

## ISSUE ADRESSED BY THIS POLICY

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The introduction of human cells/fluids/tissues into animals may provide an opportunity for infectious agent amplification and exposure. An incidental exposure event is deemed **possible** and imparts a **moderate** negative consequence upon personnel (investigators and ACS staff), environmental (animal welfare), and reputation of the University. Specific pathogen-free testing for prominent Bloodborne Pathogens reduces the likelihood of exposure events but does not necessarily negate the inherent consequences associated with exposure to pathogens excluded from the panel. Thus, the overall risk associated with the current practice is deemed to be **moderate**. Mitigation of this risk will warrant additional action.

## HAZARD MITIGATION

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The following is a breakdown of the risks associated with the various procedures and appropriate mitigation efforts:

1. Preparing the human cell/fluid/tissue inoculum: **high risk activity**
  - a. These activities must be handled in accordance with BSL-2 containment and practices as defined by federal agencies Centers for Disease Control and Prevention (BMBL 6th edition) and National Institutes of Health.
2. Inoculating the human cells/fluids into live animals: **moderate to high-risk activity**
  - a. This activity must be performed in accordance with ABSL-2 containment and practices including the use of Universal precautions, which include the following practices:
    - i. If applicable, the use of safety-engineered sharps devices.
    - ii. The use of an annually certified biosafety cabinet for any potential aerosol generating procedures. Injections can be performed outside of a BSC granted personnel don mucous membrane protection (either a face shield or safety glasses/goggles worn with a surgical mask).
    - iii. Cages containing animals inoculated with human-derived products must be clearly labeled at the time of delivery of human-derived materials to the animals to indicate the hazard.
3. Housing of animals inoculated with human derived materials: **low risk activity**
  - a. Housing of animals will be designated by the BSO/IBC and IACUC to be at **ABSL-1+Hu** to indicate that additional precautions per section 4.b. below and waste handling practices per section 6 below beyond standard ABSL-1 housing may be required.
  - b. Animals must be caged in individually ventilated cages (IVC) using a negative airflow mode of operation.

- c. Cages can be maintained in any standard housing room (ABSL-1) assigned by ACS. Cages must be labeled appropriately to indicate that animals have been inoculated with human derived cells/tissue.

**4. Routine cage changes: *low risk activity***

- a. Animal welfare shall be visually assessed prior to handling. In most cases, a productive infection is associated with observable symptoms. If handled in an animal transfer station and handled using protective barriers (direct contact with animals is minimized by wearing appropriate PPE in addition to the use of tunnels when transferring animals between cages), the risk of exposure is greatly mitigated.

**b. Exceptions include:**

- i. Animals that appear ill (e.g., hunched posture, ruffled fur, lethargic, displaying active hemorrhage/weeping wounds or ulcerated lesions) must be handled in accordance ABSL-2 containment and practices plus Universal Precautions to include handling the animals and performing cage changes inside an annually certified biosafety cabinet (BSC). Veterinarian guidance will be considered in containment determination.
- ii. For the administration of veterinary care to animals displaying behavior consistent with poor health (i.e., conditions described under 4-b-i above) when direct handling of the animals may be required, an additional pair of gloves will be worn in addition to standard PPE for safe animal handling; and all handling of animals be performed in an annually certified BSC.

**5. Inoculated animal invasive procedures: *moderate to high-risk activity***

- a. Invasive surgeries and necropsies should be handled using appropriate PPE accordance with the UF Blood Borne Pathogen Program ABSL-2 containment and practices including the use of appropriate primary containment devices (i.e., certified BSC, perfusion table, etc.). If the use of containment devices is not feasible, additional PPE affording mucous membrane protection must be worn (i.e., either a face shield or safety glasses/goggles worn with a surgical mask).

**6. Waste handling: *moderate risk activity***

- a. Carcasses that have received human source material are by definition biohazardous materials and must be collected and disposed of as regulated biomedical waste.
- b. In the absence of presumed cage contamination to human-derived products (no visual evidence of blood in cage or bedding or knowledge of their use to house animals with active hemorrhage/weeping wounds), depopulated cages can be handled in accordance with standard ACS practices. Cage wash personnel are already wearing heightened PPE precautions (notably including the use of a fit-tested N95 respirator and mucous membrane protection).

- c. If the cage is reasonably anticipated to be contaminated with human-derived or potentially infectious material (per 4.b.i), cages will require autoclave inactivation prior to disposal of bedding as regulated biomedical waste followed by cage wash.

Note: If researchers are working in a shared research environment, all personnel present in the space when human cells/fluids/tissues or inoculated animals are being manipulated must have completed the UF Bloodborne Pathogen training and adhere to the aforementioned precautions.

## CONCLUSIONS

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The greatest risk of exposure associated with the use of human-derived products in animals pertains to active manipulations of the human-derived product and invasive procedures with the inoculated animals. These procedures will warrant heightened precautions; however, lower-risk procedures can conform to standard ABSL-1 practices. Adherence to the detailed mitigation efforts will effectively lower the likelihood of exposure down to a **rare** occurrence (primarily attributed to nonconformance to the standard operating procedures), thereby reducing the overall risk of this activity to **low**. The proposed strategy imparts the following:

1. It affords research personnel with adequate protection, even when handling samples potentially contaminated with bloodborne pathogens (BBP) agents. As such, the adherence to these specified practices may negate the need for SPF BBP panel testing (however, this is still recommended when dealing with primary human specimens).
2. Since the cages are handled in accordance with standard precautions (i.e., not autoclaved), ACS obligations and per diems should not be substantially impacted.

## HUMAN CELLS IN ANIMALS – PRACTICES AND CONTAINMENT SUMMARY

Activity	Practices and Containment
Preparing the human cell/fluid/tissue inoculum	BSL-2 practices and containment
Inoculating the human derived materials into live animals	ABSL-2 Practices plus Universal Precautions to include: <ul style="list-style-type: none"> <li>• Use of safety-engineered sharps devices</li> <li>• Use of BSC for any aerosol generating procedures.</li> <li>• Injections may be given outside of BSC if appropriate PPE is worn (standard PPE + safety glasses/goggles + surgical mask)</li> </ul>
Animal housing	Standard housing room (ABSL-1) plus the housing of animals in IVC set up with negative air flow (hereby designated ABSL-1+Hu): <ul style="list-style-type: none"> <li>• Label <b>“Use of Human Cells in Animals”</b> <u>on caging and at the entrance of the room</u></li> </ul>
Cage changing	Assess animal health prior to opening the cage for any purpose: <ul style="list-style-type: none"> <li>• Always transfer animals using tunnels</li> <li>• Refer to veterinary guidance for animals that appear ill.</li> <li>• Use a BSC for animals with active hemorrhage/weeping wounds. Adhere to ABSL-2 including Universal Precautions and safety practices.</li> </ul>
Invasive procedures on inoculated animals	ABSL-2 containment practices plus Universal precautions for handling human tissue: <ul style="list-style-type: none"> <li>• Must use BSC or perfusion table for containment whenever possible. See section 5 above for exceptions</li> </ul>
Waste handling	<ul style="list-style-type: none"> <li>• Carcasses are collected and disposed of as regulated <u>biomedical waste</u>.</li> <li>• In the absence of contamination of human derived products, standard bedding disposal applies.</li> <li>• Cages known to have housed animals with active hemorrhage/weeping wounds or where contamination of human derived products is suspected, will require autoclaving prior to disposal as regulated biomedical waste to adhere with FLDOH biomedical waste regulations followed by cage washing.</li> </ul>