <i>Streptococcus</i> spp. <i>Corynebacterium</i> spp. (other than <i>C. bovis</i> or <i>kutscheri</i> ) Any other gram negative bacteria

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<u>Category/Action</u>	<u>Organisms</u>
<b>CATEGORY IV.</b>	<b><u>MICE and RATS</u></b>
<ul style="list-style-type: none"> <li>• CONTINUE SHIPMENT</li> <li>• NO RECYCLE</li> <li>• NO OTHER ACTIONS</li> <li>• PROVIDE INFORMATION TO CUSTOMERS ON REQUEST</li> </ul>	<i>Bacillus</i> spp. Fungi (molds and yeasts) All other non-pathogenic bacteria