Corporation obtaining approval, the name of its representative, and the address of its main office

Applicant Name: Takara Bio Inc.
Ikunoshin Kato, President and CEO (Seal)
Address: Seta 3-4-1, Otsu City, Shiga Prefecture, Japan

Approved Type 1 Use Regulation

Name of the Type of Living Modified Organism	Nonproliferative and genetically modified Moloney murine leukemia virus that expresses Herpes simplex type 1 thymidine kinase and human intracellular region-deleted low affinity nerve growth factor receptor, and has env protein of mouse amphotropic virus 4070A in its envelope (SFCMM-3)
Content of the Type 1 Use of Living Modified Organism	Used in clinical facilities for human gene therapy, including storage, transportation, disposal and acts incidential to them
Method of the Type 1 Use of Living Modified Organism	(1) The solution of SFCMM-3 should be sealed in containers, transported to a clinical facility in the frozen state, and stored in a freezer in a storage room that can be locked at the facility. (2) Thawing of the frozen solution of SFCMM-3, and dilution and dispensation of the solution of SFCMM-3 has to be performed in a safety cabinet in a cell preparation room where containment measures of P2 level can be conducted (hereinafter referred to as “cell preparation room”) or in a closed system in the cell preparation room. Similarly, the handling of dilution of SFCMM-3 and the cells transduced with SFCMM-3, including the transduction of the donor lymphocyte with SFCMM-3, incubation of the cells transduced with SFCMM-3, etc., are to be performed in a safety cabinet in the cell preparation room or in a closed system in the cell preparation room. Storage of dilution of SFCMM-3 and cells transduced with SFCMM-3 should be kept in a refrigerator, freezer or incubator in the cell preparation room. Note that when the dilution of SFCMM-3 or its frozen form or the cells transduced with SFCMM-3 is transported to another P2 area through an open area, it should be

	contained inside a sealed container, which should be put in a box, etc. for transportation to avoid dropping or breaking it. (3) When disposing of the solution (including dilution) of SFCMM-3 or the cells transduced with SFCMM-3, these should be sterilized and then disposed of according to the medical waste management protocol. (4) The medical waste management protocol includes the following and has to be approved and provided by the clinical facility: 1) The clinical facility prepares the annual waste management plan and notifies staff of it. The waste management plan includes the situation of waste generation, separation methods, methods of collection and transfer in the clinical facility, the range of sterilization and disinfection to be performed at the clinical facility, methods of packaging, storage methods, procedures in case of consignment to agencies, and emergency contact procedures. 2) The clinical facility prepares a report on waste disposal, and stores the report for five years. 3) Infectious waste should be disposed of as follows: a) Infectious waste has to be separated from other waste, and be packed and sealed in a transportation container for discharge. b) Collection, transportation and storage of infectious waste should be conducted using containers to avoid scattering of the content; for waste containing liquid, airtight containers should be used so that the content is not spilled. Additionally, measures should be taken to prevent decomposition or the generation of an odor. c) Collection, transportation and storage of sharp-edged waste should be conducted using puncture-resistant robust containers that avoid the risks of accidental puncture etc. d) The periods of storage of infectious waste should be as short as possible, and care should be taken that unauthorized people can not enter the storage area, and storage should be separated from other waste. In addition, signs should be posted in the storage area so that the relevant persons immediately notice the storage of

	infectious waste, together with the precautions on its handling. 4) Biological hazard symbols should be attached and displayed on transportation containers containing infectious waste. 5) When infectious waste disposal is not performed internally, but is consigned to an agency, the consignment contract should be made after confirming that the agency has been approved for infectious waste disposal by the prefectural governor according to the Waste Management and Public Cleansing Law. Note that the agency cannot re-consign the service to another agency. (5) Administration of the cells transduced with SFCMM-3 to a subject has to be performed by infusion in a private room in which negative pressure is maintained and appropriate containment measures are taken (hereinafter referred to as “negative pressure room”). Additionally, devices that come in direct contact with the cells transduced with SFCMM-3 when administrated such as injection needles, syringes, and tubes, etc., should be disposable ones, and after use, these should be appropriately disinfected in the negative pressure room, followed by disposal in accordance with the medical waste management protocol. (6) Until the third day after administration, the subject should be cared for in the negative pressure room. When the subject goes to the open area outside the negative pressure room for examinations, etc., viral leakage prevention measures including the wearing of a mask and a gown must be compulsory. Blood and body fluids of the subject during the period of being taken care of in the negative pressure room should be appropriately disinfected individually and disposed of in accordance with the medical waste management protocol. In addition, the excreta of the subject including urine and feces should be appropriately disinfected in the negative pressure room and disposed of in accordance with the medical waste management protocol until replication competent retrovirus (RCR) is no longer detected by the polymerase chain reaction (PCR) test to subject's blood which is performed on or after the day following administration. Note that the handling of blood, body fluids and excreta, etc., from the subject that are to be used as clinical samples

	should be in accordance with the handling of the solution of SFCMM-3 or the cells transduced with SFCMM-3. (7) During the period of being taken care of in the negative pressure room, devices that have been used invasively in the subject and those that have been in contact with blood, body fluid and excreta, etc., should be appropriately disinfected in the negative pressure room and be disposed of in accordance with the medical waste management protocol, or be sufficiently washed in the negative pressure room. (8) Before releasing the subject from being taken care of in the negative pressure room, confirm that RCR is negative in the peripheral blood mononuclear cells (PBMC) and the plasma of the subject. If RCR is detected, the subject should continue to be cared for in the negative pressure room. (9) If RCR is detected in the PBMC or the plasma of the subject after releasing the subject from being taken care of in the negative pressure room, immediately transfer the subject to be taken care of in the negative pressure room, and take the same measures as in (6) to (8) above.