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 (BE)
(b) Notification number: B/BE/25/BVW4
(c) Date of acknowledgement of notification: ../../….
(d) Title of the project
An Open-Label Dose-Escalation Study to Assess the Safety and Tolerability of a Single Intravitreal Injection of SPVN20 Gene Therapy in Subjects with No Light Perception Due to End-Stage Rod-Cone Dystrophy, and Who Retain Dormant Foveal Cone Photoreceptors
(e) Proposed period of release
From Q2 2025 (Belgium) until Q3 2031*
(*final study dose delivered in Q3 2026; time after Q3 2026 is safety follow up with no IMP administered).

2. Notifier

Name of institution or company: SparingVision

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 …

(b) Identity of the GMO (genus and species)
Genus: Dependoparvovirus

Species: Adeno-associated virus (AAV); AAV engineered for intravitreal injection (IVT) and containing the codon-optimized human gene of G protein-gated inwardly rectifying potassium (GIRK) channel 1, mutated for an F137S amino-acid substitution (GIRK1(F137S))

(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).

The genetic stability of SPVN20 is expected to be equivalent to a wild-type AAV. However, due to the lack of viral Rep and Cap genes, SPVN20 is expected to remain in the cells as episomes and will not replicate and produce viral particles. The genomic integrity of the SPVN20 vector genome is tested by DNA sequencing.

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) FR, IE

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 B/../../…

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.

Administration of the GMO will occur only within contained clinical sites by trained medical professionals. Medical staff will handle SPVN20 according to local guidelines for handling of biohazardous materials and will use appropriate personal protective equipment. Contaminated waste will be disposed of according to local guidelines for biohazardous waste. Workplaces and potentially contaminated areas will be disinfected appropriately in order to avoid unintended exposure to SPVN20. 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 SPVN20 is replication-incompetent by design and will not contain any complete copies of 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 by design, is not known to be pathogenic, and the amount of particles is unlikely to cause significant infections in the exposed individual.
Taking into account the results of the environmental risk assessment and the applied mitigation measures, the overall environmental risk posed from use of SPVN20 is considered negligible.

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	Dependovirus
(iii)	species	Adeno-associated virus
(iv)	subspecies	Not applicable (n/a)
(v)	strain	AAV engineered for intravitreal injection (IVT) derived from AAV2
(vi)	pathovar (biotype, ecotype, race, etc.)	n/a
(vii)	common name	AAVi

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	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 (.) N/A

(d) Is it frequently kept in the country where the notification is made?

Yes (.) No (.) N/A

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	AAV2 hosts are humans and non-human primates. SPVN20 does not have a natural habitat.

(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 sequencing

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

N/A

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 (.)

Additional information: Wildtype AAV is non-pathogenic and has 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 has no known pathogenic effects. Consequently, AAV fulfils the definition of a risk group 1 biological agent according to the Directive 2000/54/EC (a biological agent that is unlikely to cause human disease).

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
…

8. Information concerning reproduction

(a) Generation time in natural ecosystems:
The replication of recombinant SPVN20 in an infected host cell is dependent on coinfection with a helper virus such as adenovirus. The generation time of wild-type AAV in a natural ecosystem will be significantly very high, depending on the timing of the coinfection. Replication competent AAV generation time of SPVN20 is not relevant since it lacks by design the rep and cap genes that are required for the reproduction of rcAAV.

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

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

(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 (funghi)	(.)
(vi)	eggs	(.)
(vii)	pupae	(.)
(viii)	larvae	(.)
(ix)	other, specify	Wild type and recombinant AAVs, remain episomal for extended periods of time by the formation of genome concatemerization.

(b) relevant factors affecting survivability:
AAV particles are stable outside host organisms for up to several weeks under normal environmental conditions at a wide pH and temperature ranges. However, AAV are effectively degraded in sewage water, most likely due to microbial activity, by hydrolysis, and also by UV radiation at the levels found in nature, and other degrading factors (Fleischmann, 2023). Replication of AAV cannot occur outside of a host cell. AAV is readily inactivated by disinfectants such as 0.5% sodium hypochlorite, 0.45% potassium peroxymonosulfate, 0.5% peracetic acid, or 10% bleach.

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)
N/A

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 the production of SPVN20. Between the ITRs, an expression cassette to deliver a functional transgene encoding the GIRK1(F137S) gene has been inserted.

Eventually, SPVN20 is an engineered adeno-associated virus for IVT that aims to provide dormant cone photoreceptors with the GIRK channel, a protein with the ability to restore phototransduction by generating a short phototransduction cascade within the dormant cones.

Via this mechanism of action, SPVN20 aims to restore light sensitivity to the diseased retina and, potentially, some level of visual acuity and/or color vision.

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 SPVN20.

(c) Host range of the vector

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 SPVN20 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).

(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?

