

PART 1 (COUNCIL DECISION 2002/813/EC)

**SUMMARY NOTIFICATION INFORMATION FORMAT FOR THE RELEASE OF
GENETICALLY MODIFIED ORGANISMS OTHER THAN HIGHER PLANTS IN
ACCORDANCE WITH ARTICLE 11 OF DIRECTIVE 2001/18/EC**

In order to tick one or several possibilities, please use crosses (meaning x or X) into the space provided as (.)

A. General information

1. Details of notification

- (a) Member State of notification: [Spain](#)
- (b) Notification number: [B/ES/17/08](#)
- (c) Date of acknowledgement of notification: [23/03/2017](#)
- (d) Title of the project: [A pilot study of autologous differentiated T lymphocytes infusion from expanded and transduced peripheral blood to express a chimeric antigen receptor with anti-CD19 specificity in patients with resistant or refractory CD19 + leukemia or lymphoma.](#)
- (e) Proposed period of release: [from April 2017 to June 2018.](#)

2. Notifier

Name of institution or company:
[Institut d'Investigacions Biomèdiques August Pi i Sunyer \(IDIPAPS\)](#)
[Carrer del Rosselló, 149, 08036 Barcelona](#)

3. GMO characterisation [CART19a_A3B1:CD8TM:4-1BB:CD3 or ARI-0001 cells.](#)

(a) Indicate whether the GMO is a:

- | | | |
|----------------|-----|-----------------------|
| viroid | (.) | |
| RNA virus | (.) | |
| DNA virus | (.) | |
| bacterium | (.) | |
| fungus | (.) | |
| animal | | |
| - mammals | (X) | |
| - insect | (.) | |
| - fish | (.) | |
| - other animal | (.) | specify phylum, class |

other, specify (kingdom, phylum and class)

- (b) Identity of the GMO (genus and species)
Homo sapiens and Mus musculus.
Autologous T lymphocytes transduced with a lentivirus to express a chimeric (murine / human) antigenic receptor (CAR) directed against CD19 (ARI-0001 cells).
- (c) Genetic stability – according to Annex IIIa, II, A(10)
The sequences encoding CAR directed against CD19 are introduced into T cells by transduction with a lentivirus. Since the viral vector is integrated into the host genome, after the infusion, the CAR sequences will be present as an integral and stable host DNA in transduced cells as long as they persist.

Genetic stability is verified in different steps of the production process, through integration analysis of the insert (restriction pattern and transgene sequencing).

4. Is the same GMO release planned elsewhere in the Community (in conformity with Article 6(1)), by the same notifier?
Yes (.) No (X)
If yes, insert the country code(s)
5. Has the same GMO been notified for release elsewhere in the Community by the same notifier?
Yes (.) No (X)
If yes: -
- Member State of notification
- Notification number

Please use the following country codes:

Austria AT; Belgium BE; Germany DE; Denmark DK; Spain ES; Finland FI; France FR; United Kingdom GB; Greece GR; Ireland IE; Iceland IS; Italy IT; Luxembourg LU; Netherlands NL; Norway NO; Portugal PT; Sweden SE

6. Has the same GMO been notified for release or placing on the market outside the Community by the same or other notifier?
Yes (.) No (X)
If yes: -
- Member State of notification
- Notification number
7. Summary of the potential environmental impact of the release of the GMOs.

The possible environmental impact of the release of ARI-0001 cells is very low. The release of ARI-0001 cells is limited to its administration to the patient in the hospital environment and will not reach the environment to a large extent. The GMO consists of genetically modified T lymphocytes that are transduced *ex vivo* in a Good Manufacturing Practices (GMP) facilities and it is transported with standardised transport measures according to GMP and protocols, where it is infused intravenously to the patient, which means that the risk of any impact on the environment is negligible.

In the unlikely event that the cells are exposed to the environment, i.e. being released from the packaging accidentally, the cells would rapidly lose viability and therefore the vector sequences would be lost. The GMO is not able to survive, settle, spread or displace to other organisms, and is not pathogenic in animals or plants. ARI-0001 cells persist in the human once inoculated during a limited period of time, and later they are eliminated by physiological processes like any other cellular type.

According to the environmental risk assessment, the ARI-0001 product will not, in general, reach the environment.

