

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

Name of Entity: Jichi Medical University Hospital
 Name of Applicant: Yoshikazu Yasuda, Hospital Director
 Address: 331-1, Yakushiji, Shimono, Tochigi

Approved Type 1 Use Regulation

Names of types of living modified organisms	Type-2 adeno-associated virus vector (AAV-hAADC-2) incorporated with human aromatic L-amino acid decarboxylase (AADC) gene
Content of Type 1 Use of living modified organisms	Use for the purpose of human gene therapy, storage, transportation, disposal, and other acts attendant with these.
Method of Type 1 Use of living modified organisms	<p>Facility Location : 331-1, Yakushiji, Shimono, Tochigi Facility Name: Jichi Medical University Hospital and Jichi Children's Medical Center Tochigi</p> <ol style="list-style-type: none"> (1) The solution of the living modified organisms enclosed in a sealed container with a screw cap, shall be transported to the treatment facility in frozen state and stored in a freezer within the laboratory in the facility. (2) Melt, dilute, and dispense this frozen solution of the living modified organisms within a safety cabinet in the P2-level laboratory (called simply "P2 laboratory" hereinafter). The diluted solution of the living modified organisms shall be stored in a freezer within the P2 laboratory. When transporting this diluted solution in a liquid or frozen state to other areas through any open area, it shall be enclosed in a double-sealed container. (3) When disposing the living modified organisms (including its diluted solution), apply virus inactivation treatment (by high-pressure steam sterilization treatment or incineration; the same applies hereinafter) first, and dispose according to the Rules regarding the medical waste management, which was provided by this facility (called simply "Medical Waste Management Rules" hereinafter). (4) Within a safety cabinet in P2-level laboratory, fill this solution of the living modified organisms into a device consist of a dedicated syringe, tube and cannula, and install this device in the dedicated syringe pump (called "injection set" hereinafter), then double seal it and transport it to an operation room without positive pressure, for which containment measures for the environment have been taken appropriately (to be called simply "operation room" hereinafter). This operation room shall be located at the end of the operation room area, and no other operations shall be performed on the day of administration of the

	<p>living modified organism solution.</p> <p>(5) When administering the living modified organisms to a human subject, the diluted solution shall be injected into the putamen at the both sides by stereotactic brain surgery, performed in the operation room.</p> <p>Install carefully the injection set in the stereotactic brain surgery device, insert a cannula through a 12mm-diameter bone tunnel which was made on the subject's head skull, and inject this diluted solution in two directions inside the putamen by a syringe pump at a rate of 3 μl/min. When injection is completed, keep the cannula at the same position for about 3 min. and remove it slowly. Especially at the brain surface area, remove the cannula very carefully at a rate of approx. 3mm/min. The cannula must have a taper-tip structure to avoid the diluted solution leaking from cannula's tip and being aerosolized during removing the cannula. Immediately after the cannula is removed, close the subject's wound temporarily. Then repeat the same injection steps for another side of putamen. Spread a cloth doubly around the subject's head.</p> <p>(6) After administering the living modified organisms to the subject, disinfect his/her wounded part, stick wound dressing material for skin deficiency into the dermis and seal it, then cover it with a triangular bandage. For virus release prevention, make sure to have the subject dressed with a mask and a gown, and transport him/her from the operation room to a room without positive pressure, for which containment measures for the environment have been taken appropriately (called simply "individual room" hereinafter).</p> <p>(7) Apply virus inactivation treatment to the tools such as the injection set, cloths and gauze, which were used in the above steps (5) and (6), and dispose them according to the Medical Waste Management Rules. When applying the virus inactivation in the other areas, transport the items in a double-sealed container. Close off the operation room for 12 hours after the operation. Then irradiate ultraviolet light to the floor and disinfect by wiping with detergent containing quaternary ammonium salt.</p> <p>(8) The subject shall be managed in an individual room for 72 hours after administration. When the subject needs to go out of the operation room or individual room to an open area temporarily for reasons such as taking a test, obligate him/her to wear a mask and a gown to prevent virus release.</p> <p>(9) For the subject's excrement (blood, body fluid, urine, and fecal waste; the same applies hereinafter) which was excreted in the individual room during the management period, apply virus inactivation, and dispose according to the Medical Waste Management Rules. If the virus inactivation is conducted in other areas, use a double-sealed container for transportation. Also, the handling method for the subject's excrement which will be used as clinical specimen shall be based on the handling of the solution of the living modified organisms.</p>
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	<p>(10) For tools used invasively on the subject during the individual management period, as well as tools which were in contact with the subject's excrement, apply virus inactivation treatment, and dispose according to the Medical Waste Management Rules or cleanse thoroughly. If the virus inactivation treatment is conducted in other areas, use a double-sealed container for transportation.</p> <p>(11) Before releasing the subject from the individual room management, make sure that the living modified organisms in this subject's blood and urine exhibit negative results. When the living modified organisms turned out positive, the individual room management shall be continued.</p> <p>(12) When the living modified organisms are detected in the subject's blood or urine after he/she was released from the individual management, immediately bring him/her under the individual room supervision, and take the same steps as the above (8) to (11).</p>
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