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

Name: Kitasato University Hospital
Applicant: Kiyotaka Fujii, Director
Address: Kitasato 1-15-1, Sagamihara City, Kanagawa Prefecture

Approved Type 1 Use Regulation

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| Name of the Type of Living Modified Organism | Nonproliferative and genetically modified human adenovirus type 5 that expresses the Herpes simplex virus thymidine kinase gene (Adv.RSV-TK) |
| 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 of Clinical Facility : Kitasato 1-15-1, Sagamihara City, Kanagawa Prefecture<br>Name of Clinical Facility: Kitasato University Hospital<br><br>(1) The Adv.RSV-TK solution should be sealed in containers, transported to a clinical facility in the frozen state, and stored in a freezer in a P2 level laboratory at the facility (hereinafter referred to as “P2 lab”).<br>(2) Thawing, dilution and dispensing of the frozen Adv.RSV-TK solution has to be performed in a safety cabinet in a P2 lab. Diluted Adv.RSV-TK should be stored in a freezer in the P2 lab. Note that when the diluted Adv.RSV-TK or its frozen form is transported to another P2 level area through an open area, it should be kept inside a container that is doubly sealed.<br>(3) When disposing of the Adv.RSV-TK solutions (including dilutions), these should be virally inactivated (by autoclaving or by immersion in 0.5% sodium hypochlorite solution for 2 hours or longer; hereinafter the same shall apply), and then disposed of according to the medical waste management protocol defined by the facility (hereinafter referred to as "the medical waste |

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| | management protocol").<br>(4) The diluted Adv.RSV-TK should be doubly sealed, transported to a operation clean room that is pressure-controlled not to be positive and has appropriate containment measures (hereinafter referred to as "clean room"), packed in a special device comprising a puncture needle for injection, a syringe and a tube (hereinafter referred to as "injection kit") and loaded onto an injection pump.<br>(5) The administration of Adv.RSV-TK to a subject should be performed in a clean room by injecting the diluted Adv.RSV-TK into the prostate cancer lesion using a puncture guide mounted on an ultrasonographic device, the injection kit and an injection pump.<br>(6) Following completion of the administration of Adv.RSV-TK to the subject, the wounds of the subject should be disinfected. The subject, who is wearing a mask and a gown to prevent viral leakage, should be moved from the clean room to a single room that is pressure-controlled not to be positive and has appropriate containment measures (hereinafter referred to as “single room”).<br>(7) Devices including the injection kit, fabric and gauge used in (5) and (6) described above should be virally inactivated and disposed of according to the medical waste management protocol. In addition, devices including the puncture guide should be reused after viral inactivation. If the viral inactivation has to be carried out in another area, the objects should be transported in a doubly sealed container.<br>(8) The subject should be cared for in the single room until 24 hours after administration. When the subject enters the open area outside the clean room or the single room for examinations, etc., viral leakage prevention measures, including the wearing of a mask and a gown must be compulsory.<br>(9) The excreta, etc. (including blood, body fluids, urine and feces; hereinafter the same shall apply) of the subject |

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| | during the period of being taken care of in the single room should be virally inactivated and then disposed of in accordance with the medical waste management protocol. If the viral inactivation is to be carried out in another area, the objects should be transported in a doubly sealed container. Note that the excreta, etc., from the subject that are to be used as clinical samples should be handled in accordance with the handling of the Adv.RSV-TK solution.<br>(10) During the period of being taken care of in the single room, invasive devices that have been used in the subject and those that have been in contact with excreta, etc., should be virally inactivated and then disposed of in accordance with the medical waste management protocol, or be washed sufficiently. If the viral inactivation is to be carried out in another area, the objects should be transported in a doubly sealed container.<br>(11) Before releasing the subject from being taken care of in the single room, confirm that Adv.RSV-TK is negative in the blood and urine of the subject. If Adv.RSV-TK is detected, the subject should continually be cared for in the single room.<br>(12) If Adv.RSV-TK is detected in the blood or the urine of the subject during the observation period even after releasing the subject from the single room, immediately transfer the subject back to the single room, and take the same measures as in (8) to (11) above. |