



# ADENOVIRUS AND ADENOVIRAL VECTORS

Adenoviruses are non-enveloped, linear double-stranded DNA viruses and are a common cause of upper and lower respiratory tract infections. Adenoviral vectors (viral vectors are viruses that are specifically used to introduce exogenous DNA into host cells) have a high cloning capacity, can be produced in high titers, and can infect a wide variety of cell types. Adenovirus serotypes 2 and 5 are commonly used for creating recombinant adenoviral vectors.

## Potential Health Hazards

Adenoviruses are effective at targeting the human respiratory and intestinal systems, and can cause eye infections and the common cold.

Replication-defective recombinant adenovirus has caused corneal and conjunctival damage.

## Modes 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 Acquired Infections

There are reports of rare cases of illness caused by working in laboratories with clinical specimens. There is a theoretical risk of infection from exposure to laboratory cultures of wild-type adenovirus or recombinant viruses. Transmission of adenoviruses can occur through ingestion, inhalation of aerosolized droplets, mucous membrane contact, and accidental injection (for example, as the result of a needlestick).

## Host Range

Humans and animals are the natural reservoirs for wild-type adenoviruses. Recombinant adenovirus vectors infect a variety of mammalian cell types, and some strains can transform cells in culture.

## Survival

Adenoviruses are unusually stable to chemical or physical agents and adverse pH conditions. They are very stable in the environment and can survive 3 to 8 weeks on environmental surfaces at ambient temperatures. Even after treatment with ether or chloroform, they can still be infective.

## Laboratory Practices

**Biosafety Level 2** practices and facilities must be used for activities involving adenoviruses/viral vectors.

- Biohazard signs and labels must be displayed in areas and on equipment where adenoviruses are used and stored. This includes, but is not limited to, laboratory entrance doors, biological safety cabinets, incubators, refrigerators, and freezers.
- Use a biological safety cabinet (BSC) (a.k.a., tissue culture hood) for manipulations that can generate aerosols, such as pipetting, harvesting, infecting cells, filling tubes/containers, and opening sealed centrifuge canisters. If a procedure cannot be done in a BSC and only on an open bench, use a plastic shield to prevent exposure through inhalation or splashing.

- Use aerosol containment devices when centrifuging. These include sealed canisters that fit in the centrifuge bucket, covers for the centrifuge bucket, heat sealed tubes, or sealed centrifuge rotors. Rotors should be removed and opened inside a BSC. Centrifuge tubes should be filled and opened in a BSC.
- Vacuum lines must be protected with liquid disinfectant traps and/or micron filter.

## Personal Protective Equipment

Personal protective equipment (PPE) includes, but is not limited to -

- Disposable gloves (nitrile, latex, etc.).
- Lab coat when working in the laboratory. Remove when leaving the area.
- Goggles for splash protection.

## Precautions When Using Animals

When animals are infected with adenoviruses/adenoviral vectors, the Animal Biosafety Level of the project will be generally assigned to ABSL-2C. The Animal Biosafety Level protocol is sent to the principal investigator (PI) along with the IBC's letter of approval.

Animal use requests are made to the Institutional Animal Care and Use Committee (IACUC) by submitting an Animal Care and Use Form (ACURF) found at <http://research.uiowa.edu/animal/downloads/acurf.doc>.

Infected animals can excrete adenovirus, so cages and bedding are considered biohazardous for a minimum of 5 days post-exposure. Take precautions to avoid creating aerosols when emptying animal waste material. The Office of Animal Resources staff uses a changing station when emptying animal cages to minimize the creation of aerosols. Soiled cages are disinfected prior to washing.

Animal cages must be labeled with a biohazard sign.

## Recombinant Adenoviral Research

Protocols involving adenoviral vectors must be approved by the Institutional Biosafety Committee (IBC). Complete an “**rDNA Registration Document**” and submit it to Biosafety, HPO – 100 HPO. The form is available at <http://www.uiowa.edu/~hpo/biosafety/rdnareqform.doc>.

## Employee Exposure

**Eye exposure** - Rinse eyes in an eyewash for at least 15 minutes.

**Skin exposure** - Rinse skin with soap and water.

**Accidental Needlestick Injury** - Scrub contaminated skin with soap and water.

**Report Incidents and Seek Treatment** - Report actual or suspected exposure incidents to your supervisor immediately. Seek treatment at the Worker's Health Clinic, if necessary. It is located on the first floor of Boyd Tower – General Hospital. The clinic's phone number is 353-8653. If the incident occurs after 4:30 pm, during the weekend, or on holidays, proceed to UIHC's Emergency Treatment Center (ETC). The phone number is 356-2233.

- **Symptoms** - Acute respiratory illness (cold-like symptoms), pneumonia, conjunctival infection (pink eye), corneal inflammation, including possible scarification.
- **Immunizations and Prophylaxis** - None available.
- **Incubation Period** - From 1-10 days.

