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	B/BE/23/BVW3
(c)	Date of acknowledgement of notification	../../….
(d)	Title of the project LAV-YF17D/RabG will be assessed in Part 2 of clinical study AVX12A-001_AVX48A-001 entitled: *A Phase I, randomized, double-blind, multi-centre, placebo-controlled, dose-escalation study to evaluate the safety, reactogenicity and immunogenicity of AstriVax' investigational vaccine for the prevention of yellow fever (AVX70120), and of AstriVax' investigational vaccine for the prevention of rabies (AVX70481), in healthy adults aged 18 to 40 years*	
(e)	Proposed period of release	From 01/08/2024 until 31/12/2025

2. Notifier

Name of institution or company: AstriVax NV

3. GMO characterisation

(a) Indicate whether the GMO is a:

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

Specify phylum, class: Phylum: Orthornavirae
Class: Flasuviricetes
Order: Amarillovirales
Family: Flaviviridae

(b) Identity of the GMO (genus and species)
The GMO, live attenuated virus (LAV)-YF17D/RabG, includes the full genome of the live attenuated yellow fever 17D (YF17D) strain, with sequence of the rabies surface glycoprotein (RabG) inserted.
Genus: Flavivirus
Species: Yellow fever virus (YFV)
Strain: 17D-204

(c) Genetic stability – according to Annex IIIa, II, A(10)
The insertion of the 1.6kb RabG transgene into the YF17D genome is associated with a certain level of instability caused by the genetic pressure resulting from the insertion of the RabG transgene.

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 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.

The human and environmental risk assessment show that there is very low to negligible risk to public health and environment.

Public Health Risk Assessment
The likelihood of infection with LAV-YF17D/RabG virions of people not included in the clinical study is low to negligible considering:
- The virions cannot be transmitted under natural environmental conditions.
- Any potential means of spread of the GMO (through accidental self-administration of the precursor DNA vaccine PLLAV-YF17D/RabG, or through direct exposure to LAV-YF17D/RabG virions in biological material from a study participant) would involve the exposure to very low amounts of (PL)LAV-YF17D/RabG (if any), by consequence, it would be unlikely that the person would actually get infected with LAV-YF17D/RabG.

- Measures have been put in place to avoid exposure to LAV-YF17D/RabG of people not included in the clinical study (refer to Section F.4.c).

If people not included in the clinical study were to get infected with LAV-YF17D/RabG virions, the potential hazards are the same as those for the participants in clinical study:

- **Risk of adverse effects**. As the GMO has similar biological properties as its parental organism, YF17D, it can be assumed that adverse effects related to vaccination with YF17D may be similar to those related to exposure to LAV-YF17D/RabG. The majority of adverse effects related to vaccination with YF17D are mild in intensity, however, there is a small risk of serious adverse events that are of severe intensity: the incidence of serious adverse events following vaccination with commercial YF17D vaccines has been estimated at 1.6 – 4.7 per 100 000 vaccinees. The risk of occurrence of serious adverse events is considered low to negligible.
- **Risk of occurrence of a mutational event during *in vivo* replication that increases pathogenicity.** As the LAV YF17D/RabG virions replicate *in vivo*, the occurrence of a mutational event during replication that increases pathogenicity cannot fully be excluded. If this were to occur, the intensity of the hazard may potentially be severe. The same risk exists for commercial YF17D vaccines, and over the 800 million people who have been vaccinated with commercial YF17D vaccines, one occurrence of this has been identified. The likelihood of occurrence of this type of event is hence considered low to negligible.
- **Risk of recombination with other (attenuated) flaviviruses.** Recombination with other (attenuated) flaviviruses is a theoretical hazard if a co-infection were to occur in the same cells of the vaccinated host. This could theoretically lead to the emergency of novel strains with altered pathogenic potential, and the intensity of the hazard may therefore potentially be severe. However, it has been shown that the generation of viable recombinants in case of recombination between (live attenuated) flaviviruses is highly unlikely. Moreover, this would require a co-infection of LAV-YF17D/RabG with another (attenuated) flavivirus in the same host cell. Considering that clinical study AVX12A-001_AVX48A-001 will take place in Belgium, where there have not been any reports of endemic human flavivirus infections and where the LAV vaccines against yellow fever, Japanese encephalitis and dengue disease are not routinely administered, the likelihood of a co-infection is considered low to negligible. Overall, the likelihood of occurrent of this type of event is therefore considered negligible.

Taken together, the overall risk to public health is considered low to negligible.

