The SMART Program

Sentinel Mouse And Rat Testing

ELISA ASSAYS

Biotech Trading Partners
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"Representing only the very best to the very best"

인사, Bienvenue, 挨拶, Willkommen, 问候, Welkom, Benvenuto, Χαιρετισμοί, Saludos, Welcome

Thank you for your interest in the SMART Program, a system designed to bring your Rodent Sentinel Program back under *your* control.

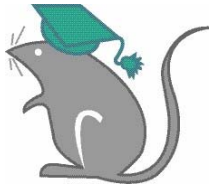
Please use this catalog as a portal to our products, a product line that is constantly expanding in both scope and technologies.

The focus of this catalog is to introduce you to our ELISA product line. All of our assays are performed at room temperature using only a small amount of animal sera, and can be completed in less than 90 minutes.

This catalog consists of:

- An overview of who we are
- A SMART ELISA Product Listing
- A SMART ELISA Procedure Chart
- Overcoming the obstacles of in-house testing by using SMART ELISA
- A package insert from a Mouse Hepatitis Kit as a representative of all SMART ELISA's (all work exactly the same)
- A brief overview of the infections we test for, including clinical symptoms and their effects on research

Please feel free to contact your distributor for more information.



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The name "Biotech Trading Partners" may be new, but the foundation is solid.

This company was formed to re-establish the partnerships that once existed between manufacturers and laboratorians; relationships forged to provide a service or product to improve the workflow and quality of results.

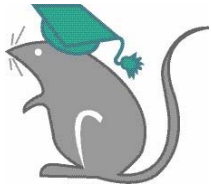
I have had 30+ years experience in this industry ranging from my beginnings as a bench tech in the New York City Health Department to President of MarDx Diagnostics. In between, I've held positions as a sales representative, sales director, technical director, and operations manager. Throughout my career I've never lost focus of customer and patient care.

Biotech Trading Partners has recently developed and released its own product line: the SMART program. This line is dedicated to EIA products for Sentinel Mouse and Rat Serology, bringing the accuracy and ease-of-use of human diagnostics to veterinary research.

Biotech Trading Partners is committed to providing superior service and support to our customers. All products can be manufactured to the specifications and expectations of our end-user. In addition, we also have the capability and interest to co-develop custom products.

Our product offerings are constantly expanding; please check our web site, www.biotechtradingpartners.com, for current offerings and more specifics.

"Representing only the very best to the very best" is not a catch phrase: it is the mission statement for Biotech Trading Partners.



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The SMART Program

Get with the program; the **SMART** program
The **S**entinel **M**ouse **A**nd **R**at **T**esting Program

Mouse EIA Serology Assays

SMART-M10	MVM, Minute Virus of Mice
SMART-M11	Sendai Virus
SMART-M12	PVM, Pneumonia Virus of Mice
SMART-M13	REO-3, REO Virus Type 3
SMART-M14	TMEV (GDVII), Theiler's Murine Encephalomyelitis Virus
SMART-M15	LCM, Lymphocytic Choriomenigitis Virus
SMART-M16	Ectromelia Virus
SMART-M17	MHV, Mouse Hepatitis Virus
SMART-M18	Polyoma Virus
SMART-M19	EDIM, Epizootic Diarrhea of Infant Mice, (Mouse Rotavirus)
SMART-M23	K, Mouse Pneumonitis Virus
SMART-M24	MCMV, Mouse Cytomegalovirus
SMART-M25	MAD 1, Murine Adenovirus FL
SMART-M26	MAD 2, Murine Adenovirus K87
SMART-M27	MPUL, Mycoplasma pulmonis
SMART-M28	MPV (*r*VP2), Mouse Parvovirus
SMART-M30	CARB, Cilia-Associated Respiratory Bacillus
SMART-M31	ECUN, *Encephalitozoon cuniculi*
SMART-M32	CPIL, Tyzzer's Disease (*Clostridium piliforme*)
SMART-M33	Hantaan Virus
SMART-M35	Murine Norovirus

Rat EIA Serology Assays

SMART-R11	Sendai Virus
SMART-R12	PVM, Pneumonia Virus of Mice
SMART-R13	REO-3, REO Virus Type 3
SMART-R14	TMEV (GDVII), Theiler's Murine Encephalomyelitis Virus
SMART-R15	LCM, Lymphocytic Choriomenigitis Virus
SMART-R20	SDAV/RCV, Rat Coronavirus/Sialodacroadenitis Virus
SMART-R21	KRV, Kilham Rat Virus
SMART-R22	H1, Toolan's Virus
SMART-R25	MAD-1,2, Murine Adenovirus FL/K87
SMART-R27	MPUL, Mycoplasma pulmonis
SMART-R29	RPV (*r*VP2) Rat Parvovirus
SMART-R30	CARB, Cilia-Associated Respiratory Bacillus
SMART-R31	ECUN, *Encephalitozoon cuniculi*
SMART-R32	CPIL, Tyzzer's Disease (*Clostridium piliforme*)
SMART-R33	Hantaan Virus

