

Adenovirus/ Adenoviral Vectors

Background

Adenovirus is a respiratory, mucous membrane, eye and gastrointestinal pathogen. Replication deficient as well as replication competent adenovirus can cause respiratory inflammation, corneal injury and conjunctival damage. This virus can remain infective even after chloroform and ether extractions. The replication deficient virus may be complemented *in vivo* – causing the vector to become replication competent.

Symptoms of Exposure

Exposure to adenovirus may cause acute respiratory illness (cold like symptoms), pneumonia, conjunctival infection (red eye) or corneal damage.

Containment Level

Adenovirus may be transmitted by aerosol, droplet and injection routes of transmission. Generally, adenovirus is classified as a Biosafety Level 2 (BSL-2) organism. Adenoviral vectors may be regulated at varying biosafety levels. At the discretion of the IBC, experiments may need to be conducted at Biosafety Level 3 (BSL3). In the IBC application, the PI must justify that the gene to be expressed is not particularly harmful, and include citations to support these statements.

Approvals

Experiments using adenovirus require local IBC approvals before initiation of experiments

Test Methods for Recombinant Virus-QC Tests

**If vectors are being obtained from a commercial supplier, please check the manufacturer's information as to the quality control concerning replication competent viruses. This information should be supplied with the IBC application.

Viral vector stocks must be checked for recombinant virus using the E1a assay prior to use *in vitro* or *in vivo*. The vector stock should be tested at a limit of sensitivity of 1 in 10⁶ virus particles compared to a known positive control (Zhang et al, 1995).

Laboratory Practices

1. No work with Adenovirus is permitted on the open bench.
2. A certified Class II biosafety cabinet inspected within the last 12 months must be used for all manipulations including (but not limited to):
 - ♦ Pipetting
 - ♦ Harvesting infected cells for RNA
 - ♦ Infection of cell culture
 - ♦ Infection of animals
3. Centrifugation must be done in closed containers and using **sealed rotors or safety cups**. Safety cups are to be opened inside the biosafety cabinet.

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4. All vacuum lines must be fitted with a HEPA filter (an example is the "Vacushield™" inline hydrophobic filter, Product # 4402 from Gelman Science, Millex FH vacuum line protector Millipore (Fisher) cat # SLFH05010, or "HEPA-VENT™" inline hydrophobic filter, Catalog # 6723-5000 from Whatman).
5. All laboratory staff working with or supervising work with adenovirus must be made aware of the hazards associated with the work, required safety practices and procedures, and proper handling of the agent.
6. All laboratory staff working with or supervising work with adenovirus must be current on their laboratory and bloodborne pathogens/biosafety training requirements.
7. Signs and labels (including the universal biohazard symbol) must be placed to indicate each area where adenovirus is used or stored (including biosafety cabinets, incubators, refrigerators, laboratory entrance doors, etc.).

Personal Protective Equipment

1. Disposable gloves.
2. Disposable gown or equivalent when introducing vector into animals or performing necropsies. Lab coats are adequate for tissue culture manipulations.
3. Goggles and/or face shield.
4. All work and manipulations of Adenovirus must be conducted in a certified Class II biological safety cabinet. If there are extenuating circumstances or this biosafety cabinet is unavailable, please contact EOHSS (at the numbers listed at the end of this SOP) as additional precautions may be required.

Instructions in the Event of Employee Exposure

- ♦ **EXPOSURE FROM SPLASH OR AEROSOLS – INHALATION**
Report the incident to your supervisor and refer to the emergency operations plan at [emergency.rutgers.edu](http://myrehs.rutgers.edu). Your supervisor should submit an accident report at <http://myrehs.rutgers.edu>.
- ♦ **EXPOSURE FROM SPLASH OR AEROSOLS – EYE CONTACT, SKIN AND/OR MUCOUS MEMBRANE**
Rinse a minimum of 15 minutes in eye wash or flush area with water, report the incident to your supervisor and refer to the Emergency operations plan for further instructions. Your supervisor should submit an accident report at <http://myrehs.rutgers.edu>.
- ♦ **NEEDLESTICK AND/OR SHARPS EXPOSURE**
Contaminated skin should be thoroughly scrubbed for several minutes with a 10% povidone solution (Betadine) and copious amounts of water. Report the incident to your supervisor and REHS immediately after scrub. Seek medical attention at [Campus Employee Health Services/Occupational Medicine Services](http://myrehs.rutgers.edu). Your supervisor should submit an accident report at <http://myrehs.rutgers.edu>.

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Animal Facility Requirements:

1. All bedding, waste and animals shall be treated as if they are contaminated with recombinant adenovirus. After all animals are removed from their primary enclosure immediately autoclave or treat with chemical disinfectant. After disinfection, dump the cage contents and begin cleaning the cage for re-use. All waste must be decontaminated by autoclaving or chemical disinfection prior to disposal.
2. Animal carcasses must be placed in autoclave bags and be designated for infectious waste disposal.
8. Special training must be given to all animal husbandry personnel on adenovirus, the hazards associated with the work, required practices and procedures and proper handling of bedding, cage washing, and all other husbandry materials associated with the experiment. Animal facility staff may provide this training in consultation with REHS.
9. All necropsies must be performed in a designated room using animal BSL-2 practices and procedures.
10. The following information must be posted in the animal room. REHS will provide a sign template to the animal facility staff for this purpose.
 - A description of special housing required to ensure safety of animal facility personnel, such as ventilated cabinets or hoods.
 - A label on the animal cage indicating the hazardous materials to be administered to live animals. (i.e., Replication deficient Ad-5)

References

CDC-BMBL, 5th ed., www.cdc.gov/od/ohs/biosfty/bmb15/BMBL_5th_Edition.pdf

Hazardous and Radioactive Waste Disposal Standard Operating Procedure, Comparative Medicine Resources
<http://njms.umdnj.edu/research/cmr/sop.cfm>

MSDS Health Canada <http://www.phac-aspc.gc.ca/msdsftss/msds3e.html>

NCI-Fredrick Safetygram (ISM-193, April 2001): <http://web.ncifcrf.gov/Campus/safety/safetygram/ism-193.pdf>

Stanford University, "Working with Viral Vectors,"
http://www.stanford.edu/dept/EHS/prod/researchlab/bio/docs/Working_with_Viral_Vectors.pdf

University of Kentucky Adenovirus Fact Sheet: <http://ehs.uky.edu/biosafety/adenovirus.html>

University of Texas Health Science Center at Houston "Guidelines for the Safe Handling of Adenoviral Vectors in Laboratory, Animal and Human Experiments" <http://www.uth.tmc.edu/safety/biosafety/adenovirus.htm>

Zhang WW, Kock, PE, Roth, JA. 1995. "Detection of wild-type contamination in a recombinant adenoviral preparation by PCR." *Biotechniques*. 18:444-447.

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Acknowledgement Page

I, _____, have read the SOP for Herpes Simplex Virus Vectors. The following people will be conducting experiments using the HSV vectors. The staff members know where to find a copy of this SOP in the laboratory and they understand the hazards and safe work practices as detailed therein.

Name	Job Title	Initials

Principal Investigator (print): _____

Principal Investigator (Signature): _____

ES

Contact Information:



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