Osaka University Regulations on Genetic Modification Experiments

(Purpose)

Article 1:

The purpose of these Regulations is to stipulate matters necessary for the implementation of genetic modification experiments (“Experiments”) at Osaka University (“University”) under Article 13 of the Osaka University Regulations on Genetic Modification Experiment Safety Management (“Safety Management Regulations”), thereby promoting research using genetic modification techniques.

(Definitions)

Article 2:

The terms used herein shall have the meanings set forth in Article 2 of the Safety Management Regulations.

(Safety of Experiments)  
Article 3:

1. Experiments shall be planned and implemented based on the containment measures at levels specified in the Ministerial Ordinance Providing Containment Measures to be Taken in Type 2 Use of Living Modified Organisms for Research and Development (Ordinance of the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of the Environment No. 1 of 2004) (“Ministerial Ordinance”), to ensure the safety thereof.
2. The President, Division Directors, Biosafety Officers, Principal Investigators and persons engaged in Experiments shall appropriately perform the respective duties specified in the Safety Management Regulations.

(Application for Approval for Experiment, Review and Reporting)

Article 4:

1. All Experiments shall be approved by the President (following confirmation by the Minister of Education, Culture, Sports, Science and Technology as the case may be) in advance following the procedures set for each of the experiment categories stated below, with a view to ensuring the safety thereof.
2. Minister-affirmed Experiment: The Experiment plan shall be approved by the President following affirmation by the Minister of Education, Culture, Sports, Science and Technology.
3. Institution-approved Experiment: The Experiment plan shall be approved by the President.
4. The period of the Experiments stipulated in the preceding Paragraph shall be up to five (5) years.
5. Laboratory and Experimental Area (collectively “Experiment Space”) to be used for the Experiments stipulated in Paragraph 1 shall be affirmed by:
6. The Biosafety Officer of the Division with which the Principal Investigator is affiliated;
7. The abovementioned Biosafety Officer and the Biosafety Officer in charge of the facility where the Experiment Space is located if said facility is not attached to the Division with which the Principal Investigator is affiliated.
8. If a Division Director has a plan to establish a new Experiment Space in the facility under his or her control to conduct an Experiment that requires P2- or higher level containment measures, the Director shall have the Biosafety Officer check the plan, notify the President thereof using the prescribed form, and obtain approval of the Genetic Modification Experiment Safety Committee.
9. The Principal Investigator shall file an application for approval for the Experiment plan (“Application”) to the President through the relevant Division Director in accordance with the procedures stipulated separately.
10. The Principal Investigator shall ensure that the relevant Biosafety Officer certifies the competence of persons to be engaged in the Experiment using the prescribed form prior to filing an Application.
11. If an Experiment that has been approved is terminated, suspended, or is not implemented, the Principal Investigator shall notify the President of the termination, suspension or non-implementation thereof using the prescribed form through the relevant Division Director.
12. If an Experiment plan is to be changed, the Principal Investigator shall have the Biosafety Officer of the Division with which he or she is affiliated confirm the change and then notify the President thereof through the relevant Division Director using the prescribed form in advance, provided, however, that the Principal Investigator shall file an application to change the Experiment plan pursuant to the provision of Paragraph 5 of this Article in the following cases:
13. A minister-affirmed Experiment is to be changed.
14. The change of the Experiment plan involves a change in the level of containment measures required therefor (except when the Experiment plan after change requires a lower level of containment measures).
15. An Experiment plan requiring P3-level (including P3A-level and P3P-level) containment measures is to be changed (except in the case stated in the preceding Item and when the Experiment plan after change requires a lower level of containment measures).
16. The change of an Experiment plan involves a change in the type of animal experiment (e.g. animal development experiment and animal inoculation experiment) (except in the cases stated in the preceding three Items and when the Experiment plan after change requires a lower level of containment measures).
17. The change of an Experiment plan involves a change in the type of plant experiment (e.g. plant development experiment, mushroom development experiment, and plant inoculation experiment) (except in the cases stated in Items (1), (2) and (3) above and when the Experiment plan after change requires a lower level of containment measures).
18. The Principal Investigator shall report on the progress of the Experiment using the prescribed form for each academic year during the Experiment period to the Biosafety Officer of the relevant Division by the last day of June of the following academic year, provided, however, that this does not apply to Experiments that were terminated or suspended during the academic year.

(Implementation of Experiments)  
Article 5:

All persons engaged in Experiments shall abide by the following rules.

1. Experiments shall be conducted in a Laboratory.
2. Experiments shall be conducted in accordance with the approved Experiment plan.
3. Containment measures at the levels stipulated in Article 6 shall be taken when conducting Experiments.
4. For each Experiment, a record shall be made and kept in storage.