SMART®

Multi-Species EIA Serology Assays

BTP-96200	QnE Hyaluronic Acid (HA) Quantitative ELISA assay

All products are Research Use Only

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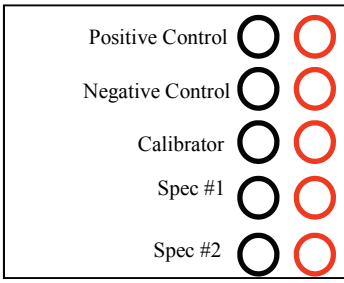
ELISA Testing by the Numbers

1

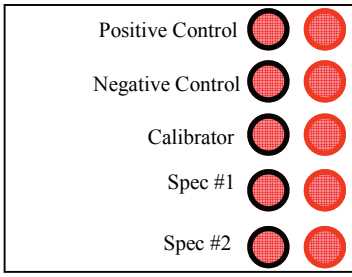


Add the Controls, and diluted Calibrator and samples to the Antigen well **(Black)** and Antigen Control well **(Red).**

Incubate for 30 Minutes at RT

WASH

2

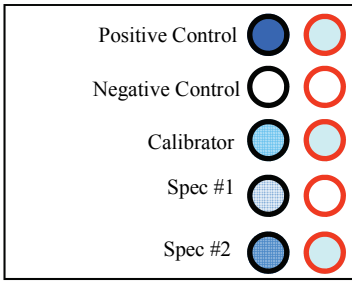


Add Conjugate to all wells.

Incubate for 30 Minutes at RT

WASH

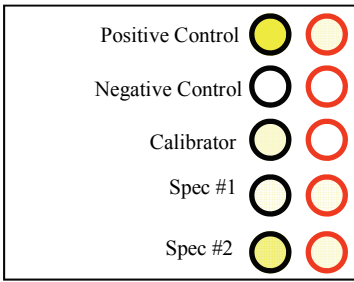
3



Add Substrate to all wells.

Incubate for 10 Minutes at RT

4



Add Stop Reagent to all wells

Read at 450/620 within 30 minutes

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SMART™

Encountering Obstacles with Sentinel Rodent Serology Testing?

Involved Reagent Ordering

Reagent Backorders

Lack of Customer Support

Complicated Procedures

Lack of Freezers and Incubators

...then get *SMART*

Complete kits, one catalog number to order

Guaranteed Standing Order policy

Dedicated support staff

Simple unified procedure with ready-to-use reagents

All testing at room temperature, reagent storage at 2-8°C

Biotech Trading Partners®

Mouse Hepatitis Virus (Mouse Sera)

Catalog # SMART-M17

For the detection of antibodies to Mouse Hepatitis Virus (MHV) in Mouse Sera by ELISA

For Use On Research Animals Only

ASSAY PRINCIPLE

The micro test wells are coated in alternating columns with Mouse Hepatitis Virus (MHV) Antigen and Control-Antigen. During the first incubation with the diluted specimen, any antibodies that are reactive with the MHV Antigen or Control-Antigen will bind to the coated wells. After washing to remove the rest of the sample, the Enzyme Conjugate is added. If antibodies have been bound to the wells, the Enzyme Conjugate will then bind to these antibodies. After another series of washes, a chromogen is added. If the Enzyme Conjugate is present, the peroxidase will catalyze a reaction that consumes the peroxide and turns the chromogen from clear to blue. Addition of the Stop Solution ends the reaction and turns the blue color to a bright yellow color. The reaction is then read with an ELISA reader and an Index Value is calculated from the Differential OD (Antigen well OD minus Control-Antigen well OD) of the specimen.

REAGENTS PROVIDED

Test Strips:	**Two** 96-breakaway well Microplates in holders coated in alternating columns with MHV Antigen and Control-Antigen. The Antigen wells are ringed in black and the Control-Antigen wells are ringed in red.
Enzyme Conjugate:	**One** 11ml bottle of anti-mouse IgG conjugated to peroxidase
Reactive Control Serum:	**One** 1ml vial of diluted reactive serum
Negative Control Serum:	**One** 1ml vial of diluted negative serum
Calibrator:	**One** 100µl vial of reactive serum
Chromogen:	**One** 11ml bottle of TMB
Wash Buffer:	**Three** 25ml bottles of concentrated (20X) buffer with surfactant
Dilution Buffer:	**Two** 30ml bottles of buffered protein solution
Stop Solution:	**One** 11ml bottle of 1M Phosphoric Acid

REAGENT STORAGE

Store the reagents, strips and bottled components between 2 - 8º C.
The diluted wash buffer may be stored at room temperature for up to 180 days, but do not use if it becomes cloudy. Do not add fresh buffer to old buffer.

