Assessment of Containment Level Requirements for Modified Vaccinia Ankara (MVA) Pox Viral Vector

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Assessment of Containment Level Requirements for Modified Vaccinia Ankara (MVA) Pox Viral Vector

- Transgene Request to Classify the MVA-MUC1-IL2 Vector at Biosafety Level 1
- Differences Between BL-2 and BL-1
- RAC Decision in 1993 to Reduce BL for NYVAC, ALVAC, and TROVAC to BL-1
- CDC Advisory Committee on Immunization Practice Overview
- Summary of OBA Consultant Reviews
- Recommendations

Transgene's Request to Classify the MVA-MUC1-IL2 Vector at BL-1

- Clinical investigation of MVA-MUC1-IL2 as a treatment vaccine in prostate cancer
- Low risk: restricted host range, low pathogenicity, and previous human experience
- Risk characteristics similar to NYVAC, ALVAC, and TROVAC
- BL-2 practices impose unnecessary precautions

Biosafety Level 2 Safeguards Not Required at Biosafety Level 1

- PI limits access to the laboratory
- Advise laboratory occupants of potential hazards
- Universal biohazard symbol posted at access
- Special care to avoid skin contamination
- “Sharps” precautions
- Biosafety manual
- Containment equipment to reduce exposures to aerosols and large volumes of concentrated virus

Basis of RAC Decision to Classify NYVAC, ALVAC, and TROVAC at BL-1

- Highly attenuated characteristics and restricted host range reduces risk
- Recognition of need to increase containment if there is reason to believe that immunizing amounts of gene products would provide an additional risk

CDC Advisory Committee on Immunization Practices Reference to Highly Attenuated Poxvirus Vectors[1]

- Lists biosafety level for MVA as BL-2; NYVAC, TROVAC, and ALVAV as BL-1
- Unable to replicate or replicate poorly (NYVAC) in mammalian host cells
- Avirulent among normal and immunosuppressed animals
- MVA is safe among humans
- No report of laboratory-acquired infections
- Vaccination not indicated for health-care workers

[1] MMWR Vol. 50 / No. RR-10

Summary of OBA Consultant Reviews

- Dr. Moss recommends BL-1 for strain of vaccinia virus.

  Basis: Highly attenuated; MVA exhibits a replication defect in most mammalian cells that severely limits the yield of infectious virus; does not spread or cause disease in immunocompromised animals; wide use in humans with no adverse side effects, even in high risk individuals.

Summary of OBA Consultant Reviews *(Continued)*

- Dr. Feinberg recommends BL-2 for MVA-MUC1-IL2 recombinant virus. Considers BL-1 appropriate for parent strain of non-recombinant MVA.

  Basis: Potential risk that inadvertent exposure to MVA-MUC1-IL2 might raise autoimmune responses against MUC1 or IL2 in healthy individuals. Not evident how BL-1 would enhance protocol simplicity while maintaining appropriate level of safety.

Summary of OBA Consultant Reviews *(Continued)*

- Dr. Spearman recommends that additional data are required to determine that MVA represents a minimal risk to lab personnel and environment.

  Basis: A careful review of documentation of safety of MVA in humans is needed. There is substantial documentation for the safety of recombinant ALVAC but the extrapolation of ALVAC data to MVA is problematic. While animal data generally supports the safety of MVA given parentally, safety data specifically examining safety are limited. For example the potential for ocular infections or inflammatory/immune-mediated complications have not been examined.

Recommendations