HARVARD MEDICAL SCHOOL

COMS Protocol Review Policy

Last Revised 3/28/2025

HMS Primary Responsible Office: Office of Biological Safety
Approval Body: Committee on Microbiological Safety (COMS)
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1. **Purpose**

   COMS reviews and approves research at Harvard University and COMS- affiliated Institutions that involve the use of COMS-Regulated Materials ("CRM") as defined in the Policy Introduction.

2. **Applicability**

   Any COMS application that is approved by the committee must follow the guidance of this policy and be in compliance with all other safety requirements imposed by COMS or by federal, state or local legislation or regulation.

3. **Implementation Procedures**

   The review process differs depending on which section of the NIH Guidelines the research falls under and the determined risk level of the work. The Principal Investigator (PI) is responsible for submitting the completed COMS protocol in eCOMS to their institutional biosafety officer (BSO). The COMS protocol requires the PI to make an initial determination of which section of the NIH Guidelines (if any) their research falls under. The BSO then conducts a risk assessment and verifies the PI's initial determination of the NIH Guideline section is correct. If the BSO risk assessment results in the protocol requiring further review based on high-risk activities, lack of precedent for the agents proposed, use of common laboratory areas, or other concerns, appointed committee review may be needed. Further information may be provided in the BSO risk assessment.

   Risk Assessment and Committee Review

   a. The institutional BSO will conduct a risk assessment of the proposed research. The results of the risk assessment will include:
      i. Recommended biosafety level
      ii. Containment: The containment, procedures and, if necessary, additional stipulations for the protocol. If available, agent-specific guidance, e.g. risk group or biosafety level, from the NIH

Guidelines, CDC/NIH BMBL, or Public Health Agency of Canada Pathogen Safety Data Sheets.

iii. The BSO shall consider the following additional factors as part of their risk assessment, as available:
   - Pathogenicity
   - Host range
   - Infectious dose (may differ based on route of transmission)
   - Agent stability
   - Concentration of agent
   - Animal study data
   - Effective treatment/prevention (e.g., availability of antibiotics or vaccine)
   - Origin of agent (e.g., academic laboratory, commercial source)
   - Strain validation
   - Predominant route(s) (Note: route(s) of exposure in laboratories may differ than routes of transmission observed in nature)
   - Delivery of genetic material to cell independently (e.g., viral vector)

b. Committee review
   i. If the Institutional BSO, COMS Office, COMS Chair or COMS Vice Chair recommends appointed committee member review, at least one committee member reviewer will be assigned. Experiments requiring appointed review potentially include:
      1. Research under Sections III-A, III-B, and III-C of the NIH Guidelines
      2. Clinical protocols
      3. Research under United States Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP)
      4. Those otherwise assessed by the BSO or COMS leadership to be of higher risk or requiring elevated level of review (e.g., risk group three organisms,)
   ii. The protocol will be reviewed at an upcoming COMS meeting.

Administratively approved protocols will be listed on the agenda.

c. Protocols requiring approval by the Institutional Review Entity (IRE) for NIH Implementation of the U.S. Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP), federal and/or local oversight(e.g. NIH Office of Science Policy (OSP) local public health agencies) are approved with condition of final approval granted by the entities as mentioned above.

Protocol Approval

Once appropriate review has been obtained and the work is approved, the COMS Office will send an approval letter signed by the COMS Chair or COMS Vice Chair to the PI indicating that the work is approved under the biosafety level and stipulations indicated in the letter.

Review Procedure for Research Involving Recombinant or Synthetic Nucleic Acid Molecules:

Research involving recombinant or synthetic nucleic acid molecules is covered under one of six sections (Sections III-A through III-F) of the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines).

1. **NIH Section III-A**

   Committee Review

   a. At the request of COMS, NIH OSP will make a determination regarding whether a specific experiment involving the deliberate transfer of a drug resistance trait falls under Section III-A-1-a and therefore requires NIH Director approval. An Institutional Biosafety Committee may also consult with NIH OSP regarding experiments that do not meet the requirements of Section III-A-1-a but nonetheless raise important public health issues. NIH OSP will consult, as needed, with one or more experts.

2. **NIH Section III-B**

   Experiments Covered (Require NIH OSP and Institutional Biosafety Committee Approval Before Initiation):

   Committee Review

   a. Applications that fall under Section III-B will be assigned at least one committee member reviewer and discussed at an upcoming COMS Meeting. Protocol initiation requires approval by the NIH Office of Science Policy (OSP) and COMS.

3. **NIH Section III-C (Experiments Involving Human Gene Transfer that Require Institutional Biosafety Committee Approval Prior to Initiation)**
    a. **See Clinical Trial Policy for special requirements**

4. **NIH Section III-D (Experiments that Require Institutional Biosafety Committee Approval Before Initiation)**

    Committee Review

    a. Applications that fall under Section III-D will be discussed at an upcoming COMS Meeting. Protocol initiation requires approval by COMS.

5. **NIH Section III-E (Experiments that Require Institutional Biosafety Committee Notice Simultaneous with Initiation)**

    Committee Review

    a. Applications that fall under Section III-E will be discussed at an upcoming COMS Meeting. Protocol initiation requires approval by COMS.

6. **NIH Section III-F Exempt Experiments**

    Committee Review

    a. Applications that fall under Section III-F will be administratively approved by the COMS Office. Protocol initiation requires approval by COMS.

B. Review Procedure for Research Not Involving Recombinant or Synthetic Nucleic Acid Molecules

Research not involving recombinant or synthetic nucleic acid molecules is covered under the definition of CRM (see Policy Introduction (II) Scope). The review process is dependent on the risk assessment conducted by the institutional BSO, input from the Director of COMS, COMS Chair and COMS Vice Chair. Should the work involve biosafety level three containment, an additional review may be required by the local health department, as detailed above in implementation procedures.

1. Bacteria, viruses, fungi, parasitic protozoa and prions that are not regulated under the NIH Guidelines
    - Experiments covered
        i. Experiments involving the use of non-recombinant CRM, regardless of their

pathogenicity to humans.

ii. **Special considerations:** Any non-NIH appointed reviews falling under BL1 containment would be assigned as standard reviews with a call to discussion at the next COMS Meeting.

iii. **Downgrade of materials** – Any downgrade of biosafety level will require appointed review. Upgrading of a biosafety containment level may be standard review and be identified for discussion at the next COMS Meeting.

2. Human or non-human primate blood, cells, tissues, fluids or secretions
    - Experiments Covered
        i. Experiments involving the use of human or nonhuman primate blood, cells, tissues, fluids or secretions.
3. Biological Toxins
    - Experiment Covered
        i. Experiments involving the use of biological toxins under the Federal Select Agent Registry Program (both regulated and non-regulated quantities).
        ii. Permissible Toxin Amounts
4. Policy Authority
    - COMS Office of Biological Safety

The Committee on Microbiological Safety shall enforce this policy.

5. Related Policies
    - Clinical Trials Policy
    - COMS Policy Introduction
6. References
    - NIH Guidelines
    - NIH Implementation of the U.S. Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP)
    - BMBL
    - CDC/USDA Select Agent Regulations