## Spill and Disposal Procedures

For spills **outside** a biological safety cabinet, leave the area while holding your breath. Once outside the area, wash hands and face with soap and water. Do not allow anyone inside the area or room where the spill occurred. Allow 30 minutes for the aerosols to settle. Enter the room wearing required protective clothing, gently cover the spill with paper towels, and apply disinfectant starting at the perimeter and working towards the center. Allow the disinfectant to remain on the spill for at least 20 minutes before initiating spill clean up. After initial clean up, disinfect the area a second time.

For spills **inside** a biological safety cabinet, cover the spill with paper towels or wipes. Gently pour disinfectant over the spill area. Let the disinfectant soak for 20 minutes before cleaning up the spill. After initial clean up, disinfect area a second time.

Contaminated materials must be disposed of as biohazardous waste.

Decontaminate adjacent surfaces with bleach solution.

## Disinfectants

Effective disinfectants require a minimum of 20 minutes contact time. Use one of the following:

- Sodium hypochlorite (use 1-10% dilution of fresh bleach)
- 5% Phenol

**Note: Alcohol is not an effective disinfectant against adenovirus species.**

## Decontamination

Autoclave cultures for 30 minutes at 121°C or 250°F (15 lbs per square inch of steam pressure).

Disinfect work surfaces using an effective germicide (see above). This may be followed by an alcohol wipe to lessen the corrosive nature of the germicide.

## Transport Requirements

Materials must be appropriately contained and labeled for transport within the University. Shipping infectious substances, diagnostic specimens, and/or shipping with dry ice off-campus require training and certification. See HPO's fact sheet "Transporting and Shipping Infectious Substances" found at <http://www.uiowa.edu/~hpo/biosafety/transportingguideSIS.pdf> for additional information.

## If You Have Questions

Contact HPO's Biological Safety Section at 5-8501.

## Information and References

Harvard University. (2000, March). Environmental Health and Safety Program. Guidance on commonly used viral vectors. Annex II. Part 2B. <http://www.hms.harvard.edu/orsp/coms/BSRs/Viral-Vector-discussion.pdf>. Retrieved June 2004.

Health Canada Office of Laboratory Security. (1999, November). Infectious Substances MSDS Web Site. Adenovirus types 1, 2, 3, 4, 5 and 7. <http://www.phac-aspc.gc.ca/msds-ftss/msds3e.html>. Retrieved June 2004.

National Cancer Institute at Frederick. (2002, May). NCI-Frederick Safetygram. Working with adenovirus and adenovirus vectors. <http://web.ncifcrf.gov/Campus/safety/safetygram/ism-193.pdf>. Retrieved June 2004.

Qbiogene, Inc. Technical Resource web page. (2002). Is the adenovirus safe to handle? <http://www.qbiogene.com/technical/faq/faq-adenovator.shtml#1>. Retrieved June 2004.

University of California, San Diego Program in Human Gene Therapy. (1998, August). Vector Development Laboratory web page. Adenovirus MSDS. <http://medicine.ucsd.edu/gt/Adenovirus.html>. Retrieved June 2004.

University of Iowa. Health Protection Office. (1995, February). Biological Safety Manual. <http://www.uiowa.edu/~hpo/biosafety/hpobsbm.pdf>. Retrieved June 2004.

*U.S. Department of Health and Human Services Centers for Disease Control and Prevention and National Institutes of Health. (1999, May). Biosafety in microbiological and biomedical laboratories (BMBL) 4th edition. <http://www.cdc.gov/od/ohs/biosfty/bmb4/bmb4toc.htm>. Retrieved June 2004.*

*U.S. Department of Health and Human Services Centers for Disease Control and Prevention and National Institutes of Health. (1999, May). Biosafety in microbiological and biomedical laboratories (BMBL) 4th edition. Section III. Laboratory biosafety level criteria. Biosafety level 2 requirements. <http://www.cdc.gov/od/ohs/biosfty/bmb4/bmb4s3.htm>. Retrieved June 2004.*

Christ, M. (2002). Preclinical evaluation of gene transfer products: Safety and immunologic aspects. *Toxicology*, 174, 13-19.

Evans M., Lesnaw, J. (1999). Infection control in gene therapy. *Infection Control and Hospital Epidemiology*, 20(8), 568-576.

Feldman, S. (2003). Components of gene therapy experimentation that contribute to relative risk. *Comparison Medicine*, 53(2), 147-158.

Marinee, K.L., Chuah, D.C., VandenDriessche, T. (2003). Biosafety of adenovirus vectors. *Current Gene Therapy*, 3(6), 527-543.

NIH Recombinant DNA Advisory Committee. (2002, January). NIH Report: Assessment of adenovirus vector safety and toxicity: Report of the National Institute of Health Recombinant DNA Advisory Committee. *Human Gene Therapy*, 13(1), 1-13.