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: The Netherlands
(b) Notification number: B/NL/17/002
(c) Date of acknowledgement of notification: 03/05/2017
(d) Title of the project
Evaluation following the administration of autologous T cells genetically modified with a retroviral vector to express Chimeric Antigen Receptors (CARs) in subjects with malignant diseases.

(e) Proposed period of release: From 01/09/2017 until 30/06/2037

2. Notifier: Stichting VUmc, Amsterdam

Name of institution or company: Autolus Limited,
58 Wood Lane, London,
W12 7RZ, United Kingdom

3. GMO characterisation

(a) Indicate whether the GMO is a:

viroid	(.)
RNA virus	(X) retrovirus
DNA virus	(.)
bacterium	(.)
fungus	(.)
animal	
- mammals	(.)
- insect	(.)
- fish	(.)
- other animal	(.)

specify phylum, class:

(b) Identity of the GMO (genus and species)
Genus: Gammaretrovirus
Species: Moloney murine leukaemia virus

(c) Genetic stability – according to Annex IIIa, II, A(10)

The replication-deficient Moloney Murine Leukaemia Virus (MoMLV) is pseudotyped with the RD114 envelope. This combination enhances particle stability and the RD114 recognition of T lymphocytes is designed for human specificity and confers less toxicity compared to alternate viral envelopes. The genetic sequence of the retroviral vector (MoMLV) and the inserted cassettes that express a Chimeric Antigen Receptor (CAR) and or a safety switch (RQR8), are confirmed post-production to contain no mutations.

The retroviral transduced autologous cells are designed to express CARs and in additional cases the RQR8 protein and the product does not contain the intact virus. Furthermore, due to the labile nature of T lymphocytes under normal conditions, the GMO is highly unlikely to survive or persist on environmental surfaces.

4. Is the same GMO release planned elsewhere in the Community (in conformity with Article 6(1)), by the same notifier?

Yes (X) No (.)

If yes, insert the country code(s) GB and DE

5. Has the same GMO been notified for release elsewhere in the Community by the same notifier?

Yes (X) No (.)

If yes:

- Member State of notification GB
- Notification number GM3297
  B/../../…not yet available

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 B/../../…

7. Summary of the potential environmental impact of the release of the GMOs.

The GMO released into the environment consists of *ex vivo* transduced, autologous T lymphocytes that are intravenously infused into the patient. Therefore, the environmental impact on release of the GMO into the environment, is considered as low. The retrovirus has been optimised and designed to be replication-deficient. Cells at the end of production are tested for the presence of Replication Competent Retrovirus (RCR) and no RCR has been detected in material developed for clinical trials. These data support the highly reduced risk in case of any GMO environmental spread.

Patients that have received the autologous gene therapy treatment will not be eligible to act as blood donors and so release can only be conceived by accidental cuts or spillage. Transmission of accidental GMO-containing biological samples (e.g. blood or bone marrow) cause the other person's immune system to recognise the foreign bodies and stimulate their destruction. If the accidental recipient's blood becomes infected and is fully HLA-identical to

the donor's immune cells, there is a very minor chance that the transduced donor cells will evade detection. In the event of accidental GMO transfer, the safety switch can be deployed by administering rituximab, as a rescue medicine, to trigger the destruction of the GMO-contaminated cells where the RQR8 safety switch is expressed.

T-lymphocytes cells are highly labile and do not survive on environmental surfaces. The investigative centres have healthcare management/biosafety procedures and staff that are trained in managing patients and safe handling of GMOs, ultimately reducing the risk of biohazardous exposure. Overall, the risk of the modified CAR and/or RQR8 retrovirus, designed as a personalised investigational medicine, poses an extremely low risk to other surrounding humans and the environment. Therefore, the environmental risk potential is considered negligible.

