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: Belgium
(b) Notification number:
(c) Date of acknowledgement of notification
(d) Title of the project
A Phase 2b, Randomized, Double-masked, Multicenter, Dose-ranging, Sham-controlled Clinical Trial to Evaluate Intravitreal JNJ-81201887 (AAVCAGsCD59) Compared to Sham Procedure for the Treatment of Geographic Atrophy (GA) Secondary to Age-related Macular Degeneration (AMD)

(e)Proposed period of release
It is anticipated that the trial will be open from August 2023 to July 2025.
All subjects treated in this study will enter an additional long-term follow-up period at the end of the trial, under a separate protocol.

2. Notifier
Name of institution or company: Janssen-Cilag International NV
Turnhoutseweg 30, B-2340 Beerse, Belgium

3. GMO characterisation

(a) Indicate whether the GMO is a:

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

other, specify (kingdom, phylum and class)

(b) Identity of the GMO (genus and species)
Family: *Parvoviridae*

Genus: Dependovirus
Species: Adeno-associated virus (AAV)
Strain: AAV2
Recombinant AAV that contains the inverted terminal repeats (ITRs) of serotype 2 packaged in a serotype 2 capsid and encodes the human CD59.

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

Evolution of AAV viruses (like all viruses) is directed by spontaneous mutations or recombination with other viruses of the same species, when such genetic modification confers a selective advantage. Non-homologous genomic recombination may occur spontaneously in nature between the viral genomes of AAV strains only under circumstances where a cell of the host organism is infected simultaneously by two different strains of AAV, which is permissive in that species (permissive cell line providing helper functions or presence of a helper virus).
AAVCAGsCD59 is expected to be highly genetically stable. AAVCAGsCD59 is generated by transient transfection of a production cell line using fully characterised, sequenced plasmids. Production of the vector in the manufacturing process and second-strand synthesis of the vector genome rely on the host DNA polymerase, characterised by high fidelity DNA polymerisation and additional proofreading exonuclease activity, leading to very low error rate of DNA replication. The genomic integrity of the AAVCAGsCD59 vector genome is tested by DNA sequencing of the vector genome.

AAVCAGsCD59 is unable to replicate independently, even in the presence of a helper virus such as adenovirus, since it lacks the rep and cap genes required for replication and packaging, respectively. AAVCAGsCD59 replication could only occur in the extremely unlikely event of a triple infection of the same host cell by AAVCAGsCD59, wild-type AAV (providing the rep and cap functions) and a helper virus. The triple infection event could result in the recombination of the AAVCAGsCD59 expression cassette with the rep and/or cap genes of the wild-type virus.

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)
HU, NL

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, ES, PT, DE, SE
- Notification number B/ES/23/02, TBC

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.

Administration of the GMO will occur only within contained clinical sites by trained medical professionals. It is therefore not anticipated that the GMO will come into direct contact with the environment. Therefore, environmental impact of the GMO is negligible.
Moreover, the clinical vector AAVCAGsCD59 is replication-incompetent by design and will not contain any replication-competent (helper) virus sequences. Even if accidental release occurs, the GMO will not be able to spread in the environment. In the case of accidental exposure and transfer of vector to an unintended human or non-human recipient, the risks are considered negligible since the vector is not able to replicate, is not known to be pathogenic, and the amount of particles is unlikely to cause significant infections in the exposed individual.

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

other, specify

2. Name

(i) order and/or higher taxon (for animals) *Parvoviridae*
(ii) genus Dependoparvovirus

(iii) species Adeno-associated virus (AAV)
(iv) subspecies N/A (Not applicable)

(v) strain AAV2
(vi) pathovar (biotype, ecotype, race, etc.) N/A
(vii) common name Adeno-associated virus 2

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) No (.)

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

Atlantic	(X)
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 (.) No (.) NA

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

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	(X) hosts are humans and non-human primates

(b) If the organism is an animal: natural habitat or usual agroecosystem: N/A

5. (a) Detection techniques
Polymerase chain reaction (PCR)

(b) Identification techniques
Polymerase chain reaction (PCR) and sequence analysis

Sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS PAGE) and Western Blot

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

AAVs have not been classified under Directive 2000/54/EC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work. AAV fulfils the definition of a group 1 biological agent according to the Directive 2000/54/EC (a biological agent that is unlikely to cause human disease).