SERUM COLLECTION AND HANDLING

This test utilizes the specimen's serum: coagulate the blood and remove the serum. The use of "bloody" sera is contra-indicated. Serum samples should be refrigerated as soon as possible after collection and tested within 48 hours. If the specimen is not to be tested within 48 hours after collection, the serum sample should be frozen at 0°C or lower.
Avoid repeated freezing and thawing of samples.
Vortex (mix well) samples, controls, and calibrator before using.
Do not use pooled specimens as this will adversely affect the performance of the assay.

Test samples and the calibrator are diluted 1:51 in the dilution buffer (5µl of sera + 250µl of dilution buffer)
The Negative and Reactive Controls are ready to use; **do not dilute.**
All Reagents must be at room temperature before beginning the assay.

MATERIALS REQUIRED BUT NOT PROVIDED

Pipettes capable of delivering 5µl, 50µl, and 250µl
Squeeze bottle for washing strips or automated plate washer (see procedural notes)
Distilled or reagent grade water and graduated cylinder
Tubes for sample and calibrator dilution
Absorbent paper
A dual wavelength (bichromatic) ELISA plate reader with a 450nm and a 620 to 650nm filter. If a bichromatic reader is not available, a single wavelength ELISA reader with a 450nm filter can be used.

PROCEDURE

See attached procedure guide. All procedures and reagents are at room temperature (15 – 25° C).

READING RESULTS

ELISA Reader: Zero reader on air. Set for bichromatic readings at 450/620-650nm or for a single wavelength of 450nm
Positive – Index Value of 1.0 or greater
Negative – Index Value of less than 1.0

INTERPRETATION OF RESULTS

Each Control, Calibrator, and Specimen has an OD result from the Antigen Well and the Control-Antigen Well. The OD of the Control-Antigen Well is subtracted from the OD of the Antigen Well to yield the Differential OD.

For Example:

	Antigen Well OD	Control-Antigen Well OD	Differential OD
Negative Control:	0.12	0.04	0.08
Reactive Control:	1.82	0.03	1.79
Calibrator:	0.38	0.10	0.28
Specimen 1:	1.10	0.19	0.91
Specimen 2:	0.25	0.02	0.23

The Index Value of the controls and specimens is obtained by dividing the Differential OD of the specimen or control by the Differential OD of the calibrator.

Calculation of the Example:

Differential OD of the Calibrator	0.28		
Index Value of Negative Control	0.08/0.28	0.29 Index	Valid
Index Value of Reactive Control	1.79/0.28	6.39 Index	Valid
Index Value of Specimen 1	0.91/0.28	3.25 Index	Positive
Index Value of Specimen 2	0.23/0.28	0.82 Index	Negative

An Index Value of **1.0 or greater** is considered Positive.
An Index Value of **less than 1.0** is considered Negative.

Negative Index Values are considered to be **0.00**

If using the SMART-Calc Excel Program, just enter the OD value from the reader into the appropriate well on the Excel grid and SMART-Calc will perform all of the calculations automatically.

QUALITY CONTROL

The use of controls allows validation of the test. The results should not be used if a control, or the calibrator, is out of range. A run is valid if all three of the following conditions are met:

Negative Control - Index Value of less than 0.60
Reactive Control - Index Value between 1.50 and 6.50
Calibrator - The Differential OD must be greater than 0.00

EXPECTED VALUES

The normal value is Negative. Studies have shown that antibodies may take up to 21 days to appear after exposure; therefore, Negative specimen results should be reviewed in relation to a possible exposure date. All Positive specimen results should be confirmed by an alternate method.

TROUBLESHOOTING

Negative Control has an Index greater than 0.59

Suggestion: wash more vigorously. Remove excessive liquid from the wells by slapping plate, well side down, against an absorbent towel. Do not allow test wells to dry out.

Reactive Control has an Index Value of less than 1.50 or more than 6.50

Suggestion: check the three "T's": Time, Temperature, and Technique. Time: insure that the timing on the incubation stages is adhered to. Temperature: temperatures above 25^{o}C may adversely affect the assay; Technique: check all pipettes to insure that they are properly delivering the correct volume to produce a 1:51 dilution of the calibrator and specimens. Also check your wash procedure to insure vigorous washing and removal of excess wash buffer.

