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

Name: National Cancer Center
Applicant: President, Setsuo Hirohashi
Address: 5-1-1 Tsukiji, Chuo-ku, Tokyo

Approved Type 1 Use Regulation

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| Name of the Type of Living Modified Organism | Nonproliferative and genetically modified Moloney murine leukemia virus that expresses Herpes simplex virus 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 a clinical facility for human gene therapy, including storage, transportation, disposal and acts incidential to them |
| Method of the Type 1 Use of Living Modified Organism | Address of the clinical facility: 5-1-1 Tsukiji, Chuo-ku, Tokyo<br>Name of the clinical facility: National Cancer Center Hospital<br><br>(1) The solution of SFCMM-3 should be sealed in containers, transported to the clinical facility in the frozen state, and stored in a freezer in a P2 level laboratory at the facility (hereinafter referred to as "P2 laboratory").<br>(2) Thawing of the frozen solution of SFCMM-3, and dilution and dispensing of the solution of SFCMM-3 has to be performed in a safety cabinet in a P2 laboratory or in a closed system in the P2 laboratory. 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 P2 laboratory or in a closed system in the P2 laboratory. Dilution of SFCMM-3 and cells transduced with SFCMM-3 should be stored in a refrigerator, freezer or incubator in the P2 laboratory. 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. |

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| | (3) When disposing of the solution (including dilution) of SFCMM-3 or the cells transduced with SFCMM-3, these should be sterilized (by autoclaving for not less than 20 minutes at 121°C or above, or soaking in 0.5% sodium hypochlorite solution for not less than two hours; the same in the followings) and then disposed of according to the medical waste management protocol established by National Cancer Center Hospital (hereinafter referred to as "medical waste management protocol").<br>(4) Administration of the transduced cells to a subject has to be performed by infusion in a private room that is undergoing appropriate containment measures (hereinafter referred to as “clean room”). Additionally, devices that come in direct contact with the cells transduced with SFCMM-3 at the time of administration, such as injection needles, syringes, and tubes, etc., should be disposable ones, and these should be appropriately sterilized followed by disposal in accordance with the medical waste management protocol. Note that when sterilization is performed in the area outside of the clean room, the wastes should be contained inside a double sealed container and transported.<br>(5) Until the third day after administration, the subject should be cared for in the clean room. When the subject goes to the open area outside the clean room for examinations etc., viral leakage prevention measures including the wearing of a mask and a gown must be compulsory.<br>(6) Blood and body fluids of the subject during the period of being taken care of in the clean room should be appropriately sterilized 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 sterilized and disposed of in accordance with the medical waste management protocol until the existence of replication competent retrovirus (hereinafter referred to as "RCR") is denied by the polymerase chain reaction test using subject's blood which is performed on or after the day following administration. Note that the handling of 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.<br>(7) During the period of being taken care of in the clean room, devices etc. that have been used invasively in the subject and those that have |

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| | been in contact with excreta etc. of the subject should be appropriately sterilized and be disposed of in accordance with the medical waste management protocol, or be sufficiently washed. Note that when sterilization is performed in the area outside of the clean room, the wastes should be contained inside a double sealed container and transported.<br>(8) Before releasing the subject from being taken care of in the clean room, confirm that RCR is negative in the peripheral blood mononuclear cells (hereinafter referred to as "PBMC") and the plasma of the subject. If RCR is detected, the subject should continue to be cared for in the clean room.<br>(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 clean room, immediately transfer the subject to be taken care of in the clean room, and take the same measures as in (5) to (8) above. |