SNIF: GMOB-2023-15228

Domain:
GMO

Authorisation type:
Deliberate release of GMO or a combination of GMOs for any other purpose than for placing on the market

Application type:
Summary notification for the release of genetically modified higher organisms other than higher plants in line with Decision 2002/813/EC Annex, Part 1.

Recipient Member State:
Netherlands

Competent Authority:
Ministry of Infrastructure and Water Management

Notification number:
B/NL/23/005

Acknowledgement date:
2023-06-01

A- General information

Details of notification

Details of notification
IM-MV_23-005
Member State of notification
Netherlands
Title of the project
Vaccination of chickens , under field conditions, with two recombinant herpesvirus of turkey to monitor the immunological responses in time. One herpesvirus with an insection of HA H5 gen of a LPAI virus (Vectormune HVT-AIV) and one existing recombinant herpesvirus of turkey, with a VP2 gene of infectious bursal disease, with a HA H5 gene construct (Vaxxitek HVT-IBD-H5).
Proposed period of release
Starting date
2023-06-01
Finishing date
2030-01-30

Notifier

Name of institute or company
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Country
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GMO characterisation

(a) Indicate whether the GMO is a:

Viroid
No
RNA virus
No
DNA virus
Yes
Bacterium
No
Fungus
No

Animal
No
Other
No

(b) Identity of the GMO (genus and species)

Two different vaccines are applied: Both vaccines contain a live cell-associated Herpesvirus of turkey (HVT) based on the HVT FC-126 strain. HVT or Meleagrid herpes virus 1 (MeHV-1) belongs to the family of the Herpesviridae, subfamily Alphaherpesvirinae, genus Mardivirus One vaccine contains the HVT FC126 strain an insertions of the HA H5 gene of Influenza virus. One vaccine contains the HVT FC126 strain with an insection of the VP2 gene of infectious bursal disease, in which an insertion of HA H5 construct is added.

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

The recipient organism, HVT FC-126 strain, has been isolated from a commercial turkey flock and found to be non-pathogenic for both turkeys and chickens. The genetic stability of the recombinant HVT is confirmed by sequence evaluation and confirmation of the expression of the inserted genes

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

No

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

No

Has the same GMO been notified for release or placing on the market outside the Community by the same or other notifier?

No

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

No environmental impact is expected. - HVT is a naturally non-pathogenic virus. Its natural host is the turkey, but the virus can also replicate in chickens, but only after an intramuscular or subcutaneous application. Replication in other avian species is very unlikely. HVT causes no clinical disease in turkeys, chickens and other avian species. The virus can spread via inhalation of dust particles shed from the skin from infected (or vaccinated) birds to turkeys but spreading to chickens is highly unlikely. Shedding from vaccinated chickens is limited and transient in nature. - Genetic modifications made by introducing the HA H5 genes does not change the non-pathogenic phenotype of the parent virus and the recombinants are therefore still non-pathogenic. There are no risks for recombination either with other viruses or the host, therefore no new properties can be introduced in the environment. - HVT and recombinant HVTs are not capable of replicating in mammalian cells and cannot infect humans. As the HVT recombinants are non-pathogenic, the level of risk for both humans and the environment can be considered as effectively zero.

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

1. Recipient or parental organism characterisation

Indicate whether the recipient or parental organism is a:

Viroid
No
RNA virus
No
DNA virus
Yes
Bacterium
No
Fungus
No
Animal
No
Other
No

2. Name

(i) Order and/or higher taxon (for animals)
Herpesvirales
(ii) Genus
Mardivirus
(iii) Species
Meleagrid herpesvirus 1

(iv) Subspecies

(v) Strain
FC 126

(vi) Pathovar (biotype, ecotype, race, etc.)

3. Geographical distribution of the organism

(a) Indigenous to, or otherwise established in, the country where the notification is made:
yes
(b) Indigenous to, or otherwise established in, other EC countries:
yes
Indicate the type of ecosystem in which it is found:
continental
(c) Is it frequently used in the country where the notification is made?

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

4. Natural habitat of the organism

(a) Is the organism a microorganism ?
No
(b) Is the organism an animal?
No

5(a) Detection Techniques

Detection Techniques
The virus can be grown in primary or secondary cultures of chicken cells such as embryonic fibroblasts and causes a typical cytopathic effect (CPE). These plaques can be seen macroscopically or visualized by Giemsa-, Naphtalene black- or serospecific staining. HVT in blood samples from infected chickens can be identified by plating lymphocytes on monolayers of primary or secondary chicken cells. Detection can also be performed on DNA extracted from the virus using the polymerase chain reaction (PCR).