(Containment Measures)  
Article 6:

Containment measures to be taken for each type of Experiment shall be as stipulated below:

1. For Experiments using microorganisms, containment measures at the levels stipulated in Item 1 of Article 5 of the Ministerial Ordinance shall be taken.
2. For large-scale cultivation experiments, containment measures at the levels stipulated in Item 2 of Article 5 of the Ministerial Ordinance shall be taken.
3. For animal experiments, containment measures at the levels stipulated in Item 3 of Article 5 of the Ministerial Ordinance shall be taken. When animal experiments requiring P1- or P2-level containment measures are to be conducted in the same Laboratory at the same time, the areas for these experiments shall be clearly defined or P1- or P2-level containment measures, or P1A- or P2A-level containment measures, shall be taken respectively.
4. For plant experiments, containment measures at the levels stipulated in Item 4 of Article 5 of the Ministerial Ordinance shall be taken. When plant experiments requiring P1- or P2-level containment measures are to be conducted in the same Laboratory at the same time, the areas for these experiments shall be clearly defined or P1- or P2-level containment measures, or P1A- or P2A-level containment measures, shall be taken respectively.

(Precautions to be Taken during an Experiment)

Article 7:

The following conditions shall be met during an Experiment:

1. LMO contained in waste (including liquid waste) shall be inactivated before disposal of the waste.
2. LMO that adheres to facilities, equipment, and devices shall be inactivated before disposal or reuse thereof (or before washing if they are to be used after being washed).
3. Laboratory tables shall be cleaned to inactivate LMO after completing the Experiment for the day and immediately after an LMO adheres thereto.
4. The windows and doors of the Laboratory shall be closed (except when entering and leaving the Laboratory).
5. In any operations, aerosol generation shall be kept to a minimum.
6. LMO shall be placed in a container that is designed to prevent the leakage and spread thereof when it is to be inactivated outside of the Laboratory or taken outside of the Laboratory for any other purpose during the Experiment.
7. Appropriate measures shall be taken to prevent an LMO from adhering to persons who handle it or infecting such persons, including mandating hand-washing after handling an LMO.
8. Mechanical pipettes shall be used wherever possible; mouth pipetting shall be forbidden.
9. It shall be prohibited to eat, drink, smoke and keep any food in the Laboratory.
10. Injection syringes shall not be used whenever other methods are available.
11. The Laboratory shall always be kept clean and tidy.
12. Persons engaged in the Experiment shall follow the instructions given by the Principal Investigator on what to wear for the Experiment.
13. Appropriate measures shall be taken to prevent those who do not know about the Experiment from entering the Laboratory.
14. Other instructions given by the Principal Investigator shall be followed.

(Containment Measures to be Taken during Storage)  
Article 8:

The following containment measures shall be taken for storage of an LMO:

1. LMO shall be placed in a container that is designed to prevent leakage thereof. The container shall be conspicuously labeled as containing the LMO.
2. The container in which an LMO is placed pursuant to the preceding Item shall be stored in a specifically designated area. If it is stored in a refrigerator or any other storage equipment, the refrigerator or equipment shall be conspicuously labeled as storing the LMO.
3. LMOs requiring P1- or P2-level containment measures shall be stored in the Laboratory in principle, and LMOs requiring P3-level containment measures shall be stored in the Laboratory at all times.

(Containment Measures to be Taken during Transport)  
Article 9:

The following containment measures shall be taken for transport of LMO:

1. LMO shall be placed in a container that is designed to prevent the LMO from leaking, escaping, or otherwise spreading.
2. LMO that requires P3-level (including P3A-level and P3P-level) containment measures shall be placed in a container that is designed to prevent the LMO from leaking, escaping, or otherwise spreading even if the container breaks due to an accident or for any other reason during ordinary transport.
3. The container shall be marked on the most visible part of its surface to the effect that careful handling is required.

(Measures to be Taken for Domestic Transport)  
Article 10:

1. When LMO is to be transferred, supplied or entrusted for use to a person, information on specified matters shall be provided to said person using the prescribed form pursuant to Paragraph 1 of Article 26 of the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Act No. 97 of 2003) (“Act”).
2. When information is to be provided pursuant to the preceding Paragraph, the contents thereof shall be checked by the Biosafety Officer of the relevant Division.
3. A person who accepts transferred or supplied LMO or who is entrusted an LMO for use shall be given information on specified matters from the party transferring or supplying the LMO or entrusting the LMO for use and shall ask the Biosafety Officer of the relevant Division to check the information in advance.

