

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

Name: Jichi Medical University Hospital

Applicant: Kazuyuki Shimada, Director

Address: Yakushiji 3311-1, Simotsuke City, Tochigi Prefecture

Approved Type 1 Use Regulation

Name of the Type of Living Modified Organism	Nonproliferative and genetically modified human adeno-associated virus type 2 that expresses the human amino acid decarboxylase gene (AAV-hAADC-2)
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	<p>Address of Clinical Facility: Yakushiji 3311-1, Simotsuke City, Tochigi Prefecture</p> <p>Name of Clinical Facility: Jichi Medical University Hospital</p> <p>(1) The AAV-hAADC-2 solution should be sealed in containers, transported to a clinical facility in the frozen state, and stored in a freezer in a laboratory at the facility.</p> <p>(2) Thawing, dilution and dispensing of the frozen AAV-hAADC-2 solution has to be performed in a safety cabinet in a P2 level laboratory (hereinafter referred to as "P2 lab"). Storage of the diluted AAV-hAADC-2 should be kept in a freezer in a P2 lab. Note that when the diluted AAV-hAADC-2 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.</p> <p>(3) When disposing of the solution (including dilutions) of AAV-hAADC-2, these should be virally inactivated (by autoclaving or incineration; hereinafter the same shall apply), followed by disposal according to the medical waste management protocol defined by the facility (hereinafter referred to as "the medical waste management protocol").</p> <p>(4) The diluted AAV-hAADC-2 should be packed in a special device comprising a syringe, a tube and a cannula loaded on a</p>

	<p>syringe pump (hereinafter referred to as "injection kit") in a safety cabinet in a P2 lab, doubly sealed, and transported to an operation room that is pressure-controlled not to be positive, and is undergoing appropriate containment measures (hereinafter referred to as "operation room"). In addition, the operation room should be located at the end of the operation room area, and no other operation should be conducted in the operation room on the day of the administration of AAV-hAADC-2.</p> <p>(5) The administration of AAV-hAADC-2 to a subject should be performed in the operation room by injecting the diluted AAV-hAADC-2 into the putamen on both sides by stereotaxic operation.</p> <p>After carefully loading the injection kit on the stereotaxic equipment, the cannula is inserted through a hole with a diameter of approximately 12 mm in the skull of the subject, and the diluted AAV-hAADC-2 is injected slowly by two-direction syringe pump into the putamen. After finishing the injection, the cannula is kept in position for about three minutes, and is then slowly removed. Removal from the surface of the brain should be performed particularly carefully at a rate of approximately 3 mm/minute. By using a cannula with a tapered end, spilling of the diluted AAV-hAADC-2 from the cannula end or aerosolization of the dilution during removal is prevented. After removal of the cannula, the wound of the subject should be closed immediately, but temporally. Injection into the other putamen should be done in the same way.</p> <p>Additionally, two sheets of fabric should be spread around the head.</p> <p>(6) Following the completion of administration of AAV-hAADC-2 to the subject, the wounds of the subject should be disinfected, sealed by applying wound dressings to replace dermal loss, and covered with a triangular bandage. The subject, who is wearing a mask and gown to prevent viral leakage, should be moved from the operation room to a single room that is pressure-controlled not to be positive and has appropriate containment measures (hereinafter referred to as "single room").</p> <p>(7) Devices including the injection kit, fabric and gauge used in above mentioned (5) and (6) should be virally inactivated and disposed of according to 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</p>
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	<p>container. Note that the operation room should be closed for at least 12 hours after the operation. Then, the floor should be UV radiated and further disinfected by wet mopping using a cleaner containing quaternary ammonium salt.</p> <p>(8) The subject should be cared for in the single room until 72 hours after administration. When the subject enters the open area outside the operation room or the single room for examinations, etc., viral leakage prevention measures including the wearing of a mask and a gown must be compulsory.</p> <p>(9) The excreta, etc. (including blood, body fluids, urine and feces) of the subject 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 viral inactivation has to be carried out in another area, the objects should be transported in a doubly sealed container. Note that excreta, etc., from the subject that are to be used as clinical samples should be handled in accordance with the handling of the AAV-hAADC-2 solution.</p> <p>(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.</p> <p>(11) Before releasing the subject from being taken care of in the single room, confirm that AAV-hAADC-2 is negative in the blood and the urine of the subject. If AAV-hAADC-2 is detected, the subject should be continually cared for in the single room.</p> <p>(12) If AAV-hAADC-2 is detected in the blood or the urine of the subject after releasing the subject from being taken care of in the single room, immediately transfer the subject back to the single room, and take the same measures as in (8) to (11) above.</p>
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