OIST

BIOSAFETY MANUAL

OKINAWA INSTITUTE OF SCIENCE AND TECHNOLOGY GRADUATE UNIVERSITY

Table of Contents

PREFACE

The OIST Biosafety Manual is intended to be a resource for information, guidelines, policies, and procedures that will enable and encourage researchers and graduate students who work in the laboratory environment to work safely and reduce or eliminate the potential for exposure to biological hazards. The information presented here also reflects the requirements set forth in statutes and instruments thereof, guidelines of regulatory authorities and OIST rules. It is intended that the Faculty Member, Section Leader and supervisory personnel will supplement this information with instruction and guidance regarding specific practices and procedures unique to the work being done by those in their laboratories.

Your questions, comments and suggestions concerning the Manual are welcomed and can be made on-line at research_safety@oist.jp.

Japanese statues and instruments thereof accessible from links are translated into English and provided to you. Please note that not all of the English texts are prepared by the central government, but some of them are provided by OIST. Both of the English texts are provided only as provisional references, and in some cases, Japanese connotations or implications of wordings in Japanese provisions may not be reflected in their English versions.

I INTRODUCTION

A. SCOPE

This Manual is applicable to all laboratory, research, service and support activities that may involve exposure to biohazardous agents or materials and that come under the purview of the OIST Institutional Biosafety Committee (IBC) or OIST Institutional Human Subjects Research Review Committee (IHC).

Activities specifically addressed are those involving:

☐ Living Modified Organisms
☐ Various bacteria, fungi, parasitic agents and viruses having pathogenicity
☐ Animals and plants being infected by pathogens
☐ Invasive Alien Species
☐ Animals and animal derived materials subject to regulatory control under the Act on Domestic Animal Infectious Diseases Control
☐ Plants, plant pests and soils subject to regulatory control under the Plant Protection Act
☐ Experimentally infected research animals
☐ Blood and body tissue
☐ Any other matters that can cause hazards to human body, the community, and the environment and matters being contaminated by these

The Manual does not address issues of radiation or chemical safety. These are covered in the Rules for Prevention of Radiation Hazards, the Rules for the Management of Chemical Materials, relevant Manuals and Research Safety Section WEB Site. In addition, when conducting Human Subjects Research including the clinical research and the research associated with samples derived from humans and data on humans, also see the Rules for Human Subjects Research, various guidelines concerning bioethics prepared by the central government and Research Safety Section WEB Site. When blood and body tissues of humans and apes are found to be infected by pathogens, handle them in accordance with the BSL of the pathogens. If you are not sure whether they are affected by pathogens, unless otherwise indicated, handle them as BSL2 materials. In addition, provide measures for preventing infection to blood-derived pathogens and toxins.

B. REGULATIONS AND GUIDELINES

Following OIST basic policies, rules and procedures (PRP) and statutes and instruments thereof, regulatory rules and guidelines form the basis for the practices in the Manual.

☐ OIST Rules for Recombinant DNA Experiments
☐ OIST Rules for Biosafety Management
☐ Act for the Conservation and Sustainable Use of Biological diversity through Regulations on the Use of Living Modified Organisms (Cartagena Act)
☐ Act Concerning the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (Infectious Diseases Act)
☐ National Institute of Infectious Diseases (NIID) Safety Management Regulations for Pathogens and Toxins
☐ NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH)
☐ WHO Laboratory Biosafety Manual (WHO)

Before starting any experiment, read carefully OIST rules, statutes and instruments thereof, and any other provisions listed above and familiarize yourself with the contents.

Cartagena Act:

- ☐ Procedures pertaining to the Type 1 Use (for works performed outside laboratory rooms)
  Approval of Institutional Rules for Type 1 Use by the competent minister, Biological Diversity Risk Assessment Report, etc.
- ☐ Procedures pertaining to the Type 2 Use (for works performed inside laboratory rooms)
  Containment measures
- ☐ Institutional Biosafety Program
  Establishment of committee
  Appointment of an expert member
  Education and Training
  Establishment of reporting and communication system under emergency
- ☐ Procedures pertaining to the importation/exportation of Living Modified Organisms
- ☐ Provision of information on Living Modified Organisms

Infectious Diseases Act:

- ☐ Select Biological Agents and Toxins are classified into four categories, namely, Type 1 to Type 4, and importation, transfer/receipt, transport, etc. thereof are controlled in accordance with the Type. It also provides criteria for several requirements in relation to pathogens, such as facility, storage, use, transport and disinfection requirements.

National Institute of Infectious Diseases (NIID) Safety Management Regulations for Pathogens and Toxins:

- ☐ Management structure to secure the safety of Pathogens and Toxins
- ☐ Biosafety Level (BSL)/Animal Biosafety Level (ABSL) classifications
- ☐ Standards for safety facility, equipment and operation concerning laboratory rooms

Obtaining, possession, use, or transfer of any Select Biological Agents and Toxins is strictly regulated by Infectious Diseases Act. It requires government permits and inspection as well as significant measures of lab security, personnel training, and accurate record keeping regarding the status of possessed Select Biological Agents and Toxins.

Handling and disposal of biohazards is regulated and monitored by the Ministry of the Environment and must be performed in compliance with the OIST Rules for the Management of Wastes, the OIST Manual for the Management of Wastes and the Manual on Disposal of Infectious Wastes based on the Waste Disposal Act (Ministry of the Environment).

The requirements for packaging and shipment of biological materials are provided in the Postal Act and Terms and Conditions of Domestic Postal Services for domestic transport and in the Universal Postal Convention of the Universal Postal Union, WHO Guidance on regulations for the Transport of Infectious Substances for transnational transport. In addition, air transport must be carried out in accordance with the provisions of IATA Dangerous Goods Regulations. Information on shipping procedures that comply with these regulations is found at Research Safety Section WEB Site.

C. THE BIOLOGICAL SAFETY PROGRAM AT OIST

The biological safety program at OIST developed from the OIST's commitment to address and comply with the relevant Acts and Guidelines to ensure a higher level of safety. The key components of the program for ensuring the higher safety level are:

- ☐ OIST Institutional Biosafety Committee
- ☐ Research Safety Section Leader
- ☐ Biosafety Officer
- ☐ Faculty Member, Section Leader and Lead Investigator
- ☐ Laboratory worker
- ☐ Health Center

The roles and responsibilities of each are described below:

OIST Institutional Biosafety Committee:

The membership of OIST Institutional Biosafety Committee includes representative faculty, persons from outside the OIST who have excellent knowledge of Biosafety. The committee's current membership is listed on the Research Safety Section WEB Site. The main responsibilities of IBC are:

☐ Reviewing experimental protocols regarding Living Modified Organisms and Pathogens and Toxins.
☐ Reviewing the implementation and termination report.
☐ Advising about rules, manuals and personnel training concerning biological materials.

Research Safety Section Leader

The Research Safety Section Leader manages and supervises the implementation of experiments involving biological materials to ensure the overall safety of the research, and manage the procedures to establish necessary facilities and equipment for safe and proper implementation of experiments.

Biosafety Officer

☐ Provides a pre-application review of experimental protocols involving biological materials to ensure compliance with statutes and instruments thereof and OIST institutional rules, and advises the Lead Investigator as necessary.
☐ Establishes plans for renovations of experimental facilities and equipment as necessary, in order for the proper implementation of experiments involving biological materials.
☐ Provides necessary personnel training to the Lead Investigator, researchers and students.
☐ Confirms that experiments involving biological materials are conducted according to the approved experimental protocols.

Faculty Member, Section Leader and Lead Investigator

☐ Completes applications for all research projects involving the use of biological materials.
☐ Accepts direct responsibility for the health and safety of those working with biological materials in his/her laboratory.
☐ Ensures proper lab orientation, training and instruction for laboratory worker in safe practices and protocols, including instruction in good microbiological techniques and handling needed to work safely with the biological materials involved.
☐ Ensures that laboratory worker receives any necessary medical surveillance.
☐ Ensures compliance by laboratory worker with the relevant rules, regulations, guidelines and policies.
☐ Ensures biosafety cabinets are equipped as needed.
☐ Ensures personal protective equipment is provided and used.
☐ Reports immediately to Biosafety Officer and Research Safety Section Leader any significant violations of statutes and instruments and guidelines, problems with containment measures and any significant research-related accidents and biohazards.

Laboratory Worker：

☐ Participates in appropriate personnel training and acts as trained.
☐ Becomes familiar with biological materials being used in the lab and the potential risks associated with exposure.
☐ Follows laboratory practices and protocols.
☐ Complies with applicable OIST rules and manuals, statutes and instruments thereof and guidelines.
☐ Completes any necessary medical surveillance.
☐ Reports accidents, spills, or contamination incidents to Lead Investigator.

Health Center

☐ Provides first-aid measures to any injured personnel and makes an appropriate arrangement such as medical review and transfer to medical institutions.
☐ Provides special medical examination.

D. OIST INSTITUTIONAL RULES, INTERNATIONAL GUIDELINES AND RELEVANT STATUTES AND INSTRUMENTS THEREOF

OIST Institutional Rules

- ☐ OIST Recombinant DNA Experiments Rules.
- ☐ OIST Biosafety Management Rules.
- ☐ OIST Institutional Biosafety Committee Rules.

International Guidelines

- ☐ NIH Guidelines for Research Involving Recombinant DNA Molecules
- ☐ WHO Laboratory Biosafety Manual

Relevant Statutes and Instruments thereof and the equivalents

Statutes and Instruments thereof, etc. concerning Recombinant DNA Experiments

- ☐ Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms
- ☐ Implementing Regulations for the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms
- ☐ The Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms for Research and Development
- ☐ Matters to Specify Certified Host-Vector Systems in accordance with the Provisions of the Ministerial Ordinance Stipulating containment Measures to Be Taken in Type 2 Use of Living Modified Organisms
- ☐ Explanation of the "Public Notice amending a part of the Matters to Specify Certified Host-Vector Systems in accordance with the Provisions of the Ministerial Ordinance Stipulating Containment Measures to Be Taken in Type 2 Use of Living Modified
- ☐ Basic Matters under the Provisions of Article 3 of the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms
- ☐ Materials for explaining the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the
- ☐ A Guide for "R&D Type 2 Ministerial Ordinance"
- ☐ Containment Measures Check Lists
- ☐ Applicant's Manual for Certification of Containment Measures in Type 2 Use
- ☐ Cases of Stipulations Violation the Act

Statutes and Instruments concerning Pathogens and Toxins

- ☐ Act Concerning the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases
- ☐ National Institute of Infectious Diseases Safety Management Regulations for Pathogens and Toxins
- ☐ BSL Classification

Other Relevant Statutes and Instruments thereof

- ☐ Invasive Alien Species Act
- ☐ Act on Domestic Animal Infectious Diseases Control
- ☐ Plant Protection Act
- ☐ Act on the Protection of Fishery Resources

Ⅱ Research Project Application and Approval

A. INTRODUCTION

Faculty Members and Lead Investigators are responsible for the preparation of an application for all research involving Living Modified Organisms and Pathogens and Toxins (biological materials) including the required Protection Level of containment measures and Biosafety Level (BSL) for Pathogens and Toxins to the proposed research. Applications are required for the following:

☐ Living Modified Organisms
☐ Pathogens and Toxins: Viruses, bacteria, fungi, parasites, prions, and toxins produced by microorganisms, which constitute factors hazardous to the human body, society and the environment as well as materials contaminated with these items.
☐ Blood and body tissue

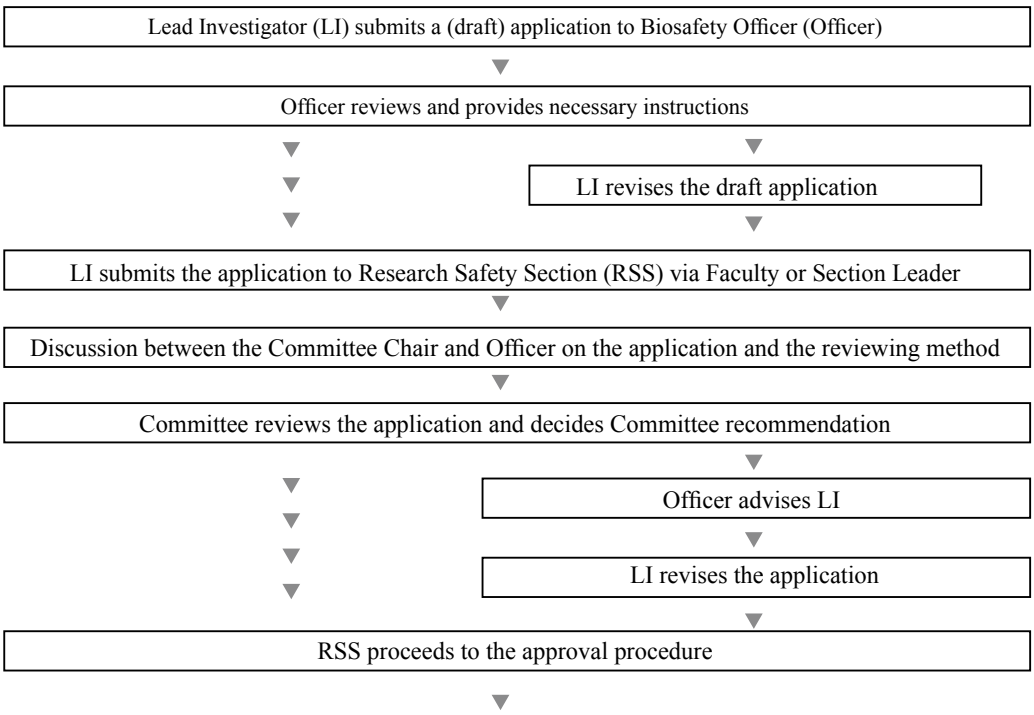
OIST Institutional Biosafety Committee (IBC) reviews all of the application forms submitted. In order for an application form to be reviewed by the IBC, it must meet formal requirements and provide measures for securing safe handling of materials involving biohazards with indication of appropriate Protection Levels of containment measures and Biosafety Levels (BSL).
When applying for Recombinant DNA Experiment using pathogens (Select Biological Agents and Toxins provided for in the Infectious Diseases Act and Pathogens and Toxins of BSL2 or above), submission of an application form for Recombinant DNA Experiment will suffice.

