MONTANA STATE UNIVERSITY
Research Integrity & Compliance

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Phone: (406) 994-6732
IBC Approval Date: 6/10/2026

MSU Large-scale (greater than 10L) Biological Materials Policy

Scope

This policy applies to researchers conducting large-scale use of biological materials, such as microorganisms with or without recombinant or synthetic nucleic acids, toxins, human-derived materials, or animal-derived materials. Large-scale means greater than 10 liters of biological materials in one container. Large-scale containers can include fermenters, bioreactors, carboys, or specialty equipment, or waste collected in volumes greater than 10 liters in one container.

Responsibility

Principal Investigators (PIs) and research staff conducting large-scale research are required to follow this policy and other plans/policies as outlined.

References

Appendix M of the Biosafety in Microbiological and Biomedical Laboratories (BMBL), Centers for Disease Control (CDC).

Section III-D-6 and Appendix K of the National Institutes of Health Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines).

MSU Biosafety Manual.

Definitions

BSL1-LS: Biosafety Level 1-Large Scale is for biological materials that require BSL-1 containment at the laboratory scale.

BSL2-LS: Biosafety Level 2-Large Scale is for large-scale use of biological materials that require BSL-2 containment at the laboratory scale.

Closed system: An item that prevents biological material from escaping into the environment or exposing personnel such as a closed vessel used for the propagation and growth of cultures; screw-cap tubes/bottles used for sampling, further processing, or final production.

HEPA filters: High Efficiency Particulate Air filters.

IBC: Institutional Biosafety Committee. The MSU IBC reviews and approves large-scale biological materials research for compliance with the NIH Guidelines, MSU policies and procedures, and other federal, state and local policies. The MSU IBC reviews the handling of all large-scale research, even that which does not include recombinant or synthetic nucleic acids or may be exempt from the NIH Guidelines, so that MSU, acting through the IBC, can ensure that all large-scale research is appropriately reviewed, and recombinant DNA research is appropriately classified.

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Validated autoclave cycle: Annual verification and monthly validation of autoclave cycle parameters with large volumes of liquid are mandatory. New cycle parameters, waste items, or changes in the way waste is loaded into the autoclave must be verified before waste is removed from the facility.

- Verify each cycle and type of waste load annually by preparing a load that mimics the autoclave load (example: 4 x 20L carboys of liquid waste). Annual verification is conducted by placing several biological indicators (BIs) throughout the load to demonstrate that the conditions are adequate to achieve sterilization. Annual verification records are maintained in the Laboratory Specific Biosafety Manual.
- Monthly validation is conducted per the Autoclave Quality Assurance Program and records are maintained via the Autoclave Quality Assurance Form.

Validated inactivation procedure: A procedure that renders a microorganism non-viable but allows the microorganism to retain characteristics of interest for future use; the efficacy is confirmed by data generated from a viability testing protocol. For material that contains recombinant or synthetic nucleic acids, use the organism that will serve as the host for propagating the recombinant or synthetic nucleic acid molecules.

Training

All researchers utilizing large-scale use of biological materials must complete required training courses and applicable occupational health requirements per the biosafety training website. Additional training on lab specific standard operating procedures must be documented in the lab specific biosafety manual, such as training in aseptic techniques and in the biology of the organisms used; donning and doffing of personal protective equipment (PPE) and an understanding of when PPE is required for product protection vs. personal protection; and emergency response procedures including spill response protocols.

Policy

All policies and procedures outlined in the MSU Biosafety Manual must be adhered to. Prior to initiating any large-scale use of biological materials, an approved IBC protocol is required. PIs must meet with the Biosafety Officer to conduct a risk assessment and to determine risk mitigation strategies. The IBC has the authority to determine the biosafety containment level (BSL) to which the work must be conducted at. This policy applies to microorganisms, material containing recombinant or synthetic nucleic acids, viral vectors, and biological materials used in volumes greater than 10L in one container.

The table below describes the requirements at each biosafety level for working with biological materials at a large-scale.

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Requirements	BSL1-LS	BSL2-LS
Spills and accidents are immediately reported to the Principal Investigator and Biosafety Officer.	Yes	Yes
Cultures of viable organisms must be handled in a closed system or other primary containment equipment which is designed to *reduce/prevent* the potential for escape of viable organisms.	Yes *Reduce*	Yes *Prevent*
Culture fluids must not be removed from a closed system or other primary containment equipment unless the viable organisms have been inactivated by a validated inactivation procedure. Culture fluids that contain viable organisms intended as final product may be removed from the primary containment equipment by way of closed systems.	Yes	Yes
Sample collection from a closed system, the addition of materials to a closed system, and the transfer of culture fluids from one closed system to another must be conducted in a manner which *minimizes/prevents* the release of aerosols or contamination of exposed surfaces.	Yes *Minimize*	Yes *Prevent*
Exhaust gases removed from a closed system or other primary containment equipment must be treated by filters which have efficiencies equivalent to HEPA filters or by other equivalent procedures (e.g., incineration) to *minimize/prevent* the release of viable organisms to the environment.	Yes *Minimize*	Yes *Prevent*
A closed system or other primary containment equipment that contained viable organisms must not be opened for maintenance or other purposes unless it has been sterilized by a validated autoclave cycle except when the culture fluids contain viable organisms intended as final product.	Yes	Yes
A closed system used for the propagation and growth of viable organisms and other primary containment equipment used to contain operations involving viable organisms must: • Contain sensing devices that monitor the integrity of containment during operations, • Rotating seals and other mechanical devices must be designed to prevent leakage or must be fully enclosed in ventilated housing that is exhausted through HEPA filters or through other equivalent treatment devices, and • Be permanently identified and this identification must be used in all records reflecting testing, operation, and maintenance, and kept in the Laboratory Specific Biosafety Manual.	No	Yes
A closed system used for the propagation and growth of viable organisms must be tested for integrity of the containment features. Testing must be: • Done prior to the introduction of viable organisms and following modification or replacement of essential containment features, • Procedures and methods used in the testing must be appropriate for the equipment design, and • Records of tests and results must be kept in the Laboratory Specific Biosafety Manual.	No	Yes
Each closed system and primary containment equipment used to contain viable organisms must be labeled with the universal biosafety symbol.	Yes	Yes
Emergency plans must include methods and procedures for handling large losses of culture on an emergency basis.	Yes	Yes