Environmental Protection Authority
Te Mana Rauhī Taiao

New Zealand Government

Approval

Date of Decision	21 August 2020
Application number	APP204075
Application type	To develop in containment genetically modified organisms under sections 40(1) and 42A of the Hazardous Substances and New Organisms Act 1996
Applicant	The Malaghan Institute of Medical Research
Date Application received	7 August 2020
Consideration date	20 August 2020
Decision-made by	Siobhan Quayle, Group General Manager, Regulatory Systems and Operations[1]
Purpose of the Application	To develop genetically modified human cells for the packaging and testing of 3rd generation self-inactivating lentiviral vectors, to be used to genetically modify human T cells for the expression of genes that regulate the activity of human immune cells.

Decision

1.1. After reviewing all of the information contained in the application, the EPA Staff Assessment Report, and comments received from the Department of Conservation, I am satisfied that the application meets the requirements of section 42A of the Act.

[1] The Group General Manager of Regulatory Systems and Operations has made the decision on this application under delegated authority in accordance with section 19 of the Act.

1.2. Therefore, **I approve** application APP204075 to develop, as a project, the genetically modified organisms described in Table 1 and the Schedule **with controls**, as listed in Table 2.

	21/08/2020
Siobhan Quayle **Group General Manager, Regulatory Systems and Operations**	**Date**

Table 1: Approved organism description

Host organisms	Cultured cell lines of the following species: *Homo sapiens* L. 1758 (human). Human lentiviral packaging cell lines, primary leukaemia cell lines for vector titre testing, and human primary T cells with genes encoding Chimaeric Antigen Receptors
Category of host organism	These organisms are Category 1 host organisms because: • they are clearly identifiable and classifiable • they are characterised to the extent that their main biological characteristics are known • they are not normally able to (and do not contain infectious agents normally able to) cause disease in humans, animals, plants or fungi • they do not normally infect, colonise or establish in humans, and • they do not produce desiccation-resistant structures such as spores or cysts that can be normally disseminated in the air.
Modification	Vectors will be 3rd generation replication-defective self-inactivating lentiviral vectors and consist of plasmids containing viral packaging gene constructs, envelope protein constructs, and transfer vectors containing: promoters and gene regulatory elements, packaging signals, secretory signals, polyadenylation signals, flanking long terminal repeat sequences and origins of replication, genes for viral envelope proteins, reverse transcriptase, integrase, matrix, capsid and nucleocapsid proteins, envelope proteins, protease. Donor genetic material is sourced from humans, and mammalian viruses. The modifications will consist of functional coding sequences for chimaeric antigen receptors, including antibody single chain variable fragment recognising the CD19 cell surface protein, transmembrane domains, and immune cell co-stimulatory domains. The modifications will exclude: • Genetic material that increases the pathogenicity, virulence, or infectivity of the host organism • Genes that encode for vertebrate toxins with an LD_{50} < 100 µg/kg, and • Those that result in the GMO having a greater ability to escape from containment than the unmodified host organism.
Category of modification	The modifications are Category B because these modifications are carried out under a minimum of PC2 containment as defined in the Regulations. They do not increase the pathogenicity, virulence or infectivity of the host organism to laboratory personnel, the community or the environment and do not result in the GMO having a greater ability to escape from containment than the unmodified host organism.
Minimum containment level required	PC2

Table 2: Controls

The approval holder must ensure compliance with the following controls.	
1)	This approval is limited to the development of the GMOs described in Table 1 and the Schedule ("approved organisms") to undertake genetic modification of cell lines from humans to enable the packaging of 3rd generation self-inactivating lentiviral vectors and the creation of Chimaeric Antigen Receptor T cells.
2)	The approved organisms must not escape containment.
3)	The approved organisms must be developed within a containment facility that complies with: • The MAF/ERMA New Zealand Standard: Facilities for Microorganisms and Cell Cultures[2]: 2007a • The Australian/New Zealand Standard AS/NZS 2243.3:2002 Safety in laboratories: Part 3: Microbiological aspects and containment facilities[3], and • Physical Containment level 2 (PC2) requirements of the above Standards (at minimum) for developments involving the efficient disruption of specific endogenous genes or the precise modification of endogenous sequences in cultured human cell lines.
4)	The approval holder must ensure that within 24 hours of the discovery of any breach of containment (includes the escape of an organism(s) or a failure in the structural integrity of physical containment), the Ministry for Primary Industries biosecurity inspector responsible for supervision of the facility, has received notification (written or verbal)[4] of the breach and the details of any remedial action taken.

Schedule: List of organisms, and approval numbers of organisms approved for development

Organism	Approval number
Human (*Homo sapiens* L 1758) viral vector packaging cell lines, leukaemia cell lines and human patient-derived primary T cell lines	GMD102668

[2] Any reference to MAF/ERMA New Zealand or AS/NZS Standards in these controls also refers to any subsequent version approved or endorsed by the EPA.

[3] Any reference to MAF/ERMA New Zealand or AS/NZS Standards in these controls also refers to any subsequent version approved or endorsed by the EPA.

[4] The biosecurity inspector's contact details can be found in the facility containment manual.