(Procedures for Importing and Exporting LMO)

Article 11:

1. A person who wishes to export LMO shall comply with the provisions of Articles 27 and 28 of the Act, ask the Biosafety Officer of the relevant Division to check the validity of doing so, and notify the President using the prescribed form in advance.
2. A person who wishes to import LMO shall receive information from the exporting party in the form stipulated in Item 1 of Article 37 of the Regulations related to the Enforcement of the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Ordinance of the Ministry of Finance, the Ministry of Education, Culture, Sports, Science and Technology, the Ministry of Health, Labour and Welfare, the Ministry of Agriculture, Forestry and Fisheries, the Ministry of Economy, Trade and Industry, and the Ministry of the Environment No. 1 of 2003). The person shall then ask the Biosafety Officer of the relevant Division to check the validity of importing the LMO, and notify the President using the prescribed form in advance.
3. The procedures stipulated in the preceding two Paragraphs shall be applied when importing from and exporting to both party and non-party countries to the Cartagena Protocol on Biosafety to the Convention on Biological Diversity.

(Education and Training)  
Article 12:

When a Biosafety Officer has provided education and training pursuant to Article 11 of the Safety Management Regulations, he or she shall report thereon to the President using the prescribed form without delay.

(Biosafety Cabinet and HEPA Filter Standards)

Article 13:

The biosafety cabinet and HEPA filter standards shall be as stipulated in the Attachment.

(Inspection of Biosafety Cabinet)   
Article 14:

1. The HEPA filter in a biosafety cabinet installed in a P2-level (including P2A-level and P2P-level) Laboratory shall be cleared of contamination by sealing the biosafety cabinet and using 10 g/m3 formaldehyde fumigation immediately before its replacement and during inspection.
2. When a biosafety cabinet is to be installed in a P3-level (including P3A-level and P3P-level) Laboratory, it shall be positioned in a manner that allows regular inspection, replacement of the HEPA filter, and formaldehyde fumigation to be conducted without moving the cabinet.
3. The biosafety cabinet stated in the preceding Paragraph shall be subjected to the following three tests upon installation, and tests (1) and (2) at least once a year thereafter:
4. Air speed and airflow test
5. HEPA filtration performance test
6. Hermetic seal test

(Miscellaneous Provision)

Article 15:

Matters necessary for promotion of genetic modification research not specified herein shall be set forth separately.

Supplementary Provision

These Regulations shall come into effect on April 1, 2004.

Supplementary Provision

These Regulations as amended shall come into effect on April 18, 2006.

Supplementary Provision

These Regulations as amended shall come into effect on April 1, 2009.

Supplementary Provision

These Regulations as amended shall come into effect on April 21, 2009.

Supplementary Provision

(Date of Enforcement)

1. These Regulations as amended shall come into effect on June 1, 2012.

(Transitional measures for application for approval for Experiment plans)

2. The Principal Investigator who is to apply for approval for an Experiment plan to be conducted or changed after the date of enforcement of these Regulations as amended under Paragraph 1 of Article 4 may file said application even before the date of enforcement pursuant to the provision of Article 4.

Supplementary Provision

These Regulations as amended shall come into effect on April 1, 2013.

Supplementary Provision

These Regulations as amended shall come into effect on October 1, 2013.

Supplementary Provision

These Regulations as amended shall come into effect on January 1, 2016.

Supplementary Provision

These Regulations as amended shall come into effect on February 21, 2018.

Attachment (Article 13)

Class I

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| Application | Used for handling microorganisms and pathogens of a low to medium hazard level, where clean air is not required in the workspace. |
| Structure/standards | The biosafety cabinet has a front opening and an exhaust port. The inflow of air from the front opening prevents the outflow of contaminant aerosols, and the exhaust air is HEPA-filtered before exiting the cabinet.  The average airflow speed (exhaust air volume/area of front opening) shall be at least 0.40 m/s. |

