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/25/BVW6
(c)	Date of acknowledgement of notification	../../….
(d)	Title of the project	

MV-NiV will be assessed in the clinical study EU-CT 2025-522293-37-00 entitled: *A phase 1, placebo-controlled, randomised, participant- and assessor-blind, single-centre study to assess the safety and immunogenicity of 2 dosages of Nipah measles vector vaccine (MV-NiV) administered subcutaneously either a single dose or as 2 consecutive doses at 4-week interval, in healthy non-exposed volunteers, aged 18-40 years.*

(e)	Proposed period of release	From 01/01/2026 until 31/03/2028

2. Notifier

Name of institution or company: University of Tokyo

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: *Negarnaviricota*
Class: *Monjiviricetes*
Order: *Mononegavirales*
Family: *Paramyxoviridae*

(b) Identity of the GMO (genus and species)
The GMO, live attenuated virus (LAV)-MV-NiV, includes the full genome of a live-attenuated measles virus (MV) strain from the Edmonsion lineage, genetically engineered to express the glycoprotein G of the Nipah virus. The NiV-G gene is inserted into the MV genome between the nucleoprotein and phosphoprotein genes.
Genus: *Morbillivirus*
Species: *Measles morbillivirus*
Strain: Edmonston

(c) Genetic stability – according to Annex IIIa, II, A(10)
The insertion of the NiV-G transgene into the measles virus genome (between the N and P genes) introduces moderate genetic pressure, but the MV-NiV construct has demonstrated high stability. Serial passaging of MV-NiV in Vero cells (up to five passages) showed no mutations in the NiV-G insert and only minor, low-frequency mutations in the vector backbone, none of which became dominant. These results confirm that MV-NiV maintains genetic integrity under manufacturing conditions.

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 release of LAV-MV-NiV is considered of negligible risk to the environment.
LAV-MV-NiV virions do not have a natural host range beyond humans, cannot be transmitted under natural environmental conditions, and are highly sensitive to environmental factors (e.g. heat, UV light, desiccation, disinfectants). As such, they cannot survive for long periods outside the host, and there are no safety concerns associated with MV-NiV shedding or spill into the environment. Potential routes of transmission to third parties are limited to accidental self-administration of the product by clinical site staff during handling or administration, or

direct exposure to biological material from a vaccinated subject (e.g. via blood, tissues, or body fluids).
Although the MV-NiV vector is replication-competent, shedding is minimal or absent based on preclinical data. Nonetheless, transmission via biological fluids (e.g. blood transfusion, organ transplant, or vertical transmission during pregnancy or breastfeeding) cannot be fully excluded. To mitigate this, risk management measures have been implemented, including eligibility restrictions, contraceptive use, and donation bans (e.g. no blood or organ donation for 3 months post-vaccination). The risk of MV-NiV transmission to third parties is therefore considered low to negligible.
Were transmission to occur, potential adverse effects would mirror those following vaccination and include:

1. Mild, self-limiting adverse events (e.g. fever, fatigue, rash);
2. Rare uncontrolled replication in severely immunocompromised individuals;
3. A theoretical reversion to a wild-type-like phenotype, although no such reversions have been reported for Edmonston-based strains; and
4. Expression of the Nipah virus G glycoprotein, which is non-functional and has no known toxicity or oncogenicity.

While the magnitude of some of these effects could be moderate in highly vulnerable individuals, the likelihood of transmission and occurrence of serious adverse effects is low to negligible, supported by the long-standing safety record of Edmonston-derived measles vaccines and the non-functional nature of the inserted transgene.
In summary, although some theoretical risks exist, the overall risk to healthcare professionals, close contacts (including vulnerable populations), and the general environment is considered negligible, due to the biological characteristics of the vector, its environmental fragility, and the robust risk management strategies in place.

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	*Morbilivirus*
(iii)	species	*Measles morbilivirus*
(iv)	subspecies	-
(v)	strain	Edmonston
(vi)	pathovar (biotype, ecotype, race, etc.)	-
(vii)	common name	Nipah measles vector vaccine (MV-NiV)

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)

MV-NiV is the commercial vaccine against Nipah virus. It does not have a natural habitat.

