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ESTABLISHING BIOLOGICAL RISK AND APPROPRIATE CONTAINMENT FOR ADENO-ASSOCIATED VIRUS (AAV) GENE THERAPY AGENTS

Risk Groups

The NIH Guidelines and WHO categorize wild-type infectious agents into risk groups[1,2]

Group 1	Group 2	Group 3	Group 4
Agents that are not associated with disease in healthy adult humans	Agents that are associated with human disease that is rarely serious and for which preventive or therapeutic interventions are *often* available	Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions *may be* available (high individual risk but low community risk)	Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available (high individual risk and high community risk)

LOWEST RISK → HIGHEST RISK

Biosafety Levels (BSLs)

An agent's risk group determines its BSL and its handling protocol[1–3]

Level 1	Level 2	Level 3	Level 4
• Standard microbiological practices • Open bench or table permitted • Lab coat and gloves • Sink for washing hands • Means for controlling access (e.g. door)	• Access to work area is limited when work is conducted • PPE includes mask and eye protection of face shield • BSC for procedures that may cause exposure to aerosol or splashes • Access to autoclave • Work area includes self-closing doors and access to eye wash station	• Receive immunization for microbes used • Access restricted at all times • BSC for all open procedures • Exhausted air cannot be recirculated • Two sets of self-closing locked doors for entrance • Immediate access to autoclave	• Dedicated lab clothing • Shower upon exit • Class III BSC or full-body air-supplied suit • Separate building or isolated zone • Dedicated air supply and processed exhaust
Example: *AAV*	***Example:*** *Staphylococcus aureus*	***Example:*** *Mycobacterium tuberculosis*	***Example:*** *Ebola virus*

LOWEST LEVEL → HIGHEST LEVEL

Safety Features of AAV Vectors

Recombinant AAV* (rAAV) is considered a Risk Group 1 agent – infection with AAV is not associated with disease in humans[1,4]

rAAV vectors are replication-incompetent (non-infectious) by design[5,6]

Absent of hazardous genes, rAAV vectors can be handled at BSL-1 containment (BSL-2 containment may be considered for genes of unknown significance)[1,6]

rAAV vectors are susceptible to common disinfectants approved for bloodborne pathogens (e.g. EPA Lists B, D, and E)[6,7]

* In which the transgene does not encode either a potentially tumorigenic gene product or a toxin molecule, and construct is produced in the absence of a helper virus.

Summary

- Basic biological risk and containment criteria have been established by the NIH[1], CDC[3], and WHO[2]
- The biological risks from working with AAV vectors are considered very low[1,4]
- AAV vectors can be handled at BSL-1, the lowest biosafety level[1,5]
- Nevertheless, care should be taken to mitigate exposure to AAV vectors[5]
- All materials contaminated with AAV vectors should be disposed of as biohazardous waste[5]

References

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AAV, adeno-associated virus; **BSC**, biological safety cabinet; **BSL**, biosafety level; **CDC**, Centers for Disease Control and Prevention; **EPA**, Environmental Protection Agency; **NIH**, National Institutes of Health; **PPE**, personal protective equipment; **rAAV**, recombinant adeno-associated virus; **WHO**, World Health Organization.