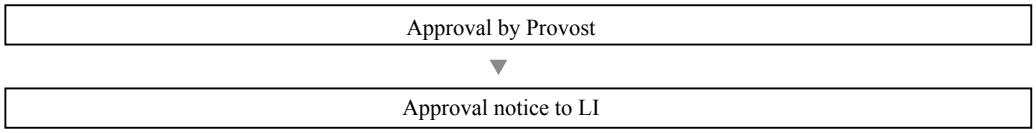
When applying for Human Subjects Research and the use of samples derived from humans, see OIST Rules for Human Subjects Research.

B. APPROVAL PROCESS

The Approval process is initiated by submission of a draft application form to the Biosafety Officer for experiments involving biological materials. No experiment can be commenced unless approval is obtained.
The chart provided below indicates the steps involved in this process:

Approval process for application





In addition, when an experiment and research in operation is completed/terminated or discontinued, submission of a Termination Report is required.
When continuing (renewing) an approved application, an application for renewal with addendum of a "Status Report" must be submitted before the scheduled date of the Committee meeting immediately before the expiry date of the approval.

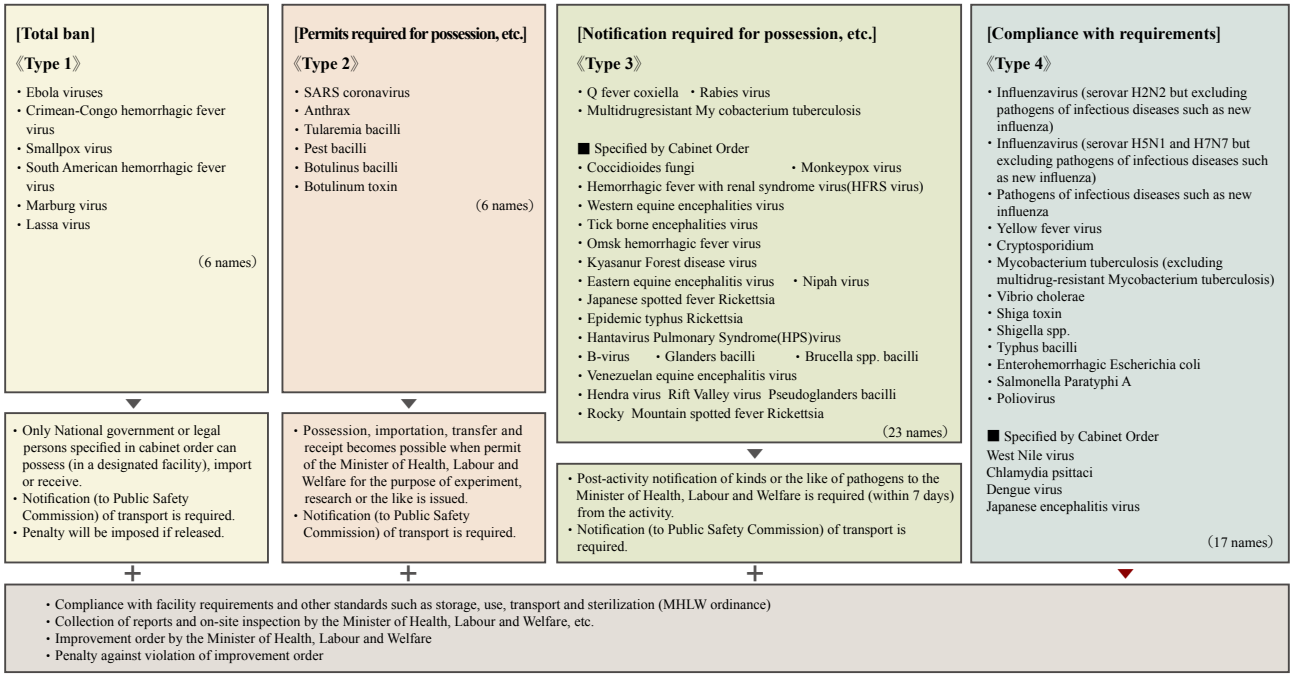
Copies of the application forms can be downloaded from the Research Safety Section WEB Site. The WEB Site also provides applicable OIST rules and manuals, relevant statutes and instruments thereof, guidelines and other reference materials which may be useful for preparing an application. When determining an appropriate Protection Level of containment measures and Biosafety Level (BSL), see relevant ministerial ordinances and the BSL Classification provided in the National Institute of Infectious Diseases Safety Management Regulations for Pathogens and Toxins.

C. ADDITIONAL APPROVALS AND REQUIREMENTS

Type 1 Use of Living Modified Organisms, and Pathogens and Toxins of P3 and BSL3 or above
At OIST, researchers can only carry out experiments that fall under Recombinant DNA Experiments of Type 2 Use (work involving handling of Living Modified Organisms within the environment provided with required containment measures such as in a laboratory room) stipulated in the Cartagena Act. In order to perform Type 1 Use of Living Modified Organisms (works involving handling of Living Modified Organisms without providing containment measures such as performing plant cultivation tests in the field), OIST needs to prepare a new internal Rules and receive approval by the competent minister.
In addition, facilities for experiments of P3 or BSL3 levels or above have not been established yet (a space is reserved but facility requirements such as airlocks and sterilization equipments have not been installed yet). Thus, if any of you have a plan to carry out such experiment, consult with the Research Safety Section promptly.

Select Biological Agents and Toxins
The Ministry of Health, Labour and Welfare stipulates Select Pathogens and Toxins (Type 1, Type 2, Type 3 and Type 4 Pathogens and Toxins) as those having pathogenicity and considered to be potential risks on human life and health and provides a list thereof in Infectious Diseases Prevention Act. Activities such as possession, importation, transfer, acquisition, personnel training, disinfection, record keeping, facility requirements, storage requirements and transport of Select Pathogens and Toxins are subject to regulatory control. Failure to comply with the established regulations can result in significant civil and criminal penalties.
Therefore, any Faculty Member, Section Leader or Lead Investigator considering the acquisition, holding and use of certain Select Pathogens and Toxins must contact the Biosafety Officer to discuss the specifics of the requirements.
In determining whether to use Select Pathogens and Toxins, researchers are encouraged to give careful consideration to the personal responsibilities, financial costs, and lengthy application and permit process involved with compliance. It should be noted that any plans for use of certain Select Pathogens and Toxins could easily take several months to get the appropriate permits and approvals and establish the security and protocols necessary to comply with the regulatory requirements. If any plan involves Type 1 and Type 2 Pathogens and Toxins, in particular, be fully aware of these requirements.

Overview of comprehensive measures for the prevention of infectious diseases and appropriate management of Select Pathogens and Toxins



Live Viruses

Individuals who will be working with certain live pathogenic viruses in the laboratory must complete medical review and informed consent process where necessary prior to such work. Contact Biosafety Officer for further information and directions for completing this process.

In addition, a worker who works with live pathogenic viruses must confirm risks of such viruses, safety precautions and emergency measures prior to the work, obtaining information from Faculty Member, Section Leader or Lead Investigator.

A worker who works with said viruses must inform the Faculty Member or Section Leader and follow instructions thereof when the worker:

☐ Becomes pregnant;
☐ Is exposed to live pathogenic virus by accident or injury; or
☐ Has a change in immune status.

Blood and Body Tissue

In cases, where work involves the use of blood, body fluids or unfixed human tissue, there is the danger of exposure to bloodborne pathogens. Work with any of these materials in a laboratory setting requires that Laboratory staff be enrolled in the Bloodborne Pathogens Program.

Work with any of the bloodborne pathogens requires each research unit to develop an Exposure Control Plan that documents how the risk of exposure will be reduced or eliminated. Specifically, the Plan describes the followings:

☐ Persons who have potential risks of exposure to blood and live tissues and tasks or duties that may cause exposure to these
☐ Engineering and work practice controls in place
☐ Personal protective equipment provided and used
☐ Good housekeeping practices initiated
☐ Hepatitis B (HBV) vaccination
☐ Medical follow-up after exposure
☐ Proper hazard signage and labeling
☐ Record-keeping
☐ Personnel training for workers

Individuals who have potential risks of exposure must participate in the personnel training provided by the Faculty Member, Section Leader or Lead Investigator on the following matters:

☐ Work procedures for the protection against bloodborne pathogens;
☐ Appropriate personal protective equipment;
☐ Safe work practices; and
☐ Reporting all exposures to Health center.

In addition, when human blood or tissue donors are involved, the Faculty Member, Section Leader or Lead Investigator must take the following measures in accordance with the OIST Human Subjects Research Rules:

☐ Submits the application for approval of research plan to the OIST Institutional Human Subjects Research Committee via Research Safety Section; and
☐ Gets the informed consent of prospective donors.

Donors will not be able to donate without the informed consent. In addition, drawing of blood must be performed only by those having required qualification such as a physician and nurse.

Biohazards Associated with Animal Handling

When research involves handling of laboratory animals, laboratory worker must be aware of the potential allergens, zoonoses and physical hazards, e.g. bites and scratches, which may be encountered by researchers and staff.
If any researcher desires to handle laboratory animals, please contact the Animal Resources Section prior to the handling, as such handling requires participation in an orientation session and submission of an application.

Security Trade Control

The “Foreign Exchange and Foreign Trade Control Act” (Foreign Exchange Act) stipulates export control on weapons, general-purpose goods which are likely to be diverted to weapons, general-purpose goods which can be used to develop weapons and all goods that are likely to be diverted to weapons of muss destruction. Researchers must note that the scope of export control covers biological agents such as some of pathogens and toxins. In addition, the scope of exportation is not limited to the export of actual goods but also covers the provision of technologies such as know-how and protocols. Goods and technologies subjected to this control are classified into List Control and Catch All Control.

Ⅲ Working Safely with Biological Materials and Biological Safety Levels

A. EXPOSURE CONTROL

The term "containment" is used in describing safe methods for managing infectious agents in the experiment areas where they are being handled or maintained. The purpose of containment is to reduce or eliminate exposure of laboratory workers and any other relevant personnel, and the outside environments to potentially hazardous agents.
The three elements of containment include laboratory practice and technique, safety equipment, and facility design.

■ Safe Laboratory Practice and Technique
The most important element of containment is strict adherence to appropriate procedures and techniques for handling biological materials. Persons working with infectious agents or infected materials must be aware of potential hazards, and must be trained and proficient in the practices and techniques required for handling such material safely. The Faculty Member, Section Leader and Lead Investigator are responsible for providing or arranging for appropriate training of laboratory workers.

The Faculty Member, Section Leader and Lead Investigator should identify specific hazards that will or may be encountered, and consider practices and procedures needed to minimize or eliminate risks. Personnel should be advised of special hazards and are expected to follow the required practices and procedures.

■ Safety Equipment (Primary Barriers)
Safety equipment includes biological safety cabinets, enclosed containers, and other engineering controls designed to eliminate or minimize exposures to hazardous biological materials. The biological safety cabinet (BSC) is the principal device used to provide containment of infectious splashes or aerosols generated by many microbiological procedures. More information on BSCs may be found in Section IV B.

Safety equipment may also include items for personal protection such as personal protective clothing, respirators, face shields, safety glasses or goggles. In some situations, personal protective clothing may form the primary barrier between personnel and the infectious materials.

