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Introduction

Balancing Animal Welfare, Human Safety, and Research in Agriculture High Containment

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Abstract

Livestock research is paramount to understanding the risks associated with unintentional and intentional introductions of emerging, reemerging, and transboundary animal diseases, including their relationship to both the security of the economy and the nation's food supply. Research involving large animal species conducted in maximum containment Biosafety Level (BSL)-3Ag and BSL-4 facilities include Health and Human Services and United States Department of Agriculture Select Agents that can have severe consequences on both animal agricultural industry and public health. This themed issue of *ILAR* spans the spectrum of concerns related to this special niche within the animal research community with an emphasis on a review of available research, current trends, and novel approaches relevant to those conducting large animal research with high-risk agents and those charged with regulating those facilities and programs. Articles are authored by those embedded in the high- and maximum-containment community, directly involved with the work, detailing the unique challenges associated with BSL-3 and BSL-4 livestock research.

Key words: Animal welfare, biocontainment research, BSL-3Ag, BSL-4, BSL-4Ag, livestock vaccine, zoonoses

Large animal research is paramount to understanding the risks associated with emerging or reemerging zoonotic diseases. Although these events have been uncommon, their impact can be long lasting when they do occur. Recent examples of the economic hardships resulting from emerging zoonotic diseases include the 2014–2015 highly pathogenic avian influenza outbreak, which devastated the United States poultry industry with over $3 billion dollars in economic losses, or the ongoing COVID-19 pandemic, with cumulative costs in the United States estimated to reach $16 trillion.[1,2] Gaining a strong understanding of high-consequence Biosafety Level (BSL)-3 Ag and BSL-4 agents is essential to prepare for and provide adequate risk assessments to ensure the safety of both human and animal health as well as food security. In this special issue of *ILAR*, the contributors review a breadth of topics pertaining to high- and maximum-containment research. Each article discusses critical elements and challenges to working in this specialized niche environment.

The use of animals in BSL3-Ag and BSL-4 research is essential for providing risk assessments to inform policy makers on preparations in the face of looming zoonotic disease incursions. Dr Klages'[3] contribution reviews important regulatory Institutional

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Animal Care and Use Committee–related aspects to consider when carrying out animal studies in high containment. Many moving parts and important details are involved in conducting research that takes into account the welfare of animals, protection of personnel, the public, and the integrity of the science.

To complement institutional considerations for safe and humane animal use, accrediting bodies such as Association for Assessment and Accreditation of Laboratory Animal Care International provide additional oversight. The comprehensive review by Harper et al[4] provides a thorough perspective to the unique considerations of high containment. The use of risk group 3 and 4 pathogens provides additional challenges to ensure animal welfare is met. The challenges of high containment are discussed under the perspective of Association for Assessment and Accreditation of Laboratory Animal Care International with the ultimate goal of ensuring standardization and excellence in animal care and use.

Vector-borne diseases offer special challenges due to the acquisition, rearing, and operational use of arthropods. Higgs et al[5] review considerations that should be addressed prior to undertaking arthropod research. This thoughtful review provides insights into handling and maintenance of infection with arthropods under high-containment conditions.

Waste management is a critical component often overlooked in planning for agricultural animal studies in high containment. Large animal research generates copious volumes of waste in many forms that present significant challenges in the adequate treatment of effluent. Henneman et al[6] provide a detailed account of different waste streams and considerations for processing. The need for thorough consideration of work flows prior to construction of new facilities or renovation of existing ones cannot be understated in an effort to ensure operations and maximum capacity are maintained.

Both large and small animals require specialized containment zones to ensure BSL-3Ag and BSL-4 work is performed in a safe manner. The contribution by DeTolla et al[7] provides an evaluation of the use of semi-rigid isolators for housing laboratory animals infected with risk group 3 agents. This work highlights modification of traditional isolators that may be useful for containment conditions.

An important outcome from large animal maximum-containment research is the development of countermeasures against high-consequence zoonotic emerging or reemerging pathogens, where a OneHealth approach is important for protecting both human and animal health. Brake et al[8] discuss the challenges and opportunities in the development and licensing of veterinary vaccines against high-consequence pathogens.

Translational research is extremely important to improving our understanding of human disease. Small animal models are useful; however, they are limited in their ability to recapitulate aspects of disease concerning human health. Schiffman et al,[9] provide a comprehensive review of ferrets as a model for the study of filoviruses and their role in the evaluation of countermeasures for therapeutic use in humans.

The human–domestic animal–wildlife interface has increasingly recognized significance in emerging and reemerging infectious diseases. The study of wildlife is important to understanding the roles of nondomestic species in transmission and amplification and as potential reservoirs. Falendysz et al[10] review the many safety, scientific, and logistic challenges associated with wildlife studies in biocontainment and outline important considerations for animal welfare and the adaptation of existing techniques and technologies as well as for the development of novel approaches for wildlife.

Zoonotic diseases often present with limited clinical signs in both wildlife and domestic animals. Large animal research is critical to better understand the susceptibility of livestock to risk group 4 pathogens along the human–domestic animal transmission interface. Lewis and Pickering[11] review large animal research in high containment with a focus on ebolaviruses and henipaviruses. The studies discussed have been instrumental to the development of large animal models and the preparation for future zoonotic disease outbreaks.

As can be imagined, there are many challenges to safely, effectively, and ethically conducting research involving animals in high and maximum containment. This themed issue is focused on bringing together expertise in this field and sharing novel approaches for dealing with these challenges. The information provided in this issue helps strengthen the foundation of biocontainment programs relevant to those engaged in animal-based research as well as expand the basic understanding of this work to the broader research and regulatory community.

Potential conflicts of interest. All authors: No reported conflicts.

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