Environmental Risk Assessment

LAV-YF17D/RabG virions do not have a natural host range, cannot be transmitted under natural environmental conditions, and cannot survive for long period of time as such in the environment. There are hence no safety concerns associated with LAV-YF17D/RabG shedding or spill into the environment and the risk to the environment 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	(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)	-
(ii)	genus	Flavivirus
(iii)	species	Yellow fever virus (YFV)
(iv)	subspecies	-
(v)	strain	17D-204
(vi)	pathovar (biotype, ecotype, race, etc.)	-
(vii)	common name	Yellow fever virus 17D (YF17D)

3. Geographical distribution of the organism

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

(b) Indigenous to, or otherwise established in, other EC countries:
(i) Yes (.)

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

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

(ii) No (x)
(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 …	(x)

YF17D is the commercial vaccine against yellow fever. It does not have a natural habitat.

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

5. (a) Detection techniques

Detection of the parental virus, YF17D is most commonly done through the detection of viral RNA by using PCR methods. Alternatively, YF17D virions can be detected through cell culture methods (*e.g.* plaque assay).

(b) Identification techniques

Identification of parental virus, YF17D, can be done through the identification of viral RNA, which is done through PCR methods.

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:
The recipient organism, YF17D, is not classified by the Directive/5000/54/EC of the European Parliament and of the Council. Nevertheless, in the Belgian biohazard classification list, it is classified as risk class 2 for humans.

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

8. Information concerning reproduction

(a) Generation time in natural ecosystems:
The parental virus, YF17D, is the commercial vaccine against yellow fever and does not have a natural ecosystem.

(b) Generation time in the ecosystem where the release will take place:
YF17D requires a human host for replication. The exact generation time is unknown, however, following administration of commercial YF17D vaccine, the YF17D virions replicate in the vaccinated host, and are detectable in the blood of a subset of vaccinated persons in the first week after immunization, with a peak detection around 5 days after immunization.

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

(c) Factors affecting reproduction:
YF17D replication in the vaccinated host is self-limiting and stops with the appearance of neutralizing antibodies about 8-9 days after immunization.

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	(x) Not applicable. The parental virus, YF17D, cannot form survival structures

(b) relevant factors affecting survivability:
YF17D is a fragile, lipid-enveloped RNA virus that cannot replicate outside a suitable host, or form survival structures. It is sensitive to desiccation and thermally instable. It can hence not survive for long periods of time as such in the environment.
YF17D is derived from wild type YFV which is inactivated by heat (50-60°C for at least 30 minutes), ultraviolet light, gamma radiation, or by organic chemicals / disinfectants (3-8% formaldehyde and 2% glutaraldehyde; 2-3% hydrogen peroxide, 500-5,000 ppm available chlorine, alcohol, 1% iodine, or phenol iodophors).

10. (a) Ways of dissemination
YF17D cannot be disseminated under natural environmental conditions. YF17D can only be disseminated through direct exposure to biological material from a vaccinated person (*e.g.* blood transfusion, organ transplant, through pregnancy or breastfeeding).

(b) Factors affecting dissemination
Not applicable. YF17D cannot be disseminated under natural environmental conditions.

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 for the Applicant.
Note that the recipient organism, YF17D, has been used as the basis of 2 marketed vaccines, Imojev® and Dengvaxia® (both developed by Sanofi Pasteur; the latter one is authorised for use in the European union). As opposed to LAV-YF17D/RabG however, these vaccines were developed by replacing the genes encoding 2 structural proteins of YF17D (prM and E) with those of specific Japanese Encephalitis and Dengue strains, respectively. This leads to chimeric virions with surface expression of the immunizing antigens.

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 purpose of the genetic modification is for LAV-YF17D/RabG virions to express the RabG protein in all cells infected by the LAV, in order induce an immune response against rabies virus in the vaccinated host, for the prevention of rabies.

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 (.) No (x)

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	(.)
cosmid	(.)
transposable element	(.)
other, specify …	

(b) Identity of the vector
…
(c) Host range of the vector
…

(d) Presence in the vector of sequences giving a selectable or identifiable phenotype

	Yes	No
antibiotic resistance	(.)	
other, specify	…	

Indication of which antibiotic resistance gene is inserted
…

(e) Constituent fragments of the vector
…

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

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

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 insert is composed of the coding sequence of the rabies surface glycoprotein (RabG).

(b) Source of each constituent part of the insert
Rabies virus

(c) Intended function of each constituent part of the insert in the GMO
Induction of an immune response against rabies virus

(d) Location of the insert in the host organism

- on a free plasmid (.)
- integrated in the chromosome (.)
- other, specify … Integrated in the viral RNA genome

(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 (.)
- insect (.)
- fish (.)
- other animal (.)
(specify phylum, class) …

other, specify …

2. Complete name

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

3. Is the organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?
Yes (x) No (.) Not known (.)
If yes, specify the following:

(c) to which of the following organisms:

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

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

Yes (x) No (.) Not known (.)

