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/24/BVW6
(c)	Date of acknowledgement of notification	../../….
(d)	Title of the project LAV-YF17D/HBc will be assessed in clinical study AVX37-101 entitled: *A randomised, double-blind, placebo-controlled, multi-centre, Phase I study to evaluate the safety, reactogenicity and immunogenicity of AstriVax' investigational therapeutic hepatitis B virus (HBV) vaccine (AVX70371) in adult patients with chronic HBV (CHB) infection.*	
(e)	Proposed period of release	From 01/03/2025 until 31/12/2026

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/HBc, includes the full genome of the live attenuated yellow fever 17D (YF17D) strain, with the sequence of the core antigen from the hepatitis B virus (HBc) inserted.
Genus: Flavivirus
Species: Yellow fever virus (YFV)
Strain: 17D

(c) Genetic stability – according to Annex IIIa, II, A(10)
Extensive passaging of LAV-YF17D/HBc in in vitro cell culture has shown that it is genetically stable.

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, RO

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 outcome of the human and environmental risk assessment is that there is very low to negligible risk to public health and environment.

Public Health Risk Assessment
The likelihood of infection with LAV-YF17D/HBc virions of people not included in the clinical study is low to negligible considering:
- The virions can most probably not be transmitted under natural environmental conditions.
- Measures have been put in place to avoid exposure to LAV-YF17D/HBc of people not included in the clinical study (refer to Section F.4.c).
- If exposure to LAV-YF17D/HBc to people not included in the clinical study were to occur (through accidental self-administration of the precursor DNA vaccine AVX70371, or through direct exposure to LAV-YF17D/HBc virions in biological

material from a study participant), this would involve the exposure to very low amounts of LAV-YF17D/HBc particles (if any), by consequence, it would be unlikely that the person would actually get infected with LAV-YF17D/HBc.

If people not included in the clinical study were to get infected with LAV-YF17D/HBc virions, the potential hazards are the same as those for the participants in the 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/HBc. 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 therefore considered low to negligible.
- **Risk of occurrence of a mutational event during *in vivo* replication that increases pathogenicity.** As the LAV YF17D/HBc 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 emergence 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/HBc with another (attenuated) flavivirus in the same host cell. Considering that clinical study AVX37-101 will take place in Europe, where endemic human flavivirus infections are rare, and where live attenuated vaccines against yellow fever, Japanese encephalitis and dengue are not part of the routine immunization schedule, the likelihood of a co-infection with other (attenuated) flaviviruses is considered low to negligible. Overall, the likelihood of recombination with other (attenuated) flaviviruses is therefore considered negligible.

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

Environmental Risk Assessment

LAV-YF17D/HBc virions do not have a natural host range, can most probably not be transmitted under natural environmental conditions, and cannot survive for long period of time as such in the environment. There are hence no environmental safety concerns associated with LAV-YF17D/HBc 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
(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 (.)
* The parental organism, YF17D, is the commercial vaccine against YFV. In Belgium, it is administered to people travelling to endemic regions by physicians affiliated with an accredited travel clinic.

(d) Is it frequently kept in the country where the notification is made?
Yes (x) * No (.)
* The parental organism, YF17D, is the commercial vaccine against YFV. In Belgium, it is administered to people travelling to endemic regions by physicians affiliated with an accredited travel clinic.

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)

Not applicable. 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 classified as risk class 2 for humans in the Belgian biohazard classification list. It is not classified by the Directive/5000/54/EC of the European Parliament and of the Council.

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 for a brief period after immunization, with a duration of 1-5 days and 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, at 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 can most probably not be disseminated under natural environmental conditions. The only plausible means of dissemination is through direct exposure to biological material from a recently vaccinated person (if the material were to contain YF17D particles).

(b) Factors affecting dissemination
Not applicable. YF17D can most probably not 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)
The Applicant is conducting a clinical study (study AVX1248-101, EU CT number 2024-511194-29) in which the GMO LAV-YF17D/RabG is assessed. LAV-YF17D/RabG includes the full genome of YF17D with the sequence of the rabies surface glycoprotein inserted. The notification number for the release of LAV-YF17D/RabG is B/BE/23/BVW3.

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/HBc virions to express HBc, in order induce an immune response against HBc in the vaccinated host.

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 core antigen of the hepatitis B virus (HBc).

