University of Utah

Institutional Biosafety Committee
Standard Operating Procedures and Policies

Subject: Containment for Injection of Human Cells into Animal Models

SOP Number 16_03_01

Approval Date 03_17_22 Supersedes Date 16_03 Page 1 of 2

The potential hazards associated with the handling of human/nonhuman primate cell culture are mainly the contamination of the cells with pathogenic agents and/or the tumorigenicity of the cells. Agents such as bacteria, fungi, and mycoplasmas generally cause some kind of visual effect on the cells or culture media allowing for detection of contamination. However, many viruses do not cause cytopathic effect (CPE), can be latent or are undetectable with current technology.

Primate and other mammalian cell lines can harbor viruses with a broad host range. Human cell lines are most likely to be contaminated with the highly pathogenic viruses including hepatitis B virus and HIV (human immunodeficiency virus). It must be understood though, that Primate cells can contain dangerous pathogens, most notably herpes B virus and Marburg virus both of which have caused fatal infections in humans. Rodent cell lines can carry lymphocytic choriomeningitis virus (LCMV), Reo-3 virus and hantavirus with documented cases of human disease and death.

In 1994, OSHA issued an interpretation of the applicability of the Bloodborne Pathogen (BBP) Standard towards human cell lines. According to the interpretation, human cell lines are considered to be potentially infectious and within the scope of the BBP Standard unless the specific cell line has been characterized to be free of recognized bloodborne pathogens. The American Type Culture Collection (ATCC) recommends that all human cell lines be accorded the same level of biosafety consideration as a line known to human risk group 2 pathogens (BSL-2) unless they have been screened for human pathogens.

In addition, the 6th Edition of the NIH/CDC publication, *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) recommends that human and other primate cells should be handled using Biosafety Level-2 (BSL-2) practices and containment.

Based on these recommendations, the University of Utah Institutional Biosafety Committee and Attending Veterinarian (AV) requires Animal Biosafety level 2 (ABSL-2) practices to be followed when animals are injected/implanted with human cell lines (primary or established), human tissues or human tumors. This work must be registered with the IBC through BioRAFT.

If a PI wishes to use lower containment (ABSL-1), the PI must submit a request to the IBC as part of their registration in BioRAFT. The IBC Chair, and/or Biosafety Officer (BSO) will review the application, with review by the full IBC if deemed appropriate by the Chair or BSO.

Biologics that require testing for human pathogens (See **Appendix A**) with review and approval by the IBC prior to in vivo rodent use at ABSL-1:

a. Human-derived cell lines, transplantable tumors, serum, tissues, body fluids, and antibody preparations that have not been passed through rodents or have not been exposed to rodents.

Possible exemptions from testing requirements, but not from review and approval by the AV and/or by the IBC:

a. Commercially obtained biological material for which the vendor (e.g. ATCC[+]) can supply negative screening results for murine and/or human pathogens on UofU's exclusion lists.
b. If ABSL-2 practices will be followed when using human-derived biological material in rodents.

Pathogen Testing: Recommended Testing Laboratories

a. Charles River Laboratories http://www.criver.com/products-services/basic-research/health-monitoring-diagnostic-services/cell-line-research-biologics-screening
    i. Human Infectious Agent Panels
        1. U Utah IBC Human Biologics CLEAR Panel (9 Agent Human CLEAR)
        2. Human HEP/HIV panel plus LCMV and HTLV*
b. IDEXX BioResearch https://www.idexxbioanalytics.com/hubfs/IBA_Q1_2022_NA_DOS.pdf
    i. h-IMPACT 1 (Human Pathogen) Testing panel
    ii. h-IMPACT 3 (Human Pathogen) Testing panel plus LCMV and *Corynebacterium bovis*[#]

c. Other laboratories may be used, but must be pre-approved by the AV and/or by the IBC.

Copies of the biologics testing results should be retained and accessible (uploaded in the EHS Safety Administrative Management (SAM) System).

Notes:
+ As of January 2010, all human cell lines accessioned in the ATCC general collection are tested for the adventitious agents HIV, HBV, HCV, HPV, EBV, and CMV. As of August 2012, the Hepatitis C test was removed from the ATCC virus panel test. Testing for *Corynebacterium bovis* is evaluated through their routine sterility testing for bacteria (using a BacT/ALERT 3D system), which is done on each lot. All cell lines must be mycoplasma free when deposited but ATCC recommend periodic testing when being cultured: they sell mycoplasma testing kits and services.

*Established human cell lines without testing for LCMV or HCV will be considered by the IBC on a case by case basis. LCMV typically causes lytic infections of human cells while no cell lines supporting HCV replication have been identified to date.

#Human samples obtained from patients are unlikely to harbor *Corynebacterium bovis* and an exemption to testing will be considered by the IBC.

In addition, the University of Utah AV has requirement for testing of cell lines for animal pathogens prior to injection into animals at ABSL-1, such as testing for murine materials.

APPENDIX A: List of Agents Excluded from University of Utah Human Biologics^

1. Human Immunodeficiency Virus Type 1 and 2 (HIV)
2. Hepatitis A Virus (HAV)
3. Hepatitis B Virus (HBV)
4. Hepatitis C Virus (HCV)
5. Human T-lymphotropic Virus (HTLV)
6. Lymphocytic Choriomeningitis Virus (LCMV)
7. *Mycoplasma spp.*
8. *Corynebacterium bovis*

^Testing for additional agents may be required based on the source of the material. These will be determined by the IBC.