■ Facility Design (Secondary Barriers)
The design of a facility is important in providing a barrier to protect those working inside and outside the laboratory and to protect people or animals in the community from infectious agents which may be accidentally released from the laboratory.
Facilities must be commensurate with the laboratory's function and the recommended Protection Level of containment measures and Biosafety Level for the agent being manipulated. Specific safety requirements for facility design are found in “Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms for Research and Development”, “Technical standards for positions, structures and installations provided for in the Act Concerning the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases” and “Standards for safety facility provided for in the National Institute of Infectious Diseases Safety Management Regulations for Pathogens and Toxins”.

The secondary barrier(s) needed will depend on the risk of transmission of specific agents. For example, all OIST research falls within the Protection Levels of 1 and 2, and Biosafety Levels of 1 and 2 at present and exposure risks involve direct contact with the agents, or inadvertent contact in experiment areas. Secondary barriers in these laboratories include separation of the laboratory work area from public access, availability of inactivation equipment (e.g., autoclave), hand washing facilities and disinfectants.

B. LABORATORY BIOLOGICAL SAFETY LEVELS

There are two kinds of Biological Safety Levels. One is the Experiment Classification which applies to Recombinant DNA Experiment and defines Class 1 to Class 4 depending on the pathogenicity to Mammalian and Avian species. Taking into consideration the combination of Classes of Experiment Classifications of nucleic acid donor organism and host and other conditions, one of the four Protection Levels of containment measures from P1 to P4, is determined. The other is the Biosafety Level, which defines four risk levels from BSL1 to BSL4, depending on the risk revels on human life and health and applies to Pathogens and Toxins. These two biological safety levels are likely to be compatible in terms of risk levels, facility requirements and so on. However, it should be noted that some of the microorganisms are classified differently between these two Biological Safety Levels.

Living Modified Organisms

Experiment Classifications of nucleic acid donor organism and host which are Living Modified Organisms are provided for in the "Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms for Research and Development" which is one of the instruments of the "Cartagena Act".

Experiment Classification:

Class 1	Of microorganisms, mushrooms and parasites, those which are not pathogenic to animals belonging to Mammalia and Aves (including Homo, Hereinafter "mammals") and are stipulated by the Minister of Education, Culture, Sports, Science and Technology, animals (including Home and excluding parasites) and plants
Class 2	Of microorganisms, mushrooms and parasites, those which are low in pathogenicity to mammals and are stipulated the Minister of Education, Culture, Sports, Science and Technology
Class 3	Of microorganisms and mushrooms, those which are high in pathogenicity to mammals and low in propagation and are stipulated by the Minister of Education, Culture, Sports, Science and Technology
Class 4	Of microorganisms, those which are high in pathogenicity to mammals and high in propagation and are stipulated by the Minister of Education, Culture, Sports, Science and Technology

Specific names of living organisms according to the Classes above are listed in the Appendix 2 of the "Matters to Specify Certified Host-Vector Systems in accordance with the Provisions of the Ministerial Ordinance Stipulating Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms for Research and Development".

After reviewing and confirming the Classes in the Experiment Classification for the nucleic acid donor organism and the host, a Protection Level of containment measures to be taken (one of P1 to P4) should be determined. Although specific containment measures to be taken are different among experiments using microorganisms, large scale culture experiments, experiments using animals and experiments using plants, basic matters to consider are same among all experiments. Determination of containment measures must be made considering various conditions, which is a very complicated task.
If anything is unclear, consult Biosafety Officer (research_safety@oist.jp).

How to determine the containment measures :

① Class of host/donor organism and Protection Level of containment measures are same:
Where one of ② to ③ is applicable.
Measures to be taken:
Take containment measures of the same number as the Class in the Experiment Classification for either host or nucleic acid donor organism, which is not smaller than the other. However, if the Experiment Classification for transgenic animals producing experiment or transgenic plants producing experiment, numbers for the Experiment Classification for the host and the Protection Level of containment measures should be equal.

② Class of host/donor organism is higher than Protection Level of containment measures:
Where a Certified Host-Vector System is used.
Measures to be taken:
Take containment measures of Protection Level 1 when the Experiment Classification of nucleic acid donor organism is Class 2 or lower, or take containment measures of Protection Level 2 when nucleic acid donor organism is of Class 3.

③ Class of host and Protection Level of containment measures are same:
Where using identified donor nuclei acids in which irrelevance to pathogenicity and transmissibility to mammals can be inferred.
Measures to be taken:
Take containment measures of Protection Level 2 or 1, when the Experiment Classification of host is Class 2 or 1.

④ Class of host/donor organism is lower than Protection Level of containment measures:
Where without using Certified Host-Vector Systems, in which to pathogenicity and transmissibility to animals and ability of causing relevance significant increase to mammal host's pathogenicity can be inferred.
Measures to be taken:
Take containment measures of Protection Level 2 or 3, when either the Experiment Classification of host or that of nucleic acid donor organism whichever is smaller is Class 1 or 2. However, if the Experiment Classification involves transgenic animals producing experiment or transgenic plants producing experiment, take containment measures of Protection Level 2 or 3 when the Experiment Classification of host is Class 1 or 2.

⑤ Original containment measures:
When all conditions below are met:

Large scale culture experiment:

- LMOs using Certified Host-Vector Systems
- Nuclei acid donor organisms are of class 1
- Identified donor nuclei acid
- Irrelevance to pathogenicity and transmissibility to mammals can be inferred in light of scientific knowledge.

► **L S C**

Experiment using animals:

- Identified donor nuclei acid, for which irrelevance to pathogenicity and transmissibility to mammals can be inferred in light of scientific knowledge.
- Donor nucleic acids integrated in nucleic acids of chromosomes of hosts and without containing transposable elements.
- It is inferred in light of scientific knowledge that the kinetic ability related to escape does not increase in comparison with that of host.
- Animals without carrying living modified organisms of microorganisms.

► **Specified Breeding Section**

Experiment using plants:

- Identified donor nuclei acid, for which irrelevance to pathogenicity and transmissibility to mammals can be inferred in light of scientific knowledge.
- Donor nucleic acids integrated in nucleic acids of chromosomes of hosts and without containing transposable elements.
- It is inferred in light of scientific knowledge that the dispersibility and hybridity of pollen, spores and seeds (hereinafter referred to as "pollens") do not increase in comparison with that of host.
- Plants without carrying living modified organisms of microorganisms.

► **Specified Screened Room**

Facility requirements for the P1 level are not so strict that ordinary biological laboratories can meet the requirements. As for P2 level, unless otherwise indicated, a safety cabinet and an autoclave must be installed. In addition, experiments in P2 facilities must be carried out in a closed room, not in an open lab.
Please review Appendix 2 of the Type 2 Use Ministerial Ordinance and confirm the details of containment measures of P1 to P4.

Pathogens and Toxins

The National Institute of Infectious Disease (NIID) has established four levels of Biosafety, based on the degree of hazard associated with an organism, to describe the combination of laboratory practices and techniques, safety equipment, and facilities needed to protect against exposure. These four Biosafety Levels (BSL) require successively more restrictive practices and facilities as work moves from the least restrictive BSL1 to work with the highest hazard level of BSL4. Exposure to biohazardous agents is intended to be prevented or limited by establishing and following the appropriate BSL practices and conditions. Research in OIST facilities is currently limited to BSL1 and BSL2. (See the BSL list provided in the NIID regulations.)

BSL1 applies to the basic level of containment and essentially represents good microbiological practice with no special primary or secondary barriers required. This applies to work with defined and characterized strains of viable microorganisms not known to consistently cause disease in healthy adult humans. This includes such organisms as the bacteria Bacillus subtilis, non-pathogenic strains of E. coli and yeast.

BSL2 applies to work with a broad spectrum of moderate-risk agents that are generally present in the environment at large and are associated with human disease of varying severity.

All of the viral agents used in research, such as adenovirus, cytomegalovirus, and other herpes viruses fall within the BSL2 level of work. Other microorganisms assigned to this containment level include salmonella spp., toxoplasma spp., hepatitis B, and proliferation deficient strains of HIV. With the use of good microbiological techniques, much of this work can be done on open bench tops as long as there is limited potential for splashes and aerosol creation. However, work inside a biosafety cabinet is strongly recommended, as long as it is applicable. In addition to BSL1 conditions, this level of work also requires that:
☐ Laboratory workers have specific training in handling any pathogenic agents used
☐ Access to the laboratory is limited when BSL2 work is being done
☐ Gloves and other suitable personal protective equipment are worn
☐ Extreme precautions are taken with contaminated sharps
☐ Biological Safety cabinets are used when there is potential for splash or aerosol creation

BSL3 and BSL4 apply to work with exotic agents of increasingly greater potential for causing serious human illness or death. No work at the BSL3 or 4 is currently being done and facilities that would meet the requirements of these biosafety levels are not available at OIST. In order to conduct BSL3 experiments, installations and equipments must meet a higher level of biosecurity, and thus, contact Research Safety Section promptly, as soon as your intended experiment project becomes tangible.

A summary of requirements at each laboratory biosafety level can be found at “Safety installations and administrative guidelines for laboratory handling pathogens and toxins (NIID)”.

C. ANIMAL BIOSAFETY LEVELS (ABSL)

A similar set of four biosafety levels are provided for work with vertebrate animals infected with agents which may infect humans. These Animal Biosafety Levels, ABSL 1 to ABSL 4, provide standardized practices, equipment, and facilities that are comparable to the laboratory biosafety levels described above. However, there are unique hazards associated with infected animals that must be understood by those personnel with animal contact and addressed in the animal facility. Animal activity can create aerosols and bites and scratches can occur.

Please contact Animal Resources Section or Animal Experiment Coordinator at cm@oist.jp for further information.

Ⅳ LABORATORY PROCEDURES AND EQUIPMENT

A. GUIDELINES FOR GOOD LABORATORY PRACTICES IN RECOMBINANT DNA EXPERIMENT AND EXPERIMENT HANDLING PATHOGENS AND TOXINS

(This section is prepared based on the OIST institutional rules, the Cartagena Act, the NIID Safety Management Regulations for Pathogens and Toxins, WHO Laboratory Biosafety Manual and the NIH Guidelines for Research Involving Recombinant DNA Molecules.)

*Indented and bulleted items indicate additional requirements for work at P2/BSL2.

1. Immediately notify Faculty Member(FM), Section Leader(SL) or Lead Investigator(LI) if occurrence of an accident, injury, illness, or overt exposure (spills of research materials) associated with laboratory activities is suspected. And, FM, SL or LI contacts Biosafety Officer. As appropriate, consult Health Center for any necessary medical surveillance and/or treatment at medical institutions.
   Note: By law, OIST is obligated to report to the relevant authorities of any significant research-related accidents/injuries and violations of Cartagena Act and Infectious Disease Act.

2. For those intending to work with Living Modified Organisms or Pathogens and Toxins defined in the OIST Rules for Recombinant DNA Experiment or Biosafety Management, complete the Biosafety training and the required medical review via Health Center as necessary. For certain live virus work, serum draw and preservation thereof may be required depending on the virus involved. Contact Biosafety Officer for details.

3. Be aware that access to the laboratory is limited or restricted at the discretion of ELI when a biological experiment or work with biological materials is in progress. Laboratory should have doors to control access. Laboratories containing materials of P2/BSL2 or above must have security system that can limit access to certain personnel.

5. Understand that the FM, SL and LI must ensure that all laboratory workers receive appropriate personnel training, necessary on-going training, supervision regarding on hazards associated with the agents involved and the necessary precautions to prevent exposures (spills).

6. Understand that personal health status may impact an individual's susceptibility to pathogens, and necessary medical surveillance and any conditions in this regard should be discussed with FM, SL, LI and Health Center as appropriate.

   □ When work involves handling of highly hazardous specific pathogens, additional entry requirements such as appropriate immunizations and serum sampling are imposed. In such a cases, only personnel meeting the specific entry requirements are permitted in the laboratory.

7. Ensure that when infectious agents are in use in the laboratory, an international biohazard warning symbol and sign must be posted on the lab access door. Besides this symbol and sign, such information as room number, name of Pathogens and Toxins, BSL and name of LI and phone number in case of emergency must be indicated in the laboratory.
   For Recombinant DNA Experiments, the proper sign must be displayed on laboratory access doors. Containers, refrigerators and freezers in which Living Modified Organisms or Pathogens and Toxins are placed must be labeled stated sign.

▲ Sign on laboratory access and storages, etc. where Pathogens and Toxins are handled

▲Symbol and sign inside a laboratory room where Pathogens and Toxins are handled

▲Indication on laboratory access for P1 Level Recombinant DNA Experiment

▲Indication on laboratory access for P2 Level Recombinant DNA Experiment

▲ Indication during P2-Level Recombinant DNA Experiment is in operation

▲ Indication on access to transgenic animal breeding section

▲ Indication on container for transporting Living Modified Organisms

▲Indication on storage and freezer for Living Modified Organisms

8. Wash hands frequently with soap and always after handling biological materials, after removing gloves and before leaving the laboratory.
   - ☐ Under emergency situations, use an emergency shower and eye washer where necessary.