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

6. Composition of the insert

(a) Composition of the insert
The expression cassette consists of a cone-targeting synthetic promoter (composed of an enhancer-promoter combination), a gene encoding hGIRK1(F137S) and regulatory elements (an intron, a polyadenylation signal, and a WPRE sequence), all flanked by AAV ITRs.

(b) Source of each constituent part of the insert
- Cone-targeting promoter: Homo sapiens
- SV40 intron: Simian Virus 40
- WPREmut6: Woodchuck hepatitis virus
- Gene encoding GIRK1(F137S) expression cassette: Homo sapiens
- Polyadenylation signal: bovine
- ITRs: AAV2

(c) Intended function of each constituent part of the insert in the GMO
- Promoter: Intended to drive cone-targeted gene expression.
- GIRK1(F137S) cDNA: G-protein-gated inward rectifying potassium channel, from human origin. Codon optimized complementary deoxyribonucleic acid (cDNA) sequence encoding a mutated GIRK1 protein with a F137S substitution allowing the formation of functional homotetramers.
- SV40 intron: intronic element to increase transgene expression
- Polyadenylation signal: Ends mRNA transcription and promotes mRNA stability.
- AAV ITRs: Required for vector genome packaging and replication in producer cells, as well as stable episome formation in transduced cells.
- WPREmut6: Woodchuck Hepatitis Virus Posttranscriptional Regulatory Element to increase transgene expression

(e) 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.

(f) 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 (GIRK1(F137S)) 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) N/A
(ii) family name for plants N/A
(iii) genus *Homo*
(iv) species *Sapiens*
(v) subspecies N/A
(vi) strain N/A
(vii) cultivar/breeding line N/A
(viii) pathovar N/A
(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 (.) 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 The survivability of the recombinant SPVN20 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 by design even in the presence of a helper virus. Therefore, though it can 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 No pathogenic effects of wild-type AAV in humans are known. The introduction of the expression cassette is not expected to result in the development of pathogenicity. Thus, neither the wild-type AAV nor SPVN20 are known or expected to be pathogenic. Removal of viral

genes during the construction of the vector would be expected to further reduce any risk of pathogenesis.

2. Genetic stability of the genetically modified organism
The genetic stability of SPVN20 is confirmed on every batch by genetic sequencing. After administration to the patient, the genome is assembled to form larger double stranded DNA concatemers. However, no new virus particles are being formed in the subjects. These concatemers persist in the cell as stable episomal structures and are transcriptionally active. Based on the known genetic stability of the wild type AAV, and the absence of an intrinsic mechanism for the genetic variation or instability, the genetic traits of SPVN20 are expected to be stable.

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 to the recombinant viral DNA

(b) Techniques used to identify the GMO
PCR with primers specific to the recombinant viral DNA
Genetic sequencing

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):
Department of Ophthalmology
Ghent University & Ghent University Hospital
C. Heymanslaan 10
9000 Gent
Belgium

(b) Size of the site (m^2):
(i) actual release site (m^2):
Not applicable. A specific size for the site of release cannot be defined as SPVN20 will be administered to patients as part of a clinical trial.
(ii) wider release site (m^2):
Not applicable. A specific size for the site of release cannot be defined as SPVN20 will be administered to patients as part of a clinical trial.

(c) Proximity to internationally recognised biotopes or protected areas (including drinking water reservoirs), which could be affected:
Not applicable. SPVN20 will be administered by a one-time single intravitreal injection in a hospital setting. Thus, it is not anticipated to come into contact with any recognized biotopes or protected areas.

(d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO
Administration of SPVN20 will occur only within a controlled hospital setting; therefore, it is not anticipated that it will come into contact with plants, animals or soil.

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 intravitreal 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).
In Study SPVN20-CLIN-01, SPVN20 is administered as a single intravitreal. Nine (9) patients overall and four (4) patients in Belgium are foreseen.

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

(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 standard hospital procedures. All waste from the procedure will be regarded as hazardous medical waste and waste treatment will follow the standard hospital

procedures. For UZ Gent, all leftovers will be discarded as hazardous medical waste in plastic containers. These containers are closed and collected within 24 hours from the waste disposal rooms located in the hospital and transported to the recycling parc on-site. A registered waste transporter collects the hazardous medical waste 3 times a week from the campus for incineration at Indaver.

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 as there is no prior clinical experience with SPVN20. It is not anticipated that the GMO will be released into the environment.

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	…
(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)
SPVN20 has been designed to result in expression of the GIRK1(F137S) gene to treat patients with no light perception due to end-stage rod-cone dystrophy (RCD), and who retain dormant foveal cone photoreceptors. 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 by design 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 by design 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)
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 1 year 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 (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 material used in this trial is disposable and will be regarded as hazardous medical waste. For UZ Gent, all leftovers will be discarded as hazardous medical waste in plastic containers. These containers are closed and collected within 24 hours from the waste disposal rooms located in the hospital and transported to the recycling parc on-site. A registered waste transporter collects the hazardous medical waste 3 times a week from the campus for incineration at Indaver.

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.