OCCUPATIONAL AND ENVIRONMENTAL HEALTH AND SAFETY
THE UNIVERSITY OF UTAH

FACT Sheet

Recombinant Adenoviral Vectors

The following provides information on the use and containment of recombinant adenoviral vectors. Investigators should use these guidelines as part of their risk assessment when planning experiments with these vectors and preparing applications to the Institutional Biosafety Committee (IBC). Note the listed containment levels are the minimum that should be employed with these vectors: some experiments, such as the expression of toxins or oncogenes, may require higher levels of containment. The appropriateness of the containment should be considered as part of the investigator's risk assessment and will be reviewed by the IBC.

NIH Risk Group	RG2 Adenoviruses are non-enveloped icosahedral viruses containing double-stranded DNA.
Biocontainment Level	BSL-2. 1st Generation: Deletion of regions E1, E3 genes (less safe) 2nd Generation: Deletion of regions E1, E2, E3, E4 genes (more safe) Expression of oncogenes or toxins may raise BSL containment requirements
Infectious to Humans/Animals	Yes
Route of Transmission	Wild-type adenoviruses are spread directly by oral contact and droplets. They are indirectly spread by handkerchiefs, eating utensils and other articles freshly soiled with respiratory discharge of an infected person. It is possible for a person who is infected, but asymptomatic, to shed virus for many months or years.
Laboratory Hazards	Inhalation of aerosolized droplets, mucous membrane contact, parenteral inoculation, or ingestion. Adenovirus is unusually stable in the environment. Adenovirus can still be infective after having been extracted with ether and/or chloroform.
Disease	Apart from respiratory involvement, illnesses and presentations of adenovirus include gastroenteritis, conjunctivitis, cystitis, and rash illness. Symptoms of respiratory illness caused by adenovirus infection range from the common cold syndrome to pneumonia, croup, and bronchitis. Patients with compromised immune systems are especially susceptible to severe complications of adenovirus infection. *Pharyngoconjunctival fever* is a specific presentation of adenovirus infection: • high fever that lasts 4–5 days • pharyngitis (sore throat) • conjunctivitis (inflamed eyes, usually without pus formation like pink eye) • enlargement of the lymph nodes of the neck • headache, malaise, and weakness • Incubation period of 5–9 days

	Replication-defective recombinant adenoviral vectors have caused corneal and conjunctival damage.
Treatment/Prophylaxis	Most infections are mild and require no therapy or only symptomatic Treatment/Prophylaxis. Because there is no virus-specific therapy, serious adenovirus illness can be managed only by treating symptoms and complications of the infection.
Pathogenesis	Can infect a variety of non-dividing cells. Stays episomal (does not integrate)
Replication Competent	Possible
RCV Testing	The probability of producing replication competent virus (RCV), although low, increases with each successive amplification. RCA is produced when adenoviral DNA recombines with E1-containing genomic DNA in HEK 293 cells. It is suggested to use early amplification stocks when needed to produce additional quantities of adenovirus. RCV testing is recommended for 1st generation vectors. PCR for E1 prior to use or plate on non-susceptible cell types
Disinfection	Effective disinfectants require a minimum of 20 minutes contact time. Use one of the following: • RECOMMENDED: Sodium hypochlorite (0.5%: use 1:10 dilution of fresh bleach) • 5% Phenol Note: Alcohol is NOT an effective disinfectant against non-enveloped viruses such as adenovirus.
Animals	ABSL-2: When animals are infected with adenoviruses/adenoviral vectors, the Animal Biosafety Level of the project will be generally assigned to ABSL-2. Animals must be injected in a Biological Safety Cabinet. Infected animals can excrete adenovirus, so cages and bedding are considered biohazardous for a minimum of 5 days post-exposure (replication incompetent vectors). Take precautions to avoid creating aerosols when emptying animal waste material: adenovirus is excreted by animals. Soiled cages are disinfected prior to washing. Animal cages must be labeled with a biohazard sign. After 5 days animals can be transferred to ABSL-1 standard conditions. The animals will be transferred to a clean cage, and the ABSL-2 cage will stay in the ABSL-2 quarantine space for appropriate waste disposal and cleaning. Once animals have been transferred to ABSL-1, they can be used handled as with other ABSL-1 animals. For first generation vectors or infection of animals containing human cells or tissues, ABSL-2 containment may be required for longer periods. This will be determined by the IBC. ABSL-2 or ABSL-1 for xenografts of transduced human/animal cells. Determined by IBC.

Sources:
http://web.stanford.edu/dept/EHS/prod/researchlab/bio/docs/Working_with_Viral_Vectors.pdf
http://www.dartmouth.edu/~ehs/biological/biosafety_docs/110_1_ibc_viral_vector_policy.pdf