PROCEDURAL NOTES

The kit Calibrator and Controls must be included on each plate tested.

Allow all reagents and samples to come to room temperature before testing. It is normal for the concentrated wash buffer to crystallize when cold. The crystals will re-dissolve once the solution returns to room temperature.

Do not use reagents beyond the expiration date printed on the label.

The dropper tips are removable from the reagent bottles to allow pipetting of reagents.

Do not inter-mix conjugates, calibrators, controls, or coated plates between different kits or different lot numbers of the same kit: these components are balanced to work together as a unit. The wash buffer, substrate, stop reagent, and dilution buffer are universal reagents and can be inter-changed between all SMART ELISA kits.

There are several types of automated plate washers available. If using an automated plate washer, you will need to validate the performance of your particular washer on the SMART assays. This can be done as simply as performing a side-by-side comparison of results achieved by manual washing versus automated washing. At the conclusion of each wash cycle, invert the tray and slap the wells hard against a paper towel 3-4 times to remove excess buffer.

This product is warranted to perform as described in the labeling provided that: the product is stored and used as directed; used before the expiration dating; and adequate quality control is performed. No other warranty is implied, nor are we liable for any consequential damages arising out of the aforesaid warranty.

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A graduate of the SMART program

EIA PROCEDURE GUIDE

Mouse Hepatitis Virus (Mouse Sera), Catalog #SMART-M17

INITIAL SETUP

1. Bring one bottle of the 20x Wash Solution to 500ml with distilled water. **MIX WELL**
2. Prepare the plate map. The columns alternate between **black-ringed Antigen wells** and **red-ringed Control-Antigen wells**. Each Control, Calibrator, and specimen requires two wells: an Antigen coated well and a Control-Antigen coated well.

Well Location	Identification
A1 & A2	Reactive Control
B1 & B2	Negative Control
C1 & C2	Calibrator
D1 & D2	Specimen #1
E1 & E2	Specimen #2
F1 & F2	Etc.

3. Controls are ready to use, do not dilute
4. Set up calibrator and specimen dilution tubes according to the plate map.
5. Prepare 1:51 dilution of the calibrator and specimens as follows:
   Add 250µl of Dilution Buffer to all dilution tubes
   Add 5µl of each specimen or calibrator to appropriate tube. **MIX WELL**

SERUM INCUBATION STAGE

6. Break-off the required number of Antigen and Control-Antigen wells and place into the plate holder. (Unused wells must be kept sealed in a dry environment)
7. Add 50µl of the pos and neg controls to the appropriate wells.
8. Transfer 50µl of each specimen and calibrator dilution tube to the appropriate wells.
9. Incubate at room temperature for **30 MINUTES.**

WASH STAGE

10. After 30 minutes, dump the tray. Refill each well to the top with wash buffer and dump.
11. Repeat the above step four more times for a total of **5 WASHES.**
12. After the last wash, dump the tray and slap the wells hard against a paper towel 3-4 times to remove excess buffer.

CONJUGATE INCUBATION STAGE

13. Add 50µl (1 drop) of conjugate to each well.
14. Incubate at room temperature for **30 MINUTES.**

WASH STAGE

15. After 30 minutes, dump the tray. Refill each well to the top with wash buffer and dump.
16. Repeat the above step four more times for a total of **5 WASHES.**
17. After the last wash, dump the tray and slap the wells hard against a paper towel 3-4 times to remove excess buffer.

SUBSTRATE STAGE

18. Add 50µl (1 drop) of CHROMOGEN to each well.
19. Incubate at room temperature for **10 MINUTES.**
20. **DO NOT DUMP AFTER THIS INCUBATION PERIOD.**

STOP STAGE

21. Add 50µl (1 drop) of STOP SOLUTION to each well.
22. Brace the plate with one hand and gently tap along the opposite side of the plate with the other to evenly distribute the Stop Solution in each well.
23. Read the plate at bichromatic 450/620-650nm wavelengths (or a single wavelength of 450nm) within 30 minutes of adding the Stop Solution.

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Cilia-Associated Respiratory Bacillus (CARB)

Background: Cilia-Associated Respiratory Bacillus (CARB) is a filamentous bacterium of unknown taxonomy found parallel to and among the cilia of the respiratory tract. The bacterium is frequently found concurrently colonized with *Mycoplasma pulmonis*; however, CAR bacillus is capable of causing respiratory disease as a mono-infection.

Transmission: Direct contact is the likely mode of transmission. The bacillus is not readily transmitted by fomites. The incidence of infection is not known.