5(b) Identification Techniques

Identification Techniques
HVT virus can be identified by labeling viral foci with the aid of the immuno fluorescence method using specific anti-HVT antibodies. Alternatively, detection can be performed on DNA extracted from the infected cells/virus using the polymerase chain reaction (PCR). A primer set composed of HVT genome specific primers can be used to specifically detect HVT.

6. Is the recipient organism classifies under existing Community rules relating to the protection of human health and/or the environment?

No

7. Is the recipient organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?

no

8. Information concerning reproduction

(a) Generation time in natural ecosystems:
The natural host is turkey. The generation time in the natural host and in chickens can be estimated between 12 and 48 hours. HVT causes a persistent infection and can be detected during the whole life of the animal. Spreading of the virus between turkeys occurs through the release of dust particles from feather follicles. Spreading of virus between chickens can only take place for a short period of time post vaccination.
(b) Generation time in the ecosystem where the release will take place:
The generation time in chickens can be estimated between 12 and 48 hours. HVT causes a persistent infection in chickens and can be detected during the whole life of the animal. Spreading of the virus between chickens is highly unlikely.
(c) Way of reproduction
Asexual

(d) Factors affecting reproduction:
Host dependent replication.

9. Survivability

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

(i) endospores
No
(ii) cysts
No
(iii) sclerotia
No
(iv) asexual spores (fungi)
No
(v) sexual spores (fungi)
No
(vi) eggs
No
(vii) pupae
No
(viii) larvae
No
Other
Yes
Specify
None
(b) Relevant factors affecting survivability
HVT vaccine viruses are being produced in chicken embryo fibroblast (CEF) cells and stored in liquid nitrogen. The virus can only survive in viable CEF cells. Factors that influence the survival of CEF cells (high temperatures, desiccation, pH, etc.) also affect the stability of the virus. After vaccination of chickens the virus could spread via dust from the feather follicles. These dust particles can be relatively stable and but are not infectious for chickens.

10(a) Ways of dissemination

From four weeks post vaccination of chickens the virus will not spread to other chickens via dust from the feather follicles. Spread of HVT is only seen in turkeys and is normally not observed in other avian species such as chickens. Infection through inhalation of dust is the natural way of infection
10(b) Factors affecting dissemination
From four weeks post vaccination of chickens the virus will not spread to other chickens via dust from the feather follicles. Spread of HVT is only seen in turkeys and is normally not observed in other avian species such as chickens. Infection through inhalation of dust is the natural way of infection

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)

B/NL/21//002, B/NL/11/006, B/NL/15/011

C. Information relating to the genetic modification

1. Type of the genetic modification

Insertion of genetic material
Yes
Deletion of genetic material
No
Base substitution
No
Cell fusion
No
Other
No

2. Intended outcome of the genetic modification

One vaccine: The inserted HA-gene of LPAI will be transcribed and express the HA-protein, after vaccination with the HVT recombinant. Other vaccine: The inserted HA-gene construct of LPAI will be transcribed and express the HA-protein, after vaccination with the HVT recombinant, which also carries the VP2 gene.

3(a) Has a vector been used in the process of modification?

Yes
3(b) If yes, is the vector wholly or partially present in the modified organism?
No

6. Composition of the insert

(a) Composition of the insert

One insertion with DNA fragments containing the HA-gene of LPAI sequence with regulatory (promotor and terminator) sequences.

(b) Source of each constituent part of the insert

The inserted DNA is composed of HA of a LPAI H5 subtype or a LPAI H5 construct and cytomegalovirus (CMV) and polyadenylation sequences

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

The inserted region contains the HA-gene of LPAI virus or the HA-gene construct and promoter and terminator sequences. The inserted HA is transcribed and express proteins which induce an immune response against AIV in vaccinated chickens. The function of the promoter sequences is to facilitate the transcription of the genes and the function of the terminator sequences is to facilitate termination of transcription.

(d) Location of the insert in the host organism

On a free plasmid
No
Integrated in the chromosome
No
Other
Yes
Specify
Integrated in the viral genome

(e) Does the insert contain parts whose product or function are not known?

No

D. Information on the organism(s) from which the insert is derived

1. Indicate whether it is a:

Viroid
No
RNA virus
Yes
DNA virus
No
Bacterium
No
Fungus
No
Animal
No
Other
No

2. Complete name

(i) Order and/or higher taxon (for animals)
n.a.
(ii) Family name (for plants)
Orthomyxoviridae
(iii) Genus
Influenza Virus
(iv) Species
Influenza Virus, type A
(v) Subspecies
n.a.
(vi) Strain

1. LPAI originates from mute swan/Hungary/4999/2006 and 2. A computationally optimized sequence of LPAI (Computationally Optimized Broadly Reactive Antigen (COBRA)) based upon known HPAI HA sequences to an artificial HA construct.
   (vii) Cultivar/Breeding line
   n.a.
   (viii) Pathovar
   n.a.
   (ix) Common name
   n.a.