If yes, give the relevant information under Annex III A, point II(A)(11)(d):
RabG mediates entry of the rabies virus into host cells as is as such involved in the pathogenic or harmful properties of the rabies virus. However, the GMO (LAV-YF17D/RabG) only includes the genetic sequence of the RabG glycoprotein from the rabies virus. The RabG protein as such is not enough to create infectious particles.

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 (x) No (.)

If yes, specify
The donor organism, rabies virus, is classified by the EC Directive/5000/54/EC as human pathogen Risk Group 3. However, as indicated above, LAV-YF17D/RabG only contains the genetic sequence of the RabG protein from the rabies virus, which is not enough to create infectious rabies particles.

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 …

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

Yes (.) No (x) Not known (.)

Specify …

(e) 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 insertion of the 1.6kb RabG transgene into the YF17D genome is associated with a certain level of instability caused by the genetic pressure resulting from the insertion of the RabG transgene.

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)

4. Description of identification and detection methods

(a) Techniques used to detect the GMO in the environment
Detection of LAV-YF17D/RabG virions can be done through the detection of viral RNA by using PCR methods, or by detection of virions, which can be done through cell culture methods.

(b) Techniques used to identify the GMO
Identification of the GMO at the level of its new trait(s) can be done through PCR methods.

F. Information Relating to the Release

1. Purpose of the release (including any significant potential environmental benefits that may be expected)
LAV-YF17D/RabG will be assessed in Part 2 of the Phase I clinical study AVX12A-001_AVX48A-001. This is the first clinical study to support the development of a new vaccine for the prevention of rabies.

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):
Clinical study AVX12A-001_AVX48A-001 will be conducted at 2 clinical study sites in Belgium:
- Centre for Evaluation of Vaccination (CEV) / Vaccinopolis, Drie Eikenstraat 663, 2650 Antwerp (Edegem), Belgium
- Center of Vaccinology (CEVAC), University Hospital Ghent, C. Heymanslaan 10, 9000 Ghent, Belgium

(b) Size of the site (m^2): N/A
(i) actual release site (m^2): … m^2
(ii) wider release site (m^2): … m^2
A total of 48 study participants are planned to be administered PLLAV-YF17D/RabG vaccine in Part 2 of clinical study AVX12A-001_AVX48A-001.

(c) Proximity to internationally recognised biotopes or protected areas (including drinking water reservoirs), which could be affected:
Not applicable: the GMO, LAV-YF17D/RabG, is a fragile, lipid-enveloped RNA virus that cannot replicate outside a suitable host, or form survival structures. It is sensitive to desiccation and thermally instable. It cannot survive as such in the environment for long periods of time.

(d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO
Not applicable: the GMO, LAV-YF17D/RabG, is a fragile, lipid-enveloped RNA virus that cannot replicate outside a suitable host, or form survival structures. It is sensitive to desiccation and thermally instable. It cannot survive as such in the environment for long periods of time. It does not have a natural host range and cannot be disseminated under natural environmental conditions.

4. Method and amount of release

(a) Quantities of GMOs to be released:
Upon administration of the plasmid DNA vaccine, PLLAV-YF17D/RabG, the GMO (LAV-YF17D/RabG) is produced in the cells of the vaccinated host, relying on the human transcription and translation machinery. The LAV-YF17D/RabG virions subsequently self-replicate in the vaccinated host. Self-replication is self-limiting and stops with the appearance of neutralizing antibodies. As a consequence, the quantity of GMO that will be released will depend on intrinsic factors such as the number of transfected cells and the time to neutralization of the LAV-YF17D/RabG virions.

(b) Duration of the operation:
Part 2 of clinical study AVX12A-001_AVX48A-001 is planned to start in August 2024. The end date of Part 2 of the study is estimated to be in December 2025.

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

Potential routes of spread of the GMO are limited to accidental self-administration of the precursor DNA vaccine PLLAV-YF17D/RabG, or to direct exposure to LAV-YF17D/RabG virions.

