HARVARD MEDICAL SCHOOL

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I. Purpose

a. Harvard University's Committee on Microbiological Safety (COMS) serves as the Institutional Biosafety Committee (IBC) for Harvard as well as the COMS-Affiliated Institutions.

II. Scope

COMS is responsible for reviewing all work with COMS-Regulated Materials ("CRM"), as defined in the Policy Introduction (II) Scope at Harvard and the Affiliated Institutions. The Affiliated Institutions recognize and agree that Harvard has the authority to establish policies and procedures that COMS shall follow in its initial and continuing review and approval of applications, proposals, and activities. For research conducted at or sponsored by an Affiliated Institution, the Affiliated Institution is responsible for ensuring that its laboratories and personnel are in compliance with all training and other safety requirements imposed by COMS or by federal, state or local legislation or regulation.

For research that falls under the purview of the NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules ("NIH Guidelines"), COMS reviews all projects conducted at or sponsored* by COMS-affiliated institutions. For research that does not fall under the NIH Guidelines, COMS reviews all projects using CRM conducted at COMS-affiliated institutions. Projects using these materials at institutions under COMS purview may not commence without COMS approval. Research is defined as the systematic investigation or

experimentation for the purpose of teaching, scientific (laboratory or fieldwork), or clinical advancement for activities involving CRM.

COMS-Regulated material(s) or CRM are defined as:

- Recombinant or synthetic nucleic acids as defined in the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), including gene drive modified organisms;
- Human or nonhuman primate blood, cells, tissues, fluids, and secretions;
- Biological toxins subject to the National Select Agent Registry Program; and
- Bacteria, viruses, fungi, parasitic protozoa, and prions.

III. Function

So that the biological aspects of the research and teaching are conducted in a safe manner using established biosafety standards, principles and practices, COMS shall establish, maintain, and update policies and procedures on the proper use and handling of CRM. COMS also shall establish minimum standards and best practices for the oversight and administration of research with CRM that may pose safety, health, or environmental risks, including, for example, requirements for education and training and for laboratory safety policies. All COMS materials must comply with applicable biosafety standards and applicable federal, state, and local laws and regulations and shall take into consideration relevant worker safety, public health, agricultural and environmental protection, and ethical standards.

*Sponsor may be defined several ways in the regulations, the most salient are: 1) an individual who supervises the research training experience of individual fellows supported by a fellowship award; or 2) any financial support of the research (i.e., a subaward where the Subrecipient will be conducting research requiring COMS/IBC review); or 3) as defined in 21 CFR 50.3: "a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization." i.e., develops the protocol/investigation, which may be conducted at multiple sites. Questions about sponsorship should be directed to the COMS Office and they will be reviewed on a case-by-case basis. Should the COMS office determine that a project requires COMS review, the institutional biosafety officer will be notified.

IV. Roles and Responsibilities

Harvard

Harvard is responsible for establishing COMS and thus has the authority to establish policies and procedures that COMS shall follow in its initial and continuing review and approval of applications, proposals, and activities. For research conducted at or sponsored by Harvard, Harvard is responsible for compliance with all training and other safety requirements imposed by COMS or by federal, state, or local legislation or regulation. Specifically, Harvard shall:

A. Establish and implement policies for the safe conduct of research and teaching involving CRM;
B. Establish and maintain COMS in compliance with the NIH Guidelines;
C. Appoint a Biological Safety Officer (BSO) to serve as a member of COMS;
D. Ensure adequate expertise and training (using ad hoc consultants as deemed necessary) to evaluate gene drive modified organism (GDMO), Dual Use Research of Concern (DURC), and pathogens of enhanced pandemic potential (PEPP) research;
E. Choose as members of COMS only people with appropriate expertise, as outlined in the NIH Guidelines and the COMS Policy Introduction.
F. For research conducted at or sponsored by Harvard, provide appropriate training on laboratory safety and implementation of the NIH Guidelines to all Principal Investigators and laboratory staff;
G. For research conducted at or sponsored by Harvard, establish mechanisms for having all research involving CRM reviewed by COMS;
H. For clinical trials conducted at or sponsored by Harvard, establish mechanisms for compliance with the NIH Guidelines and COMS Policies by all Principal Investigators (PIs) including, for example, the requirements that:
    1. All aspects of NIH Guidelines Section III-C must be appropriately addressed by any PI who is conducting human gene therapy trials; and