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

5. (a) Detection techniques

Reverse transcription polymerase chain reaction (RT-PCR) for measles viral RNA is the preferred and most sensitive method for detecting acute infection, especially during early illness or in vaccinated individuals with modified disease presentation. Alternatively, parental measles virus virions can be detected through cell culture-based methods, such as infection of Vero cells expressing SLAM (Signaling Lymphocytic Activation Molecule), where cytopathic effects such as syncytia formation are typically observed. Historically, viral detection was also performed using immunofluorescence staining of infected cells or by seroconversion in susceptible animal models, though such approaches are now largely replaced by molecular methods.

(b) Identification techniques

Identification of parental virus, measles virus (Edmonston strain), 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, measles virus Edmonston strain, is classified as risk class 1 for humans in the Belgian biohazard classification list.

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, measles virus (Edmonston strain), spreads rapidly in human hosts with a short incubation period of 10-14 days from infection to symptom onset. The generation time (from infection to peak virus shedding) is estimated at ~7-10 days, based on the onset of viremia and peak infectivity after exposure.

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

The MV-NiV vector, like other attenuated measles vaccines, typically shows limited or no viremia and minimal shedding. Replication is largely restricted to local

lymphoid tissues, and peak detection of RNA in biological fluids (e.g., blood) occurs around day 11 post-vaccination in primate models. Therefore, generation time in vaccinated hosts is similar or slightly delayed (~10–12 days) compared to wild-type infection, due to attenuation.

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

(c) Factors affecting reproduction:
Attenuated strains show limited replication in non-permissive hosts and have lower *in vivo* replication efficiency than wild-type strains. Pre-existing immunity can reduce replication, and the virus mainly replicates in lymphoid and epithelial tissues.

9. Survivability

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

(i)	endospores	(.)
(ii)	cysts	(.)
(iii)	sclerotia	(.)
(iv)	asexual spores (fungi)	(.)
(v)	sexual spores (fungi)	(.)
(vi)	eggs	(.)
(vii)	pupae	(.)
(viii)	larvae	(.)
(ix)	other, specify	(x) Not applicable. The parental virus, measles virus, cannot form survival structures

(b) relevant factors affecting survivability:
The Edmonston strain of measles virus is a fragile, lipid-enveloped RNA virus that cannot replicate outside a host and does not form spores or latent reservoirs. It is highly sensitive to environmental factors such as heat, desiccation, UV light, and common disinfectants (e.g. 1% sodium hypochlorite, 70% ethanol, hydrogen peroxide, peracetic acid). Under ideal laboratory conditions, it may remain viable on non-porous surfaces for up to 2 hours, but typically loses infectivity within 30–60 minutes. In aerosol form, viability may last up to one hour in poorly ventilated spaces but declines rapidly with airflow, temperature, or light exposure. The attenuated Edmonston strain is no more environmentally stable than wild-type virus and poses no risk of environmental persistence.

10. (a) Ways of dissemination
The Edmonston strain of measles virus is primarily transmitted via respiratory routes. Infection occurs through inhalation of virus-laden aerosols or large droplets released when an infected person coughs, sneezes, or breathes. Aerosols can remain airborne in enclosed, poorly ventilated spaces, while larger droplets typically infect through direct contact with mucous membranes. Fomite transmission is less common but possible, as the virus can survive on non-porous surfaces for up to two hours under ideal conditions. The virus does not replicate outside the human host and is not spread through water, soil, food, or insects. The attenuated Edmonston strain used in vaccines and vectors like MV-NiV is minimally shed and has not been associated with person-to-person transmission.

(b) Factors affecting dissemination
Dissemination of the Edmonston strain is influenced by factors such as ventilation, environmental conditions, and host immunity. Poorly ventilated spaces increase aerosol persistence, while heat, low humidity, and UV light rapidly inactivate the virus. Pre-existing immunity and the attenuated nature of the strain reduce viral shedding and transmission. Close, prolonged contact poses the highest risk, while brief exposure presents minimal risk.

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)
None

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 to induce protective immunity against Nipah virus infection by using a safe, well-characterized measles virus vaccine backbone to express the Nipah virus glycoprotein G.

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	(x)
(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 plasmid-based reverse genetics in mammalian cells (Vero cells)	

6. Composition of the insert

(a) Composition of the insert

The insert is composed of the coding sequence of the Nipah virus glycoprotein (NiV-G) from the Malaysia strain of Nipah virus.