3. Is the organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?

no
(b) are the donated sequences involved in any way to the pathogenic or harmful properties of the organism?
no

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

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 related to exposure to biological agents at work?

Yes

If yes, specify the following:

According to EU Directive 2000/54/EC, Avian Influenza can be considered as a class 2 organism. Exposure of humans to infected birds can cause respiratory symptoms. As a complication mortality can occur, depending on the adaption of the AI strain to humans.

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

no

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?
no
Specify
The replication and amount of virus shedding is the same or reduced compared to the recipient HVT FC-126 strain. There is no difference in survivability of the GMOs compared to the recipient HVT: the virus has the same properties as described under B.9.b.
(b) Is the GMO in any way different from the recipient as far as mode and/or rate of reproduction is concerned?
no
Specify
The in-vitro growth characteristics are not different from the recipient HVT FC-126. The GMOs is propagated like the recipient in chicken embryo fibroblasts (CEF). Also the in vivo growth characteristics are the same compared to the recipient
(c) Is the GMO in any way different from the recipient as far as dissemination is concerned?
no
Specify
Dissemination of the GMOs has been studied in chickens in comparison to the recipient HVT FC-126 strain; no apparent qualitative differences between the GMOs and HVT FC-126 in terms of virus localization and chronology of virus appearance in tissues tested except for reduced replication are acceptable. Therefore, the dissemination rate of the GMOs from vaccinated chickens is the same or decreased compared to the recipient virus.
(d) Is the GMO in any way different from the recipient as far as pathogenicity is concerned?
no
Specify
Insertion of the genes does not change the non-pathogenic nature of the HVT FC-126 recipient. HVT FC-126 is a naturally non-pathogenic virus.

2. Genetic stability of the genetically modified organism

The genetic stability of the GMOs is confirmed by sequence evaluation and confirmation of the expression of the inserted genes.

3. Is the GMO significantly pathogenic or harmfull in any way (including its extracellular products), either living or dead?

no
(b) Give the relevant information 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
The virus can be grown in primary or secondary cultures of chicken cells such as embryonic fibroblasts and causes a typical cytopathic effect (CPE). These plaques can be seen macroscopically or visualized by Giemsa-, Black plaque assay (BPA) or serospecific staining. GMOs in blood samples from infected chickens can be identified by plating lymphocytes on monolayers of primary chicken cells. Detection can also be performed on DNA extracted from the virus using the polymerase chain reaction (PCR).

(b) Techniques used to identify the GMO

The GMOs can be visualized by labeling viral foci with the aid of the immune-fluorescence method using specific HVT antibodies or antibodies raised against the inserted proteins. Alternatively, detection can be performed on DNA extracted from the virus using PCR. Specific primers in the HVT genome HA gene can be selected for this purpose.

F. Information relating to the release

1. Purpose of the release (including any significant potential environmental benefits that may be expected)

The GMOs will be used in the Netherlands for the active immunization of chickens. The purpose of the release applied for is to perform field trials to monitor the immune response of the chickens and to provide chickens, that are raised and vaccinated under field conditions, for HPAI H5 challenge experiments.

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?

No

3. Information concerning the release and the surrounding area

(a) Geographical location (administrative region and where appropriate grid reference):

Overijssel and Flevoland

(b) Size of the site (m2)

(i) actual release site (m2)
poultry holding with a capacity of max. 30000 animals
(ii) wider release area (m2)
n.a.

(c) Proximity to internationally recognised biotopes or protected areas (including drinking water reservoirs), which could be affected:

Location not within a radius of 500 meters of a water reservoir.

(d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO

Chickens are kept in other houses on the same sites. No turkey farms are located within a radius of 1000m from the locations. Interaction of the GMOs with migratory species will be very unlikely to occur as they cannot enter the houses where the vaccinated chickens are kept.

4. Method and amount of release

(a) Quantities of GMOs to be released:

Per GMO a maximum of 100.000 chickens will be vaccinated that is 100.000 doses (2500 - 8000 pfu /dose).

(b) Duration of the operation:

Vaccinated birds will be kept for maximum 80 weeks

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

Standard business operations will be applied. The vaccinated chickens and the produced table eggs will not be for human consumption, unless it is authorised by the responsible authority

5. Short description of average environmental conditions (weather, temperature etc.)

The Netherlands has a temperate maritime climate: summers are relatively cool (average day temperature 17.3C) and winters cold (average day temperature 3.9C). Average temperature over the year is Rain is expected year-round (800 900 mm rain in a year), with more days with rain in fall.