B. Information relating to the recipient or parental organism from which the GMO is derived

1. Recipient or parental organism characterisation:

(a) Indicate whether the recipient or parental organism is a:

(select one only)

- viroid (.)
 - RNA virus (.)
 - DNA virus (.)
 - bacterium (.)
 - fungus (.)
 - animal (.)
 - mammals (X)
 - insect (.)
 - fish (.)
 - other animal (.)
- (specify phylum, class)

other, specify

2. Name

- (i) order and/or higher taxon (for animals): *Homo sapiens*
- (ii) genus : *Homo*
- (iii) species: *H.sapiens*
- (iv) subspecies: -
- (v) strain: -
- (vi) pathovar (biotype, ecotype, race, etc.): -
- (vii) common name: human

3. Geographical distribution of the organism

- (a) Indigenous to, or otherwise established in, the country where the notification is made:
 Yes (X) No (.) Not known (.)

- (b) Indigenous to, or otherwise established in, other EC countries:
[Not applicable for humans.](#)

- (i) Yes (.)

If yes, indicate the type of ecosystem in which it is found:

Atlantic	..
Mediterranean	..
Boreal	..
Alpine	..
Continental	..
Macaronesian	..

- (ii) No (.)

- (iii) Not known (.)

- (c) Is it frequently used in the country where the notification is made?
Yes (.) No (.)

- (d) Is it frequently kept in the country where the notification is made?
Yes (.) No (.)

4. Natural habitat of the organism

- (a) If the organism is a microorganism

water	(.)
soil, free-living	(.)
soil in association with plant-root systems	(.)
in association with plant leaf/stem systems	(.)
other, specify	

- (b) If the organism is an animal: natural habitat or usual agroecosystem:
[Human](#)

5. (a) Detection techniques

[Common techniques of blood cell analysis. From the apheresis of the patient, the lymphocytes are selected by their size \(density\) as the first step \(removal of platelets and obtaining mononuclear cells \[PBMCs\]\) by three different options: centrifugation, elutriation or ficoll.](#)

- (b) Identification techniques
[Please refer to section 5.a.](#)

6. Is the recipient organism classified under existing Community rules relating to the protection of human health and/or the environment?

Yes (.) No (X)

If yes, specify : -

...

7. Is the recipient organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?

Yes (.) No (X) Not known (.)

If yes:

- (a) to which of the following organisms:

humans (.)
animals (.)
plants ()
other (.)

- (b) give the relevant information specified under Annex III A, point II. (A)(11)(d) of Directive 2001/18/EC

The cells from which the OMG (autologous T cells) are derived are patient specific and do not survive outside the patient from which they are derived. Cells are not pathogenic and do not persist or replicate in either the environment or other organisms.

As a prior quality control, before the apheresis is performed and prior to the introduction of the patients in the trial, all patients included will be tested for different serologies, excluding those individuals who present some positive serology according to RD 1301/2006. Also, the microbiological controls necessary to process the cells obtained in the laboratory of advanced therapies of the Hospital Clínic of Barcelona (HIV 1 and 2, HVB, HVC, CMV, Lues, HTLV, T. Cruzi) will be performed.

If there is a period of time of 2 months between the blood test and leukapheresis, the serology will be repeated (the tests will be performed in the microbiology department of the Hospital Clínic de Barcelona).

8. Information concerning reproduction

Not applicable for autologous human T cells transduced with the CAR receptor.

- (a) Generation time in natural ecosystems:

- (b) Generation time in the ecosystem where the release will take place:

- (c) Way of reproduction: Sexual .. Asexual ..

- (c) Factors affecting reproduction:

9. Survivability

Not applicable for autologous human T cells transduced with the CAR receptor.

(a) ability to form structures enhancing survival or dormancy:

- | | | |
|--------|------------------------|-----|
| (i) | endospores | (.) |
| (ii) | cysts | (.) |
| (iii) | sclerotia | (.) |
| (iv) | asexual spores (fungi) | (.) |
| (v) | sexual spores (funghi) | (.) |
| (vi) | eggs | (.) |
| (vii) | pupae | (.) |
| (viii) | larvae | (.) |
| (ix) | other, specify | |

(b) relevant factors affecting survivability:

Not applicable, genetically modified T lymphocytes cannot survive in the environment.

10. (a) Ways of dissemination

Human T lymphocytes can only be transmitted from human to human through injection or infusion. Given the inability of human T lymphocytes to survive in the environment, their participation in any environmental process is not expected. In the case that human T lymphocytes are infused between individuals, the recipient's immune system is expected to eliminate them.