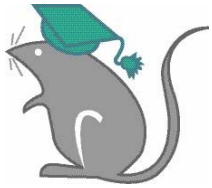
Clinical Signs: Chronic respiratory disease similar to mycoplasmosis has been described.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: CARB is primarily a respiratory pathogen and has been shown to cause chronic suppurative cranioventral bronchopneumonia as well as a co-pathogen in other respiratory infections.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with CARB serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M30, CARB ELISA, Mouse
SMART-R30, CARB ELISA, Rat



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Ectromelia Virus

Background: Ectromelia virus, the agent of mousepox, is a DNA poxvirus of the vaccinia subgroup.

Transmission: Natural infections occur via the fecal-oral route, urine contamination or by direct contact. Skin abrasions are thought to provide the main route of entry. Inoculation of mice with poxvirus-infected tumor cells or serum products have also caused disease outbreaks. Severity of disease is dependent on the mouse strain. Incidence of disease is rare, with sporadic epizootics usually resulting from passage of infected cells or other biological material into naive mice.

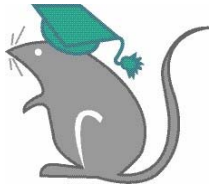
Clinical Signs: In acute Ectromelia infections, there is high morbidity and high mortality with affected animals exhibiting hunched posture, conjunctivitis and facial swelling. Subacute to chronically infected animals develop a cutaneous vesicular body rash which often progresses to swelling, necrosis and sloughing of the extremities. Deaths are sporadic.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: Ectromelia alters a host's immune response in various ways, especially in studies involving transplantable tumors.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with Ectromelia serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M16, Ectromelia ELISA, Mouse



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Encephalitozoon cuniculi (ECUN)

Background: *Encephalitozoon cuniculi* (ECUN) is an obligate intracellular microsporidian protozoan.

Transmission: Ingestion and inhalation are the likely modes of transmission.

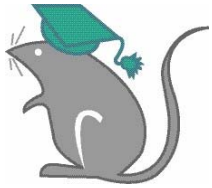
Clinical Signs: Almost always sub-clinical, but may have renal involvement, torticollis and other nervous signs with mortality.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA.

Effects on Research: ECUN causes focal granulomatous lesions in the lung, kidney, liver and brain. It is also involved in granulomatous intestinal pneumonia, intestinal nephritis, and menigoencephalitis.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with ECUN serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M31, ECUN ELISA, Mouse
SMART-R31, ECUN ELISA, Rat



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Epizootic Diarrhea of Infant Mice (EDIM)

Background: EDIM, also known as Mouse Rotavirus, is an RNA virus of the rotavirus group A.

Transmission: EDIM is highly contagious and transmission occurs by fecal-oral, direct contact, and aerosol routes. Adult mice are viral carriers and shed the virus to their susceptible young. The incidence of rotavirus infection is common.

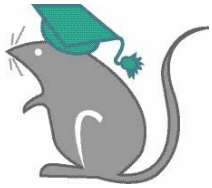
Clinical Signs: Clinical signs are generally limited to mice under 14 days old and the animals present with watery, mustard-colored stools, lethargy, and distend abdomens. Feces often dry on the perineum causing impaction and, if not removed, death. Surviving mice usually exhibit stunted growth.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: Rotavirus can alter host physiology in multiple ways thus confounding research. Examples are: increased susceptibility to the pathologic effects of co-pathogens; altered results of dietary and nutritional studies; and altered results in gastrointestinal physiology studies.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with EDIM serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M19, EDIM ELISA, Mouse



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Lymphocytic Choriomeningitis (LCM) Virus

Background: LCM virus is an arenavirus (RNA virus).

Transmission: *In utero* or perinatal infections (within 1 day post-partum) produce a persistent, subclinical infection. If a mouse is infected after 24 hours of age, antibody production occurs. The virus is continually shed in urine, saliva and milk but the antibodies are difficult to detect due to low production and to binding with the virus to cause circulating antibody-virus complexes.

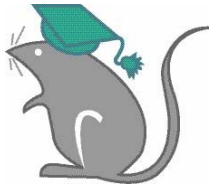
Clinical Signs: Two types of infections are known to occur. The persistent tolerant form results when the infection is acquired *in utero* or within a few days after birth. There is life-long viremia and shedding of virus. There is modest growth retardation, and at 7-10 months of age, immune complex glomerulonephritis occurs and is associated with emaciation, ruffled fur, hunched posture, ascites and some deaths. The second, nontolerant (acute) infection occurs when the mice are exposed after the first week of life. Viremia develops, but there is no shedding of virus. The outcome is usually death within a few days or weeks.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA.