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

1. Recipient or parental organism characterization:

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

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

other, specify …

2. Name

(i)	order and/or higher taxon (for animals)	Retroviridae
(ii)	genus	Gammaretrovirus
(iii)	species	Moloney Murine Leukemia
(iv)	subspecies	Oncovirinae type C
(v)	strain	
(vi)	pathovar (biotype, ecotype, race, etc.)	
(vii)	common name	MoMuLV

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:
(i) Yes (X)

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

Atlantic	..
Mediteranean	X.
Boreal	X.
Alpine	X.
Continental	X.
Macaronesian	X.

(ii) No (.)
(iii) Not known (.)

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

(d) Is it frequently kept in the country where the notification is made?
Yes (X) 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	In mice

(b) If the organism is an animal: natural habitat or usual agroecosystem:
Free living.

5. (a) Detection techniques
Polymerase Chain Reaction (PCR) for detection of the inserted transgenes and or vector analysis from patient blood samples. Flow cytometry from patient blood samples will be used to measure GMO-modified T-lymphocytes from treated patients.

(b) Identification techniques
See 5a.

6. Is the recipient organism classified under existing Community rules relating to the protection of human health and/or the environment?
Yes (X) No (.)
If yes, specify: Risk Group 2 per the classification in Annex 4 of the Dutch Regulation on Contained Use of GMO (Ministry of Infrastructure and the Environment).

7. Is the recipient organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?
Yes (X) No (.) Not known (.)

If yes:

(a) to which of the following organisms:

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

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

MoMuLV is an ecotropic virus and only infects dividing murine cells. The retrovirus is transmitted in the blood from the infected maternal mouse mother to its offspring. Transmission may be spread by germline infection. The wild type virus is oncogenic in mice. In rhesus monkeys, lymphomas were observed in immunocompromised animals. These data suggest a pathogenic mechanism by which chronic productive retroviral infection may permit insertional mutagenesis that results in cell transformation and tumour formation in haemapoietic stem cells but not in mature lymphocytes. *In vivo* infection in humans appears to require direct injection with amphotropic or pseudotyped virus. However, in these studies, a replication-deficient MoMuLV retroviral vector is used. No clinical manifestations of disease have been noted in humans exposed to the MoMuLV retrovirus, to date.

8. Information concerning reproduction

(a) Generation time in natural ecosystems:

Not applicable to the modified replication-deficient retroviral vector.

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

The strain of MoMuLV used is replication-deficient.

(c) Way of reproduction: Sexual .. Asexual

Not applicable.

(c) Factors affecting reproduction:

Retroviral vectors are enveloped viruses and are inactivated by desiccation, detergents, heat sterilisation and high salt concentrations. The approximate of MoMuLV half-life is between 5 and 8 hours at 37^{o}C in aqueous solution.

9. Survivability

(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	Not appliccable

(b) relevant factors affecting survivability:
Temperature, UV-radiation, humidity, chemical disinfection.

10. (a) Ways of dissemination
The wild type MoMuLV can be transferred in mouse from mother to child via blood or germ cells infection. The virus only infects dividing cells. Infections of humans can only occur if the virus is directly infused into the blood. Dividing, but not non-dividing, human cells can only be infected by pseudotyped MoMuLV, but not by wild type MoMuLV.

(b) Factors affecting dissemination
The retrovirus will not be disseminated as the virus is replication-deficient and chance of recombination with other retroviruses is low.

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)
Prior genetic modifications related to the parenteral organism without the specific genetic inserts expressing CAR and or RQR8 are B/NL/11/003 and B/NL/11/001.

C. **Information relating to the genetic modification**

1. Type of the genetic modification

(i)	insertion of genetic material	(X)
(ii)	deletion of genetic material	(X)
(iii)	base substitution	(.)
(iv)	cell fusion	(.)
(v)	others, specify	…

2. Intended outcome of the genetic modification
To express of Chimeric Antigen Receptors (CARs) on transduced T-lymphocyte cells that are genetically engineered to target malignant patient cells. This harnesses the T-lymphocytes immunity to induce cell death of the ‘cancerous cells’.

