Bloodborne Pathogens and Primate Material

Blood and other potentially infectious material (OPIM) have long been recognized as a potential threat to the health of employees who are exposed to these materials through penetration of the skin or mucous membrane exposure. The primary agents of concern are human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV). There are over 60 other microorganisms that are transmitted via blood or OPIM and can cause disease.

OSHA requires that anyone handling human blood or OPIM follow 29 CFR 1910.1030 “Occupational Exposure to Bloodborne Pathogens; Needlesticks and Other Sharps Injuries; Final Rule”. This federal regulation mandates training for all personnel handling blood or OPIM. The intent is to prevent or reduce exposure to any of these sometimes fatal diseases.

All personnel handling human blood, tissues or fluids are required to take the Bloodborne Pathogens Training offered by the Biosafety Office before work has started and take refresher training annually. PIs are also responsible for developing an Exposure Control Plan.

A special note about human cell lines;

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.

Of the pathogenic agents, viruses are of particular concern. Other 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 prior to work with the cells. However, many viruses do not cause cytopathic effect (CPE), can be latent or are undetectable with current technology.

Contamination of the cell culture may stem from the donor (endogenous) or from contamination by the user or from the materials used in the culture process (e.g. serum, proteins, fetal extracts, hormones, etc.).

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 and other mammalian cell lines can harbor viruses with a broad host range. 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, Reo-3 virus and hantavirus with documented cases of human disease and death.

Some of the bovine sourced culture media products may contain bovine viral diarrhea virus (BVDV), infectious bovine rhinotracheitis virus, and parainfluenza virus type 3. BVDV can bind to cells from many species and noncytopathic strains may establish persistent infections in bovine and nonbovine cell lines.

Oncogenic viruses (e.g. Hepatitis B and C viruses, HIV, Epstein Barr virus (EBV), human T-lymphotropic virus (HTLV), human herpesvirus 8, simian virus 40) are able to transform cells
into malignant forms. HTLV-1 is known to be oncogenic for humans and others are known to be oncogenic for primates including feline sarcoma virus, EBV, and the human papillomavirus.

The other hazard associated with human cell lines is the tumorigenicity of continuous cell lines. There has been one reported case of a laboratory worker who developed a tumor after an accidental needlestick with a human colonic adenocarcinoma cell line.

In 1991, the Occupational Safety and Health Administration (OSHA) issued the Bloodborne Pathogens (BBP) Standard to protect employees who have occupational exposure to human blood or other potentially infectious materials. While human blood, most body fluids, unfixed human tissues and organs were clearly included within the scope and application of the standard, the inclusion of human cell lines was ambiguous.

In 1994, OSHA issued an interpretation of the applicability of the 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 hepatitis viruses, HIV, Epstein-Barr virus, papilloma viruses and other recognized bloodborne pathogens.

In alignment with this interpretation, 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 carry HIV (BSL-2). Moreover, the 5th 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 (BSL2) practices and containment.

The CDC’s stance on cell cultures taken from the 5th edition of the BMBL:

“Cell cultures: Workers who handle or manipulate human or animal cells and tissues are at risk for possible exposure to potentially infectious latent and adventitious agents that may be present in those cells and tissues. This risk is well understood and illustrated by the reactivation of herpes viruses from latency, the inadvertent transmission of disease to organ recipients, and the persistence of human immunodeficiency virus (HIV), HBV, and hepatitis C virus (HCV) within infected individuals in the U.S. population. There also is evidence of accidental transplantation of human tumor cells to healthy recipients which indicates that these cells are potentially hazardous to laboratory workers who handle them. In addition, human and animal cell lines that are not well characterized or are obtained from secondary sources may introduce an infectious hazard to the laboratory. For example, the handling of nude mice inoculated with a tumor cell line unknowingly infected with lymphocytic choriomeningitis virus resulted in multiple LAIs. The potential for human cell lines to harbor a bloodborne pathogen led the Occupational Health and Safety Administration (OSHA) to interpret that the occupational exposure to bloodborne pathogens final rule would include human cell lines.

**A Note About ATCC:** ATCC **DOES NOT** test their cell lines for the presence of human viruses. Because of this ATCC recommends that all cell lines be treated at the same level as a line known to contain HIV which is BSL-2. Also, the biosafety designation that the ATCC gives
to their lines refers to the shipping requirements not the laboratory requirements. So if a cell line is rated BSL-1, it means it can be shipped as a biological substance, category B, UN 3373 per DOT/IATA. Category B substances are those that generally are not capable of causing permanent disability or life-threatening or fatal disease in otherwise healthy humans or animals upon exposure.

It is best to consult with the BSO to determine the appropriate actions.

The table below taken from the Belgian Biosafety Server describes some of the properties that should be taken into consideration when performing a risk assessment.

<table>
<thead>
<tr>
<th>Source (species of origin)</th>
<th>Cell types or tissues</th>
<th>Culture type</th>
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<tbody>
<tr>
<td>The closer the genetic relationship of the cell culture is to humans, the higher the risk is to humans since contaminating pathogens usually have specific species barriers. !! Be aware that some contaminating organisms might cross the usual species barrier (e.g. H5N1 influenza, BSE, SARS, etc.)</td>
<td>Consider the tumor inducing potential of cell types.</td>
<td></td>
</tr>
</tbody>
</table>

- avian and invertebrate cells
- epithelial and fibroblastic cells
- well-characterized cell lines
- gut mucosa
- endothelium
- primary cell lines
- neural tissues
- hematopoietic cells