Effects on Research: LCM has a high degree of zoonotic potential which allows this virus to readily infect transplantable tumors and cell lines. LCM has a wide range of effects which will interfere with studies in immunology, oncology, and physiology.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with LCM serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M15, LCM ELISA, Mouse
SMART-R15, LCM ELISA, Rat



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Mouse Adenovirus (MAD-1 and MAD-2)

Background: Mouse Adenovirus consists of two strains; FL (Mouse Adenovirus-1 and K87 (Mouse Adenovirus-2). MAD-1 is found in both mice and rats, with MAD-2 primarily in mice.

Transmission: MAD-1 is transmitted in urine, feces and nasal secretions; MAD-2 primarily by feces.

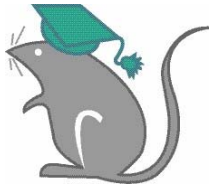
Clinical Signs: There are usually no clinical symptoms.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: Mouse Adenovirus can alter host immune systems resulting in multi-systemic interactions including spleen, intestine, brain, salivary glands, and myocardium. Mouse Adenovirus can also cause neonatal encephalitis and suckling runting.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with Mouse Adenovirus serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M25, MAD-1 ELISA, Mouse
SMART-M26, MAD-2 ELISA, Mouse
SMART-R25, MAD-1 ELISA, Rat



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Mouse Cytomegalovirus (MCMV)

Background: Mouse Cytomegalovirus (MCMV) is a betaherpesviurus usually affecting the salivary glands.

Transmission: MCMV is transmitted by saliva, tears, and urine.

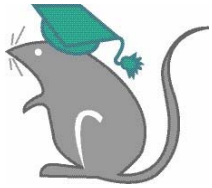
Clinical Signs: There are usually no clinical symptoms, but immunocompromised mice develop disseminated cytomegalic inclusion disease.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: MCMV primarily affects the submandibular salivary gland and has shown to evolve into multi-systemic dissemination. Infants can develop focal necrosis, cytomegaly, and inclusions in many tissues. Young adults develop subclinical pulmonary infection with alveolar septal thickening and edema; eosinophillic intranuclear and intracytoplasmic inclusions particularly in salivary gland acinar epithelial cells.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with MCMV serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M24, MCMV ELISA, Mouse



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Mouse Hepatitis Virus (MHV)

Background: MHV is an RNA Coronavirus. Several MHV strains (approximately 25) have been described and display tropisms for different tissues but all share the ability to replicate in the intestinal tract.

Transmission: Fecal-oral, direct contact, aerosols, and fomites have been reported. Vertical transmission has been reported in experimental infections, but doesn't appear to occur in spontaneous infections. The incidence of MHV infection is very common.

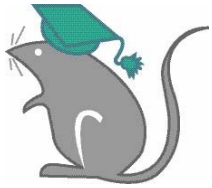
Clinical Signs: Adult infections are usually asymptomatic. Clinical signs depend upon the strain of the virus and are most evident in infant mice. Typically these include diarrhea, poor health, and death. Eventually the infected mice become asymptomatic if they survive to adulthood.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: The effects on research are too numerous to list since MHV alters the host immune response and is a contaminant of cell lines.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with MHV serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M17, MHV ELISA, Mouse



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Mouse Parvovirus (MVM and MPV)

Background: Parvoviruses are single stranded DNA viruses. The two important parvoviruses of mice are: Minute Virus of Mice (MVM) and Mouse Parvovirus (MPV).

Transmission: Direct contact with urine, feces, nasal secretions, milk, and fomites are the primary means of viral spread.

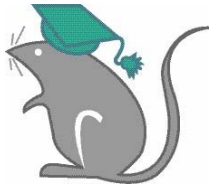
Clinical Signs: Naturally-occurring parvovirus infections do not produce clinical signs or lesions in infected mice. In immunocompetent mouse hosts, MVM appears to cause a short-lived infection while MPV causes persistent infections of lymphoid tissue (especially mesenteric lymph nodes).

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: MVM and MPV can alter host immune systems in multiple ways thus confounding research. Examples are: interference with the selection of transplantable tumor phenotypes; interference with mitogenic responses, ascites production, and antibody production; and may cause immunosuppression of the host.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with MVM and MPV serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M10, MVM ELISA, Mouse
SMART-M28, MPV-rVP2 ELISA, Mouse



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Mouse Pneumonitis Virus (K-Virus)

Background: Mouse Pneumonitis Virus (K-Virus) is a papovavirus causing intestinal pneumonia with a proliferation of intestinal endothelium.

Transmission: K-Virus is transmitted by orofecal and urine.