2. No research participant may be enrolled in a human gene transfer experiment until approval has been obtained from COMS, the local Institutional Review Board (IRB), and any other relevant regulatory bodies.

I. For research conducted at or sponsored by Harvard, determine the necessity for health surveillance of personnel involved in connection with CRM projects, and if appropriate, establish and maintain a health surveillance program for such projects. Such a program shall be required if personnel are:

1. Engaged in large-scale research or production activities involving viable organisms containing CRM that require Biosafety Level Three (BL3) containment; or

2. Engaged in animal research involving viable recombinant or synthetic nucleic acid molecules-containing microorganisms that require BL3 or greater containment.

J. Work with COMS and Biosafety Officers to report any significant problems, violations, or any significant research-related accidents or illnesses to applicable federal, state, and local agencies, following the COMS Incident Reporting and COMS Clinical Trial policies;

K. Provide COMS-approved training as outlined in the COMS Training policy;

L. Hold an annual public meeting, in accordance with the Boston Public Health Commission Laboratory Regulation. The COMS encourages members of the public to attend this public meeting to learn more about the review process. To request attendance at a meeting, contact COMS@hms.harvard.edu.

Committee on Microbiological Safety (COMS)

As the IBC responsible for review and approval of all research involving CRM to be conducted at or sponsored by Harvard or any of the COMS-Affiliated Institutions, COMS shall:

A. Maintain membership of at least five members selected for their collective experience and expertise in recombinant or synthetic nucleic acid molecules technology and for

their ability to assess the safety of recombinant or synthetic nucleic acid molecules research and identify any potential risk to public health or the environment. COMS membership shall include:

1. At least two members not affiliated with Harvard or any of the COMS-Affiliated Institutions (apart from their membership on COMS) and who represent the interest of the surrounding community with respect to health and protection of the environment;
2. At least one individual with expertise in plants, plant pathogens, or plant pest containment principles as outlined in Appendix L, Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Plants, of the NIH Guidelines;
3. At least one member with expertise in animals, as outlined in Appendix M, Physical and Biological Containment for Recombinant or Synthetic Nucleic Acid Molecule Research Involving Animals, of the NIH Guidelines.
4. At least one member representing Harvard's laboratory technical staff;
5. The Institutional BSO when an Affiliated Institution conducts research involving CRM requiring BL3, BL4, or Large-Scale containment (greater than 10 liters of biological culture);
6. On a rotating basis, Institutional BSOs from COMS-Affiliated Institutions that do not conduct recombinant or synthetic nucleic acid molecules research at BL3, BL4, or Large Scale (greater than 10 liters of biological culture);
7. Members with expertise and training in recombinant or synthetic nucleic acid molecules research involving human research participants;
8. Members with expertise in recombinant or synthetic nucleic acid molecules technology, biological safety, and physical containment;
9. Ad hoc members knowledgeable in institutional commitments and policies, applicable law, standards of professional conduct and practice, community, and the environment. These members can include those knowledgeable of GDMOs;
10. Ex officio members who provide expertise in institutional policy and procedures, biosafety, biosafety policy, or regulatory requirements to COMS. Ex officio members

may also have an oversight role for some business operations of COMS or related business or compliance areas. Ex officio members do not have voting privileges unless temporarily assigned by the Chair or Vice-Chair at the start of a meeting to ensure quorum. The ex officio member may decline the assignment.