9. Do not eat, drink, smoke, chew gum, handle contact lenses, or apply cosmetics in the laboratory. Persons wearing contact lenses in the laboratory should also wear goggles or a face shield.

10. Bringing food, medications or cosmetics into the laboratory is not recommended. Store food outside the experiment areas in refrigerators.

11. Do not pipette by mouth; only mechanical pipetting devices are permitted.

12. Perform all procedures carefully to minimize the creation of splashes or aerosols.

13. Establish and follow policies for safe handling of sharps. Use a high degree of caution when handling any sharp item contaminated biological materials, such as needles and syringes, slides, pipettes, capillary tubes, and scalpels. Substitute plasticware for glass whenever possible. Handle broken glassware with brush and dustpan, tongs, or forceps - not directly with hands.

14. Do not bend, shear, break, recap, or remove used needles from disposable syringes or otherwise manipulate such units by bare hand before disposal. Dispose of needles and syringes in the disposal container provided in the laboratory for this purpose.
   - ☐ Restrict needles and syringes or other sharp instruments in the laboratory for use only when there is no alternative.
   - ☐ Use only needle-locking syringes or disposable syringe needle units (with the integrated needle and syringe) for injection or aspiration of infectious material.

15. Always wear lab coats, gowns, or other designated laboratory uniforms to prevent contamination or soiling of street clothing.
   - ☐ Wear lab coats, gowns, smocks, or other provided protective garments while working with hazardous materials. When leaving the lab, remove and leave coats and other protective clothing in the lab for either disposal or laundering.

16. Wear gloves if the skin on the hands is broken or if a rash is present. Protective eyewear should be worn for procedures that involve anticipated splashes of microorganisms or other hazardous materials to the face.
   - ☐ Wear gloves when manipulating infectious materials or agents or when hands must otherwise contact contaminated surfaces. Remove and change gloves when overtly contaminated or when torn or punctured. Do not wear contaminated gloves outside the lab. Do not wash or reuse disposable gloves. Consider alternatives to latex gloves to prevent allergic response.
   - ☐ Wear appropriate face protection (goggles, mask, face shield or other splatter guard) for anticipated splashes or sprays of infectious materials to the face when agents must be handled outside the BSC. Persons wearing contact lenses should also wear eye protection.

17. Decontaminate equipment and work surfaces at completion of work, at the end of the day, and following spills of biological materials. If a spill occurs, cover the spill with paper towels and soak the towels with a 1 to 10 dilution of chlorine bleach or other suitable disinfectant. Allow the material to soak for approximately 20 minutes before discarding materials in bag with biohazard sticker. Bench tops are impervious to water and resistant to solvents, acids, alkalis, and chemicals used for surface decontamination. Laboratory surfaces and spaces between fixtures are designed to be easily cleaned; no carpets or rugs.

18. Work on open bench tops is permitted; use of special containment equipment such as a biological safety cabinet (BSC) is not generally required for agents assigned to P1 and BSL1.
    □ Work in the open laboratory is permitted, except that a properly maintained biological safety cabinet is required whenever:

    Procedures with a potential for creating infectious aerosols or splashes are conducted. These may include centrifuging, grinding, blending, vigorous shaking or mixing, sonic disruption, opening containers of infectious materials whose internal pressures may be different from ambient pressures, inoculating animals intranasally, and harvesting infected tissues from animals or embryonate eggs.

    High concentrations or large volumes of infectious agents are used . Such materials may be centrifuged in open laboratory if sealed rotor heads or centrifuge safety cups are used, and if these rotors or safety cups are opened only in a biological safety cabinet.

    Be aware that air sampling studies have shown that most of the common manipulations of bacterial and viral cultures in research laboratories release aerosols of viable organisms. This must be considered when evaluating need for use of the biological safety cabinet or other physical containment device.

19. Dispose of all biohazards including potentially biohazardous and associated wastes as outlined in the Manual for the Management of Wastes.
    □ Cover containers of all cultures, tissues, specimens of body fluids, or other potentially infectious waste to prevent leakage during collection, handling, processing, storage, transport, or shipping.

20. Do not bring animals or plants irrelevant to research or experiment into the experiment areas.

B. BIOLOGICAL SAFETY CABINETS (BSCS)

Types of BSCs

BSCs are classified as Class I, Class II or Class III cabinet with Japanese Industrial Standards (JIS) code: K3800-2009. When properly maintained and operated, they effectively contain and capture microbial contaminants and infectious agents using HEPA (High Efficiency Particulate Air) filters. (See Figure 1.)

BSCs should not be confused with clean benches. Unlike a BSC, a clean bench is equipments only designed for preventing contamination of materials being worked with, by providing clean air into the working space, and thus is not intended for worker's safety. Also, some clean benches have air curtains, but they are not equivalent to air barriers of BSCs which satisfy several different microbiological test performances. Air curtains of clean benches are not subject to such microbiological tests and are not suitable for work with infectious or toxic material. (See Figure 2.) (Although clean benches, like BSCs, have HEPA-filtered air, with clean benches the air flows over the experimental material toward the user rather than being drawn away.)

BSCs should also not be confused with conventional fume hoods that do not filter microorganisms.

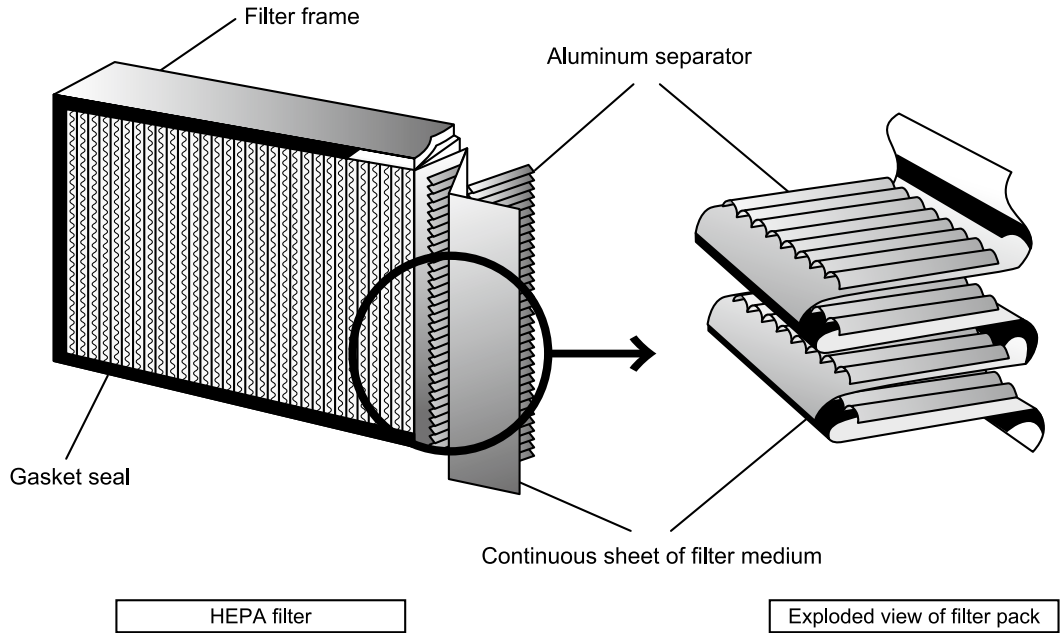


Figure 1. Diagram of HEPA filter.

These filters are typically constructed of continuous sheets of paper-thin filter medium, pleated to increase surface area, divided by aluminum separators, and affixed to a frame. The HEPA filter is a high performance air filter which traps 99.97% or grater of particles of 0.3 μm in diameter at rated air flow, and its initial pressure loss is 245 Pa or less.

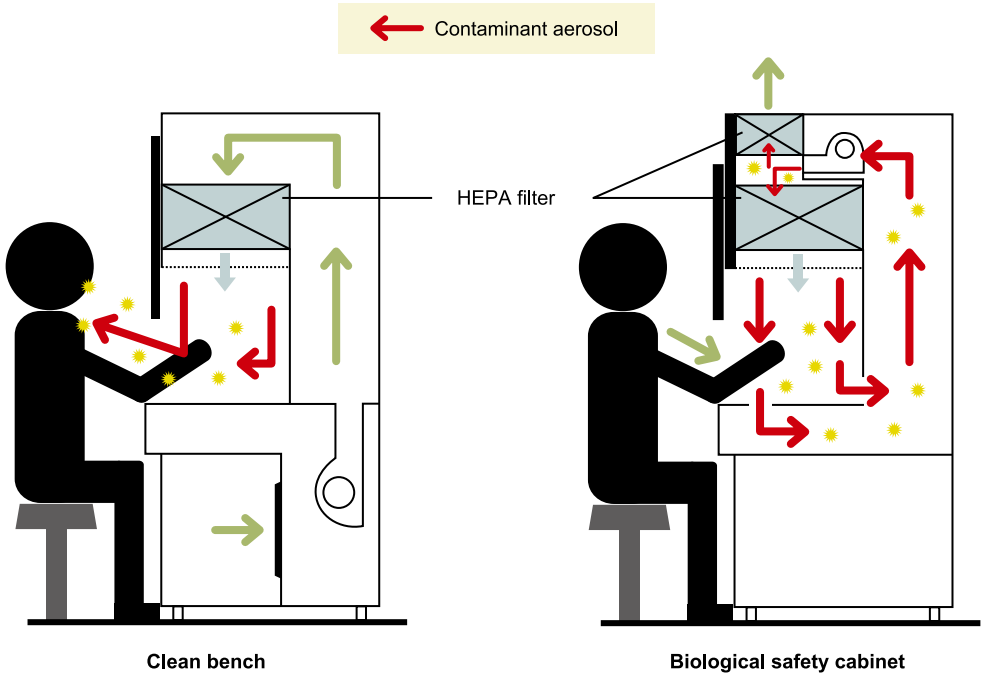


Figure 2. Difference in the structure between clean benches and BSCs

The structure of a clean bench is designed only for keeping specimens free from germs, while the structure of a BSC is, in addition to keeping the germ-free environment for the specimen, because of the introduction of negative pressure, air-barrier (class II) and HEPA filter, a BSC is capable to containing aerosol created in the work area. These two types of equipment are very similar in their appearances but their functions are very different.

Class I BSCs are used for work which does not require clean air in the working space, as they prevent outflow of contaminated aerosol using the inflow of air from the front opening. Thus, they provide personnel and environmental protection, but not product protection. (See Figure 3).

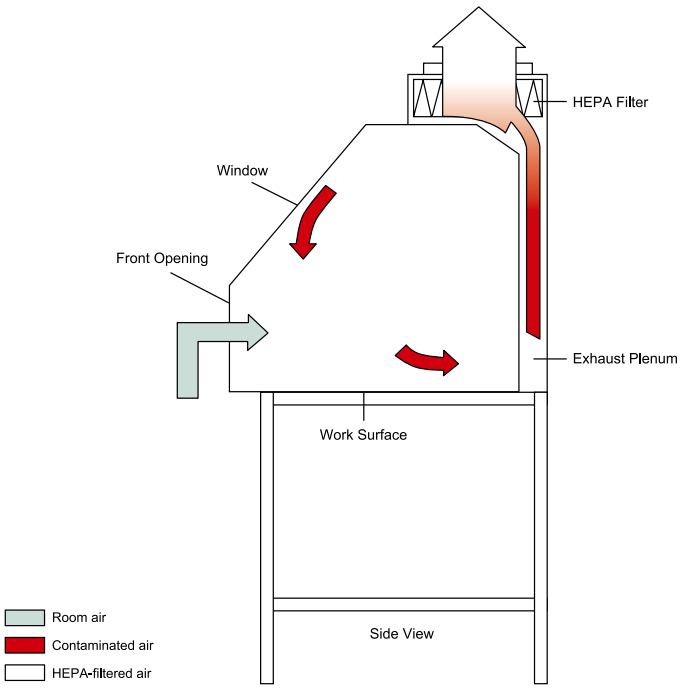


Figure 3. Class I Biological Safety Cabinet

Class II BSCs are the most commonly used BSC on campus. These cabinets provide personnel, environmental and product protection. In class II, HEPA-filtered clean air is supplied to the work space, where the clean air goes toward the work surface and is split into two branched air flows, to the front intake grill and to the rear intake grill located at the far side of the work surface, passes through the fan, and then the HEPA filter for circulation and discharge. Also, the air taken from the front opening goes under the work surface from the front intake grill, passes through the fan, and then the HEPA filter for circulation and exhaust. (See Figure 4.) When using a large volume of volatile flammable chemicals, contact the appropriate section (Facility Operation and Use Section) prior to use, and make sure that there is no problem in terms of structure or facility design.