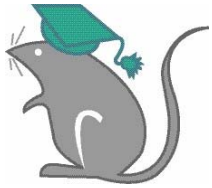
Clinical Signs: There are usually no clinical symptoms, but immunocompromised mice develop disseminated cytomegalic inclusion disease.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: K-Virus will cause dyspnea and death in suckling mice and will contaminate mouse tumors and tissue cultures. K-Virus can cause intranuclear inclusions in the vascular endothelium of the jejunum, ileum, lung, and liver; pulmonary congestion and edema; and alveolar septal thickening.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with K-Virus serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M23, K-Virus ELISA, Mouse



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Mycoplasma pulmonis

Background: *Mycoplasma pulmonis* (MPUL) is typically a chronic disease of the upper and lower respiratory tract.

Transmission: Direct contact, aerosol, and intrauterine (congenital) are three known modes of transmission.

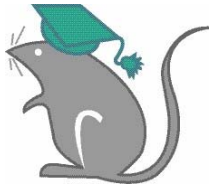
Clinical signs: Most infections are subclinical with *Mycoplasma* carried in the upper respiratory tract and uterus. The acquisition of primary viral or bacterial respiratory pathogens enhances subclinical mycoplasmal infections. Early signs of overt disease may include a red (porphyrin) oculonasal discharge, and nasal stridor. As the organism travels along the respiratory tract, otitis media, labored breathing, ruffled coat, anorexia, chattering (mice), snuffling (rats), coughing, and hunched posture may be observed.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: MPUL shortens the life span of the mouse or rat and significantly interferes with many research protocols.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with MPUL serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M27, MPUL ELISA, Mouse
SMART-R27, MPUL ELISA, Rat



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Pneumonia Virus of Mice (PVM)

Background: PVM is an RNA paramyxovirus of the pneumovirus group.

Transmission: The primary route of infection is by aerosol and direct contact with infected animals during the first two weeks of infection when the virus is shed. The disease is usually enzootic in a colony in which susceptible animals are regularly introduced. The incidence of disease in research colonies is low for PVM.

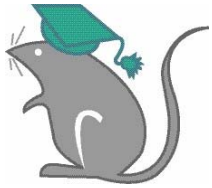
Clinical Signs: In immunocompetent mice and rats, the infections are short-lived and without clinical signs. In immunocompromised animals, chronic pneumonia with wasting occurs. The infection is fatal.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: The effects of PVM in immunocompetent animals can interfere with immunological and toxicological studies and measurements of pulmonary cell kinetics and metabolism.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with PVM serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M12, PVM ELISA, Mouse
SMART-R12, PVM ELISA, Rat



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Polyoma Virus

Background: Polyoma virus is a papovavirus.

Transmission: Direct contact, through contaminated feed and bedding, is the primary means of viral spread. It is highly contagious and shed in all secretions of an animal.

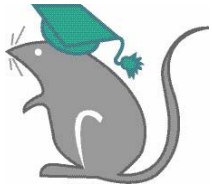
Clinical Signs: There are usually no clinical symptoms.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: Polyoma Virus can alter host immune systems resulting in spontaneous neoplasma; carcinogenesis; contaminated cell cultures, and transplantable tumors.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with Polyoma Virus serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M18, Polyoma ELISA, Mouse



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Rat Coronaviruses (SDAV and RCV)

Background: Coronavirus is an RNA virus with 2 strains identified to cause disease in rats. Rat coronavirus (RCV) causes respiratory infection while Sialodacroadenitis virus (SDAV) infects the upper respiratory tract, Hardarian and exorbital lacrimal glands, and the submandibular and parotid salivary glands. The SDAV strain causes clinical disease.

Transmission: SDAV/RCV is highly contagious and is spread by aerosol, direct contact, and fomites. No latent infection or carrier state occurs. The incidence of infection is high.

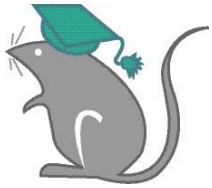
Clinical Signs: Viral infection is not fatal, and is generally subclinical. Rats infected with SDAV may exhibit a porphyrin oculonasal discharge. The submandibular salivary gland may be palpably enlarged due to sialoadenitis. Symptomatic rats are at a greater risk for inhalation anesthesia. Chronic exophthalmos can result in exposure keratitis.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA

Effects on Research: SDAV/RCV can alter host immune systems in multiple ways thus confounding research.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with SDAV/RCV serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-R20, SDAV/RCV ELISA , Rat



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Rat Parvovirus (KRV, H-1, and RPV)

Background: Parvoviruses are single stranded DNA viruses. Multiple species of parvoviruses in rats include Kilham Rat Virus (KRV or RV), Toolan's Virus (H-1), and Rat Parvovirus (RPV). Of these, KRV is the only virus species reported to cause clinical disease in rats. The other parvoviruses are antigenically distinct from KRV, and have not been associated with naturally-occurring disease. RPV causes subclinical, persistent infections in rats.

