

ASU fact sheet | Large-scale use of biological materials

This fact sheet provides guidance on the large-scale use of biological materials. “Large-scale use” is defined as greater than 10 liters of biological material (e.g., cultures, solutions) in one container. Large-scale containers include fermenters, bioreactors, carboys or specialty equipment such as “tubes.” The use of large-scale materials in research and teaching is governed by the National Institutes of Health, or NIH, [Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules](#) and by the Centers for Disease Control, or CDC, guidance document [Biosafety in Microbiological and Biomedical Laboratories](#), or BMBL. At ASU, large-scale use must be reviewed and approved by the Institutional Biosafety Committee, or IBC.

ASU oversight

The NIH Guidelines and the BMBL detail procedures for the containment and safe conduct of various forms of research, including work with large volumes of biological materials. All researchers at ASU must comply with the NIH Guidelines and BMBL even if the NIH does not fund their individual projects. In addition, a permit from the [USDA/APHIS](#) is required for the interstate movement or environmental release of genetically modified organisms.

At ASU, the IBC oversees all research, teaching, and production of biological materials in volumes greater than 10 liters in one vessel. The IBC reviews and approves large-scale use for compliance with the NIH Guidelines, ASU policies, and best laboratory practices. The ASU IBC reviews the handling of all large-scale research, even that which may be exempt from the NIH Guidelines, so that ASU, acting through the IBC, can ensure that all recombinant DNA research is appropriately reviewed and classified.

Principal Investigators, or PIs, must submit a disclosure to the IBC before beginning work with biological volumes greater than 10 liters. The IBC disclosure application is available on the [ORIA website](#). ASU Environmental Health and Safety will inspect the equipment and set-up before operation begins. As part of the IBC disclosure, the PI must submit the following standard operating procedures, or SOPs:

- Harvesting.
- Inoculation.
- Large spills.
- Medical evaluation and treatment.
- Normal operation.
- Secondary containment.
- Small spills.
- Transporting between locations.
- Validating destruction (including all mathematical calculations for disinfection).
- Waste disposal.

ASU PIs are responsible for compliance with the NIH Guidelines while conducting research or production with large-scale cultures and solutions. Additionally, the PI must notify the IBC before modifying research already approved and promptly report any problems with containment procedures, violations of the NIH Guidelines or any research-related accidents and illnesses.

Large-scale use under the NIH Guidelines

Large-scale experiments are governed by NIH Guidelines [Section III-D-6](#), Experiments Involving More than 10 Liters of Culture. This section specifies that the appropriate containment for large-scale work be decided by the IBC and that [Appendix K](#), Physical Containment for Large Scale Uses of Organisms Containing Recombinant DNA Molecules, should be used for guidance. Appendix K discusses how to select the appropriate physical containment level. It describes work practices and facility requirements for [Good Large Scale Practice](#), [Biosafety Level 1–Large Scale](#), [Biosafety Level 2–Large Scale](#), and [Biosafety Level 3–Large Scale](#). Finally, it has definitions, footnotes and a table comparing the different levels of large-scale practice.

Selection of physical containment levels

Good Large Scale Practice, or GLSP, is for work involving viable, non-pathogenic and non-toxigenic strains derived from host organisms that have a history of safe large-scale use. GLSP is recommended for organisms such as those in NIH Guidelines [Appendix C](#), which have built-in environmental limitations. The organisms that may be used at GLSP are described in [Appendix K-VII-G](#) and following:

The host organism should:	<ul style="list-style-type: none"> • Be non-pathogenic and non-toxigenic; • Have an extended history of safe large-scale use or have built-in environmental limitations that limit survival without adverse consequences in the environment. • Not contain adventitious agents.
The recombinant engineered organism should be:	<ul style="list-style-type: none"> • As safe in the large-scale setting as the host organism. • Non-pathogenic and non-toxigenic. • Without adverse consequences in the environment.
The vector/insert should:	<ul style="list-style-type: none"> • Limited in size as much as possible to the DNA required to perform the intended function. • Poorly mobilizable. • Well characterized and free from known harmful sequences.
Also, the vector/insert should:	<ul style="list-style-type: none"> • Not increase the stability of the construct in the environment unless that is a requirement of the intended function; and • Not transfer any drug resistance markers to microorganisms not known to acquire them naturally if such acquisition could compromise the drug's use.

Biosafety Level 1-Large Scale (BSL1-LS) is for biological materials that require BSL-1 containment at the laboratory scale and that **do not qualify for GLSP**. BSL2–Large Scale (BSL2-LS) is for large-scale use of organisms that require BSL2 containment at the laboratory scale and BSL3–Large Scale (BSL3-LS) is for large-scale use of organisms that require BSL3 containment at the laboratory scale. BSL2-LS and BSL3-LS are not discussed in this document.

Containment and Work Practices for GLSP and BL1-LS ([Appendices K-II](#) and [K-III](#) and [Table 1](#))

GLSP and BSL1-LS have some similar requirements for containment and work including:

- Appropriate facilities, equipment and work practices to safeguard health.
- Emergency plans for handling a large loss of biological material.
- Inactivation of waste.
- Medical treatment as appropriate.
- Personal protective equipment according to risk.
- Reporting accidents and incidents.
- Standard practices for personnel safety.
- Training and standard operating procedures.

However, there are further requirements for BSL1-LS that are not needed for GLSP (see [Appendix K-III](#) for details). These are primarily about preventing aerosol releases and include:

- A closed system or other primary containment that separates viable organisms from external environment.
- Controlling aerosols by engineering to minimize release during sampling, addition of material, transfer of cultivated cells and removal of material, products and effluent from the system.
- Inactivating the material before removal from the system (unless it is the final product).
- Sterilizing the closed system by a validated procedure before it is opened.
- Treating exhaust gases to minimize release.

In order to be classified as GLSP, documentation must be submitted to the IBC, which demonstrates that the organism has an extensive history of safe large-scale use or that there are built-in characteristics, which limit its survival in the environment. Contact ASU EHS to discuss proper classification, containment levels and operating requirements.

Environmental release

A release, leak, spill, or other loss of containment of a large-scale material is a serious issue. Loss of a culture or biological solution outside of containment, for instance onto the ground, floor or into a sewer, must be reported to ASU Environmental Health and Safety within 24 hours. There are federal and state reporting requirements for such incidents.

Questions? Contact ASU Environmental Health and Safety at 480-965-1823 or email asuehs@asu.edu.

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