(b) Source of each constituent part of the insert
Hepatitis B virus

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

(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 (.)
DNA virus (x)
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 Orthohepadnavirus
(iv) species Hepatitis B virus
(v) subspecies …
(vi) strain …
(vii) cultivar/breeding line …
(viii) pathovar …
(ix) common name Hepatitis B 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 (.)
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):
HBc is the structural subunit of the hepatitis B virus viral capsid. It is essential for capsid assembly and it plays a role in multiple steps of hepatitis B virus replication, including in viral RNA packaging, reverse transcription to DNA, viral trafficking and viral entry. Importantly however, the GMO (LAV-YF17D/HBc) only includes the genetic sequence of the core antigen of the hepatitis B virus (HBc). HBc on its own cannot create infectious particles and is therefore not pathogenic or harmful.

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, hepatitis B virus, is classified by the EC Directive/5000/54/EC as a human pathogen Risk Group 3 that may present a limited risk of infection because it is not normally infectious by the airborne route. However, as indicated above, LAV-YF17D/HBc only contains the genetic sequence of HBc, which on its own cannot create infectious hepatitis B particles and is therefore not pathogenic or harmful.

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
Extensive passaging of LAV-YF17D/HBc in in vitro cell culture has shown that it is genetically 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?

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/HBc 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/HBc will be assessed in the Phase I clinical study AVX37-101. This is the first clinical study to support the development of a therapeutic vaccine against chronic hepatitis B infection.

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 recipient or parental organism, YF17D, is the commercial vaccine against YFV and is kept in accredited travel clinics. Clinical study AVX37-101 will be conducted at the clinical study site indicated below.

3. Information concerning the release and the surrounding area

(a) Geographical location (administrative region and where appropriate grid reference):
In Belgium, clinical study AVX37-101 will be conducted at the following clinical study site. It is possible that other sites will be added in the future.
- SGS Belgium N.V., Drie Eikenstraat 655, 2650 Edegem, 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
It is expected that 8 participants will be included in Belgium.

(c) Proximity to internationally recognised biotopes or protected areas (including drinking water reservoirs), which could be affected:
Not applicable: the GMO, LAV-YF17D/HBc, 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/HBc, 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 can most probably not be disseminated under natural environmental conditions.

4. Method and amount of release

(a) Quantities of GMOs to be released:
The quantity of GMO (LAV-YF17D/HBc) that will be released will depend on intrinsic factors such as the number of AVX70371-transfected cells and the time to neutralization of the LAV-YF17D/HBc virions. Indeed, upon administration of AVX70371, the precursor DNA vaccine relies on the human transcription and translation machinery to produce the GMO (LAV-YF17D/HBc) *in situ* in the vaccinated host. The LAV-YF17D/HBc virions subsequently self-replicate in the vaccinated host, which stops with the appearance of neutralizing antibodies.

(b) Duration of the operation:
Clinical study AVX37-101 is planned to start in March 2025. The end date of the study will depend on the enrolment rate and is estimated to be in Q4 2026.

(c) Methods and procedures to avoid and/or minimise the spread of the GMOs beyond the site of the release
As the LAV-YF17D/HBc virions can most probably not be transmitted under natural environmental conditions, potential routes of spread of the GMO are limited to accidental self-administration of the precursor DNA vaccine AVX70371, or to direct exposure to LAV-YF17D/HBc virions in biological material from a study participant.

This will be avoided through the following measures:

- Provision of the DNA precursor vaccine AVX70371 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 AVX70371 handing and administration, and in biological sampling.
- Storing all biological samples in tubes with a screw cap.
- Treating all waste resulting 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 study participant.
- Requiring that study participants:
    - From the first study vaccination up to 2 months after the last study vaccination: are not in close contact 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.
    - Do not donate blood or organs from the first study vaccination up to 3 months after the last study vaccination.
    - Do not donate egg / ovum (for women) or sperm (for men) from the first study vaccination up to 2 months after the last study vaccination.
    - Are not pregnant or breastfeeding at the time of study entry, and do not become pregnant up to 2 months after the last study vaccination.
    - 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

1. Name of target organism (if applicable)

(i)	order and/or higher taxon (for animals)	…
(ii)	family name for plants	…
(iii)	genus	homo
(iv)	species	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)
The GMO, LAV-YF17D/HBc, is expected to self-replicate and to express HBc. This is expected to induce an immune response against HBc in the vaccinated host.

