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

Name: Kyushu University Hospital

Applicant: Chiharu Kubo

Address: 3-1-1 Maidashi, Higashi-ku, Fukuoka

Approved Type 1 Use Regulation

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| Name of the Type of Living Modified Organism | Nonproliferative and genetically modified simian immunodeficiency virus (SIVagm-hPEDF), derived from African green monkeys, that expresses human pigment epithelium-derived factor (hPEDF) and has the env protein (VSV-G) for human Vesicular Stomatitis Virus (VSV) in its envelope. |
| Content of the Type 1 Use of Living Modified Organism | Used in clinical facilities for human gene therapy, including storage, transportation, disposal and acts incidental to them. |
| Method of the Type 1 Use of Living Modified Organism | Address: 3-1-1 Maidashi, Higashi-ku, Fukuoka<br>Name: Kyushu University Hospital<br>(1) The SIVagm-hPEDF solution must be sealed in containers, transported to a clinical facility in the frozen state, and stored in a freezer in a lockable storage room within the facility, which is equipped with P2-level containment measures (hereinafter referred to as “P2 storage room”).<br>(2) Thawing, dilution and dispensing of the frozen SIVagm-hPEDF solution, and opening of vials, must be performed within a safety cabinet in a laboratory equipped with P2-level containment measures (hereinafter referred to as “P2 laboratory”). Diluted SIVagm-hPEDF solution must be stored in a freezer within the P2 storage room.<br>In case of moving diluted SIVagm-hPEDF solution or its frozen form, through an open area, it must be placed in a sealed container, and that container must be placed in a box or similar package, to prevent it from falling or breaking.<br>(3) When disposing of the SIVagm-hPEDF solution, or its diluted forms, it must be sterilized (either by a chemical disinfectant treatment by spraying for 30 minutes with 70% ethanol, soaking for 30 minutes in |

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| | sodium hypochlorite containing 0.1~1.0% available chlorine concentration, or autoclave treatment (hereinafter the same)), and then disposed of according to the infectious waste management protocol defined by Kyushu University Hospital (hereinafter referred to as "the infectious waste management protocol").<br>(4) Syringes for administration of the diluted SIVagm-hPEDF to subjects must be filled in a safety cabinet in a P2 laboratory. Filled syringes must be placed in a sealed container, and that container must be placed in a box or similar package, to prevent it from falling or breaking.<br>(5) Administration of SIVagm-hPEDF to subjects must be performed in an operating theater that has been subjected to appropriate environmental containment measures. After incision in the vitreum using vitreous surgery under local anesthetic, inject the diluted SIVagm-hPEDF solution into the retina.<br>(6) After administration of the SIVagm-hPEDF to the subject, cover the subject's eye with gauze and an eye patch to screen the eye and prevent virus leakage. After that, promptly move the subject to a gene therapy room that has been subjected to appropriate environmental containment measures and is not under positive pressure (hereinafter referred to as a "single room").<br>(7) Needles, syringes, gauze, sterile sheets etc. that come into direct contact with SIVagm-hPEDF at the administration stage must be disposable, and must be subjected to appropriate sterilization treatment in a room with appropriate environmental containment measures, before disposal in accordance with the infectious waste management protocol.<br>If sterilization treatments on these materials are performed in a zone other than the operating theater or the single room, they must be placed inside a container that is doubly sealed for transportation.<br>(8) The subject shall be cared for in the single room for one week after administration. If the subject must temporarily leave the single room into open areas for examinations or other reasons, viral leakage prevention measures including the wearing of a mask and a gown must be compulsory. The subject shall be accompanied by one nurse at all times, and prohibition of excretion and expectoration in open areas is mandatory. |

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| | (9) The excreta, etc. (including blood, body fluids, urine and feces (hereinafter the same)) of the subject during the period of being taken care of in the single room, other than clinical samples, should be appropriately disinfected in the single room, then solidified using a solidifying agent, collected in an autoclave bag, packed in a corrugated cardboard box for medical waste labeled with a biohazard mark, and disposed of in accordance with the infectious waste management protocol.<br>If sterilization treatments on these materials are performed in a zone other than the single room, they must be placed inside a container that is doubly sealed for transportation. Excreta, etc., from the subject that are to be used as clinical samples should be handled in accordance with the handling of the SIVagm-hPEDF solution and its diluted forms.<br>(10) During the period of being taken care of in the single room, invasive devices that have been used on the subject and those that have been in contact with excreta, etc., must be subjected to appropriate sterilization treatment in a room with appropriate environmental containment measures, before disposal in accordance with the infectious waste management protocol, or cleaned thoroughly.<br>If sterilization treatments on these materials are performed in a zone other than the single room, they must be placed inside a container that is doubly sealed for transportation.<br>(11) Before releasing the subject from being taken care of in the single room, use the RT-PCR (reverse transcription polymerase chain reaction) method to confirm that SIVagm-hPEDF is negative in the blood, urine, and tears of the subject over time (on the day of administration, and on the 1st, 3rd, and 7th days thereafter).<br>If SIVagm-hPEDF is detected more than seven days after administration, continue to take care of the subject in the single room until test result is confirmed to have become negative. If the same gene sequence is detected beyond 14 days after administration, use cultured cells to check for the presence of infectious virus. Permit the subject to leave the single room after the presence of infectious virus in samples collected from the subject is denied.<br>(12) If SIVagm-hPEDF is detected from the blood, urine, or tears of the |

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| | subject after the subject has been released from care in the single room, immediately transfer the subject to care in a single room, and apply the same measures described in (8)-(11) above. |