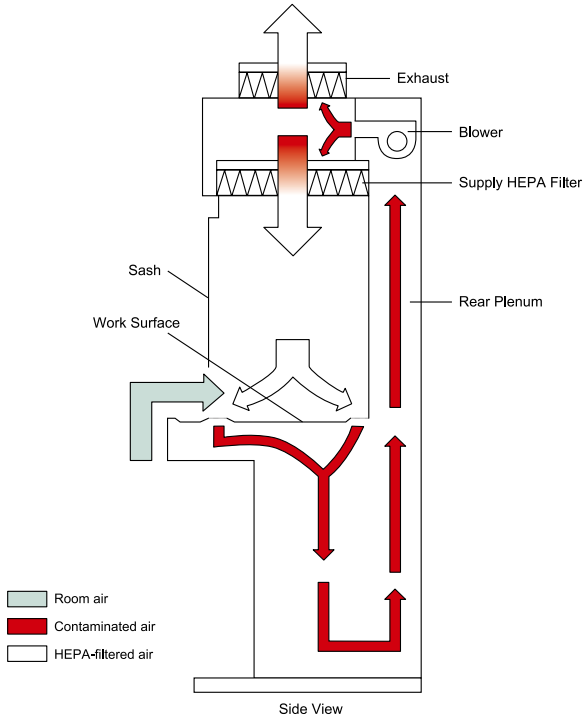


Figure 4. Class II, Type A Biological Safety Cabinet

Working in a BSC：

□ If the BSC is not left running, turn it on (for at least 10-15 minutes) prior to use, so that the internal fan of the BSC becomes stable and the air current from the front opening and the downward air-flow inside the BSC are created soundly.
□ Disinfect (decontaminate) work area (work surface, in particular) with 70% alcohol or other suitable disinfectant.
□ Place all items necessary for the planned BSC work inside the BSC.
□ In order to ensure steady air flow inside the BSC, do not cover the front intake grill and the rear intake grill.
□ Decontaminate the surface of items to bring inside the BSC, and place them so as to function efficiently. Materials and equipments should be placed at the rear side of the cabinet. In particular, aerosol-generating equipments (such as a mixer) should be placed at a place closer to the rear edge without blocking the rear intake grill. In addition, all disposal containers for contaminated items should be placed to one side of the interior of the BSC.
□ Wear appropriate personal protective equipment. At a minimum, this will include a buttoned laboratory coat and gloves.
□ Adjust the working height of the stool so that the worker's face is above the front opening.
□ Manipulations of materials within BSCs should be delayed for about 1 min after placing hands and arms inside to allow the cabinet to adjust and to blow away the dust of the surface of the hands and arms.
□ Minimize the frequency of moving hands in and out of the cabinet. Also, operators need to be careful to maintain the integrity of the front opening air inflow when moving their arms into and out of cabinets, such as moving arms slowly.
□ Work at a moderate pace to prevent the air flow disruption that occurs with rapid movements.
□ All items within BSCs, including equipment, should be surface-decontaminated and removed from the cabinet when work is completed. At the end of the work day, the work surface, the insides, back and interior of the glass should be decontaminated with disinfectants.
□ After wiping with a cloth soaked with disinfectant at the end of the work, before turning off the BSC, it should be run for 5 min in order to purge the atmosphere inside before it is switched off. Shut down the sash of the BSC, light on the UV lamp located in the hood to sterilize the surface inside the hood.

＊ Be very careful when using small pieces of materials such as kimwipes in the hood. These can be blown into the hood and disrupt the motor operations.

Performance test of the BSC

Periodical performance test consists of a series of performance tests on the BSC and confirms that it will provide the user and experimental material the protection for which it is designed. The air flows, filters, and cabinet integrity are checked to ensure that the cabinet meets minimum performance standards. Performance of the BSC is checked by three elements, including sealing capability, HEPA filter, air-flow balance at the front opening. However, these elements cannot be checked visually. Thus, in order to maintain good performance of the BSC, it should be inspected at an appropriate timing with an appropriate method. Performance tests are arranged through Biological Research Resources Section and provided by an outside vendor.

For user protection, BSCs are subject to performance test at the following timings:
・After they are received and installed (before the commencement of use)
・After they are relocated
・After HEPA-filter changes
・Annually for periodical inspection, or twice a year when handling corrosive materials
・After parts replacement; after running conditions change
・When there is any concern on the performance of the BSC

When to decontaminate the BSC (using formaldehyde)
・Before any periodical inspection or maintenance work, such as HEPA filter replacement
・Before disposing of the BSC
・Before moving the BSC to a new laboratory
・At large spills inside the BSC
・At the change of purpose of use
・Where necessary, such as at the performance test

C. DECONTAMINATION

Definitions

Decontamination is a process or treatment that renders an instrument or environmental surface safe to handle. A decontamination procedure can be as simple as cleaning up with detergent and water or as thorough as sterilization. Sterilization, disinfection, and antisepsis are all forms of decontamination.

Sterilization is the use of physical or chemical processes to destroy all microbial life, including highly resistant forms, such as bacterial spores.

Disinfection is the elimination of essentially all pathogenic not-spore-forming microorganisms but not necessarily all microbial forms from work surfaces and equipment. Effectiveness is influenced by a number of factors, including: types and numbers of organisms; amount of organic matter; the object being disinfected; the disinfectant being used; exposure time, temperature and concentration.

Antisepsis is the application of a liquid antimicrobial to the skin or other living tissue to inhibit the growth of or destroy microorganisms. Examples include hand washing with germicidal solutions or swabbing the skin before an injection.

＊ The English and Japanese texts have slightly different definitions. The above reflects the English definitions.

When to Decontaminate

All material and equipment contaminated with or containing potentially infectious agents should be decontaminated:
☐ Upon completion of procedures involving the use of biologically-active materials
☐ In the event of spills of such materials
☐ At least daily
☐ Before being washed, stored, or discarded

In most OIST laboratories, decontamination is accomplished by steam heat sterilization in an autoclave, or by surface application of or placement in a chemical disinfectant solution, such as a 1:10 bleach solution or its equivalent.

Autoclave

Autoclaving (saturated steam under pressure of approximately 15 psi to achieve a chamber temperature of at least 121 ℃ for a designated time) is the preferred and most convenient method to rapidly destroy all forms of microbial life. However, to do this, the autoclave process must reach the proper temperature and time and also prevent air form being trapped in the bag or container of treated material.

☐ The material to be sterilized must come into contact with live steam
☐ Bags or containers should be left open during autoclaving or water (up to 200ml) should be added to sealed bags to generate steam
☐ Heat indicator tape should be used with each autoclave load to indicate that sterilization has been completed
☐ Maintenance work on autoclaves such as repair or replacement of broken or corroded parts is performed by the Biological Research Resources Section through a contract maintenance service. However, each user should also be aware of the importance of securing the securing safety by performing voluntary routine checking of equipment that they use, making sure there is no contamination in the sterilization water, no corroded parts, and such like.

Chemical Disinfectant

The most practical use of chemical disinfectants is for surface decontamination and, when used in sufficient concentration, as a decontaminant for liquid wastes prior to final disposal down the drain.

General recommendations:

Liquid Decontamination:
☐ Add liquid chlorine bleach of one-ninth content of solution so as to provide a final concentration of 10%
☐ Let stand at least 20 minutes
☐ Discard down the drain
☐ Waste water is treated in a water purification treatment process using microorganisms. If discarding a large volume of chlorine bleach, contact the General Facility Management Section in advance.

Surface Decontamination:
☐ Wipe with 1:10 dilution of chlorine bleach, or
☐ Wipe with iodophor disinfectant (per label concentration), or
☐ Wipe with 70% alcohol
☐ Information on disinfectants is found on the Research Safety Section WEB Site.

D. EXPOSURE TO INFECTIOUS AGENTS

In the event of an exposure to (a spill of) an infectious agent or material, the following guidelines must be followed:

Intact skin
☐ Remove contaminated gloves and clothing
☐ Disinfect with 70% alcohol, povidone-iodine agent or others and wash thoroughly with soap and running water
☐ In the event of contamination of broken, cut or damaged skin or a puncture wound, in addition to the above, contact the Health Center and ask for a medical expert where necessary.

Eyes
☐ Immediately flush the eyes for at least 15 minutes with water, preferably using an eyewash; if no eyewash is available, pour water on the eye(s) for 15 minutes, rinsing from the nose outward to avoid contamination of the unaffected eye.
☐ Hold the eyelids away from the eyeball and rotate the eyes so that all surfaces may be washed thoroughly.
☐ Contact the Health Center and ask for a medical expert.

Ingestion or Inhalation
☐ Contact the Health Center to seek medical attention
☐ Do not induce vomiting unless advised to do so by a health care provider

* Report all exposures to the Biosafety Officer via the Faculty Member, Section Leader or Lead Investigator.

E. BIOLOGICAL MATERIAL SPILLS

Spills and Preparing for Them

In the event of a spill of biological material, the individual(s) who caused the spill is responsible for cleaning it up. OIST does not have a spill response team.

☐ Alert people in the surrounding area of the spill incident
☐ Minimize the consequences of any spill of biological material by performing all work on a plastic-backed liner to absorb spills
☐ A spill kit includes the following items:

	Item	#	Picture
1	ChemoPlus ®Gloves (Latex groves)	2	
2	ChemoPlus ®Gown (Gown)	1	
3	Safety glasses	1	
4	Respirator mask	1	
5	Shoe coverings	1	
6	Spill towels	3	
7	ChemoSorb Pads (Absorbents)	2	
8	HAZ-MAT PIG Pillow (Absorbent)	4	
9	Chemo Waste Bags (Bags for disposing wastes)	2	
10	Scoop with detachable scraper	1	
11	KEEP OUT tape	1	

	Item	#	Picture
12	Caution Sign	1	
13	Hydrogen Peroxide Solution	1	
14	20% Chlorhexidine Gluconate Soluton	1	
15	Ethanol for Disinfection	1	
16	Bleach	1	
17	Spray bottle (to prepare working solution of disinfectant)	1	
18	Bucket	1	
19	Tongs	1	
20	Bands to tie waste bags	2	
21	Fire Sand	1	
22	Mercury Collector	1	
23	Popiyodon Scrub 7.5%	1	

Spill Kit List

Spills Inside a Biological Safety Cabinet

☐ Leave the cabinet
While wearing gloves, spray or wipe the cabinet walls, work surfaces, and equipment with disinfectant equivalent to 1:10 bleach solution. If necessary, flood the work surface, as well as drain pans and catch basins below the work surface, with disinfectant for a contact time of at least 20 minutes.

☐ Soak up the disinfectant and spilled material with paper towels. Drain the catch basin into a liquid waste container. Lift the front sash and wipe all surfaces. Ensure that no paper towels or solid debris are blown into the area beneath the work surface

☐ Autoclave clean-up materials before disposal in the Waste Cabinet. Materials including bleach solution must not be autoclaved, otherwise the autoclave may be damaged. Wash hands and any exposed surfaces thoroughly after the clean-up procedure

Spills Outside a Biological Safety Cabinet

☐ P1 Level or BSL1 Spill

1. Alert others in the area of the spill.
2. Remove contaminated gloves, clothing and others. (Disinfect them and discard as wastes as necessary.)
3. Apply 70% ethanol or 7.5% povidone iodine to exposed skin such as hands and arms to disinfect, and then wash them with soak and running water thoroughly.
4. Wear clean personal protective equipment, such as gloves, gown, safety glasses and mask.
5. Cover the spill area and the surrounding area with paper towels dampened with 10% bleach or 70% ethanol or pour disinfectant around and over the spill, and leave them for 20 minutes.
6. In the case of the spill with more than one liter or one kg, report to Lead Investigator and Biosafety Officer.
7. Pick up sharp items, e.g., broken glass or needles, with forceps or appropriate cleanup tools and dispose as recombinant DNA laboratory waste or biohazard. (disinfect or autoclave the wastes as necessary.)
8. Discard disposable materials such as paper towels used to clean up the spill as recombinant DNA laboratory waste or biohazard after disinfecting or autoclaving them as necessary. Disinfect or autoclave any non-disposable materials used.

☐ P2 Level or BSL2 Spill (add followings to P1/BSL1 spill)

1. Alert others in the area of the spill. In evacuating the area, do not inhale aerosol.
2. Close lab door and post a DO NOT ENTER sign.
3. Allow aerosols to settle for at least 30 minutes before reentry to the lab.
4. Follow instructions provided by the Experiment Lead Investigator and the Biosafety Officer and take necessary actions to disinfect the area.

☐ Blood Spill

1. Alert others in the area of the spill.
2. Remove contaminated gloves, clothing and others. Discard them as biohazard.
3. Apply 70% ethanol or 7.5% povidone iodine to exposed skin such as hands and arms to disinfect, and then wash them with soak and running water thoroughly.
4. Wear clean personal protective equipment, such as gloves, gown, safety glasses and mask.
5. Cover the spill area and the surrounding area with paper towels dampened with 10% bleach or 70% ethanol or pour disinfectant around and over the spill, and leave them for 20 minutes.
6. Pick up sharp items, e.g., broken glass or needles, with forceps or appropriate cleanup tools and dispose as biohazard.
7. Discard disposable materials used to clean up or wash the spill as biohazard.
8. Wipe the surrounding area and the spill area again with disinfectant.
9. Disinfect or autoclave any non-disposable materials used.

