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

Name: IMSUT Hospital
Applicant: Kozo Imai, Director
Address: 4-6-1 Shirokanedai, Minato-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 *E.coli lacZ* gene, and has inactivation of the *γ34.5*, *ICP6* and *α47* genes (G47Δ).
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	Address of the clinical facility: 4-6-1 Shirokanedai, Minato -ku, Tokyo Name of the clinical facility: IMSUT Hospital (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. The diluted G47Δ should be stored in a refrigerator or a freezer in a P2 level laboratory. When the diluted G47Δ or its frozen form is transported to another area through an open area, it should be kept inside a double-sealed container. (3) When disposing of the G47Δ solution (including its dilution), 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 diluted G47Δ should be loaded to a designated syringe in a safety cabinet in a P2 level laboratory. The syringe should be doubly sealed, and transported to an operating room with appropriate containment measures (hereinafter referred to as "operating room"). (5) The administration of G47Δ to a subject should be performed in an operating room by injecting the buffer containing G47Δ (hereinafter referred to as "the G47Δ dilution") into the tumor. The cannula is inserted mainly through the nasal cavity of the subject, and the G47Δ dilution is slowly and manually injected. After finishing the injection, the cannula is kept in position for a few minutes, and then slowly removed. Removal of the cannula should be performed with

	particular care to prevent spilling or aerosolization of the G47Δ dilution. After injection of the total planned volume of the G47Δ dilution and the final removal of the cannula, the operation wound should be closed immediately. (6) After completion of the administration of G47Δ to the subject, the wound should be disinfected and covered with gauze. 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"). (7) Devices such as syringes and materials such as fabric sheets and gauze used in (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 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. (8) The subject should be cared in a single room until 72 hours after the G47Δ 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. (9) The excreta 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, urine and saliva sampled from the subject for research purposes should be disposed of in accordance with the handling of the G47Δ solution. (10) 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 another area, the objects should be transported in a double-sealed container. (11) Before releasing the subject from the single room care, it is necessary to confirm that G47Δ is not detected from the blood, saliva 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. (12) If G47Δ is detected from the blood, saliva or urine of the subject after the subject is released from the single room care, the subject should be transferred back to a single room immediately, and the measures described from (8) to (10) should be taken. (13) When the subject's medical condition deteriorates after G47Δ administration and the subject requires an open brain surgery for the purpose other than G47Δ administration during the period G47Δ is presumed to persist in the brain lesion, the measures described from (5) to (12) should be taken.