B. Review of CRM research conducted at or sponsored by Harvard or COMS-Affiliated Institutions in accordance with the requirements set forth in the NIH Guidelines, approving only those research projects that are found to conform with the NIH Guidelines (as outlined in the COMS Protocol Review policy). Such review and approval may involve setting containment levels as specified in NIH Guidelines Sections III-D-4-b, Experiments Involving Whole Animals, and NIH Guidelines Section III-D-5, Experiments Involving Whole Plants;
C. Periodically review recombinant or synthetic nucleic acid molecules research conducted at or sponsored by Harvard or COMS-Affiliated Institutions listed above to check compliance with the NIH Guidelines;
D. Ensure adequacy of emergency plans and procedures for addressing accidental spills and personnel contamination resulting from or related to CRM;
E. Review and administer the COMS Incident Reporting and COMS Clinical Trial policies.

Harvard COMS Office of Biological Safety

Harvard's COMS Office of Biological Safety, located at Harvard Medical School, bears administrative responsibility for COMS, and shall:

A. On behalf of all COMS-Affiliated Institutions, file an annual report with the NIH Office of Science Policy (OSP) that includes: (i) a roster of all COMS members clearly indicating the Chair, contact person, BSOs, plant expert (if applicable), animal expert, and experts in human gene therapy; and (ii) biographical sketches of all COMS members.
B. Make available to the public all COMS meeting minutes and any documents submitted to or received from federal funding agencies that these agencies are required to make available to the public;
C. Supply an annual report for the Boston Public Health Commission (BPHC) which includes: (i) a list of recombinant or synthetic nucleic acid molecules studies approved by COMS;

(ii) a roster of all COMS members; and (iii) minutes of COMS meetings.

D. Supply an annual report for the Cambridge Biosafety Committee (CBC) which includes: (i) a list of recombinant or synthetic nucleic acid molecules studies approved by COMS in the City of Cambridge; and (ii) a roster of all COMS members.
E. Notify Principal Investigators of the results of COMS review of their research proposals;
F. Establish mechanisms for communication between COMS and the relevant Institutional Review Boards (IRB) and Institutional Animal Care and Use Committees (IACUC);
G. Ensure biological safety laboratory inspections occur in accordance with the COMS Laboratory Inspection policy;
H. Ensure reporting of laboratory incidents per COMS Incident Reporting Policy and Clinical Trial Studies;
I. Maintain a secure electronic database for COMS protocol documentation;
J. Appropriately archive COMS records, including:
    1. Records of research projects reviewed by COMS;
    2. COMS minutes; and
    3. Other documents related to COMS activities.
K. Monitor national, state, and local regulatory trends and communicate any changes to the Biosafety Officers and responsible institutional representatives;
L. Develop CRM training materials.

Institutional Biological Safety Officers (BSOs)

Harvard and COMS-Affiliated Institutions are each responsible for their own compliance with all training and other safety requirements imposed by COMS or by federal, state, or local legislation or regulation. To this end, the Institutional Biological Safety Officers (BSOs) shall, for their own institutions:

A. Act as the primary liaison between the Affiliated Institution and COMS.
B. Assess the risk of proposed research applications and make recommendations to COMS as to appropriate containment, procedures and personal protective equipment;
C. Oversee all spaces where CRM is used in accordance with the COMS Inspection Policy;
D. Immediately report to COMS and their institution any significant problems, violations, or

any significant research-related accidents or illnesses, as defined in the Incident Reporting policy;

E. Develop emergency plans and procedures for handling accidental spills and personnel contamination and investigating laboratory accidents resulting from or related to CRM;
F. Provide advice and guidance on laboratory security;
G. Provide technical advice and guidance to PIs and COMS on research safety procedures;
H. Monitor:
    1. Institutional Animal Care and Use Committee (IACUC) applications;
    2. Institutional Review Board (IRB) applications;
    3. Institutional Material Transfer Agreements (MTAs); and
    4. Grants & Contracts Office submissions.