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: N/A

(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

8. Information concerning reproduction

(a) Generation time in natural ecosystems:

After entry into the host cell nucleus, wild-type (WT) AAV can follow either one of two distinct and interchangeable pathways of its life cycle: the lytic or the latent phase. For entry into a lytic phase, a latently infected cell needs to be super-infected with a helper virus, including genome rescue of the provirus DNA followed by replication and packaging of the viral genome. Finally, upon helper virus-induced cell lysis, the newly assembled virions are released.

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

N/A

(c) Way of reproduction: Sexual N/A Asexual (X)

(d) Factors affecting reproduction:

Reproduction of WT AAV is dependent on co-infection with helper virus such as adenovirus, vaccinia virus, herpes simplex virus, cytomegalovirus or human papilloma virus.

9. Survivability

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

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

AAV can persist in the host cells as episomal concatemers or integrated into the host cell DNA (the *rep* genes are required for site-specific integration into the genome of host cells).

(b) relevant factors affecting survivability:

Outside of the host, non-lipid enveloped viruses such as AAV are resistant to low level disinfectants, survive well outside of the laboratory environment. AAV particles are resistant to a wide pH range (pH 3-9) and can resist heating at 56°C for 1 hour (Berns and Bohenzky, 1987). AAV does not form survival structures but can remain infectious for at least a month at room temperature following simple desiccation or lyophilisation.

AAV is readily inactivated by disinfectants such as 0.5% sodium hypochlorite, 0.45% potassium peroxymonosulfate, 0.5% peracetic acid, or 10% bleach. AAV is also inactivated by autoclaving for 30 minutes at 121°C. It is resistant to alcohol-based disinfectants.

10. (a) Ways of dissemination

AAVs may be transmitted by ingestion, inhalation of aerosols or droplets, or contact with mucous membranes (Baldo et al., 2013).

(b) Factors affecting dissemination

Factors affecting WT AAV dissemination, in general, are exposure dose, formation of aerosols, and closeness of contacts.

WT AAVs are not able to replicate unless a co-infection with a helper virus occurs.

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).

Not applicable.

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
The intended outcome of the modifications was to remove the *rep* and *cap* genes from the WT AAV genome. The only remaining viral elements are the ITRs which are necessary for production of the AAVCAGsCD59.
Between the ITRs, an expression cassette to deliver a functional transgene encoding the human CD59 gene has been inserted.

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	(X)
bacteriophage	(.)
virus	(.)
cosmid	(.)
transposable element	(.)
other, specify	

(b) Identity of the vector
Three plasmids are used to supply all the necessary components to produce AAVCAGsCD59. These were constructed using synthetic DNA and standard molecular biology techniques to form the final plasmid constructs.

(c) Host range of the vector
Plasmids have been propagated in bacteria.

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

antibiotic resistance (X)
other, specify

Indication of which antibiotic resistance gene is inserted
kanamycin

(e) Constituent fragments of the vector
The necessary components to make AAVCAGsCD59 are provided by plasmids. These plasmids contain the transgene cassette flanked by ITRs, the *rep* genes (for replication and packaging of the transgene cassette), the *cap* gene (required to make

the capsid), and adenoviral helper genes (E4, E2A and VA RNA). The production cell line provides the E1 function *in trans*.

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

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

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

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

6. Composition of the insert

(a) Composition of the insert
AAVCAGsCD59 incorporates an expression cassette flanked by the AAV ITRs. The expression cassette includes a promoter, an intron, cDNA encoding the human CD59 gene and a polyadenylation signal.
The expression cassette is limited to the required elements designed to optimise expression of functional human CD59 protein in the eye.

(b) Source of each constituent part of the insert.
ITRs – AAV2 derived
Promoter– virus, chicken
Intron– rabbit
Therapeutic transgene – human
Polyadenylation signal – rabbit

(c) Intended function of each constituent part of the insert in the GMO
ITRs - to enable replication and packaging of the transgene cassette into the capsid as well as for second-strand synthesis and episome formation in transduced cells
Promoter - to drive specific gene expression
Intron - to enhance expression of the therapeutic transgene
Therapeutic transgene – expression of functional human CD59 protein in the eye
Polyadenylation signal - sequence to terminate transcription

(d) Location of the insert in the host organism

-	on a free plasmid	(.)
-	integrated in the chromosome	(.)

- other, specify With respect to the patient, the GMO is mainly extrachromosomal by formation of episomal concatemers.