(b) Source of each constituent part of the insert

Nipah virus Malaysia strain.
The specific sequence used aligns with GenBank accession number AY029767 and UniProt ID Q9IH62.

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

NiV-G: induction of an immune response against Nipah virus

(d) Location of the insert in the host organism

- on a free plasmid (.)
- integrated in the chromosome (.)
- other, specify … The NiV-G gene is inserted into the measles virus Edmonston strain genome, between the N (nucleoprotein) and P (phosphoprotein) genes.

(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 *Henipavirus*
(iv) species *Nipah henipavirus*
(v) subspecies …
(vi) strain Malaysian strain
(vii) cultivar/breeding line …
(viii) pathovar …
(ix) common name Nipah 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):
The donated sequence in the MV-NiV vector encodes the glycoprotein G of the Nipah virus (Malaysian strain). While NiV-G plays a role in host cell attachment in the wild-type virus, it is not pathogenic on its own. In the MV-NiV construct, the gene is expressed without the Nipah virus fusion protein, which is essential for viral entry and cell-to-cell spread. As a result, the expressed NiV-G protein cannot mediate infection or cause disease. Preclinical studies have shown no evidence of toxicity, oncogenicity, or immunopathology associated with its expression. Therefore, the donated sequence does not contribute to any pathogenic or harmful properties of the recombinant organism.

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, Nipah virus (Malaysian strain), is classified under EC Directive 2000/54/EC as a human pathogen Risk Group 4, due to its high pathogenicity and potential for severe disease. However, the MV-NiV vector contains only the genetic sequence encoding the NiV-G. This single protein is not sufficient to generate infectious Nipah virus particles, as it lacks other essential components—particularly the fusion protein—required for viral entry and replication. Therefore, the presence of the NiV-G gene in the MV backbone does not confer pathogenic properties to the recombinant organism.

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 MV-NiV vector, based on the attenuated Edmonston strain of measles virus, is genetically stable. Measles virus replicates in the cytoplasm, minimizing risks of recombination or genome integration. The NiV-G gene is inserted at a well-characterized site that supports stable expression without disrupting viral function.

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 measles virus virions can be performed by detecting viral RNA using PCR-based methods, or by isolating infectious virions through cell culture techniques.

(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 and Sanger sequencing.

F. Information Relating to the Release

1. Purpose of the release (including any significant potential environmental benefits that may be expected)
The MV-NiV vaccine is being developed as a prophylactic measure against Nipah virus infection, which causes severe, often fatal disease in humans and has pandemic potential. The vaccine uses a live attenuated measles virus (Edmonston B strain) vector, engineered to express the NiV-G of the Nipah virus (Malaysian strain).

The primary purpose of the release is to conduct a Phase 1 clinical trial in healthy adult volunteers to evaluate the safety, tolerability, and immunogenicity of MV-NiV in humans.

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, the measles virus Edmonston strain, is a live attenuated virus used globally as a component of licensed measles vaccines. It does not have a natural habitat, as it is a laboratory-adapted strain derived for human vaccination. As such, the site of release is different from the ecosystem in which the parental organism is regularly used.

3. Information concerning the release and the surrounding area

(a) Geographical location (administrative region and where appropriate grid reference):
Clinical study 2025-522293-37-00 will be conducted at one clinical study site in 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 60 healthy adults will be randomized into four groups (15 participants per group) to receive different dosing regimes on Day 0 and Day 28.

(c) Proximity to internationally recognised biotopes or protected areas (including drinking water reservoirs), which could be affected:
Not applicable: The GMO, MV-NiV, is a fragile, lipid-enveloped RNA virus based on an attenuated measles virus strain. It cannot replicate outside a suitable host, does not form survival structures, and is highly sensitive to desiccation, heat, UV light, and disinfectants. It therefore cannot persist in the environment or affect protected areas.

(d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO
Not applicable: The MV-NiV vector is a host-restricted, replication-competent measles virus that cannot infect non-human species. It is non-transmissible under natural environmental conditions, does not have an environmental reservoir, and cannot survive outside the human host for extended periods. Therefore, no interaction with flora, fauna, livestock, or migratory species is expected.