(b) Factors affecting dissemination

Human T lymphocytes can only be transmitted from human to human through injection or infusion. In the case that human T lymphocytes are infused between individuals, the recipient's immune system is expected to eliminate them.

11. Previous genetic modifications of the recipient or parental organism already notified for release in the country where the notification is made (give notification numbers)

There are no previous notifications.

C. Information relating to the genetic modification

1. Type of the genetic modification

- | | | |
|-------|-------------------------------|-----|
| (i) | insertion of genetic material | (X) |
| (ii) | deletion of genetic material | (.) |
| (iii) | base substitution | (.) |

- (iv) cell fusion (.)
- (v) others, specify

2. Intended outcome of the genetic modification

The aim of ARI-0001 cells is adoptive antitumor immunotherapy for patients with resistant or refractory CD19 + leukemia or lymphoma.

The product consist of a T-cell suspension derived from peripheral blood, obtained by a patient's leukapheresis and defined as cells expressing the CAR19 receptor on its membrane. The CAR19 receptor is designed to recognize the protein CD19, present in the tumoral cells.

These receptors have the ability to recognize intact membrane proteins, without the need for antigen processing by antigen presenting cells. CAR19 consist of a single stranded fragment of an anti-CD19 monoclonal antibody (scFv), a transmembrane region (CD8), a costimulatory molecule (4-1BB) and a signal transmitting domain (CD3ζ). Recognition of CD19 targeted by CAR19, activates the T lymphocyte because of the costimulatory and CD3 regions, causing the tumor cell dead.

3. (a) Has a vector been used in the process of modification?
Yes (X) No (.)

If no, go straight to question 5.

- (b) If yes, is the vector wholly or partially present in the modified organism?
Yes (X) No (.)

If no, go straight to question 5.

4. If the answer to 3(b) is yes, supply the following information

- (a) Type of vector
- plasmid (.)
 - bacteriophage (.)
 - virus (X)
 - cosmid (.)
 - transposable element (.)
 - other, specify

- (b) Identity of the vector

Third generation replication-incompetent lentivirus.

- (c) Host range of the vector

VSV-G envelope pseudotyped vector, and therefore, able to transduce numerous human cell types and different animal species, without replication.

- (d) Presence in the vector of sequences giving a selectable or identifiable phenotype
Yes (X) No (.)

antibiotic resistance (.)
other, specify

The phenotype (identity) is assessed by flow cytometry using monoclonal antibodies labeled with fluorochromes that recognize the CAR expressed on the membrane, corresponding to the expression of the transgene (chimeric antigen receptor directed against antigen CD19 (CAR19)).

Indication of which antibiotic resistance gene is inserted: -

- (e) Constituent fragments of the vector

A replication deficient lentiviral vector, and an insert for the expression of anti-CD19 chimeric antigen receptor (CAR19).

CAR19 is constituted by a single-stranded fragment of an anti-CD19 monoclonal antibody (scFv), a transmembrane region and part of the intracellular region (CD8), and the intracellular region consisting of a costimulatory molecule (4-1BB) and a domain that transmits the signals (CD3ζ).

- (f) Method for introducing the vector into the recipient organism

- (i) transformation (.)
(ii) electroporation (.)
(iii) macroinjection (.)
(iv) microinjection (.)
(v) infection (.)
(vi) other, specify : transduction

5. If the answer to question B.3(a) and (b) is no, what was the method used in the process of modification?

- (i) transformation (.)
(ii) microinjection (.)
(iii) microencapsulation (.)
(iv) macroinjection (.)
(v) other, specify (.)

6. Composition of the insert

- (a) Composition of the insert

The transfer plasmid is a fully synthetic, replication-deficient vector containing a deletion in the 5'U3 sequence (long terminal repeat (LTR)) and a deleted 3'U3 LTR region. Genome

transcription is produced by a human cytomegalovirus promoter fused to the 5'RU5 region. A polyadenylation signal (SV40) has been inserted downstream to the 3'LTR region.

The vector also contains other regulatory elements: (i) EF-1 α promoter for CART19 transcription, (ii) central polypurine sequence derived from HIV-1 and the central termination sequence (cPPT / CTS) for improving transduction efficiency, (iii) the HIV-1 rev response element (RRE), a highly structured 350-nucleotide RNA segment that binds to the HIV-1 Rev accessory protein to facilitate exportation of the mRNAs from the nucleus to the cytoplasm (iv) the modified posttranscriptional regulatory element of the woodchuck hepatitis virus (WPRE), a DNA sequence which, when transcribed creates a tertiary structure that enhances the expression, commonly used in molecular biology to increase the expression of genes supplied by viral vectors.