Principal Investigators

Principal Investigators are responsible for registering and performing research and teaching in compliance with all federal, state, local, and institutional (including COMS) safety regulations. For COMS registration purposes, principal investigators should have a faculty appointment at Harvard University or meet their institutional definition of a principal investigator. Directors of teaching laboratories and core facilities may also serve as Principal Investigators for COMS registrations. Instructors/Professors that will be leading classes and/or managing educational programs, must be registered prior to using materials that fall under the COMS definition of CRM. Non-faculty members may be designated as Principal Investigators for COMS registrations following approval from COMS Leadership (in consultation with the institution). COMS may grant an exception to the PI eligibility requirement. If determined to be appropriate, such exceptions will be made on a case-by-case basis.

A. In general, a PI shall:

1. Obtain COMS approval before purchase, receipt, storage, initiation, or modification of all research or teaching involving CRM;
2. Ensure that all staff listed have access to the currently approved protocol and have read the protocol before beginning work

3. Any teaching labs that involve the use of CRM will need to be registered prior to commencement of work.
4. Immediately report any significant problems, violations, or any significant research-related accidents or illnesses to their Institutional BSO, and work with COMS to report to applicable governmental agencies, following the COMS Incident Reporting and Clinical Trial policies;
5. Make sure that they and their staff have received adequate training on good microbiological techniques;
6. Adhere to institutional emergency plans and procedures for handling accidental spills and personnel contamination resulting from or related to recombinant or synthetic nucleic acid molecules or infectious agent research;
7. Comply with all applicable federal, state, and local regulations requirements for CRM.

B. Before initiating research or teaching involving CRM, the PI shall:
   1. Complete a registration form with COMS.
   2. Make an initial determination of whether the project involves CRM, Gene Drive, Dual Use Research of Concern (DURC), or pathogens of enhanced pandemic potential (PEPP);
   3. Make a determination as to the required levels of physical and biological containment in accordance with the NIH Guidelines;
   4. Select appropriate microbiological practices and laboratory techniques to be used for the research;
   5. Working with the institutional BSO as appropriate, instruct and train laboratory staff in: (i) protocol; (ii) practices and techniques required to ensure safety; and (iii) emergency plans and procedures for handling accidental spills and personnel contamination resulting from or related to CRM research.
   6. Educate laboratory staff about the reasons and provisions for any precautionary medical practices advised or requested (e.g., vaccinations or serum collection); offer consultation with occupational medicine, immunizations, and medical surveillance in accordance with current regulations and COMS recommendation.
   7. Working with the institutional BSO, to address all aspects of NIH Guidelines and COMS

Policies prior to submission of a clinical trial involving human gene transfer or other CRM (See COMS Clinical Trial Policy).

C. During the conduct of research or teaching involving CRM, the PI shall:

1. Supervise the safety performance of the laboratory or classroom staff to ensure that the required safety practices and techniques are employed;
2. Adhere to the COMS Inspection Policy and work with the Institutional BSO to correct any findings noted during an EHS inspection;
3. Adhere to and enforce the stipulations in the COMS approval letter;
4. If, during the course of experimentation, any evidence is obtained that those experiments may have increased the risk to public health by a particular biological agent or toxin, then all related research must cease immediately, and the isolates must be secured. Observations must also be reported to COMS for further review and evaluation. Continuation of research will require re-approval by COMS.
5. Investigate and report any significant problems pertaining to the operation and implementation of containment practices and procedures as outlined in the COMS Incident Reporting policy;
6. Immediately report to the institutional BSO any work errors or conditions that may result in any accident, injury or the release of CRM and work with the institutional BSO to correct any such errors or conditions;
7. Ensure the integrity of the physical containment (e.g., biological safety cabinets, biological waste containers) and the biological containment (e.g., purity and genotypic and phenotypic characteristics) for CRM.
8. Ensure that all CRM are properly disposed of and accounted for before final study closure or inactivation of the protocol.