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
Gamma-retroviral: Moloney Murine Leukemia Virus vector.

(c) Host range of the vector
Pseudotyped with RD114 envelope that recognises primate cells.

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

antibiotic resistance	(X)
other, specify	RQR8 transgene that contains two copies of a rituximab binding peptide, flanking a fragment of CD34 which binds the anti-CD34 antibody.

Indication of which antibiotic resistance gene is inserted: Ampicillin.

(e) Constituent fragments of the vector
The gamma-retroviral vector derived from SFG (a vector cassette widely used in engineering T lymphocytes). It comprises 5' and 3' wild-type Moloney Murine Leukemia Virus (MoMLV or MLV) long-terminal repeats (LTRs), the MoMLV packaging signal, the MLV Splice Acceptor and the MLV polypurine tract. The MLV packaging signal includes the MLV splice donor; The packaging signal codes for the amino-terminal portion of gag with a mutated start codon. The transgene open reading frame is inserted 3' to the splice acceptor replacing the retroviral envelope open reading frame. The expression of the transgene is via the 5' viral LTR promoter. A scaffold attachment region is inserted 3' to the transgene open reading frame.

(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 regions of the below described inserts are flanked by transcriptional control elements, 5' and 3' long terminal repeats (LTRs), a gag sequence and retroviral packaging signal.

AUTO2 insert: A CAR that recognises B-cell maturation antigen (BCMA) and Transmembrane Activator and calcium-modulator and Cyclophilin ligand Interactor (TACI) and transgene for the RQR8 safety switch.

AUTO3 insert: A CAR directed against CD19 and CAR directed against CD22.

AUTO4 insert: A CAR directed against T-cell receptor beta-1 chain C region (TRBC1) and the transgene for the RQR8 safety switch.

(b) Source of each constituent part of the insert

AUTO2: Tumour Necrosis Factor Ligand, Superfamily member 13 fragment, linked to a hinge region from a fragment of human IgG1. The transmembrane and humanised endodomain regions from CD28, OX40 and CD3ζ.

AUTO3: The single-chain variable fragment is derived from the humanised variable regions from an anti-CD19 monoclonal antibody. The transmembrane region is derived from human transmembrane domain and endodomains from human tumour necrosis factor receptor OX40 and human TCRζ.

The single-chain variable fragment is derived from a humanised anti-CD22 antibody and consists of human derived transmembrane domain and endodomains from human tumour necrosis factor receptor 41BB and human TCRζ.

AUTO4: The single-chain variable fragment is derived from a humanised variable regions from an anti-TRBC1 antibody. The transmembrane region is derived from human transmembrane domain and endodomains from human tumour necrosis factor receptor 41BB and human TCRζ.

RQR8: A fusion of two copies of a rituximab binding mimotope separated by a fragment from human CD34 which binds the anti-CD34 monoclonal antibody. These fragments are fused to the transmembrane domain and endodomain derived from human CD8.

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

Packaging elements: Retroviral vector elements (e.g. long terminal repeats and retroviral packaging signal) contribute the retroviral incorporation and integration of the sequences of interest such as the CAR and RQR8 transgenes.

Chimeric and or RQR8 transgene: The inserted transgene includes the transcriptional promoter that drives the CAR(s) and or RQR8 transgenes. The transgenes are transcribed into mRNA and the resulting protein is expressed on the cell surface of the T lymphocyte.

The single-chain variable fragment expresses the CAR as a single-chain protein that recognises specifically directed target antigens.

- Transmembrane region: The transmembrane region bridges the CAR single-chain binding domain to anchor to the cell membrane.
- Endodomains: Intracellular regions of the CAR that are designed to activate T lymphocytes following target-antigen binding. The endodomains listed in 6(b) were designed to promote T lymphocyte proliferation, cytokine augmentation, persistence and cytotoxicity to mediate anti-tumuorigenic effects.