The CAR19 transgene consists of an extracellular region with a recognition function and is formed by a unique chain sequence of the variable region of the immunoglobulins (scFv), with a variable domain of the heavy chain (VH) and a variable domain of the light chain (VL), linked together by a small peptide sequence "linker". Specifically, the scFv has been structured on the basis of N-terminal VH, followed by a 12 amino acid linker sequence with the 3X repeat sequence GlyGlyGlySer, and then the VL sequence. The VH and VL domains are derived from murine monoclonal antibody CD19 clone A3B1. The transmembrane region consists of partial CD8 sequence. The intracellular region has the function of triggering the T lymphocyte response by the CD3 domain (which transmits the signals) and a costimulatory domain (composed of the CD137/4-1BB). Also, intracellular part consists of a part of the CD8 sequence.

(b) Source of each constituent part of the insert

HIV, CMV, woodchuck and mouse genomes, and human HBV genome as indicated in the previous section (6.a).

(c) Intended function of each constituent part of the insert in the GMO

Please refer to section 6.a.

(d) Location of the insert in the host organism

- on a free plasmid (.)
- integrated in the chromosome (X)
- other, specify

(e) Does the insert contain parts whose product or function are not known?
Yes (.) No (X)
If yes, specify

D. Information on the organism(s) from which the insert is derived

1. Indicate whether it is a:

viroid (.)
RNA virus (.)
DNA virus (.)
bacterium (.)
fungus (.)
animal
- mammals (X)
- insect (.)
- fish (.)
- other animal (.)
(specify phylum, class)
other, specify

2. Complete name

(i) order and/or higher taxon (for animals) *Homo sapiens and Rodentia*
(ii) family name for plants *Hominidae and Muridae*
(iii) genus *Homo and Mus*
(iv) species *H.sapiens and Mus musculus*
(v) subspecies ...
(vi) strain ...
(vii) cultivar/breeding line ...
(viii) pathovar ...
(ix) common name *Human and mouse*

3. Is the organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?

Yes (.) No (X) Not known (.)

If yes, specify the following:

(b) to which of the following organisms:

humans (.)
animals (.)
plants (.)
other ..

(b) are the donated sequences involved in any way to the pathogenic or harmful properties of the organism

Yes (.) No (X) Not known (.)

If yes, give the relevant information under Annex III A, point II(A)(11)(d):

...

4. Is the donor organism classified under existing Community rules relating to the protection of human health and the environment, such as Directive 90/679/EEC on the protection of workers from risks to exposure to biological agents at work?

Yes (.) No (X)

If yes, specify

5. Do the donor and recipient organism exchange genetic material naturally?
Yes (.) No (X) Not known (.)

E. Information relating to the genetically modified organism

1. Genetic traits and phenotypic characteristics of the recipient or parental organism which have been changed as a result of the genetic modification

- (a) is the GMO different from the recipient as far as survivability is concerned?
Yes (.) No (X) Not known (.)
Specify

- (b) is the GMO in any way different from the recipient as far as mode and/or rate of reproduction is concerned?
Yes (.) No (X) Unknown (.)
Specify

- (c) is the GMO in any way different from the recipient as far as dissemination is concerned?
Yes (.) No (X) Not known (.)
Specify

- (d) is the GMO in any way different from the recipient as far as pathogenicity is concerned?
Yes (.) No (X) Not known (.)
Specify

2. Genetic stability of the genetically modified organism

The gene coding for the chimeric antigen receptor is introduced into T cells by transduction with an incompetent-replication lentiviral vector. The autologous genetically modified T cells are genetically stable, and the introduced gene will constitute an integral part of the host DNA.

3. Is the GMO significantly pathogenic or harmful in any way (including its extracellular products), either living or dead?
Yes (.) No (X) Unknown (.)

- (a) to which of the following organisms?

humans (.)

animals (.)
plants (.)
other (.)

- (b) give the relevant information specified under Annex III A, point II(A)(11)(d) and II(C)(2)(i)

The genome of the lentiviral vector deficient for replication is integrated as a provirus into the T cell genome. New viral particles cannot be assembled into the final host cell, since the gag gene cannot be transcribed given the absence of the gag encoding plasmid. In addition, the pol and all accessory elements are absent in this viral vector. Transgenes inserted into the lentiviral vector do not code for pathogenic factors, cytokine coding sequences, oncogenes, antibiotic resistance genes or other dangerous inserts.

