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<b>Biorisk Management Program</b>	<b>SOP 900</b>
<b>Approval Process for Inactivation Methods for Infectious Material</b>	<b>Revision v.4</b>
	<b>Approval:</b>
	<b>Approval Date:</b>

## Purpose

This document describes the process by which Principal Investigators (PIs) must petition the NIH Institutional Biosafety Committee (IBC) to gain approval to transfer biological materials that have been approved for work in a high containment space (i.e., BSL3/ABSL3, BSL4/ABSL4) to a lower biosafety level space.

## Scope

This document applies to **all** high and maximum containment laboratories at the NIH that wish to transfer biological materials to a lower biosafety level space. It describes the process to petition the NIH IBC for approval of inactivation protocols. Inactivation protocols are procedures that render a biological agent, toxin, or nucleic acid non-viable or non-functional. For a biological agent, “non-viable” means the agent/toxin is no longer capable of growing, replicating, infecting, or causing disease. For a nucleic acid, “non-viable” means that the nucleic acids are no longer capable of producing infectious forms of a virus or expression of a functional toxin without further genetic manipulation. For a toxin, the term “non-functional” means a toxin is no longer capable of exerting its toxic effect.

## Roles and Responsibilities

PIs supervising and/or conducting the work are responsible for understanding this process and obtaining written NIH IBC approval before transferring biological materials from a high containment space to a lower biosafety level space.

## Special Practices

- Each PI is required to submit validation testing and results; please see Suggested Guidelines for Validation of Inactivation Methods (Appendix 1), for each distinct inactivation method, even if the method is a widely accepted standard or has been previously published in a peer-reviewed journal.
- PIs must have a log book or tracking method (Example: appendix 2) in the laboratory or anteroom which must be used to log inactivated samples removed from the laboratory. Recorded information must include the (1) date of removal, (2) full name of the person removing sample, (3) number of samples being removed, (4) the agent the sample contained, (5) the inactivation method utilized and (5) location to where sample was removed. Procedures for recording pertinent information should be described in the laboratory inactivation standard operating procedure.
- The NIH IBC will determine the appropriate personal protective equipment (PPE) by conducting a risk assessment. All established PPE, and biosafety level requirements for

working with the agent will remain in effect before, during and after validation testing of the procedure until the protocol for transferring the agents to a lower biosafety level laboratory is approved.

- If a suspected failure of the approved method is identified or viable biological material has been accidentally removed from the high containment space then the PI must notify the respective NIH Biosafety Officer (BSO).

## Procedures

- For all new sample inactivation methods, the PI or their designee must discuss with their safety specialist and/or the NIH BSO their intent to inactivate biological materials for removal from a high containment space to a lower biosafety level space.
- A PI may develop an original inactivation method, utilize a previously published procedure or utilize one developed by another lab. In all cases the protocol must be validated in their laboratory.
- To avoid any unforeseen delays in approval, it may be beneficial for the PI to discuss the intended inactivation method and testing procedures with the NIH BSO. Following the discussion, the investigator may proceed with performing validation testing on the biological materials. Validation testing is required for any original inactivation method, existing inactivation methods developed by other labs, or procedures. This is to demonstrate that analogous results can be achieved in the PI's laboratory.
- All proposed inactivation methods, detailed validation test procedures, and validation test results must be submitted as an amendment to an existing rDNA registration (if applicable) or PRD registration, for review by the IBC. Suggested guidelines have been provided to assist PIs in the validation process (Appendix 1).
- Upon review and approval by the NIH IBC, the NIH BSO shall provide documentation to the PI listing the approved inactivation method(s) for his/her laboratory and stipulations, if any, for performing the procedure(s).
- The PI shall add the inactivation standard operating procedure(s) to his/her biosafety plan (manual), noting the applicable approved pathogen(s) that can be inactivated.
- The PI shall document personnel training on the approved inactivation method(s).
- Inactivated material may be removed from the high containment laboratory only after IBC approval is obtained, the biosafety plan updated, and staff training completed.
- The PIs Personnel shall subsequently follow the approved inactivation method and procedure(s) and all written stipulations to ensure complete inactivation of samples leaving the laboratory.
- PIs are required to provide annual training to laboratory personnel on the inactivation procedures to ensure that procedural drift does not occur.

## **Suggested Guidelines for Validation of Inactivation Methods**

Listed below are topics that the IBC considers when discussing validation studies and resulting data for the inactivation of agents/toxins. Providing the information below will speed up the approval process by reducing the chance that the IBC will request additional data or further clarification of the data provided.

1. Samples
  - a. Listing the agent/toxin used and why they were chosen.
  - b. Testing the highest titer of sample expected under experimental conditions. If this is not possible, discussing how the validation data supports the use of this inactivation method, and to what degree.
  - c. Describing the nature of the samples analyzed (e.g. tissue, cells, viral or bacterial preps, etc.).
    - i. Providing validation data for every type of sample being inactivated.
2. Assays
  - a. Methods
    - i. Providing detailed experimental conditions and standard operating procedures (SOPs) for each inactivation method.
    - ii. Indicating if multiple variables or individual steps in the procedure were tested.
    - iii. Clearly indicating the number of samples tested for each condition.
  - b. Detection assay
    - i. Describing why the assay is appropriate for the chosen agent/toxin, or type of sample.
    - ii. Giving the upper and lower limits of detection of the assay.
    - iii. Providing a detailed experimental protocol for the assay.
    - iv. If possible/practical, using a second complementary assay to confirm results.
3. Controls
  - a. Clearly defining the positive control.
  - b. Clearly defining the negative control.
4. Reproducibility
  - a. Giving the **n** number for experimental and control samples for each experiment. A minimum of n=3 for each group is recommended.
  - b. Repeating the experiment at least once following the exact same protocol/SOP. (This helps the IBC assess the reproducibility of the tested conditions.)
5. Results
  - a. Providing a complete summary of the results. Raw data are fine if presented clearly.
  - b. Stating the reduction of infectious units and what that means within the limits of detection of the chosen assay.
  - c. Giving statistical significance.
  - d. Stating the final conclusions of the study.
6. Final conditions
  - a. Based on the results, clearly detailing the final protocol and conditions to be used in the SOP.

