Safety and Risk Management

Research Involving Cell Lines

Purpose:

1. **Human and Primate Cells**. The Centers for Disease Control and Prevention (CDC)/National Institutes of Health (NIH) "Biosafety in Microbiological and Biomedical Laboratories" (BMBL): 5th edition, Appendix H, identifies hazards associated with laboratory research involving human cells/cell lines, non-human primate (NHP) cells/cell lines, and primary cells from other mammalian species. These hazards include potential exposure to HBV, HIV, and other viral pathogens including (but not limited to) SV-40, EBV, HCV, HDV, CMV, viral genomic material, and bacterial pathogens including Mycobacterium tuberculosis. The BMBL also identifies tumorigenic human cells as potential hazards as a result of self-inoculation. The BMBL recommends that all human, NHP cells, other primary mammalian cells, and human or NHP tumorigenic cells be handled under Biosafety Level-2 (BSL-2) practices and containment, requiring utilization of a biological safety cabinet (BSC), personal protective equipment, and proper decontamination of work surfaces and waste materials. The BMBL further recommends that all employees working with human cells and/or tissues be properly trained in accordance with the OSHA Bloodborne Pathogens Standard, be enrolled in a bloodborne pathogens program, offered appropriate immunizations, and that affected employees work under the policies and guidelines of an Exposure Control Plan.

2. **Non-human/non-NHP cells.** While BMBL recommendations cover only cells of human and primate origin, several other agencies with recognized biosafety expertise including the National Research Council, cell line providers (ATCC, QIAGEN, etc.), and the European Union recommend that cells/cell lines of any origin (human, primate, non-primate mammalian, and other source animals) be handled under BSL-2 conditions unless certified to be free of adventitious agents via completion of a thorough risk assessment and demonstrative analysis. In addition to viral and bacterial threats, the European Union – European Medicines Agency document: "Viral Safety Evaluation of Biotechnical Products Derived from Cell Lines of Human or Animal Origins" also indicates the potential for the introduction of bovine spongiform encephalopathy prions (BSE) contamination into established cell lines via use of contaminated animal-derived products (including animal serum products) and/or through the use of improper work methods.

Process.

1. Unless satisfactorily certified and documented by the principal investigator (via PCR or other approved analytical method or submission of validation provided by product manufacturer) to be free of adventitious agents, the following cells/cells lines must be handled under BSL-2 conditions and registered with the Institutional Biosafety Committee (IBC) through submission of a Memorandum of Understanding and Agreement (MUA).

a. All cell lines (primary and established) of human and NHP origin.
b. All cell lines derived from lymphoid or tumor tissue (of human, NHP, murine, or other mammalian origin).
c. All cell lines exposed to or transformed by any oncogenic virus.
d. All cell lines exposed to or transformed by amphotropic packaging systems.
e. All non-fixed human clinical material (e.g., samples of human tissues and fluids obtained after surgical resection or autopsy).
f. All known/potential mycoplasma-containing cell lines.

2. The IBC requires that the following categories of cell cultures by managed at BSL-1 and strongly recommends these cultures be managed under BSL-2 conditions:
   a. All lower mammalian cells/cell lines which are new to the laboratory, at least until such time as verified to be free of adventitious agents.
   b. All cell lines (primary or established) of animal origin other than mammalian (avian, amphibian, reptilian, etc.), at least until such time as verified to be free of adventitious agents.
   c. All cells passaged through bovine growth media (bovine serum albumin, fetal calf serum, etc.) unless product has been certified by manufacturer to be free of bovine spongiform encephalopathy prions (BSE); or PI has conducted a acceptable risk assessment demonstrating that the product poses minimal risk of BSE contamination.
   d. Other cells, cell lines, tissues, and related materials not specifically identified under this policy.

Direct questions or comments to the Biosafety Officer at 828- 4404.