4. Description of identification and detection methods

- (a) Techniques used to detect the GMO in the environment

Given the characteristics of the product as well as the route of administration, it is not likely that the GMO could be released into the ecosystem as well as its dissemination from the release site. In this way no monitoring, control or emergency plan activity has been planned.

- (b) Techniques used to identify the GMO

Please refer to section 4.a.

F. Information relating to the release

1. Purpose of the release (including any significant potential environmental benefits that may be expected)

The aim of ARI-0001 cells is adoptive antitumor immunotherapy for patients with resistant or refractory CD19 + leukemia or lymphoma with a life expectancy of less than two years.

CD19 is a 95 kDa glycoprotein present on the surface of B lymphocytes from the earliest stages of their development to their final differentiation into plasma cells. The expression of CD19 is exclusively restricted to cells of lymphoid B strain, excluding pluripotent stem cells. CD19 is also expressed in most cases of non-Hodgkin's lymphoma-B, acute lymphocytic leukemia-B, chronic lymphocytic leukemia, tricholeukemia, and even some cases of acute myeloid leukemia.

ARI-0001 is expected to offer a therapeutic alternative for patients with relapsed or refractory B cell neoplasms who are not eligible for transplantation of hematopoietic progenitors or who have failed a transplant and may offer a more durable response than therapies of current rescue. ARI-0001 may also have sufficient potential to replace transplantation of hematopoietic progenitors, expanding patient eligibility and obviating the need to find compatible donors, along with potentially lower rates of mortality and morbidity.

There is no anticipated negative or positive effect on the environment.

2. Is the site of the release different from the natural habitat or from the ecosystem in which the recipient or parental organism is regularly used, kept or found?

Yes (.) No (X)

If yes, specify

3. Information concerning the release and the surrounding area

- (a) Geographical location (administrative region and where appropriate grid reference):

The Hematology Room located on the 4th floor of the General Building of Hospital Clínic in Barcelona, Spain.

The Pediatric oncohematology room located on the 8th floor of the Hospital San Joan de Déu in Barcelona, Spain.

- (b) Size of the site (m²):

(i) actual release site (m²): The extension of the site does not exceed 300 m² for Hospital Clínic and 200 m² for Hospital San Joan de Déu.

(ii) wider release site (m²): -

- (c) Proximity to internationally recognised biotopes or protected areas (including drinking water reservoirs), which could be affected:

It will not affect other environmental areas outside the product administration room in the hospital. Measures to contain and manage sanitary waste during the administration of ARI-001 to patients will prevent the release of the GMO into the environment. Personal protective equipment shall be used to prevent the exposure of ARI-0001 cells from the health personnel involved in administering the product. Cell processing is done under closed and sterile production systems.

- (d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO

Not applicable since the product will not contact with the environment.

4. Method and amount of release

- (a) Quantities of GMOs to be released:

A maximum of 3 infusions will be administered at a dose of 0.5×10^6 - 10×10^6 cells / kg of the patient (> 20% of the cells are CAR19+), taking into account that i) a maximum of 10 patients included in a clinical trial ii) a single intravenous infusion per patient will be administered.

- (b) Duration of the operation:
30-45 minutes.

- (c) Methods and procedures to avoid and/or minimise the spread of the GMOs beyond the site of the release

The health staff will work according to Good Clinical Practice with the protocols of each hospital. The GMO shall be treated as Group III residue.

5. Short description of average environmental conditions (weather, temperature, etc.)

The hospital rooms for the administration of the OMG will comply with the necessary hygiene conditions required for the treatment of immunodepressed patients.

6. Relevant data regarding previous releases carried out with the same GMO, if any, specially related to the potential environmental and human health impacts from the release.

There have been no previous releases of the GMO.

G. Interactions of the GMO with the environment and potential impact on the environment, if significantly different from the recipient or parent organism

1. Name of target organism (if applicable)

(i)	order and/or higher taxon (for animals)	Primate
(ii)	family name for plants	Hominidae
(iii)	genus	Homo
(iv)	species	Homo sapiens
(v)	subspecies	Homo sapiens sapiens
(vi)	strain	...
(vii)	cultivar/breeding line	...
(viii)	pathovar	...
(ix)	common name	Human

2. Anticipated mechanism and result of interaction between the released GMOs and the target organism (if applicable).

ARI-0001 therapy is designed to treat B cell neoplasms. The aim is to act on CD19 of neoplastic cells with T cells expressing the anti-CD19 CAR receptor, as it has been shown to be effective in eliminating B cell neoplasms, and therefore, has the potential for clinical benefit in patients with no other treatment option.