4. Method and amount of release

(a) Quantities of GMOs to be released:
The MV-NiV vaccine is a live, replication-competent, recombinant measles virus administered subcutaneously. In this study, 60 healthy adult participants will be randomized into four groups (15 per group) and will receive one or two doses of the vaccine according to the schedule below:
- Group 1: Placebo on Day 0 and Day 28
- Group 2: 1×10^3 $TCID_{50}$ on both Day 0 and Day 28 (total: 2×10^3 $TCID_{50}$)
- Group 3: 1×10^4 $TCID_{50}$ on both Day 0 and Day 28 (total: 2×10^4 $TCID_{50}$)

- Group 4: Placebo on Day 0 and 1×10^4 $TCID_{50}$ on Day 28 (total: 1×10^4 $TCID_{50}$)

The MV-NiV virions replicate transiently in host cells and are self-limiting, as replication ceases upon the development of neutralizing antibodies. Therefore, the actual quantity of GMO present per subject post-administration may vary depending on individual immune response and viral clearance. Based on preclinical studies, viral replication is confined to the vaccinated host, with minimal to no shedding, and no release into the environment is anticipated.

(b) Duration of the operation:
The clinical study evaluating the MV-NiV vaccine is planned to start in January 2026. Each subject will be followed for about 7 months from the first vaccination visit, including a 6-month safety follow-up period, with the overall study expected to conclude by March 2028.

(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 MV-NiV vaccine by clinical staff during handling or administration, or to direct exposure to MV-NiV virions through contact with biological materials from vaccinated individuals.
To minimize the risk of MV-NiV dissemination beyond the clinical trial site, several containment and safety measures will be implemented. These include:

- Standard biosafety level 1 (BSL-1) procedures, appropriate for handling attenuated measles virus vectors, including the use of personal protective equipment (PPE) and proper hand hygiene.
- All clinical waste, including materials used for vaccination and biological sampling, will be treated as biohazardous waste and disposed of following site-specific biosafety protocols.
- Vaccinated subjects will be excluded from close contact (within 28 days of vaccination) with vulnerable populations. i.e. immunocompromised individuals and children under 6 months.
- Blood, tissue, and organ donation will be prohibited for at least 3 months post-vaccination.
- Clinical site staff will be trained to handle the investigational product to prevent accidental self-administration or spillage.

5. Short description of average environmental conditions (weather, temperature, etc.)
Not applicable: the GMO cannot be transmitted under any environmental conditions.

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 target organism is the human subject receiving the MV-NiV vaccine. Upon subcutaneous administration, the MV-NiV virions infect host cells using measles virus entry receptors (e.g., CD150/SLAM or CD46), initiating limited, self-limiting replication of the attenuated measles vector. During this process, the inserted NiV-G is expressed. The intended result is the induction of a protective immune response against Nipah virus through the production of neutralizing antibodies and cellular immunity specific to NiV-G. As a live attenuated vector, the MV-NiV vaccine also boosts immunity against measles virus. No adverse or unintended pathogenic interactions are anticipated.

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/

No, MV-NiV is not expected to become more competitive or invasive post-release, and the risk of unintended selection or persistence is negligible.

- MV-NiV is based on the attenuated Edmonston strain of measles virus, which has a long history of safe use in humans and is not naturally transmissible or persistent in the environment.
- The recombinant virus is host-restricted to humans and cannot infect or replicate in other species, eliminating ecological competition or spread.
- The inserted NiV-G gene does not confer any replication or fitness advantage, nor does it alter tissue tropism or environmental survivability.
- Replication is self-limiting, controlled by the host's immune response, and there is no evidence of reversion to virulence or gain-of-function mutations in similar measles-based vectors.
- The virus is highly sensitive to environmental conditions and does not form spores or latent forms that would enhance persistence.

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, MV-NiV, cannot be disseminated under natural environmental conditions and does not have a natural host range beyond humans. As a live attenuated virus, MV-NiV may transiently replicate and biodistribute within the vaccinated subject, and theoretical dissemination to others could occur through exposure to biological materials (e.g. blood or secretions). Additionally, accidental self-administration by clinical staff during handling or

administration is a potential, though unlikely, route of exposure. The GMO is therefore only capable of limited dissemination within its target organism—participants—and cannot become established or invasive in the environment.