(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 (X)
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)	Primates
(ii)	family name for plants	…
(iii)	genus	Homo
(iv)	species	Homo sapiens
(v)	subspecies	…
(vi)	strain	…
(vii)	cultivar/breeding line	…
(viii)	pathovar	…
(ix)	common name	Human

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 Patients receive genetically modified autologous T lymphocytes and the survival rates are similar to unmodified autologous T lymphocytes.

(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 Reproduction rates between GMO and unmodified T lymphocytes are believed to be the same.

(c) is the GMO in any way different from the recipient as far as dissemination is concerned?
Yes (.) No (X) Not known (.)
Specify The GMO and unmodified T lymphocytes do not contain viral particles or RCRs and therefore, dissemination would be restricted.

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

Specify GMO is not believed to be pathogenic.

2. Genetic stability of the genetically modified organism
The genetically modified T lymphocytes stably express the transgenes but further data in humans is required to address this currently.

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 replication-deficient retroviral vector integrates as a provirus into the genome of T lymphocytes. There is no risk of viral particles being produced due to the absence of the other elements require for retroviral transduction/further replication. The transgenes of interest do not contain any other hazardous inserts.

4. Description of identification and detection methods

(a) Techniques used to detect the GMO in the environment
Flow cytometry to detect the transduced CAR/RQR8-expresing cells.

(b) Techniques used to identify the GMO
Flow cytometry to detect the transduced CAR/RQR8-expresing cells.

F. Information relating to the release

1. Purpose of the release (including any significant potential environmental benefits that may be expected)
To harness T lymphocyte immunity that target malignant cells, to in turn promote the death of specifically-targeted, tumor cells.

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 (X) No (.)
If yes, specify The parental MoMLV is only infectious in *Mus musculus* (mice). Autologous human T-lymphocytes will be genetically modified with a pseudotyped MoMLV retroviral vector.

3. Information concerning the release and the surrounding area

(a) Geographical location (administrative region and where appropriate grid reference):
VU medisch centrum (Free University Medical Center), Amsterdam, The Netherlands.

(b) Size of the site (m^2): 67.650 m^2 (hospital premises)
(i) actual release site (m^2): 16 m^2 (administration room)
(ii) wider release site (m^2): not applicable (gene therapy application)

(c) Proximity to internationally recognized biotopes or protected areas (including drinking water reservoirs), which could be affected:
Not applicable.

(d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO
Not applicable.

4. Method and amount of release

(a) Quantities of GMOs to be released:
15-450 million positively transduced GMO T lymphocytes.

(b) Duration of the operation:
Autologous GMO T lymphocytes will be administered to a patient as either a single or split dose generally approximately 2 weeks apart (± 7 days), following pre-conditioning chemotherapy treatment. The total time of GMO administration with be up to 30 minutes for each (single or split dose) infusion. Approximately, 120 patients are anticipated for treatment at the VU Medical Center for each study authorised.

(c) Methods and procedures to avoid and/or minimize the spread of the GMOs beyond the site of the release
The cryopreserved GMO-containing cells are shipped in a specialised freezing bag and transfer to the bedside of the patient receiving administration in an isolated room. Following thawing, the GMO-containing cells are intravenously infused into the patient using a special microinfusion syringe-pump connected to a catheter. After infusion, the catheters will be removed and the catheter, tubing and syringe will be packed, sealed and destroyed according to standard operating procedures at the VUmc for contaminated materials. The patient will remain hospitalised for up to 7-30 days post-administration.

5. Short description of average environmental conditions (weather, temperature, etc.)
Hospital environment: activities are carried out within a hospital.

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.
Not applicable as this is planned to be the first in human studies with this 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) Primates
(ii) family name for plants …
(iii) genus Homo

(iv)	species	Homo sapiens
(v)	subspecies	…
(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)
Not applicable as the genetically modified T lymphocytes are not expected to survive outside the human body. If the modified T lymphocytes are accidentally transferred to another human, the T lymphocytes will most likely be recognised as non-self by the immune system and be destroyed. Alternatively, the safety switch can be triggered via administration of rituximab to inactivate and deleted the GMO-containing cells.

