

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

Name: Mie University Hospital

Applicant: Atsumasa Uchida

Address: 2-174, Edobashi, Tsu, Mie Prefecture, Japan

Approved Type 1 Use Regulation

Name of the Type of Living Modified Organism	Nonproliferative and genetically modified Moloney murine leukemia virus that expresses HLA-A2402-restricted MAGE-A4-specific T cell receptor alpha and beta genes, and has env protein of Gibbon ape leukemia virus in its envelope (MS-bPa)
Content of the Type 1 Use of Living Modified Organism	Used in a clinical facility 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: 2-174, Edobashi, Tsu, Mie Prefecture, Japan Name: Mie University Hospital</p> <p>(1). The solution of MS-bPa should be sealed in containers, transported to the clinical facility in the frozen state, and stored in a freezer in a P2 level laboratory at the facility (hereinafter referred to as "P2 laboratory").</p> <p>(2). Thawing of the frozen solution of MS-bPa, and dilution and dispensing of the solution of MS-bPa has to be performed in a safety cabinet in a P2 laboratory or in a closed system in the P2 laboratory. Similarly, the handling of dilution of MS-bPa and the cells transduced with MS-bPa, including the transduction of the lymphocytes of patients with MS-bPa, incubation of the cells transduced with MS-bPa, etc., are to be performed in a safety cabinet in the P2 laboratory or in a closed system in the P2 laboratory. Dilution of MS-bPa and cells transduced with MS-bPa should be stored in a refrigerator, freezer or incubator in the P2 laboratory. Note that when the dilution of MS-bPa or its frozen form or the cells transduced with MS-bPa is transported to another P2 area through an open area, it should be contained inside a sealed container, which should be put in a box etc. for transportation to avoid dropping or breaking it.</p> <p>(3). When disposing of the solution (including dilution) of MS-bPa or the cells transduced with MS-bPa, these should be sterilized (by an autoclave, or soaking in 0.5% sodium hypochlorite solution for not less than two hours; the same in the followings) and then disposed of according to the medical waste management protocol established by Mie University Hospital (hereinafter referred to as "medical waste management protocol").</p> <p>(4). Administration of the MS-bPa transduced cells to a subject has to be performed by infusion in a single room that is pressure-controlled not to be positive and has appropriate containment measures (hereinafter</p>

	<p>referred to as “single room”). Additionally, devices etc. that come in direct contact with the cells transduced with MS-bPa at the time of administration, such as injection needles, syringes, and tubes, etc., should be disposable ones, and these should be appropriately sterilized followed by disposal in accordance with the medical waste management protocol. Note that when sterilization is performed in the area outside of the single room, the wastes should be contained inside a double-sealed container and transported.</p> <p>(5). Until the third day after administration, the subject should be cared for in the single room. When the subject goes to the open area outside the single room for examinations etc., viral leakage prevention measures including the wearing of a mask and a gown must be compulsory.</p> <p>(6). Blood and body fluids of the subject during the period of being taken care of in the single room should be appropriately sterilized individually and disposed of in accordance with the medical waste management protocol. In addition, the excreta of the subject including urine and feces should be appropriately sterilized and disposed of in accordance with the medical waste management protocol until the existence of replication competent retrovirus (hereinafter referred to as "RCR") is denied by the polymerase chain reaction test using subject's blood which is performed on or after the day following administration. Note that when sterilization is performed in the area outside of the single room, the wastes should be contained inside a double-sealed container and transported. Also, note that the handling of excreta etc. from the subject that are to be used as clinical samples should be in accordance with the handling of the solution of MS-bPa or the cells transduced with MS-bPa.</p> <p>(7). During the period of being taken care of in the single room, devices etc. that have been used invasively in the subject and those that have been in contact with excreta etc. of the subject should be appropriately sterilized and be disposed of in accordance with the medical waste management protocol, or be sufficiently washed. Note that when sterilization is performed in the area outside of the single room, the wastes should be contained inside a double-sealed container and transported.</p> <p>(8). Before releasing the subject from being taken care of in the single room, confirm that RCR is negative in the peripheral blood mononuclear cells (hereinafter referred to as "PBMC") and the plasma of the subject. If RCR is detected, the subject should continue to be cared for in the single room.</p> <p>(9). If RCR is detected in the PBMC or the plasma of the subject after releasing the subject from being taken care of in the single room, immediately transfer the subject to be taken care of in the single room, and take the same measures as in (5) to (8) above.</p>
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