charles river
accelerating drug development. exactly.

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. For **VAF/Elite®** mice, isolator-based housing is used 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; they are not free of all known organisms. Instead they are distinguished from VAF/Plus® animals raised in Charles River barrier rooms by the confirmed absence of specific additional bacterial species.

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 between 30 and 75 cages with open (wire) tops. 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 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.

Quarterly (every 13 weeks), for 3 of the 4 quarters in the year, serum is collected from 4 animals in each isolator for antibody screening for the most prevalent and important viruses (Prevalent Profile). At the fourth quarterly monitoring, once each year, mice from each isolator are submitted for comprehensive health monitoring including serology for a full panel of agents (Assessment Plus profile), serum LDH evaluation (for LDV virus), bacteriology of the respiratory and gastrointestinal tracts, complete parasitology of the pelt and GI tract, and a complete necropsy with histopathology of all lesions. In addition, at the quarterly monitoring, samples are collected for PCR to screen for *Streptobacillus moniliformis* and for all *Helicobacter* spp. Every 4 weeks, to insure that the isolator retains a bacterial profile consistent with **VAF/Elite®** status, microbiologic samples are collected from each isolator.

Health monitoring reports are provided by Charles River on our website (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 that 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 β-hemolytic *Streptococcus*. When that has occurred, we have immediately recycled that isolator.

The attached list of infectious agents 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, Category I organisms comprise the VAF exclusion list, detection of which 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. 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 be thoroughly investigated and reported.

Category II comprises organisms, some of which may sometimes be present in barrier rooms but are excluded from **VAF/Elite®** animals, and 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.

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 for thoughtful 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 877-274-8371 (877-CRIVER1) or send an e-mail to askcharlesriver@crl.com.

Sincerely,

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

07 October 2011

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

Category/Action	Organisms		
CATEGORY I.	**MICE**	**RATS**	**MICE and RATS**
• STOP SHIPMENT FROM ISOLATOR • IMMEDIATE RECYCLE • NOTIFY **ALL** CUSTOMERS	EDIM MPV MHV MVM TMEV (GD-7) MNV SEND PVM REO ECTRO MAV K POLY MCMV ECUN HANT LDV LCMV MTLV	RMV KRV RPV H-1 RTV SEND PVM REO SDAV MAV ECUN HANT LCMV	CAR bacillus Tyzzer's Disease *Corynebacterium kutscheri* *Mycoplasma pulmonis* *Citrobacter rodentium* (mice) *Helicobacter hepaticus* *Salmonella* spp. *Streptobacillus moniliformis* Helminths Pathogenic protozoa External Parasites

Category/Action	Organisms
CATEGORY II.	**MICE and RATS**
• STOP SHIPMENT • IMMEDIATE RECYCLE • NOTIFY CUSTOMERS THAT RECEIVED ANIMALS FROM THE ISOLATOR • PROVIDE INFORMATION TO OTHER CUSTOMERS ON REQUEST	*Pasteurella pneumotropica* β-hemolytic *Streptococcus* spp. Coagulase-positive *Staphylococcus* spp., including *S. aureus* (*S. xylosus* for SJL mice only) *Klebsiella* spp. *Pseudomonas aeruginosa* *Proteus mirabilis* *Streptococcus pneumoniae* *Pasteurella multocida* *Pneumocystis* spp. *Corynebacterium bovis* (immunodeficient only) *Helicobacter bilis* other *Helicobacter* spp. *Bordetella bronchiseptica*