3. Any other potentially significant interactions with other organisms in the environment
Not applicable as the retroviral vector (MoMLV) is replication-deficient and highly labile on environmental surfaces and have a very limited survival outside the human body. Cross-contamination with other species is highly unlikely.

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
This is generally unlikely due to differences between murine and human retroviral homology and potential recombinations are highly unlikely to occur in patients. The fact that the GMO-containing cells are incapable of producing infectious viruses would be a further barrier to dissemination. Treated patients will not be permitted to act as blood donors and the GMO-containing cells have an extremely low chance/survival rate outside the human body.

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

(i)	order and/or higher taxon (for animals)	…Not applicable.
(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:

Highly unlikely as per G5.

(b) from other organisms to the GMO:
Highly unlikely as per G5.

(c) likely consequences of gene transfer:
These GMO-containing cells akin to the unmodified T lymphocytes are capable of proliferation into T lymphocytes that will retain the same anti-tumorigenic properties and hence, may be a positive benefit to maintain a persistent anti-cancer response.

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 additional stimulations have been performed in the natural environment.

9. Possible environmentally significant interactions with biogeochemical processes (if different from the recipient or parental organism)
None: MoMLV particles have a short half-life and are extremely labile on environmental surfaces. Modified T lymphocytes are not intended for consumption but for treatment of patients with hematological malignancies. The GMO-containing cells will not be disseminated into the ecosystem, except via accidental blood release as previously mentioned. Treated patients are restricted from being blood donors and cells have an extremely limited survive external from the human body.

H. Information relating to monitoring

1. Methods for monitoring the GMOs
Flow cytometry to detect the transduced cells.

2. Methods for monitoring ecosystem effects
If accidental blood release occurs, flow cytometry of the accidental recipient blood can be taken to assess for any presence.

3. Methods for detecting transfer of the donated genetic material from the GMO to other organisms
As above in H2, where applicable for certain species e.g. humans.

4. Size of the monitoring area (m^2)
Not applicable.

5. Duration of the monitoring
The duration of monitoring will be up to 15 years following last treatment with the GMO.

6. Frequency of the monitoring
Blood samples will be taken a multiple time points for example, before treatment, 1, 3, 6 and 12 months post-treatment for at least 5 years and then annually for 6-15 years post-last treatment. If the samples are sufficiently negative, the remaining samples may be taken but archived until warranted analysis.

I. Information on post-release and waste treatment

1. Post-release treatment of the site
No specific procedures are required for post-release in addition to the regular institutional clinical management procedures.

2. Post-release treatment of the GMOs
Not applicable.

3. (a) Type and amount of waste generated
Waste includes items like sets of catheters, tubing and syringes used for GMO-containing administration, empty infusion bags that contained the product, any applicable wound-dressings and materials used for collecting biological samples (e.g. blood, biopsies etc.). The amount of this waste per patient is estimated to be less than 1 kilogram.

3. (b) Treatment of waste
All waste that contains of may (potentially) contain GMO will be disposed of as clinical waste for incineration by an external party according to the regular institutional procedures and in compliance with national waste regulations.

J. Information on emergency response plans

1. Methods and procedures for controlling the dissemination of the GMO(s) in case of unexpected spread
The risk of unintended spread of the GMO is very limited as the GMO will be closely controlled for direct release into the receiving patient. Any accidental exposure will be reported to a health care professional and the Environmental Safety Officer (ESO) of VUmc. Also any accidental spill will be reported to the ESO. Accidental personal exposures and spills will be treated according to the regular institutional protocols for exposure and spill incidents. These protocols require proper immediate disinfection and clean-up. Waste resulting from accidents will be treated as per I.3(b).

2. Methods for removal of the GMO(s) of the areas potentially affected
Study personnel will follow the regular institutional procedures for accidental exposure or spills (see also J.1).

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
Not applicable.