- Individuals may not work alone when procedures involve macaques.
- An informed consent process regarding discretionary use of antiviral drugs must be developed.

Record:	10041
IBC NUMBER:	**SC03-077R,** amendment
NAME:	Yoshihiro Kawaoka, Professor
DEPT:	Pathobiological Sciences, SVM
PROTOCOL TITLE:	***Molecular biology of hemorrhagic fever viruses***
REVIEWERS:	
Primary:	S. Schultz-Cherry
Secondary:	M. Malkovsky
MOTION:	**Approve, with requirements**
MADE BY:	S. Schultz-Cherry
SECONDED BY:	M. Malkovsky
COMMITTEE ACTION:	**Adopted unanimously by voice vote**
PROJECT LEVEL:	3, 2, 2(RG2,PIM), 2-N
REFERENCE:	III-D

NOTES:

- Research on the pathogenesis of Ebola and Lassa fever viruses was described in the protocol renewal (May 2003). This amendment describes development of replication incompetent viral-like particles for vaccine development, screening antiviral compounds, and use of lentiviral vectors to express viral proteins. Cell lines will be generated that stably express filovirus, [redacted], VSV, or RSV glycoproteins.
- Ebola, Lassa fever, Marburg, [redacted] viruses are risk group 4 agents. Infectious virus will not be produced in these studies. RSV and VSV Indiana strain are risk group 2 agents; replication-deficient lentiviral vectors are also handled minimally with BSL-2 precautions and containment.
- The replication incompetent self-inactivating HIV, enveloped with glycoproteins from RG2 and RG4 viruses, will be handled under BSL-2 containment. These constructs will be administered to mammalian cells. While these constructs are engineered to be replication incompetent, they retain the ability to infect cells with the risk of insertional mutagenesis and must be treated with appropriate precautions. Personnel should be informed of these risks.
- Section IV.A(iii) lists activities that will be done under BSL-2 and BSL-3 containment. Full length Ebola DNA will be handled under BSL-3 containment according to the BSL-3 manual yet section V.C (p.14) is inconsistent in stating that it will be performed at BSL-2.
- Virus-like particles lack at least one gene necessary for viral replication and they can replicate only in cells expressing deleted gene products. The inability to revert to replication competency will be tested by passage in cells multiple times under BSL-4 containment. The IBC requests additional assurance by PCR testing for deleted sequence.
- The only animal to be used in conjunction with these experiments is mice. Section IV.A(iii) indicates that transgenic mice will be generated that express Ebola virus sGP or GP1. No microbes will be administered to animals.
- Disinfection procedures described in section IV.F includes surface disinfection with 1% bleach or 70% EtOH and autoclaving infected cell lines.
- BSL-2 precautions were described by submission of the table of precautions. Surgical masks are used when handling animals under BSL-2 containment. Use of N100s is indicated in the table of precautions and will be used when working in the BSL-3 area.

OFFICE OF BIOLOGICAL SAFETY
30 N. MURRAY STREET
MADISON, WI 53715-1227
263-2037; 265-8700 (fax)

- The research facilities include use of BSL-2 and BSL-3 labs and animal housing.
- The protocol was approved with the following requirements:
    1. Use PCR to confirm the absence of deleted gene sequences as an additional test to demonstrate that viral-like particles are replication defective.
    2. Biosafety level 3 must be used when handling full-length Ebola cDNA. While this point was clarified in the version of the protocol received 12/6/05, contradictory phrases remain embedded in sections of the protocol that need to be corrected.
    3. Provide training to personnel about the inherent risks posed by the lentiviral vector. Although not competent to replicate, these viral vectors retain the ability to infect cells and to integrate into the genome with the possibility of insertional mutagenesis for which no treatment is available.

Record:	10059
IBC NUMBER:	**SC05-141R**, new
NAME:	Dongsheng Cai, Assistant Professor
DEPT:	Medical School, Physiology
PROTOCOL TITLE:	***Mediator of the metabolic syndromes***
REVIEWERS:	
Primary:	M. Albertini
Secondary:	S. Schultz-Cherry
MOTION:	**Approve, with contingencies**
MADE BY:	M. Albertini
SECONDED BY:	S. Schultz-Cherry
COMMITTEE ACTION:	**Adopted unanimously by voice vote**
PROJECT LEVEL:	2, 2(RG2,PIM), 2-N, GLP(CM,DT)
REFERENCE:	III-D

NOTES:

- This protocol is the first one from this investigator. The research focuses on the role of inflammatory pathways in metabolic physiology and pathogenesis. The administration of adenoviral vectors to tissue culture and animals brings this protocol to the committee's attention.
- Project objectives should more thoroughly describe the planned experiments.
- Genes of interest include inflammatory kinases and inflammatory kinase inhibitors expressed in nonpathogenic *E. coli*, adenovirus, neuronal cell culture, and mouse brains.
- The adenoviral AdCre1 vector (Microbix Biosystems) utilizes a Cre/lox site-specific recombination system to regulate gene expression. Construct info such as whether the vector is replication-deficient was not provided, but the deletions could be confirmed by information provided by the company.
- Exposure response to adenovirus is appropriate: report to PI with medical follow up if necessary (Incorrectly placed in V.B rather than IV.B).
- Precautions and containment are described but are not specific to the facilities, materials, and procedures.
- A number of potentially-hazardous chemicals are administered to animals including carcinogens streptozotocin and BrdU and some hormones with reproductive effects (PMSG, hCG, thyroxin). Precautions for handling of hazardous chemicals should be expanded (e.g., prep of stock solutions in a fume hood, precautions for animal care staff handling animals that have been administered hazardous chemicals).