

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

Name: The University of Tokyo Hospital
 Applicant: Kadowaki Takashi, Director
 Address: 7-3-1 Hongo, Bunkyo-ku, Tokyo

Approved Type 1 Use Regulation

Name of the Type of Living Modified Organism	Replication-conditional, recombinant human herpes simplex virus type 1 that expresses the <i>E.coli lacZ</i> gene, and has inactivation of the $\gamma 34.5$, <i>ICP6</i> and $\alpha 47$ genes (G47 Δ).
Content of the Type 1 Use of Living Modified Organism	Used in clinical facilities for human therapy, including storage, transportation, disposal and acts incidental to them.
Method of the Type 1 Use of Living Modified Organism	<p>Address of the clinical facility: 7-3-1 Hongo, Bunkyo-ku, Tokyo Name of the clinical facility: The University of Tokyo Hospital</p> <ol style="list-style-type: none"> (1) The G47Δ solution should be sealed in containers, transported to the clinical facility in a frozen state, and stored in a freezer in a laboratory at the facility. (2) Thawing, dilution and dispensing of the frozen G47Δ solution should be performed in a safety cabinet in a P2 level laboratory at the facility with appropriate containment measures. The diluted G47Δ should be stored in a refrigerator or a freezer in a P2 level laboratory. When the G47Δ solution or its frozen form, or the diluted G47Δ or its frozen form is transported through an open area, it should be kept inside a double-sealed container. (3) When disposing of the G47Δ solution or the diluted G47Δ, it should be virally inactivated (by autoclaving or using disinfectant such as 70% isopropanol, 70~90% ethanol, 0.2% sodium hypochlorite, 10% povidone iodine, 0.1~0.5% chlorhexidine gluconate, and 0.05~0.2% benzalkonium chloride; hereinafter the same shall apply), followed by disposal according to the medical waste management protocol defined by the University of Tokyo Hospital (hereinafter referred to as "the medical waste management protocol"). (4) The administration of G47Δ to a subject should be performed in an operating room with appropriate containment measures by injecting the buffer containing G47Δ (hereinafter referred to as "the G47Δ

dilution") into the tumor. The needle is inserted by a transrectal ultrasound-guided transperineal technique, and the G47 Δ dilution is slowly and manually injected. After finishing the injection, the syringe is kept in position for a few minutes, and then slowly removed. Removal of the needle from the skin should be performed with particular care to prevent spilling or aerosolization of the G47 Δ dilution.

- (5) After completion of the administration of G47 Δ to the subject, the wound should be disinfected, covered with gauze, and the head of the subject covered with a cap. The subject, wearing a mask for precaution against viral leakage, should be transferred from the operating room to a single room with appropriate containment measures and without a positive air pressure (hereinafter referred to as "single room").
- (6) Devices such as syringes and materials such as fabric sheets and gauze used in above mentioned (4) and (5) 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 double-sealed container. The floor of the operating room should be cleaned by mopping using disinfectant. Note that the air in the operating room is refreshed every five minutes (twelve times an hour) by ventilation.
- (7) The subject should be cared in a single room until 72 hours after the G47 Δ administration. When the subject leaves the operating room or the single room temporarily and enters an open area for examinations, etc., he/she should avoid blood sampling, urination, and evacuation if possible, and must wear a mask to prevent viral leakage.
- (8) The excreta, including urine and feces, of the subject during the single room care should be virally inactivated and then disposed of in accordance with the medical waste management protocol. The blood and urine sampled from the subject for research purposes should be disposed of in accordance with the handling of the G47 Δ solution and the G47 Δ dilution.
- (9) During the single room care, devices that have been used invasively on the subject and those that have been in contact with the subject's excreta, etc., should be virally inactivated and then disposed of in accordance with the medical waste management protocol, or washed sufficiently. If the viral inactivation is to be carried out in an area outside the single room, the objects should be transported in a double-sealed container.

	<p>(10) Before releasing the subject from the single room care, it is necessary to confirm that G47Δ is not detected from the blood or urine of the subject. If G47Δ is detected, the subject should be continually cared in a single room until G47Δ is no longer detected.</p> <p>(11) If G47Δ is detected from the blood or urine of the subject after the subject is released from the single room care, reinstatement of the subject to a single room care will be considered. Measures similar to above mentioned (7) to (10) would be taken if deemed necessary.</p>
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