Institutional Biosafety Committee (IBC) Guidance on Biosafety Level Assignment for Adeno- Associated Virus (AAV)

Background:

Adeno-associated virus (AAV) and recombinant adeno-associated virus (rAAV) are commonly used for gene expression with fewer associated biosafety concerns when compared to viral vectors that are persistent and able to integrate into the genome. The following is guidance for determining the appropriate biosafety designation when working with AAV/rAAV vectors.

NIH Guidance:

The *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines*) identify AAV types 1-4 and rAAV constructs in which the transgene does not encode either a potentially tumorigenic gene product (for example, an oncogene) or a toxin molecule, and are produced in the absence of a helper virus, as risk group 1 (RG1) agents which are not associated with disease in healthy adults humans (*NIH Guidelines Appendix B-1*).

IBC Guidance:

The UToledo IBC will utilize the following criteria for determining appropriate biosafety containment and handling of AAV/rAAV:

- Propagation with or without helper virus, including the use of adenovirus
- Presence of transgenes encoding oncogenes or toxins
- Propagation in insect cell lines versus human cell lines
- Assurance of purification techniques and quality control methods used when propagation of virus occurs in human cell lines

Specific Requirements for Use of AAV/rAAV Use at BSL-1/ABSL-1

The UToledo IBC will consider designating AAV or rAAV for use at BSL-1/ABSL-1 if the following three criteria are met:

1. Transgene does not express an oncogenic protein or toxin (*NIH Guidelines* reference *Section III-B-1*)
2. AAV/rAAV is generated without using adenovirus or any other helper virus
3. AAV/rAAV is propagated in non-human cell lines

Specific Requirements for Use of AAV/rAAV Use at BSL-2/ABSL-2

AAV or rAAV ***must*** be used at BSL-2/ABSL-2 if:

1. Transgenes express an oncogenic protein or toxin
2. Helper virus is used to generate AAV/rAAV
3. AAV/rAAV is propagated in human cell lines ***without*** further purification before use*

* AAV/rAAV that is propagated in human cell lines with purification before use requires proof of purification in IBC protocol and requires IBC determination of biosafety level on a case-by-case basis.