F. BIOLOGICAL WASTE HANDLING

Recombinant DNA Laboratory Waste

Dispose of items falling under the following categories as “Recombinant DNA laboratory waste”.

☐ Living modified organisms (LMOs) waste
☐ Plastic ware used for recombinant DNA experiments
☐ Other items that contain or are exposed to LMOs

Be sure to sterilize recombinant DNA laboratory waste prior to disposal.
Liquid items ― If the items are completely sterilized by use of autoclaving or appropriate disinfectant, you can dispose of them by placing them in the sink after filtration to each solids. However, if you are discarding wastes containing a large volume of chlorine bleach, contact General Facility Management Section in advance.
Solid item ― After sterilization, dispose of them by placing in the Waste Cabinet with a sticker indicating “Recombinant DNA” laboratory waste on the container or bag.

Biohazards

Some wastes associated with biological materials must be disposed of in special ways because they may have been contaminated with infectious organisms or agents. These biohazards that are potentially infectious and may cause biohazards are defined by OIST institutional rules. These wastes include the following:

☐ Blood, serum, plasma and body fluids
☐ Pathological wastes arising out of an autopsy, etc.
☐ Sharp instruments with blood stains on them
☐ Items used for an experiment involving pathogenic microorganisms
☐ Items that the Special Industrial Waste Officer has deemed must undergo the same treatment as biohazardous wastes

For disposal of these wastes, the laboratory workers should act as follows:

☐ Before disposal, sterilize or disinfect waste materials associated with viral, bacterial or other agents infectious to humans (by autoclave, 1:10 bleach solution or other chemical treatment using appropriate disinfectant) as far as possible
☐ Place all biohazards, except for sharps, directly into the appropriate bag or container with a “Biohazard” sticker attached
☐ Place sharps into labeled sharps containers
☐ Put all the wastes into the waste cabinet as well as other laboratory wastes

IMPORTANT LABELLING REQUIREMENT: Laboratory workers must apply an adhesive-backed sticker with the details filled in to each bag or container (such as autoclaved bags or filled sharps containers) placed into the waste cabinet. The stickers are stocked in the drawer of the waste cabinet. Apply this sticker to all bags and containers placed inside the waste cabinet before they are to be picked up by janitors.

Other wastes generated in the experiment areas are discarded as other categories of laboratory wastes, i.e., special industrial waste, liquid, burnable, glasses and metals. For details of how these various wastes are to be handled in laboratories, see Manual for the management of wastes.

G. PACKAGING AND SHIPPING BIOLOGICAL MATERIALS

Definitions

Packaging and shipping of biological materials must be done in a way that ensures the contents will not leak and that the package will arrive in good condition.
In addition, when shipping biological materials internationally by postal service, the transport must be carried out in compliance with the methods stipulated in the provisions of the Universal Postal Convention of the Universal Postal Union (UPU). Please see the Implementing Regulations concerning ordinary postal service of the Universal Postal Convention for details. Also, if transport is to be carried out by air, the transport must comply with the IATA Dangerous Goods Regulations. In the case of domestic transport within Japan, biological materials may be transported in accordance with the Postal Act and the Terms and Conditions of Domestic Postal Services. Applicable methods in the case of domestic transport by air are almost same as the international rules for transport by air.
As a general rule for transport of goods, the sender (shipper) is responsible for any damage caused by leakages or such like that occur during transport due to inappropriate packaging, excluding incidents of lost or stolen goods.
In addition, in order to prevent biohazards, items must be packed by a researcher or technical staff who is familiar with the contents or the risks involved.

The definitions below apply to the packaging and shipping instructions that follow:

- ☐ Etiologic agent means a viable microorganism or its toxin which causes, or may cause, human disease
- ☐ Diagnostic specimen means any human or animal material including, but not limited to, excreta, secretion, blood and its components, tissue, and tissue fluids, and such like, which is reasonably believed to contain an etiologic agent, and is being shipped for diagnosis purposes
- ☐ Biological product means a biological prepared and manufactured in accordance with regulations that govern the manufacture of vaccines, reagents, etc.
- ☐ Domestic shipping means shipping to or from Japanese locations to other Japanese locations

Packaging

All biological materials including diagnostic specimens and biological products that may contain an etiologic agent must be packaged to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling and transportation (passage through cancellation machines, sorters, conveyors, etc). Contents should not leak to the outside of the shipping container, even if leakage of the primary container occurs.

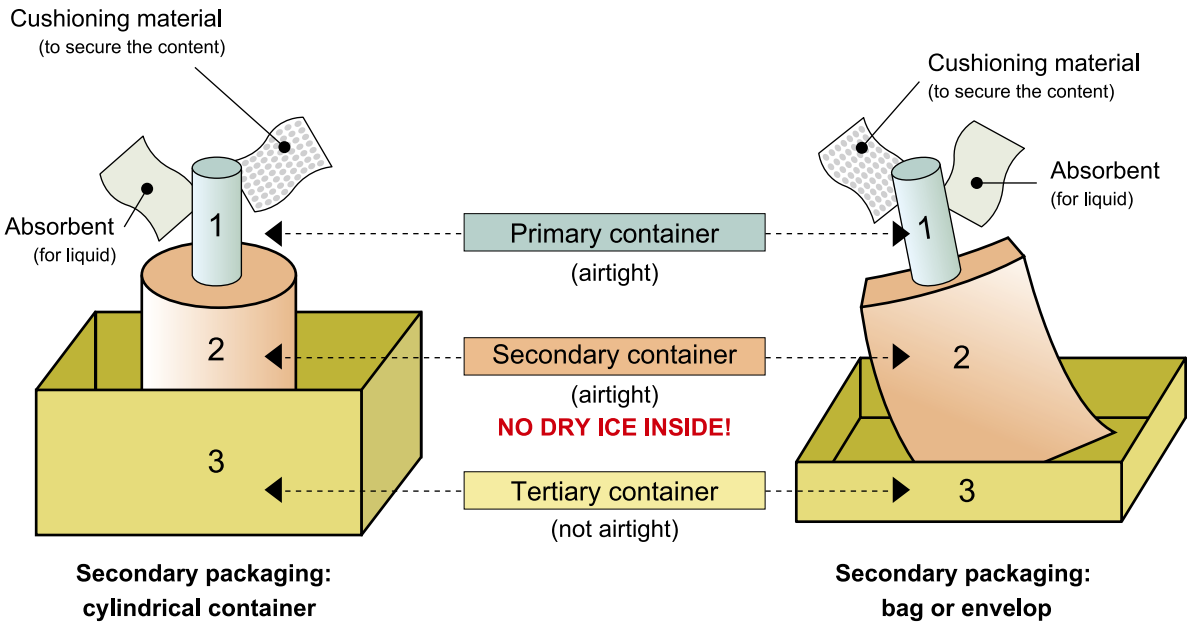
Specific packaging requirements apply to materials which are known to contain, or reasonably believed to contain certain etiologic agents and Pathogens and Toxins. Be sure to read carefully the methods of transporting Select Pathogens and Toxins provided for in the Infectious Diseases Act and WHO Guidance on Regulations for the Transport of Infectious Substances for Etiologic Agents and Pathogens and Toxins.

In addition, for Living Modified Organisms (LMOs), post the designated label on the shipping container. When shipping LMOs of Class 2 or above in the Experimental Classification, check if they fall under either Category A or B below:

Category A and B (See the WHO Guidance on regulations for the Transport of Infections Substances)

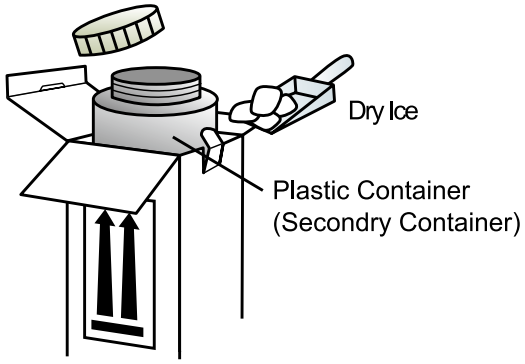
For shipping Category A Pathogens and Toxins, be sure to use containers for Category A and the basic triple packaging system. For Category B, use containers for Category B.
Both containers are manufactured and sold by domestic and foreign manufacturers. Samples are available at the Research Safety Section.

Structure of the basic triple packaging system



- The primary container must be a sturdy leak-proof receptacle containing the Pathogens and Toxins.
- The secondary container must be a highly airtight, leak-proof packaging of the United Nations packaging specification to enclose the primary container.
  Thus, NEVER PUT DRY ICE INSIDE !
- The tertiary container must be of an unbreakable, suitable cushioning material of the United Nations packaging specification to enclose and protect the secondary container from the impact during transport.

CAUTION!



Never place dry ice inside the air-tight plastic container (secondary container).
Otherwise, **the container will explode during transport**.
If you package the material with dry ice, place dry ice in the tertiary container or the overpack.

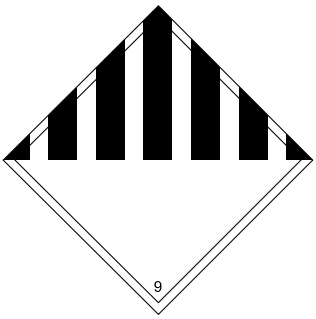
- ☐ Place material in a securely enclosed, watertight primary container (test tube, vial, etc.). Enclose this primary container in a secondary, durable watertight container. Several primary containers may be enclosed in a single secondary container as long as the total volume of material in all the primary containers enclosed does not exceed 50 ml
- ☐ Place absorbent nonparticulate material (e.g. paper toweling, not sawdust or vermiculite, etc.) in the spaces at the top, bottom and sides between the primary and secondary containers. Use enough absorbent material to absorb the entire contents of the primary container(s) in case of breakage or leakage
- ☐ Enclose each set of primary and secondary containers in an outer shipping container constructed of corrugated fiberboard, cardboard, wood or other material of equal strength. Do not use bags, envelops and similar materials
- ☐ If you package the material with dry ice, place dry ice between the secondary and outside containers
- ☐ Place shock absorbent material so as to prevent the secondary container from becoming loose inside the outer container as the dry ice sublimates

Labeling

The outer shipping container of all materials containing etiologic agents which are being shipped or transported must bear a special label, as illustrated below. These labels are available from your laboratory supply vendor.
Different labels are used for international labeling and labeling for domestic transport.

International labeling system

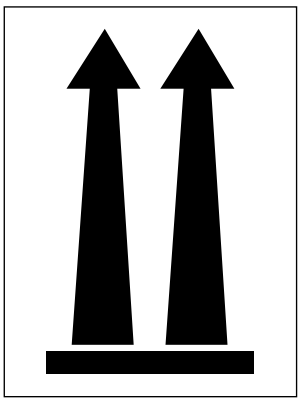
▲ Infectious substance



▲ Miscellaneous dangerous substances

▲ Non-flammable, Non-toxic gas

◀ Cryogenic liquid



◀ Right side up with care (RSWC)

Domestic transport
(Add the following label to the above international labels.)

▲ Put on the outer packaging for shipping Living Modified Organisms

▲ Put on the outer packaging for domestic shipping of Pathogens and Toxins using the postal service.

＊ In addition, the name of the item (content) must be described on the outer packaging for the shipment.

H. TRANSPORTATION METHOD

Federal Express or UPS

☐ For such shipments, internationally or domestically, follow the International Air Transport Association (IATA) Dangerous Goods Regulations. (Receipt of shipment notice is not required since the shipment is traceable through the specific carrier)

☐ Contact the specific carrier's dangerous goods agent prior to shipment to check the availability of the service and any additional packaging and labeling requirements

Notice of Delivery

In the event that a package sent by OIST is not received by the recipient by 5 days after the anticipated delivery of the package, the sender must notify the Research Safety Section Leader.

I. IMPORTATION/EXPORTATION CONTROL

Pathogens and Toxins

Importation of Pathogens and Toxins is governed by Japanese statutes. In general, a permit issued by the Minister of Health, Labour and Welfare is required prior to any possession, importation, transfer and acquisition for Type 2 Pathogens and Toxins. No Type 1 Pathogens and Toxins can be handled in OIST for any purpose. You must check whether biological materials that you intend to import or export are subject to regulatory control well before the import or export.
More information on Pathogens and Toxins may be found in Section Ⅱ C.