(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

The following information relates to the organism from which the inserted therapeutic transgene (CD59) 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) 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: N/A

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):
N/A

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 N/A

5. Do the donor and recipient organism exchange genetic material naturally?

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

WT AAV can integrate in a site-specific manner into chromosome 19 (a site termed AAVS1) by a *rep*-dependant mechanism (Dutheil et al., 2000). Approximately 0.1% of infecting WT AAV genomes integrate at AAVS1 (Deyle and Russell, 2009).

In the absence of *rep*, as is the case with recombinant AAV (rAAV) vectors, chromosomal integration is rare. DNA delivered by rAAV vectors predominantly persists as extrachromosomal elements (episomes) rather than integrating into host cell genomes.

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 The survivability of the recombinant AAV is not expected to be different from the WT virus.

(b) is the GMO in any way different from the recipient as far as mode and/or rate of reproduction is concerned?

Yes (X) No (.) Unknown (.)

Specify The rAAV genome lacks *rep* and *cap* gene sequences and is therefore replication-deficient even in the presence of a helper virus.

(c) is the GMO in any way different from the recipient as far as dissemination is concerned?

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

Specify The rAAV genome lacks *rep* and *cap* gene sequences and is therefore replication-deficient even in the presence of a helper virus.
Therefore, though it has the capacity to transduce cells, the lack of replicative capacity will severely restrict dissemination.

(d) is the GMO in any way different from the recipient as far as pathogenicity is concerned?

Yes (.) No (X) Not known (.)
Specify Neither WT AAV nor the GMO are pathogenic to humans or other organisms in the environment.

2. Genetic stability of the genetically modified organism
The GMO is expected to be highly genetically stable.
During the production process, The GMO is generated by transient transfection of a production cell line using fully characterised, sequenced plasmids. Production of the vector in the manufacturing process and second-strand synthesis of the vector genome rely on the host DNA polymerase, characterised by high fidelity DNA polymerisation and additional proofreading exonuclease activity, leading to very low error rate of DNA replication. The genomic integrity of the vector genome is tested by DNA sequencing of the vector genome. Once administered to the patient, the formation of replication-competent viral particle transporting the therapeutic cassette is consider highly unlikely mainly because 1) it would require simultaneous co-infection with a helper virus and a WT AAV to obtain a replication-competent viral particle within the same cell, and 2) the packaging efficiency will be profoundly affected during packaging of DNA above 5 kb.

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? N/A

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

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

4. Description of identification and detection methods

(a) Techniques used to detect the GMO in the environment
PCR with primers specific of the recombinant viral DNA

(b) Techniques used to identify the GMO
Molecular identity: PCR and sequence analysis

F. Information relating to the release

1. Purpose of the release (including any significant potential environmental benefits that may be expected)
The GMO is to be used in a clinical trial to treat a disease.

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):
- UZ Gent: Corneel Heymanslaan 10, 9000 Gent
- UZ Leuven Gasthuisberg: Herestraat 49, 3000 Leuven
- CHU Liège: Avenue de L'Hòpital 1, 4000 Liège
- ZNA Middelheim: Lindendreef 1, 2020 Antwerpen
- Ziekenhuis Oost-Limburg:, Synaps Park 1, 3600 Genk

(b) Size of the site (m^2):
(i) actual release site (m^2): N/A
(ii) wider release site (m^2): N/A

(c) Proximity to internationally recognised biotopes or protected areas (including drinking water reservoirs), which could be affected:
N/A as the GMO will be administered in a controlled hospital setting.

(d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO.
N/A as the GMO will be administered in a controlled hospital setting.

4. Method and amount of release

(a) Quantities of GMOs to be released:
The GMO is administered to humans enrolled in a clinical trial in a controlled hospital setting and is not intended to be released. Based on the intraocular route of administration, none to minimal release in the form of shedding (e.g. in tears) in quantities unable to cause significant infection is expected (EC, Good Practice on the assessment of GMO related aspects in the context of clinical trials with AAV clinical vectors).

(b) Duration of the operation:
The GMO will be given as an intravitreal injection, in the timeframe of hours.

(c) Methods and procedures to avoid and/or minimise the spread of the GMOs beyond the site of the release.
The GMO is introduced into the human body and is not expected to be released (see Section 4(a)).
The GMO will be prepared and administered by trained medical professionals to patients that have met the study entry criteria and have been enrolled into the study. In-house transport (i.e. at the clinical site) takes place according to local guidelines. All clinical waste from the procedure will be disposed according to the local policy. Standard operating procedures for disposal within the medical facility will be consistent with the guidance given in the WHO Laboratory Biosafety Manual, 3rd Ed (2004) for BSL1/2. In the medical facility, this will involve temporary containment in sharps bins or clearly marked bags (e.g. biohazard, medical waste) prior to autoclaving and/or incineration either on- or off-site as per local institutional guidelines for handling potentially biohazardous materials.