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

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 organisms (if applicable)

Applicable?
Yes
(i) Order and/or higher taxon (for animals)
Galliformes
(ii) Family name (for plants)
Phasianidae
(iii) Genus
Gallus
(iv) Species
Gallus Gallus
(v) Subspecies
Gallus Gallus Domesticus
(vi) Strain
n.a.
(vii) Cultivar/Breeding line
n.a.
(viii) Pathovar
n.a.
(ix) Common name
Chicken

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

Applicable?
Yes
Specify
Vaccination of chickens with the GMOs will result in replication of the GMO in the chicken, resulting in the induction of an immune response.

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

The GMOs are non-pathogenic and spreading of the GMO between chickens is highly unlikely to occur.

4. Is post-release selection such as increased competitiveness, increased invasiveness for the GMO likely to occur?

no

5. Types of ecosystems to which the GMO could be disseminated from the site of release and in which it could become established

The natural host of HVT is the turkey. This means that HVT or the GMOs can infect turkeys via the natural route (via inhalation of feather follicle dust). The GMOs are non-pathogenic for turkeys. If spreading to turkey would occur, this would not cause harm to the turkey. Spreading to turkeys is very unlikely to occur as no turkey farm is located with a radius of 1000 m of the location

6. Complete name of non-target organisms which (taking into account the nature of the receiving environment) may be unintentinally significantly harmed by the release of the GMO

(i) Order and/or higher taxon (for animals)
n.a.
(ii) Family name (for plants)
n.a.
(iii) Genus
n.a.
(iv) Species
n.a
(v) Subspecies
n.a
(vi) Strain
n.a
(vii) Cultivar/Breeding line
n.a.
(viii) Pathovar
n.a.
(ix) Common name
n.a.

7. Likelihood of genetic exchange in vivo

(a) from the GO to other organisms in the release ecosystem:
The HVT backbone has been modified by the insertion of the HA-gene of AIV. The phenotype of this vaccine strains is the same as that of the HVT FC-126 backbone. The potential for recombination of the GMOs with a wild type HVT could only result in the virus reverting to the wild state (i.e. losing the inserted genes), which would result in the wild type HVT which is also non-pathogenic. The potential for recombination of the GMOs with virulent Mareks Disease virus would be no greater than can occur with current vaccines containing HVT. HVT is commonly present in vaccinated chickens that may become double-infected with virulent MDV. Further, serotype 3 (HVT) is often given with a serotype 1 MDV strains as a polyvalent vaccine. As there have never been reports on the recombination of HVT with either the virulent MDV or the serotype 2, this possibility can be considered extremely small. Recombination with viruses from the donor sequences is also not possible: AIV are RNA viruses and have different genetic material and a different site of replication.
(b) from other organisms to the GMO:
see under a
(c) likely consequences of gene transfer**
see under a

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 simulated natural environments (e.g. microcosms etc.):

Animal studies with HVT GMO strains have demonstrated that insertion of the donor genes does not change the non-pathogenic nature of the virus. These results indicated that the GMOs will not have any impact on chickens or other avian species living in close contact with vaccinated chickens.

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

There are no known or predicted involvements in biogeochemical processes.

H. Information relating to monitoring

H. Information relating to monitoring

1. Methods for monitoring the GMOs
No specific monitoring will occur.
2. Methods for monitoring ecosystem effects
No specific monitoring will occur.
3. Methods for detecting transfer of the donated genetic material from the GMO to other organisms
Not applicable since transfer is highly unlikely
4. Size of the monitoring area (m2)
Not applicable
5. Duration of the monitoring
Not applicable
6. Frequency of the monitoring
Not applicable

I. Information on post release and waste treatment

I. Information on post release and waste treatment

1. Post-release treatment of the site
After removal of bedding material and faeces at the end of the experiment, the site will be cleaned and disinfected according to standard business operations.
2. Post-release treatment of the GMOs
Not applicable
3(a) Type and amount of waste generated
The nature and amount of waste like faeces, bedding material, waste water, vaccination related waste and natural mortality and euthanized birds, eggs and birds at end of lay as usual.
3(b) Treatment of waste
Waste from the vaccination and the laboratory waste will be collected and destroyed as medical waste. Eggs and natural mortality, euthanized birds and birds at end of lay will be discarded by the rendering company, unless consumption is authorised by the responsible authority The bedding and the waste water, is likely to be free of GGO, and will be used as fertilizer or will be burned in a power plant.

J. Information on emergency response plans

J. Information on emergency response plans

1. Methods and procedures for controlling the dissemination of the GMO(s) in case of unexpected spread
Not applicable
2. Methods for removal of the GMOs of the areas potentially affected
Not applicable
3. Methods for disposal or sanitation of plants, animals, soils etc. that could be exposed during or after the spread
Not applicable
4. Plans for protecting human health and the enironment in the event of an undesirable effect
Not applicable