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:
The likelihood of genetic exchange from the MV-NiV GMO to other organisms in the release ecosystem is negligible. MV-NiV is a non-integrating, negative-sense RNA virus that replicates exclusively in the cytoplasm of human cells and lacks reverse transcriptase or any mechanism for integration into host or microbial genomes. It does not infect non-human organisms, and no known horizontal gene transfer mechanisms are associated with measles virus vectors. Additionally, the inserted NiV-G gene is stably encoded. Therefore, genetic exchange in vivo is not expected to occur.

(b) from other organisms to the GMO:
Recombination with other viruses is highly unlikely. Measles virus belongs to the *Paramyxoviridae* family and does not recombine naturally, even with related RNA viruses. Genetic exchange would require co-infection of the same host cell with a compatible virus and homologous recombination machinery, which is not known to occur with measles vectors.

(c) likely consequences of gene transfer:
If gene transfer between the MV-NiV GMO and other viruses were to occur, the formation of viable recombinants is highly unlikely, due to the measles virus's cytoplasmic replication, non-segmented genome, and low recombination frequency. Therefore, no negative consequences are anticipated. However, as with any live viral vector, the theoretical possibility of gene exchange leading to novel strains with altered properties cannot be entirely excluded, although such events have never been observed with measles virus vectors in clinical or environmental settings.

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 behavior 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
Shedding of MV-NiV virions (in urine and buccal and nasopharyngeal samples) and viraemia (presence in blood) will be assessed in the subjects participating in the clinical study.

2. Methods for monitoring ecosystem effects
The safety and immunogenicity of the GMO will be monitored throughout the clinical study. There are no additional specific plans for monitoring the environment during the release as the GMO is not expected to survive in the environment in case of shedding.

3. Methods for detecting transfer of the donated genetic material from the GMO to other organisms
Not applicable. The GMO can only potentially be disseminated within its target organism (humans).

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

5. Duration of the monitoring
Subjects in the clinical study 2025-522293-37-00 will be followed up for 6 months after the vaccination. Shedding samples will be taken at 14 days post-vaccination.

6. Frequency of the monitoring
Participants will attend a minimum of 7 on-site visits and participate in 2 safety follow-up phone calls. The schedule is:
   - **V1 (Day -28):** Screening and consent
   - **V2 (Day 0):** First vaccination
   - **C1 (Day 1):** Phone follow-up, with electronic diary for Days 1–7
   - **V3 (Day 14):** Safety follow-up (Week 2)
   - **V4 (Day 28):** Second vaccination
   - **C2 (Day 29):** Phone follow-up, with electronic diary for Days 29–35
   - **V5 (Day 42):** Safety follow-up (Week 6)
   - **V6 (Day 56):** Safety follow-up (Week 8)
   - **V7 (Day 210):** End-of-study visit (Week 30)

   Each visit includes safety assessments such as adverse event reporting, lab tests, and immunogenicity evaluations.

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.

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

3. (a) Type and amount of waste generated
The type of waste generated will result from the handling, preparation and administration of the MV-NiV vaccine, as well as from biological sampling procedures carried out during the clinical study. This includes items such as syringes, needles, alcohol wipes, dressings, gloves and other single-use medical materials potentially contaminated with the investigational product or human biological fluids. The amount of waste generated at the clinical trial 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
All waste resulting from handling, preparation and administration of the MV-NiV vaccine, as well as from biological sampling procedures carried out during the clinical study 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 MV-NiV vaccine 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
Areas potentially contaminated with the MV-NiV GMO (e.g., surfaces, materials used in vaccine handling or sampling) will be decontaminated using validated chemical disinfectants known to effectively inactivate enveloped viruses. These include 1% sodium hypochlorite, 70% ethanol, hydrogen peroxide, or peracetic acid. The recommended contact time of 10 minutes will be respected.

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 MV-NiV vaccine by clinical staff or direct exposure to MV-NiV virions

through contact with biological materials from vaccinated individuals. These risks will be avoided through the biosafety and handling measures described in Section F.4.(c).

The environment. MV-NiV virions do not have a natural host range beyond humans and are highly sensitive to heat, dessication, and disinfectants. As such, they cannot survive for long periods in the environment. There are hence no safety concerns associated with MV-NiV shedding or accidental environmental release.