3. Any other potentially significant interactions with other organisms in the environment
Not applicable, the GMO does not have a natural host range.

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 GMO is expected to self-replicate in the vaccinated host until the appearance of neutralizing antibodies at about 8-9 days after immunization. Similar to its parental virus (YF17D), the GMO (LAV-YF17D/HBc) cannot be transmitted under natural environmental conditions does not have a natural host range. Post-release selection is therefore unlikely to occur.

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, LAV-YF17D/HBc, can most probably not be disseminated under natural environmental conditions. It does not have a natural host range. As it is possible that the LAV-YF17D/HBc virions biodistribute in and shed from the body of the vaccinee, the GMO could be disseminated to other people in case of exposure to biological material from a subject in clinical study AVX37-101 (if the material were to contain LAV-YF17D/HBc virions). Additionally, accidental self-administration of the precursor DNA vaccine AVX70371 by clinical site staff involved in the handling, dilution or administration of the vaccine could potentially lead to the dissemination of the GMO. The GMO can hence only potentially be disseminated within its target organism (humans).

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 …

Not applicable: the GMO can only potentially be disseminated within its target organism (humans).

7. Likelihood of genetic exchange in vivo

(a) from the GMO to other organisms in the release ecosystem:
Genetic exchange between the GMO and other (attenuated) flaviviruses is theoretically possible if a co-infection were to occur in the same cells of the vaccinated host. 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/HBc with

another (attenuated) flavivirus in the same host cell. Considering that clinical study AVX37-101 will take place in Europe, where endemic human flavivirus infections are rare, and where live attenuated vaccines against yellow fever, Japanese encephalitis and dengue are not part of the routine immunization schedule, the likelihood of a co-infection with other (attenuated) flaviviruses is considered low to negligible. Overall, the likelihood of recombination with other (attenuated) flaviviruses is therefore considered negligible.

(b) from other organisms to the GMO:
Similar to the above: while genetic exchange between the GMO and other (attenuated) flaviviruses is theoretically possible, the likelihood of occurrence is considered negligible.

(c) likely consequences of gene transfer:
Even if recombination of the GMO with other (attenuated) flaviviruses were to occur, the generation of viable recombinants is highly unlikely. In other words, there would most likely not be consequences of a 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.):
The behaviour and characteristics of the GMO and its ecological impact have not been studied in stimulated natural environments.

9. Possible environmentally significant interactions with biogeochemical processes (if different from the recipient or parental organism)
Not applicable. There is no known or predicted involvement of the GMO (or its recipient or parental organism) in biogeochemical processes.

H. Information Relating to Monitoring

1. Methods for monitoring the GMOs
The safety and immunogenicity of the GMO, as well as its effect on CHB infection disease markers, will be monitored throughout clinical study AVX37-101.

2. Methods for monitoring ecosystem effects
There are no specific plans for monitoring ecosystem effects, as the GMO cannot be disseminated under natural environmental conditions, does not have a natural host range and 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 clinical study AVX37-101 will be followed up for 6 months after the last study vaccination.

6. Frequency of the monitoring
Regular follow-up visits will be conducted up to 6 months after the last study vaccination.

I. Information on Post-release and Waste Treatment

1. Post-release treatment of the site
No specific decontamination procedure is required following administration or accidental spilling of the precursor DNA vaccine AVX70371 vaccine. The standard decontamination procedure of the site will be used.
In case of accidental spilling of a biological sample from a vaccinated study participant (which potentially contains the GMO, LAV-YF17D/HBc), the area will be chemically decontaminated with an organic disinfectant.

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 AVX70371, or from biological sampling from participants in clinical study AVX37-101, *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 AVX70371 (*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 contains the GMO, LAV-YF17D/HBc), 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 can most probably not be transmitted under natural environmental conditions, does not have a natural host range and cannot survive as such in the environment.

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 AVX70371, or to direct exposure to LAV-YF17D/HBc virions in biological material from a study participant. This will be avoided through the measures described in Section F.4.(c).
The environment. LAV-YF17D/HBc virions do not have a natural host range, can most probably not be transmitted under natural environmental conditions, and cannot survive for long period of time as such in the environment. There are hence no environmental safety concerns associated with LAV-YF17D/HBc shedding / spill into the environment.