3. Any other potentially significant interactions with other organisms in the environment.

No other interactions are expected.

4. Is post-release selection such as increased competitiveness, increased invasiveness for the GMO likely to occur?

Yes (.) No (X) Not known (.)
Give details

5. Types of ecosystems to which the GMO could be disseminated from the site of release and in which it could become established

Any ecosystem except the patients that will receive the autologous ARI-0001.

Exposure to ARI-0001 cells will be made by intravenous infusion to the patients. Immunosuppressed persons who are not patients will not receive this therapy. People with a functional immune system in case of accidental injection would eliminate these cells. Contact of simple exposure to the blood of a treated patient will not cause transmission of the GMO since it is rapidly inactivated under ambient conditions.

6. Complete name of non-target organisms which (taking into account the nature of the receiving environment) may be unintentionally significantly harmed by the release of the GMO

No applicable given the type of product, the target population and the route of administration in a hospital environment.

- | | | |
|--------|---|-----|
| (i) | order and/or higher taxon (for animals) | ... |
| (ii) | family name for plants | ... |
| (iii) | genus | ... |
| (iv) | species | ... |
| (v) | subspecies | ... |
| (vi) | strain | ... |
| (vii) | cultivar/breeding line | ... |
| (viii) | pathovar | ... |
| (ix) | common name | ... |

7. Likelihood of genetic exchange *in vivo*

- (a) from the GMO to other organisms in the release ecosystem: **any likelihood**
- (b) from other organisms to the GMO: **any likelihood**
- (c) likely consequences of gene transfer: **any likelihood**

8. Give references to relevant results (if available) from studies of the behaviour and characteristics of the GMO and its ecological impact carried out in stimulated natural environments (e.g. microcosms, etc.):

No study has been carried out.

9. Possible environmentally significant interactions with biogeochemical processes (if different from the recipient or parental organism)

No possible interaction.

H. Information relating to monitoring

1. Methods for monitoring the GMOs

Given the characteristics of the product, as well as the route of administration (ARI-0001 cell suspension will be transferred to the patient using conventional intravenous infusion systems with closed and sterile systems), it is unlikely that the GMO can be released into the ecosystem as well as its spread from the release site, since T cells cannot survive outside their ecosystem (human blood). In this way no monitoring, control or emergency plan activity has been planned.

Treatment of waste generated by the administration of ARI-0001 cells will be performed according to the standards established by the respective Hospitals where the release will be performed.

2. Methods for monitoring ecosystem effects

Not applicable

3. Methods for detecting transfer of the donated genetic material from the GMO to other organisms

Not applicable

4. Size of the monitoring area (m²)

Not applicable

5. Duration of the monitoring

Not applicable

6. Frequency of the monitoring

Not applicable

I. Information on post-release and waste treatment

1. Post-release treatment of the site

The place of release will be cleaned with disinfectant substances with special viricidal capacity, immediately after release.

2. Post-release treatment of the GMOs

GMO material, as well as the materials in contact with GMO, will be managed as Group III residues.

3. (a) Type and amount of waste generated

The following waste is expected to be generated: ARI-0001 cell infusion bags, intravenous infusion sets, needles, gloves, gowns, masks, bandages / plaster (10 patients in total).

3. (b) Treatment of waste

GMO material, as well as the materials in contact with GMO, will be managed as Group III residues.

J. Information on emergency response plans

1. Methods and procedures for controlling the dissemination of the GMO(s) in case of unexpected spread

In case of contamination the personnel involved in the preparation, packaging or administration of the cellular product will be notified to the principal investigator and the Occupational Hazard Prevention Service. All personnel will be given instructions on the procedures to be followed in case of accidental release.

2. Methods for removal of the GMO(s) of the areas potentially affected

The place will be cleaned with disinfectant substances with special viricidal capacity.

3. Methods for disposal or sanitation of plants, animals, soils, etc. that could be exposed during or after the spread

Not applicable.

4. Plans for protecting human health and the environment in the event of an undesirable effect

The emergency response in case of accidental injection of health personnel will consist of disinfection of the injection site and follow-up in the case of symptoms related to an immune reaction against the ARI- 0001.