5. Short description of average environmental conditions (weather, temperature, etc.)
Not applicable: given that the GMO is prepared for administration and given to subjects in a clinical environment, it is not anticipated that the GMO will be released into the environment.

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.
None

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)
AAVCAGsCD59 has been designed to result in expression of the CD59 gene to treat patients with age-related Macular Degeneration (AMD), more specifically with dry AMD. The vector is delivered via intravitreal injection into the eye.

3. Any other potentially significant interactions with other organisms in the environment.
The GMO will be administered in a clinical site setting and is replication-deficient, therefore it is highly unlikely that the GMO will come in contact with other organisms or the environment. As the AAV vector cannot replicate, the inserted genetic trait cannot be transferred to the environment at large.

4. Is post-release selection such as increased competitiveness, increased invasiveness for the GMO likely to occur?
Yes (.) No (X) Not known (.)
Give details: The AAV vector is replication-deficient and is therefore at a competitive disadvantage when compared to WT AAV strains.

5. Types of ecosystems to which the GMO could be disseminated from the site of release and in which it could become established
The GMO is a replication-deficient and is not expected to spread to the environment in any significant quantities.

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
None

(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:
Negligible

(b) from other organisms to the GMO:
Negligible

(c) likely consequences of gene transfer:
Negligible

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 specific studies on the potential ecological impact of the GMO have been conducted or are considered necessary.

9. Possible environmentally significant interactions with biogeochemical processes (if different from the recipient or parental organism)
The GMO is not known to have any impact on biogeochemical processes.

H. Information relating to monitoring

1. Methods for monitoring the GMOs
Viral shedding from patients who receive the GMO as part of the clinical trial will be closely monitored using qPCR.

2. Methods for monitoring ecosystem effects
There are no specific plans for monitoring the environment during the release, other than monitoring viral shedding from clinical trial participants as the GMO is not expected to be released into the environment.

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

4. Size of the monitoring area (m^2)
N/A

There are no specific plans for monitoring the environment during the release, other than monitoring viral shedding from clinical trial participants as the GMO is not expected to be released into the environment.

5. Duration of the monitoring
Viral shedding from patients who receive the GMO as part of the clinical trial will be assessed up to 6 months post administration.

6. Frequency of the monitoring
Samples will be taken as per the clinical study protocol

I. Information on post-release and waste treatment

1. Post-release treatment of the site
Any surface contaminated with the GMO will be decontaminated according to applicable site-specific policies and procedures, using a disinfectant with validated efficacy against AAV.

2. Post-release treatment of the GMOs
Elimination or inactivation of left-overs of the GMO is performed in a manner consistent with the local policy and standard practice of the institution for potentially biohazardous materials.

3. (a) Type and amount of waste generated
GMO waste may consist of vials, administration sets (tubing, syringes, needles, and related accessories), and personal protective equipment as worn by the clinical staff (e.g. gloves, gowns).

3. (b) Treatment of waste
All waste generated (material in contact with the GMO during the preparation and administration of the GMO) will be disposed of according to the local policy. Standard operating procedures for disposal within the medical facility will be consistent with the guidance given in the WHO Laboratory Biosafety Manual, 3rd Ed (2004) for BSL1/2. In the medical facility, this will involve temporary containment in sharps bins or clearly marked bags (e.g. biohazard, medical waste) prior to autoclaving and/or incineration either on- or off-site as per local institutional guidelines for handling potentially biohazardous materials.

J. Information on emergency response plans

1. Methods and procedures for controlling the dissemination of the GMO(s) in case of unexpected spread.
In the event of an accidental spillage of the GMO, any surface contaminated with the GMO will be decontaminated according to applicable site-specific policies and procedures with a disinfectant with validated efficacy against AAV.

2. Methods for removal of the GMO(s) of the areas potentially affected.
See Section J.1.

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

   N/A - administration of the GMO will occur in a controlled hospital setting with trained staff. Decontamination of plants, (non-human) animals and soils will not be required.

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

   The GMO will be administered at clinical trial sites by trained healthcare professionals following local rules for handling and disposal of genetically modified organisms and biological hazards. All patients will be monitored for adverse events as detailed in the clinical trial protocol.

   Considering the negligible risk for the environment, no specific plans for protecting the environment are deemed necessary.

References

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