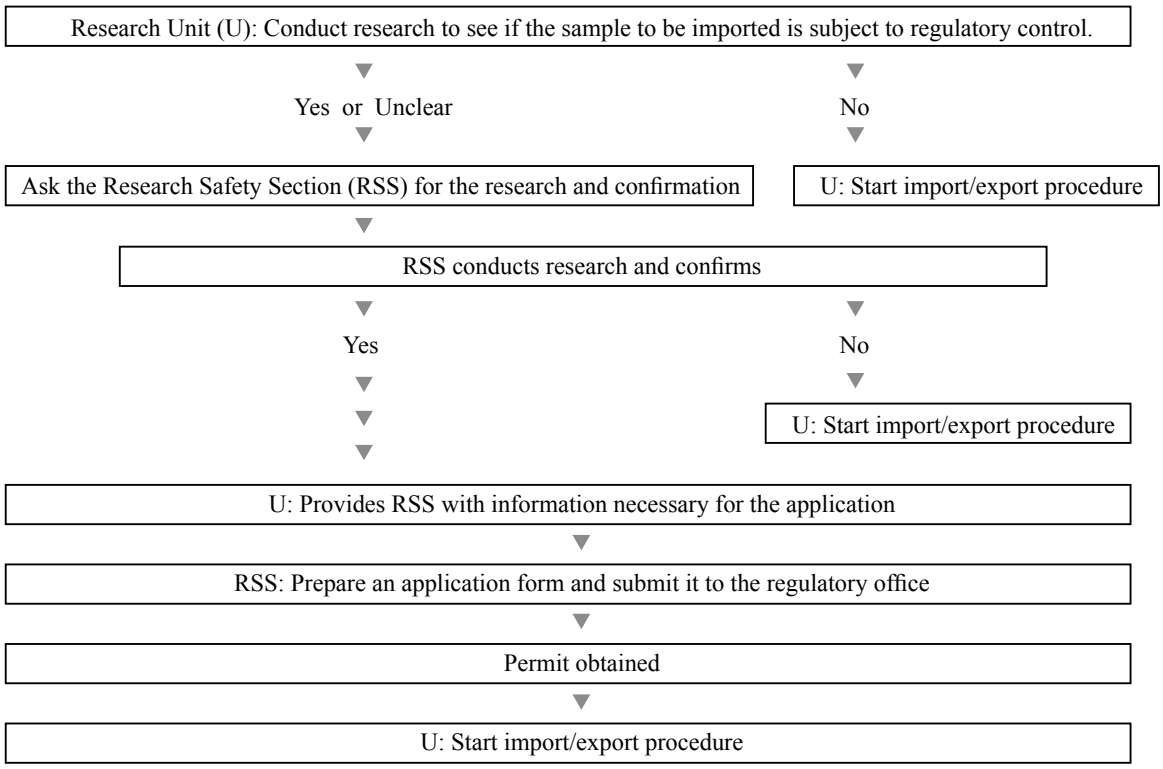
Animals, plants and soils

The Animal Quarantine Service of the Ministry of Agriculture, Forestry and Fisheries (MAFF) is a regulatory authority that functions to prevent any infectious diseases in domestic animals, rabies and such like from being brought into Japan and regulates importation of animals, materials derived from animals and pathogens for domestic animals. In addition, the Plant Protection Station of MAFF is the regulatory authority that imposes a quarantine on importation and movements inside Japanese territory of plants, pests and soils in order to prevent invasion/spread of diseases and pests which are potential threats to plants.

Materials which are subject to regulatory control include those often used in research such as animal tissues, blood, cells or cell lines, RNA/DNA extracts, hormones, enzymes, antiserums and antibodies.
Not only plants including cultivated plants such as seedlings, grafts, bulbs and seeds, and plants for human consumption such as vegetables, fruits, cut flowers, wood, grain and beans, but also living insects/microorganisms detrimental to plants are subject to plant importation quarantine control. On the other hand, highly sophisticated processed plants such as lumbers and tea, insects/microorganisms harmless to plants and dead insect samples are not subject to the import control in the context of the plant quarantine system.

Areas subject to import ban and regulated items are frequently changed in accordance with the condition of infectious diseases of livestock animals and plant pests that occurred inside and outside Japan, so you should check to see whether there is any applicable regulatory controls at the Animal Quarantine Service website (Top page, Database), Plant Protection Station website (Top page, Database) and Research Safety Section WEB site well before the importation. In addition, research on the details of regulatory controls is very complicated and may take a lot of time and effort. The OIST Research Safety Section has developed its original database, the “List of Controlled Pathogens and Toxins”, based on the information of statutes and regulatory provisions, so that the researchers can easily check the regulated items by themselves. However, the information obtained from this List is merely provisional and requires further confirmation.
In addition, before working with any items subject to regulatory controls, contact the Research Safety Section, since there are some formality requirements such as obtaining a permit and submitting a notification to the authorities.
Please take the following steps when submitting an application for permit to import or export goods subject to the import/export control to the regulatory authorities:

Import/Export procedures for biological materials:



J. STORAGE, RECEIPT AND TRANSFER

When storing Living Modified Organisms, Pathogens and Toxins, blood and any other biological materials, they must be kept in a container capable of preventing leakage. Also, log books must be prepared for record keeping, and must be kept during the storage, so that they can be disclosed upon request. In addition, the inventory must be checked regularly, so that any instances of lost or missing items can be found immediately.

When acquiring or taking-out Living Modified Organisms or Pathogens and Toxins, submission of a "Notification of Acquiring of Biological Agents" or "Notification of Taking-Out of Biological Agnts" to the Research Safety Section is required. Also, if such materials are transferred to another institute by assignment, an "Information Disclosure Form for Biological Agents" must be prepared. Please check the descriptions in the sheet with the Research Safety Section and then send them to the recipient of the assignee.

V FORMS

1 Application for Recombinant DNA Experiments
2 Termination Report/Status Report of Recombinant DNA Experiments
3 Living Modified Organisms Log Book
4 Form 11 (Related to Article 35) (Related to Export to member countries of Cartagena Protocol)
5 Application for Experiments Handling Pathogens and Toxins
6 Termination/Status Report of Experiments Handling Pathogens and Toxins
7 Pathogens and Toxins Log Book
8 Notification of Acquiring of Biological Agents
9 Notification of Taking-Out of Biological Agents
10 Information Disclosure Form for Biological Agents
11 Biohazard Sign

Application for Approval of Recombinant DNA Experiments

Committee Report Date		Approval Date	
Reference “		*provided by the Research Safety Section for new applications	
Date Received			
Biosafety Officer, Signature/Seal			
Research Safety Section Leader, Signature/Seal			

Date of Application: Month Date, Year

To: the Provost

I hereby apply for approval to conduct (modify or renew) the following Recombinant DNA experiment, in accordance with Paragraph 1, Article 9 of the OIST Graduate University Recombinant DNA Experiment Rules.

Lead Investigator

Name(Print) Signature/Seal

Phone# : （e-mail）:

Total years of experience in Recombinant DNA experiment:_____years

Faculty

Name(Print) Signature/Seal

Protocol Title:_____

Name of Unit :_____

Scheduled Experiment Duration: Month Date, Year >>> Month Date, Year

*As a general rule, each approved Experimental Protocol shall be valid until March 31st, three years after the date of approval.

1. Main Items

Protocol Title	☐ New ☐ Modification/Renewal ☐ (Corresponding to Article 11of the Rules)	
For Modification; Category of Change	☐ Researcher ☐ Inserted DNA ☐ Others ( )	☐ Location of Experiment, Storage or Disposal of Living Modified Organisms ☐ Host Organism
Aim of Experiment		
Experimental Protocol	*Explain the experimental protocol with drawings or diagrams.	
Title and Summary of Experiment for Public Information	*Title and summary may be posted on the OIST external website and others.	
Type of Experiment	☐ Experiment Using Microorganisms ☐ Large-Scale Cultivation Experiment ☐ Experiment Using Animals ☐ Animal Development Experiment ☐ Animal Inoculation Experiment ☐ Experiment Using Plants ☐ Plant Development Experiment ☐ Plant Inoculation Experiment ☐ Mushroom Development Experiment ☐ Cell Fusion Experiment	☐ Institute-Approved Experiment *1 ☐ Minister-Confirmed Experiment *2
Physical Containment Level	☐ P1 ☐ P2 ☐ P3 ☐ P1A ☐ P2A ☐ P3A ☐ Other ( )	
Living Modified Organisms From Other Institutions	☐ Yes (☐ Microorganisms ☐ Animals ☐ Plants) ☐ No Acquiring From: _____	
Animal Experiment	☐ Yes*3 ☐ No	

*1: Experiments specified in Article 4 1 of the Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms in Research and Development.

*2: Experiments specified in Annexed Table No. 1 of the Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms in Research and Development..

*3: If the submitted application involves animal experiment, a copy will be forwarded to the Animal Resources Section.

2. Location of Experiment, Storage and Disposal of Living Modified Organisms

Location #	Building Name and Room Number (or Room Name)	Required Protection Level and Safety Installation	Remarks

*Attach a floor map on which the experiment room is indicated. PDF files of floor map are available at the web site of buildings and facilities management division and research safety section.

3. Information on Inserted DNA

#	Organism From Which Inserted DNA Were Cloned*1	Name of Gene with Indication of cDNA or Genomic DNA	Identified or Unidentified	Experiment Classification*2	Accession Number and Other Necessary Information

*1: Genes of widely used vectors do not need to be mentioned, but if the vector harbors genes derived from infectious organisms (e.g. retrovirus), the information of the vector and gene should be mentioned.

*2: See Article 3 of the Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms in Research and Development.

4. Combination of Host Organism and Inserted DNA

Host Organism*1	Vector*2	Experiment Classification	Inoculated Animal/Plant/ Cultured Cell, etc.	Inserted DNA #	Experiment Location #	Protection Level	Ground for Protection Level*3

*1: In the case of active/live virus or viroid, the virus or viroid is considered as a host organism.
*2: Attach the vector map
*3: Describe the ground by referring to Article 5 of the Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms in Research and Development.

5. List of Researchers Implementing the Recombinant DNA Experiment

	Name	Title/Position	Total Years of Recombinant DNA Experiment Experience	Date of Training*1	Remarks
1				(MM DD 20YY)	
2				(MM DD 20YY)	
3				(MM DD 20YY)	
4				(MM DD 20YY)	
5				(MM DD 20YY)	

*1: as of the date when an application was submitted to the secretariat.

6 Remarks

Termination Report of Recombinant DNA Experiments/
Status Report of Recombinant DNA Experiments

Committee Report Date		Approval Date	
Reference #			
Date Received			
Biosafety Officer, Signature/Seal			
Research Safety Section Leader, Signature/Seal			

Date of Application: Month Date, Year

To: the Provost

I hereby report the completion/progress of Recombinant DNA experiment as follows, in accordance with Paragraph 6, and 7, Article 9 of the OIST Graduate University Recombinant DNA Experiments Rules.

Lead Investigator

Name(Print) Signature/Seal

Phone# : (e-mail) :

Total years of experience in Recombinant DNA experiment:_____years

Faculty

Name(Print) Signature/Seal

Protocol Title:_____

Name of Unit :_____

Scheduled Experiment Duration: Month Date, Year >>> Month Date, Year

OIST

1. Main Items

Protocol Title	☐ New ☐ Modification/Renewal ☐ (Corresponding to Article 11of the Rules)
For Modification; Category of Change	☐ Researcher ☐ Location of Experiment, Storage or Disposal of Living Modified Organisms ☐ Inserted DNA ☐ Host Organism ☐ Others ( )
Aim of Experiment	
Summary of Results	*Explain the experimental protocol with drawings or diagrams.
Title and Summary of Experiment for Public Information	*Title and summary may be posted on the OIST external website and others.
Type of Experiment	☐ Experiment Using Microorganisms ☐ Large-Scale Cultivation Experiment ☐ Experiment Using Animals ☐ Animal Development Experiment ☐ Animal Inoculation Experiment ☐ Experiment Using Plants ☐ Plant Development Experiment ☐ Plant Inoculation Experiment ☐ Mushroom Development Experiment ☐ Cell Fusion Experiment ☐ Institute-Approved Experiment *1 ☐ Minister-Confirmed Experiment *2
Physical Containment Level	☐ P1 ☐ P2 ☐ P3 ☐ P1A ☐ P2A ☐ P3A ☐ Other ( )
Living Modified Organisms From Other Institutions	☐ Yes (☐ Microorganisms ☐ Animals ☐ Plants) ☐ No Acquiring From: _____
Animal Experiment	☐ Yes*3 ☐ No

*1: Experiments specified in Article 4 1 of the Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms in Research and Development.

*2: Experiments specified in Annexed Table No. 1 of the Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms in Research and Development..

*3: If the submitted application involves animal experiment, a copy will be forwarded to the Animal Resources Section.

2. Location of Experiment, Storage and Disposal of Living Modified Organisms

Location #	Building Name and Room Number (or Room Name)	Required Protection Level and Safety Installation	Remarks

*Attach a floor map on which the experiment room is indicated. PDF files of floor map are available at the web site of buildings and facilities management division and research safety section.

