

Introduction

Institutional Biosafety Committees (IBCs) are required by the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acids (NIH Guidelines) to review research with genetically modified organisms.¹ Frequently, IBCs will additionally review non-NIH Guidelines covered research with human or other potentially infectious materials as outlined in the 49 CFR Part 1910.1030 OSHA Bloodborne Pathogen Standard (BBP) as part of the scope of biosafety coverage for the institution.²

IBCs utilize the risk assessment process started by the Principal Investigator (PI) that incorporates known scientific literature, work practices, facility design, and personal protective equipment as specified in the Centers of Disease Control guidance document, Biosafety in Microbiology and Biomedical Laboratories (BMBL) 5th edition. The difference in work practices, personal protective equipment, and facility design requirements are designated as Animal Biosafety Levels, 1-4.³

In addition, Institutional Animal Care and Use Committees (IACUCs) typically rely on the IBC to approve research with biological materials and provide a scientific review of containment requirements for projects involving animals.

Context

Xenotransplantation, commonly referred to as xenografts, is the transplantation of living cells, tissues or organs from one species to another.⁴ As discussed earlier, IBCs may elect to review and approve the appropriate ABSL with regards to human materials xenotransplanted into animals. Taking into consideration the OSHA BBP, the OSHA ABSA Clarification letter, and a search of current IBC practices, presently IBCs employ three different possibly ABSL designations for xenotransplantation containment with human materials into live animals. They are:

1. ABSL-2 for the entirety of the research
2. ABSL-2 for a specified time period, then drop to ABSL-1
3. ABSL-1 for the entirety of the study

What is not clear from the standard is whether human cell lines known not to contain BBP must be treated as BBP. Most institutions treat human materials as BSL-2, and apply the same designation as ABSL-2.

This review of the scientific literature and current U.S. government regulations was conducted in order to provide a baseline risk assessment for biosafety professionals, animal care professionals, IACUCs and IBCs tasked for animal and biosafety review.

Regulations

In addition to the OSHA BBP Standard, the BMBL 5th edition, and the NIH Guidelines, a clarification letter from OSHA to the American Biological Safety Association (ABSA), OSHA recommended "Screening of the cell lines or "strains for viruses characterized as bloodborne by the Standard."⁵ This clarification letter guides the current risk assessment process for human cell lines, but does not cover research animals.

In June, 2012, a second clarification letter to OSHA was submitted on whether ABSL-2 containment is required for xenotransplantation of human cell lines free of BBP.⁶ While OSHA declined to publish a clarification letter, in telecommunications OSHA representatives indicated that the ABSL designation is the determination of the IBC and scientific experts who review the research. When considering the ABSL designation, the PI and IBC need to consider the impact of zoonotic disease,

The scientific literature documents several cases in research of zoonotic transmission of agents to humans, including LCMV in 1989.⁷ However, 21st century biosecurity practices in animal facilities and sentinel testing reduce the likelihood of animals harboring zoonotic disease.

Discussion

The Principal Investigator provides the initial risk assessment and the IBC approves use with human materials in animals, but frequently may not consider the scientific literature or biosafety regulations for their work. The ABSL determination falls to the biosafety professional, IBC, and IACUC to assess animal containment requirements. The IBC as part of the risk assessment is justified in lowering containment provided the following aspects of the risk assessment are satisfactorily addressed:

1. Procedures where human materials are introduced into animals which are susceptible to infection by human pathogens;
2. Introduction of human materials known to be infected with human pathogens.
3. Cell line is established (ABSL-1) or primary (ABSL-2)

If the cell lines are negative for 1 and 2, and are established cell lines, consideration for ABSL-1 containment should be considered by the IBC.

References

¹ National Institutes of Health. *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*. March, 2013. http://oba.od.nih.gov/oba/rac/Guidelines/NIH_Guidelines_new.pdf. Accessed 10-10-2012

² 49 CFR Part 1910.1030, *OSHA Bloodborne Pathogen Standard*. 1991. Accessed 10-10-2012.

³ Centers of Disease Control. *Biosafety in Microbiological and Biomedical Laboratories*, 5th edition. 2010. Accessed 10-10-2012

⁴ World Health Organization, *Xenotransplantation*. <http://www.who.int/transplantation/xeno/en/>. Accessed 10-10-2012.

⁵ Pel, Z. Human Xenograft Transplantation in Animal Research: Risk Assessment and Hazard Control for Animal Care Workers. *Contemporary Topics. American Association for Laboratory Animal Science*. Vol. 42, No 6. November 2003.

⁶ Jenkins, CL. *OSHA Letter of Interpretation Request Regarding ABSL-2 vs. ABSL-1 for Human Cell Lines*. June 12, 2012.

⁷ Dykewicz CA, Dato VM, Fisher-Hoch SP, et al. (March 1992). *Lymphocytic choriomeningitis outbreak associated with nude mice in a research institute*. *JAMA* **267** (10): 1349-53. PMID 1740856

Table 1. ABSL-1 vs. ABSL-2

	ABSL-1	ABSL-2
Work Practices	Standard Animal Care	Standard Animal Care PPE considerations Biohazard Waste Decontaminated
Facilities Present	Cages Benchtop	Autoclave Biosafety Cabinet
Personal Protective Equipment	Animal Biosecurity	Animal Biosecurity Biohazards
Other Considerations	None	Other Biohazards in Facility