Class II

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| Application | Used for handling microorganisms and pathogens of a low to medium hazard level during aseptic work where clean air is required in the workspace.  There are two types of biosafety cabinet. The type-A unit is used for ordinary biological tasks, and the type-B unit is used for handling substances that cannot be effectively collected by an HEPA filter, such as small quantities of potentially dangerous chemicals, radioactive substances and gaseous compounds. |
| Structure | The cabinet has a front opening and an exhaust port. The inflow of air from the front opening prevents the outflow of contaminant aerosols, and HEPA-filtered laminar flow of clean air is supplied to the workspace. The exhaust air is HEPA-filtered before exiting the cabinet.  Using the type-A unit with its positive-pressure contaminant plenum in contact with the outer wall is not recommended. The type-B unit shall be connected with a duct to exhaust air to the outside. |
| Standards | Hermetic seal  When the cabinet is pressurized with air to 50-mm H2O, the pressure drop after 30 minutes shall be within 10%. Or, when all welds and penetrations of the cabinet are covered or sprayed with soapy water or a foaming leak-detection agent, no soap bubbles shall be found. (If the positive-pressure plenum contacts the outer wall, the amount of halogen gas leakage shall be no greater than 5 × 10−7 cc/sec.)  Worker safety test  After 5 to 10 × 108 CFU (colony-forming units) of *Bacillus subtilis* spores are sprayed, no more than a total of 10 colonies shall be collected in four impingers. The number of colonies collected by a slit sampler 5 to 15 minutes after starting the test shall be no greater than 5 in each test. The test shall be conducted 3 times in succession and the above standard shall be met each time.  Sample protection test  After 5 to 10 × 106 CFU of *Bacillus subtilis* spores are sprayed, the number of colonies collected on agar plates (which means 10 cm-diameter petri dishes placed on the worktable in a manner that covers as much area thereof as possible; the same applies hereafter) shall be no greater than a total of 5 in each test. The test shall be conducted 3 times in succession and the above standard shall be met each time.  Test for prevention of cross-contamination between samples  After 5 to 10 × 104 CFU of *Bacillus subtilis* spores are sprayed, no more than a total of 2 colonies shall be collected on agar plates placed with their centers at least 355 mm away from both sides of the cabinet. The test shall be conducted 3 times in succession both from the left and the right and the above standard shall be met each time.  Air jet speed  The air jet speed at measurement points forming a lattice of no greater than 15 cm shall be within ±20% of the average. If the cabinet is so designed as to produce a gradient of air jet speed, the speed shall be calculated in each region specified by the manufacturer.  Air inflow speed  The average air inflow speed from the front opening shall be at least 0.40 m/s (at least 0.50 m/s in case of the type-B unit).  Fan  When the filter pressure loss has risen by 20%, the reduction in the airflow processed by the fan shall be within 25% without rotation control.  Airflow direction  The airflow direction shall be determined visually by using a smoke tube or a similar device. The smoke shall flow smoothly downward when the workspace is scanned by a smoke tube from one end to the other at: the position 100±10 mm above the bottom edge of the front panel; the position where the downward laminar flow in the workplace splits into the front and rear intake openings; the position 150±20 mm above the bottom edge of the front panel; and the position 20 – 30 mm inside the front panel. There shall be no locations where the smoke does not flow or where it flows upwards, and no smoke shall leak from the cabinet.  When the perimeter of the front opening is scanned at the position 30 – 40 mm outside of the front opening, the smoke that has entered the cabinet shall not leak from the cabinet, and shall not leak into the workspace.  Rise in temperature  The temperature difference between the room and the interior of the cabinet shall be within 8°C.  Noise level  The noise level shall be no greater than 67 dBA.  Brightness  The average brightness shall be between 800 and 1,200 lux.  Vibration  The vibration displacement of the worktable along 3 perpendicular axes shall be within 5 μm RMS.  Liquid-receiving pan  The liquid-receiving pan shall be easy to clean and have a capacity of at least 4 liters. |
| Consideration for  cleaning and sterilization | The surface that could be contaminated by liquid and its droplets shall be cleanable without using a special tool. The corners of the work table and the workspace shall be rounded.  The biosafety cabinet shall be so structured as to allow formaldehyde gas to be sterilized without it being relocated, and allow the front opening and exhaust port to be sealed with a metal plate, plastic sheet, adhesive tape, or the like. To enable easy cleaning, there shall be at least 80 mm space between the floor and the bottom surface of the cabinet or adhesive seal shall be applied on the floor or the stand on which the cabinet is installed. |
| Inspection | After the cabinet is used, there may arise problems that directly affect its performance, such as clogging of the HEPA filter. To ensure safe operation, it is recommended to conduct an inspection upon installing the cabinet and at least once a year thereafter. |

Class III

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| Application | Used for handling highly hazardous microorganisms and pathogens. |
| Structure/standards | The cabinet shall be sealed and the air inflow from the intake openings and the exhaust air from the exhaust port shall be HEPA-filtered. The exhaust air shall pass through a two-layer HEPA filter or through an incinerating sterilization device before being released outside. The workspace shall be maintained at a negative pressure (at least 15-mm H2O) relative to the Laboratory. Work gloves shall be available, along with an autoclave or antiseptic solution tank for bringing in and taking out samples and devices. |

HEPA filter for biosafety cabinet

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| Performance | When a test aerosol is loaded on the primary side of an HEPA filter, the supposed transmittance through the minute partitions (ratio of the aerosol concentration on the secondary side to that on the primary side) shall not exceed 0.01%. In a scanning test that is conducted under near-isokinetic sampling conditions using a relative densitometer or a particle counter with a sampling rate of 28.3 liters/min, it shall be verified that the aerosol transmittance at around 0.3 μm does not exceed 0.01% with an HEPA filter mounted in the cabinet.  An aluminum separator shall be used. It is recommended to install a differential pressure gauge that displays the pressure loss across the HEPA filter. |