

## Recombinant Adeno-Associated Viral Vectors

The following provides information on the use and containment of recombinant adeno associated viral (AAV) 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.

<b>NIH Risk Group</b>	RG1 AAV are non-enveloped icosahedral viruses with a single stranded DNA genome.
<b>Biocontainment Level</b>	BSL-1; unless it encodes oncogene/toxin or helper virus present (BSL-2)
<b>Infectious to Humans/Animals</b>	Yes (Humans/Primates)
<b>Route of Transmission</b>	<ul style="list-style-type: none"> <li>• AAV may be transmitted through direct contact with an infected individual or through indirect contact with the contaminated environment.</li> <li>• Transmission routes include respiratory, gastrointestinal and possibly sexual transmission.</li> <li>• A concern for vertical transmission from mother to fetus also exists.</li> </ul> <p>Most adults (85-90% in the US) are seropositive for AAV and about 30% have neutralizing antibodies.</p>
<b>Laboratory Hazards</b>	Inhalation of aerosolized droplets, mucous membrane contact, parenteral injection, or ingestion.
<b>Disease</b>	<ul style="list-style-type: none"> <li>• AAV is not associated with any human disease; however, there is evidence of AAV infection in the human embryo and an association of AAV with male infertility.</li> <li>• A significant correlation was found between the presence of AAV DNA in amnion fluids and premature amniorrhexis (rupture of the amnion) and premature labor.</li> <li>• Recombinant AAV vectors lose site specific integration into chromosome 19, thereby raising the theoretical concern of insertional mutagenesis.</li> </ul>

<b>Treatment/Prophylaxis</b>	Supportive care. No specific Treatment/Prophylaxis
<b>Pathogenesis</b>	<p>Infects multiple cell types. Inserts itself on human chromosome 19 and remains latent. Can be potentially reactivated later in the presence of a helper virus and produce infection. Recombinant vectors shown to cause insertional mutagenesis in murine cell lines and neural toxicity in primates and chicks.</p>
<b>Replication Competent</b>	Only in presence of helper virus (CMV, adenovirus, herpesvirus, vaccinia)
<b>RCV Testing</b>	If helper virus is adenovirus, test for presence of RCV after heat inactivation (56°C for 15min)
<b>Disinfection</b>	<p>Effective disinfectants require a minimum of 20 minutes contact time. Use one of the following:</p> <ul style="list-style-type: none"> <li>• RECOMMENDED: Sodium hypochlorite (0.5%: use 1:10 dilution of fresh bleach)</li> <li>• Alkaline solutions at pH &gt;9.</li> <li>• 5% phenol.</li> </ul> <p>Note: Alcohol is NOT an effective disinfectant against non-enveloped viruses, such as AAV.</p>
<b>Animals</b>	<p>ABSL-1: If helper virus is used follow rules for that virus. In general, ABSL-2 will be required if a helper virus used or if host animal could house helper virus: animals must be injected in a Biological Safety Cabinet. 72 hours following infection, 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.</p> <p>Special handling of bedding and cages for 48 hours post injection. Bedding disposed in biohazardous waste.</p> <p>Animal cages at ABSL-1 need not be labeled with a biohazard sign.</p>

Sources:

[http://web.stanford.edu/dept/EHS/prod/researchlab/bio/docs/Working\\_with\\_Viral\\_Vectors.pdf](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](http://www.dartmouth.edu/~ehs/biological/biosafety_docs/110_1_ibc_viral_vector_policy.pdf)