This will be avoided through the following measures:

- Provision of the DNA precursor vaccine PLLAV-YF17D/RabG in vials with a rubber stopper and a flip-off cap.
- Appropriate training of and the wearing of appropriate personal protective equipment for clinical study staff involved in PLLAV-YF17D/RabG handing and administration, or in biological sampling.
- Storing all biological samples in tubes with a screw cap.
- Treating all waste resulting from PLLAV-YF17D/RabG handling or administration, or from biological sampling from study participants, as hazardous medical waste.
- Chemical decontamination with an organic disinfectant in case of accidental spilling of a biological sample from a participant in Part 2 of the clinical study AVX12A-001_AVX48A-001.
- Requiring that study participants:
  - Do not donate blood or organs for 3 months after the study vaccination
  - Are not pregnant or breastfeeding at the time of study entry, or become pregnant to up to at least 2 months after the study vaccination.
  - Are not in close contact (*e.g.* living under the same roof, caregiver, involved in clinical care) for 2 months after study vaccination with an immunocompromised person, an infant < 6 months of age, or any individual that, in the judgement of the Investigator, may be at increased risk.
  - Are not immunocompromised.

5. Short description of average environmental conditions (weather, temperature, etc.)
Not applicable: the GMO cannot survive as such in 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.
Not applicable: this is the first release 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

This section is not applicable: the interaction of the GMO with the environment and its potential impact on the environment is similar to that of the recipient or parental organism. Indeed, aside from its recombinant viral RNA that contains the sequence of the RabG protein in addition to that of YF17D, the composition of the LAV-YF17D/RabG virions is identical to the YF17D virions (parental organism). As a result, the GMO has similar biological properties as its parental organism, including host range (i.e. they do not have a natural host), pathogenic properties (side effects), transmission route (i.e. they cannot be transmitted under natural environmental conditions) and its ability to survive outside the host (i.e. they cannot survive as such in the environment).

1. Name of target organism (if applicable)
(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 …

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

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

4. Is post-release selection such as increased competitiveness, increased invasiveness for the GMO likely to occur?
Yes (.) No (.) 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

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) …
(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:

(b) from other organisms to the GMO:

(c) likely consequences of gene transfer:

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.):

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

H. Information Relating to Monitoring

1. Methods for monitoring the GMOs
Shedding of LAV-YF17D/RabG virions and viraemia will be assessed in a subset of the study participants participating in Part 2 of clinical study AVX12A-001_AVX48A-001.

2. Methods for monitoring ecosystem effects
The safety and immunogenicity of the GMO will be monitored throughout the clinical study. There are no specific plans for monitoring the environment during the release as the GMO cannot survive as such in the environment.

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

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

5. Duration of the monitoring
Participants in Part 2 of clinical study AVX12A-001_AVX48A-001 will be followed up for 1 year after the vaccination.

6. Frequency of the monitoring
Regular follow-up visits will be conducted up to 1 year after the vaccination.

I. Information on Post-release and Waste Treatment

1. Post-release treatment of the site
Standard clinical site hygiene. No specific post-release procedures are foreseen also considering that the GMO, LAV-YF17D/RabG, is produced in the cells of the vaccinated host upon administration of the DNA vaccine, PLLAV-YF17D/RabG, *i.e.* is the GMO is not administered (released) at the study site.

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

3. (a) Type and amount of waste generated
The type of waste generated will be that resulting from handling, dilution and administration of the DNA vaccine PLLAV-YF17D/RabG, or from biological

sampling from participants in Part 2 of clinical study AVX12A-001_AVX48A-001, *e.g.* syringes, needles, wipes, dressings, gloves.
The amount of waste generated at the clinical study sites will be within the normal handling capacity that can be managed by the standard operating procedures currently in place.

3. (b) Treatment of waste
The waste will be collected and treated as hazardous medical waste, *i.e.* collected in dedicated and certified waste bins which are hermetically sealed and transported by a certified shipper to a specialized incineration facility.

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 accidental self-administration of the precursor DNA vaccine PLLAV-YF17D/RabG into the body (*e.g.* clinical site staff needle stick injury), the medical staff must report the incident to the responsible person of the clinical site.

2. Methods for removal of the GMO(s) of the areas potentially affected
In case of accidental spilling of a biological sample from a vaccinated study participant (which potentially contain the clinical vector, LAV-YF17D/RabG), the area will be chemically decontaminated with an organic disinfectant.

3. Methods for disposal or sanitation of plants, animals, soils, etc. that could be exposed during or after the spread
Not applicable as the GMO cannot be transmitted under natural environmental conditions, does not have a natural host range and cannot survive as such in the environment for long periods of time.

4. Plans for protecting human health and the environment in the event of an undesirable effect
Human health. Potential routes of spread of the GMO are limited to accidental self-administration of the precursor DNA vaccine PLLAV-YF17D/RabG, or to direct exposure to LAV-YF17D/RabG virions. This will be avoided through the measures described in Section F.4.(c).
The environment. LAV-YF17D/RabG virions do not have a natural host range, cannot be transmitted under natural environmental conditions, and cannot survive for long period of time as such in the environment. There are hence no safety concerns associated with LAV-YF17D/RabG shedding / spill into the environment.