3. Information on Inserted DNA

#	Organism From Which Inserted DNA Were Cloned*1	Name of Gene with Indication of cDNA or Genomic DNA	Identified or Unidentified	Experiment Classification*2	Accession Number and Other Necessary Information

*1: Genes of widely used vectors do not need to be mentioned, but if the vector harbors genes derived from infectious organisms (e.g. retrovirus), the information of the vector and gene should be mentioned.

*2: See Article 3 of the Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms in Research and Development.

4. Combination of Host Organism and Inserted DNA

Host Organism*1	Vector*2	Experiment Classification	Inoculated Animal/Plant/ Cultured Cell, etc.	Inserted DNA #	Experiment Location #	Protection Level	Ground for Protection Level*3

*1: In the case of active/live virus or viroid, the virus or viroid is considered as a host organism.
*2: Attach the vector map
*3: Describe the ground by referring to Article 5 of the Ministerial Ordinance Providing Containment Measures to Be Taken in Type 2 Use of Living Modified Organisms in Research and Development.

5. List of Researchers Implementing the Recombinant DNA Experiment

	Name	Title/Position	Total Years of Recombinant DNA Experiment Experience*1	Date of Training*1	Remarks
1				(MM DD 20YY)	
2				(MM DD 20YY)	
3				(MM DD 20YY)	
4				(MM DD 20YY)	
5				(MM DD 20YY)	

*1: as of the date when the an application was submitted to secretariat.

6 Remarks

OIST

Living Modified Organisms Log

Name of Unit :

No.	Host	Vector	Name of Gene Inserted	Protection Level	Storage Room # and Freezer Name or #	Reference # of Application	Storage Starting Date	Discarding Date	Notes
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									

*In Notes, write any precautions regarding handling of LMOs.

Form No. 11 (Article 35)

Name, Address and Contact Details of the Exporter Name： Address： Phone, Telex or Fax Number： Contact Person：
Name, Address and Contact Details of the Importer Name: Address: Phone, Telex or Fax Number: Contact Person:
Name and Identity of the Living Modified Organism Name Identity
Intended Date or Dates of the Trans-Boundary Movement, If Known Date:
Taxonomical Status, Common Name, Point of Collection or Acquisition, and Characteristics of Recipient Organism or Parental Organisms Related to Biosafety Taxonomical Status: Common Name: Point of Collection or Acquisition: Characteristics:
Centers of Origin and Centers of Genetic Diversity, If Known, of the Recipient Organism and/or the Parental Organisms and a Description of Environment Where the Organisms May Inhabit or Multiply
Taxonomical Status, Common Name, Point of Collection or Acquisition, and Characteristics of the Donor Organism or Organisms Related to Biosafety Taxonomical Status: Common Name: Point of Collection or Acquisition: Characteristics:

Description of the Nucleic Acid or the Modification Introduced, the Technique Used, and the Resulting Characteristics of the Living Modified Organism
Intended Use of the Living Modified Organism or Products Thereof, Namely, Processed Materials That Are of Living Modified Organism Origin, Containing Detectable Novel Combinations of Replicable Genetic Material Obtained Through the Use of Modern Biotechnology
Quantity or Volume of the Living Modified Organism to be Transferred
A Previous and Existing Risk Assessment Report Consistent with Annex III to Cartagena Protocol on Biosafety to the Convention on Biological Diversity
Suggested Methods for the Safe Handling, Storage, Transport and Use, Including Packaging, Labeling, Documentation, Disposal and Contingency Procedures, Where Appropriate
Regulatory Status of the Living Modified Organism Within the State of Export (for example, whether it is prohibited in the State of export, whether there are other restrictions, or whether it has been approved for general release) and, If the Living Modified Organism Is Banned In the State of Export, the Reason or Reasons for the Ban
Result and Purpose of Any Notification By the Exporter to Other States Regarding the Living Modified Organism to Be Transferred
A Declaration That the Above-Mentioned Information Is Factually Correct I certify that the above information is factually correct. Name ／Signature Date：

(Notes)

1. All entries except the signature should be in English, typed, or written with pen and ink in block letters. Once entered, correction by using an eraser or applying white out is not allowed. The signature must not be reproduced by any means.
2. Dates should be written in 6 digits, i.e. “01/10/03” for October 1, 2003.

Application of Approval for Experiments Handling Pathogens and Toxins

Committee Report Date		Approval Date	
Reference #		*provided by the Research Safety Section for new applications	
Date Received			
Biosafety Officer, Signature/Seal			
Research Safety Section Leader, Signature/Seal			

Application Date: Month Date, Year

To: the Provost

I hereby apply for approval to conduct (modify or renew) the following experiment handling pathogens and toxins, in accordance with Paragraph 1, Article 10 of the OIST Graduate University Biosafety Management Rules.

Lead Investigator

Name(Print) Signature/Seal

Phone# : (e-mail) :

Total years of experience handling pathogens and toxins :_____years

Faculty

Name(Print) Signature/Seal

Protocol Title:_____

Name of Unit :_____

Scheduled Experiment Duration: Month Date, Year >>> Month Date, Year

*As a general rule, each approved Experimental Protocol will expire on March 31st, three years after the date of approval.

1. Main Items

Protocol Title	☐ New ☐ Modification/Renewal ☐ (Corresponding to Article 11of the Rules)		
For Modification; Category of Change	☐ Researcher ☐ Others ( )	☐ Location of Experiment and Storage of Pathogens and Toxins ☐ Pathogens and Toxins	
Aim of Experiment			
Experimental Protocol	*Explain the experimental protocol with drawings or diagrams.		
Title and Summary of Experiment for Public Information	*Title and summary may be posted on the OIST external website and others.		
Name of Pathogens and Toxins		BSL	☐BSL1 ☐BSL2 ☐BSL3
Animal Experiment	☐ Yes*1	☐ No	

*1: If the submitted application involves animal experiment, a copy of the application will be forwarded to the Animal Resources Section.

2. Location of Experiment and Storage and Disposal of Pathogens and Toxins

Location #	Building Name and Room Number (or Room Name)	Safety Installation	Remarks

*Attach a floor map on which the experiment room is indicated. PDF files of floor map are available at the web site of buildings and facilities management division and research safety section.

3. Acquiring From:

Name of Organization Office of Contact Person Name Telephone #, e-mail		Scheduled Acquisition Date	(MM DD 20YY)

4. List of Researchers Handling Pathogens and Toxins

	Name	Title/Position	Total Years of Experience Handling Pathogens and Toxins:	Date of Training*1	Remarks
1				(MM DD 20YY)	
2				(MM DD 20YY)	
3				(MM DD 20YY)	
4				(MM DD 20YY)	
5				(MM DD 20YY)	

*1: as of the date when an application was submitted to the secretariat.

5. Remarks

Termination Report of Experiments Handling Pathogens and Toxins/
Status Report of Experiments Handling Pathogens and Toxins

Committee Report Date		Approval Date	
Reference #		*provided by Research Safety Section in the case of a new application	
Date Received			
Biosafety Officer, Signature/Seal			
Research Safety Section Leader, Signature/Seal			

Report Date: Month Date, Year

To: the Provost

I hereby report the completion/progress of experiment handling pathogens and toxins as follows, in accordance with Paragraph 6/7, Article 10 of OIST Graduate University Biosafety Management Rules.

Lead Investigator

Name(Print) Signature/Seal

Phone# : (e-mail) :

Total years of experience in handling pathogen and toxins:_____years

Faculty

Name(Print) Signature/Seal

Protocol Title:_____

Name of Unit :_____

(Scheduled) Experiment Duration: Month Date, Year >>> Month Date, Year

OIST

1. Main Items

Protocol Title			
Aim of Experiment			
Summary of Results	*Give the summary with illustrations or diagrams.		
Title and Summary of Results for Public Information	*Title and summary may be posted on the Corporation's web site and others.		
Name of Pathogens and Toxins		BSL	☐ BSL1 ☐ BSL2 ☐ BSL3
Animal Experiment	☐ Yes*1		☐ No

*1: if the submitted application involves animal experiment, a copy will be forwarded to the Animal Resources Section.

2. Location of Experiment, and Storage and Disposal of Pathogens and Toxins

Experiment Location No.	Building Name and Room Number (or Room Name)	Safety Installation	Remarks

*Attach the floor map on which experiment room is indicated. PDF files of floor map are available at the web site of buildings and facilities management division and research safety section.

3. Acquiring From:

Name of Organization Office of Contact Person Name Tel, e-mail		Scheduled Acquisition Date	(MM DD 20YY)

4. List of Researchers Handling the Pathogens and Toxins

	Name	Title/Position	Total years of experience handling pathogens and toxins:	Date of Training*1	Remarks
1				(MM DD 20YY)	
2				(MM DD 20YY)	
3				(MM DD 20YY)	
4				(MM DD 20YY)	
5				(MM DD 20YY)	

*1: as of the date when an application was submitted to the secretariat.

5. Remarks

Pathogens and Toxins Log

Research Unit:

No.	Name	BSL	Select Pathogens and Toxins or not	Storage Room # and Freezer Name or #	Application Reference #	Storage Start Date	Discarding Date	Notes
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								

*In Notes, identify matters requiring special attention when handling the pathogens and toxins.

Notification of Acquiring of Biological Agents

Reference #	
Date Received	
Biosafety Officer, Signature/Seal	
Research Safety Section Leader, Signature/Seal	
MTA	Concluded / To be Concluded / N/A

Date: Month Date, Year

To: Biosafety Officer

From:
Lead Investigator

_____
Name Signature/Seal

Name of Research Unit: _____

Faculty

_____
Name Signature/Seal

I hereby submit a Notification of Acquiring of Biological Agents, in accordance with provisions of the OIST Biosafety and/or Recombinant DNA Rules.

Information on Biological Agent: -for LMOs: host, name of inserted nuclei acid and protection level -for pathogens and toxins: name of pathogen and toxins, BSL and the category for pathogens and toxins. *The classification of the category is defined in Act Concerning Prevention of Infectious Diseases and Medical Care for Patients Suffering Infectious Diseases.	＊Strain name and type name must also be identified accordingly.
Provider Information: institute/organization, department, address, name of person in charge, phone number and e-mail address	
(Scheduled) Date of Acquisition:	

*LMO: living modified organism

Notification for Taking-Out of Biological Agents

Reference #	
Date Received	*provided by Research Safety Section
Biosafety Officer, Signature/Seal	
Research Safety Section Leader, Signature/Seal	

Date: Month Date, Year

To: Biosafety Officer

From:
Lead Investigator

_____

Name Signature/Seal

Name of Research Unit: _____

Faculty

_____

Name Signature/Seal

I hereby submit a Notification of Taking-Out of Biological Agents, in accordance with the stipulations of the OIST Graduate University Recombinant DNA and Biosafety Rules.

Information on Biological Agents -for LMO: host, name of inserted nuclei acid and protection level -for pathogens and toxins: name of pathogen and toxins, BSL and the category for pathogens and toxins. *The classification of the category is defined in Act Concerning Prevention of Infectious Diseases and Medical Care for Patients Suffering Infectious Diseases.	*Strain name and type name shall also be identified.
Institution where Biological Agents are being taken in: Institute/organization, department, address, name of person in charge, phone number and e-mail address	
(Scheduled) Duration	

Information Disclosure Form for Biological Agents

Reference #	
Date Received	＊provided by Research Safety Section
Biosafety Officer, Signature/Seal	
Research Safety Section Leader, Signature/Seal	
MTA	Concluded / To be Concluded / N/A

Date: Month Date, Year

To: (Recipient)

From:
Lead Investigator

_____
Name Signature/Seal

Name of Unit:_____

Faculty

_____
Name Signature/Seal

I hereby provide information concerning Living Modified Organisms, in accordance with Article 26 of the Act on Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Act No. 97 of 2003) or Pathogens and Toxins as follows:

Information on Biological Agent: -Type of Use, Host/Parental Organism, Gene Name of Inserted DNA, applicability of the exemption defined in Item 1/2/4 of Article 16 of the Regulations for the Cartagena Act -Name of the Biological Agent, BSL and the category of specified pathogens for pathogens and toxins.	
Recipient Information: Institute/Organization, Department, Address, Name of Person in Charge, Phone Number, e-mail Address	
Precautions and/or Instructions for Handling	
Contact Information of Biosafety Officer	Toshinori Tanaka, Ph. D. 1919-1 Tancha, Onna-son, Okinawa 904-0495, Japan Tel: +81-98-966-2385 Fax: +81-98-966-2889 E-mail: research_safety@oist.jp

OIST

BIOHAZARD

ADMITTANCE TO AUTHORIZED PERSONNEL ONLY

Biosafety Level:_____

Lead Investigator:_____

In case of emergency call:_____

Daytime phone:_____ **Home phone:**_____

Authorization for entrance must be obtained from the Lead Investigator named above.

Form #4 related to Article 12

OIST OKINAWA INSTITUTE OF SCIENCE AND TECHNOLOGY GRADUATE UNIVERSITY