Transmission: Direct contact with urine, feces, nasal secretions, milk, and fomites is the primary means of viral spread.

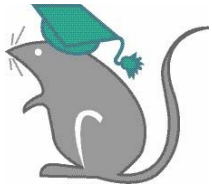
Clinical Signs: Parvovirus infections are usually subclinical. Clinical disease from KRV has been reported when the virus is introduced to a naive population. In newly infected breeding colonies, KRV causes decreased fertility, fetal resorption, small litters, and runting of pups. KRV infection in juvenile and young adult male rats may result in lethal disease from hemorrhage and necrosis of brain and gonads.

Diagnosis: Serologic assays are used for virus identification. The ELISA and IFA are the most sensitive tests but cross-reactivity does occur among the parvovirus species, especially with the IFA.

Effects on Research: Parvovirus can alter host physiology in multiple ways thus confounding research.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with ELISA serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology:
SMART-R21, KRV ELISA, Rat
SMART-R22, H-1 ELISA, Rat
SMART-R29, RPV-rVP2 ELISA, Rat



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Reovirus Type 3 (REO-3)

Background: There are three Reovirus strains. REO-3 is the only strain to cause natural infection, but all cross-react serologically

Transmission: Fecal-oral, direct contact, aerosols, and fomites have been reported.

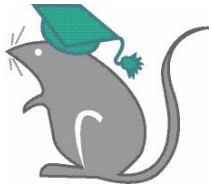
Clinical Signs: Almost always sub-clinical, but may cause CNS disease, hepatitis, diarrhea, and oily coat effect.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: Reovirus interferes with research by altering a host's immunological response and by contaminating cell cultures and transplantable tumors.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with REO-3 serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M13, REO-3 ELISA, Mouse
SMART-R13, REO-3 ELISA, Rat



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Sendai Virus

Background: Sendai virus is an RNA paramyxovirus of the parainfluenza type 1 group.

Transmission: Direct contact is the primary means of viral spread. The virus is not environmentally stable, but can be transmitted by fomites because of the quantities of virus excreted from infected mice. The incidence of infection is low.

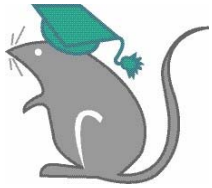
Clinical Signs: Infected mice may exhibit labored breathing and decreased fecundity. In immune deficient mice, the infection is almost always fatal. This virus is immunosuppressive and may predispose to secondary bacterial infections. Generally, no clinical signs are observed in mice in endemically infected colonies. In clinically apparent infections, signs are variable but may include chattering, mild respiratory distress to labored breathing, and decreased fecundity in adults, deaths (possibly whole litters) in neonates and sucklings, and poor growth in weanling and young adult mice. Infected rats are usually asymptomatic with minor effects on reproduction and growth of pups.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA.

Effects on Research: Sendai Virus can alter host immune systems in multiple ways thus confounding research. Examples are: interference with early embryonic development; alterations in cytokine and chemokine production; alterations in pulmonary hypersensitivity; isograft rejection; and alterations in responses to transplantable tumors, and carcinogens.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with Sendai Virus serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M11, Sendai ELISA, Mouse
SMART-R11, Sendai ELISA, Rat



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Theiler's Murine Encephalomyelitis Virus (TMEV)

Background: TMEV, also known as GD-VII, is a picornavirus and is commonly referred to as "Mouse Polio".

Transmission: TMEV is spread by direct contact and fomites.

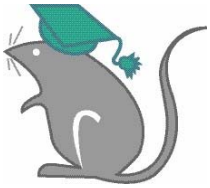
Clinical Signs: Viral infection results in demyelination and motor dysfunction. Included in the visible signs are gait disorders, tremors, ataxia, paralysis, and urinary incontinence.

Diagnosis: The most useful diagnostic test for screening mouse colonies is by ELISA or IFA

Effects on Research: TMEV will interfere with all neurological studies.

Prevention: Purchase only from approved commercial suppliers that can provide recent health monitoring data; quarantine of new arrivals for at least three weeks and screen with TMEV serology before admittance into facility; use of micro-isolator cages; and use of barrier facilities. In addition, screen all tumor lines and other murine derived biologicals by appropriate tests before their introduction into any program.

Recommended Screening Serology: SMART-M14, TMEV (GDVII) ELISA, Mouse
SMART-R14, TMEV (GDVII) ELISA, Rat



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