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

Name: Hokkaido University Hospital
Applicant: Kazuo Miyasaka, Director (Seal)
Address: Nishi 5, Kita 14, Kita-ku, Sapporo City

Approved Type 1 Use Regulation

Name of the Type of Living Modified Organism	Nonproliferative and genetically modified Moloney murine leukemia virus that contains the gene sequence of human adenosine deaminase cDNA, and has env protein of gibbon ape leukemia virus in its envelope (GCsapM-ADA)
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: Nishi 5, Kita 14, Kita-ku, Sapporo City, Hokkaido Name: Hokkaido University Hospital (1) The GCsapM-ADA 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. (2) Thawing, dilution and dispensing of the frozen GCsapM-ADA solution has to be performed in a closed system in a safety cabinet in a P2 level laboratory or in a P2 level laboratory itself. Transfer of GCsapM-ADA into the patient bone marrow cells, incubation of the cells to which GCsapM-ADA was transferred, or other handling of GCsapM-ADA dilutions and cells to which GCsapM-ADA was transferred should be similarly performed in a closed system in a safety cabinet in a P2 level laboratory or in a P2 level laboratory itself. Storage of GCsapM-ADA solution and the cells to which GCsapM-ADA was transferred should be kept in a freezer, refrigerator, or incubator in a P2 level laboratory. Note that when the diluted GCsapM-ADA or its frozen form or the cells to which GCsapM-ADA was transferred is transported to another P2 level area through an open area, it should be kept inside a doubly sealed container. (3) When disposing of the GCsapM-ADA solution (including dilutions) or the cells to which GCsapM-ADA was transferred, these should be sterilized and then disposed of according to the infectious waste management protocol defined by the facility (hereinafter referred to as "the infectious waste management protocol"). (4) Administration of the cells to which GCsapM-ADA was transferred, to a subject has to be performed by infusion in a single room that has appropriate containment measures (hereinafter referred to as “clean room”). Additionally, devices that come in direct contact with the cells to which GCsapM-ADA was transferred at the time of administration, such

	as injection needles, syringes, and tubes, etc., should be disposable ones, and after use, these should be appropriately disinfected in the clean room, followed by disposal in accordance with the infectious waste management protocol. (5) The subject should be cared for in the clean room until the third day after administration. When the subject enters the open area outside the clean room for examinations, etc., viral leakage prevention measures including the wearing of a mask and a gown must be compulsory. Blood and body fluids of the subject during the period of being taken care of in the clean room should be disinfected individually and disposed of in accordance with the infectious waste management protocol. In addition, the excreta of the subject including urine and feces should be appropriately disinfected in the clean room and disposed of in accordance with the infectious waste management protocol until the existence of replication competent GCsapM-ADA (hereinafter referred to as "RCR") is denied by the polymerase chain reaction (PCR) test using subject blood, which is performed after the day following administration. 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 GCsapM-ADA solution or the cells to which GCsapM-ADA was transferred. (6) During the period of being taken care of in the clean room, invasive devices that have been used in the subject and those that have been in contact with excreta, etc., should be appropriately disinfected in the clean room and disposed of in accordance with the infectious waste management protocol, or be washed sufficiently in the clean room. (7) Before releasing the subject from the clean room, confirm that RCR is negative in the peripheral blood mononuclear cells (PBMC) and the plasma of the subject. If RCR is detected, the subject should continually be cared for in the clean room. (8) If RCR is detected in the PBMC or the plasma of the subject after releasing the subject from the clean room, immediately transfer the subject back to the clean room, and take the same measures as in (5) to (7) above.