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	Germany
(b)	Notification number	B/DE/17/PEI3056
(c)	Date of acknowledgement of notification	10/04/2017
(d)	Title of the project Phase I clinical trial of MVA-based recombinant vaccine (MVA-MERS-S) encoding Middle East Respiratory Syndrome coronavirus spike protein	
(e)	Proposed period of release	From 2017-01-01 to 2017-09-30

2. Notifier

Name of institution or company: Universitätsklinikum Hamburg-Eppendorf (UKE)

3. GMO characterisation

(a) Indicate whether the GMO is a:

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

specify phylum, class Family: Poxviridae, Genus: Orthopoxvirus, Class: Vaccinia virus

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

Recombinant Modified Vaccinia Virus Ankara (MVA) delivering the S-glycoprotein of the Middle East Respiratory Syndrome (MERS) coronavirus, MVA-MERS-S (Song et al., 2013).
Genus: *Orthopoxvirus*
Species: *Vaccinia virus*

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

Stable, the GMO was passaged five times at a low multiplicity of infection on chicken embryo fibroblasts (CEF). The virus harvest from the final passage was tested on genetic profile with PCR and antigen expression with Western blot analysis. Previous genetic stability tests performed also demonstrated that the virus was genetically stable (Song et al., 2013).

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.

Release of GMO MVA-MERS-S considered of negligible risk to environment.

Recombinant MVAs previously classified as BSL1 GMO[1] (BVL-ZKBS), extensively studied in >90 clinical trials and field studies involving >120,000 individuals.

First MVA based vaccine products registered as pharmaceuticals by company Bavarian Nordic (http://www.bavarian-nordic.com/) with details as follows: the company utilizes its patented MVA-BN® technology platform to develop a broad infectious disease vaccine pipeline. The lead program is a non-replicating smallpox vaccine based on MVA-BN, licensed in the European Union under the trade name IMVANEX® and in Canada under the trade name IMVAMUNE®. The vaccine is being delivered to the U.S. Strategic National Stockpile for emergency use and the company is completing the Phase 3 clinical studies required to license the vaccine in the U.S..

[1] http://www.bvl.bund.de/DE/06_Gentechnik/03_Antragsteller/06_Institutionen_fuer_biologische_Sicherheit/01_ZKBS/03_Organismenliste/gentechnik_zkbs_organismenliste_node.html;jsessionid=3D9A3A7184219C26A328428747A599F1.2_cid340

The only route by which the GMO could spread into the environment is by spillage from an open and intact vial or a damaged vial, needle sting accident, leakage from the injection site or exposure to contaminated waste. However the risk that another person actually becomes infected is minimal. In the test subject, residual virus may spread from the site of injection via blood or lymph.
Data from the analysis of MVA *in vivo* distribution suggests that no virus replication takes place and the infection is strictly self-limiting: E.g. upon high dose MVA inoculation into immune-suppressed non-human primates, viral genomes can be detected in pharyngeal epithelial cells, PBMC and draining lymph nodes for up to two weeks post injection. However, it was not possible to re-isolate any viable MVA from these animals (Stittelaar et al. 2001 Vaccine 19:3700).

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) classified as BSL3 organism. The insertion of the coding sequence of the S-glycoprotein of MERS-CoV establishes MERS-CoV relevant antigenic properties in the recombinant GMO (Song et al., 2013; Volz et al., 2015; Haagmans et al., 2016) while maintaining the strict replication deficiency of the recombinant MVA (Song et al., 2013). Thus, the genetic modification and the cell substrate on which the GMO is grown do not alter the MVA replication deficiency and its potential route of spreading.

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

1. Recipient or parental organism characterisation:

(a) Indicate whether the recipient or parental organism is a:

(select one only)

viroid		(.)
RNA virus		(.)
DNA virus		(X)
bacterium		(.)
fungus		(.)
animal		
-	mammals	(.)
-	insect	(.)
-	fish	(.)
-	other animal	(.)
	(specify phylum, class)	…

other, specify …

2. Name

(i)	order and/or higher taxon (for animals)	Family: *Poxviridae* Subfamily: *Chordopoxvirinae*
(ii)	genus	Orthopoxvirus

(iii)	species	Vaccinia Virus
(iv)	subspecies	
(v)	strain	Modified Vaccinia virus Ankara (MVA)
(vi)	pathovar (biotype, ecotype, race, etc.)	…
(vii)	common name	…

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	no natural host, MVA is a laboratory strain generated by adaptation to chicken embryo fibroblasts as host cell. Historically, vaccinia virus is thought to origin from a bovine or an equine host species.

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

5. (a) Detection techniques

Modified Vaccinia virus Ankara (MVA) can be detected by propagation of specimens in chicken embryo fibroblasts (CEF). MVA genome or MVA gene products (RNA) can be detected by PCR or RT-PCR.

(b) Identification techniques

Recombinant MVA is identified by specific PCR analyses and sequencing of genomic DNA or cDNA from viral RNA

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

Classified by BVL-ZKBS as BSL1 organism (Organismus der Risikogruppe 1) Bundesgesundheitsbl - Gesundheitsforsch - Gesundheitsschutz 2002, 45:654, DOI 10.1007/s00103-002-0450-z

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:
In a replication competent environment (host cell) the life cycle of the GMO is completed within 12 hours. Virus replication restricted to few permissive host cell systems typically not encountered in natural ecosystems such as: e.g. BHK-21 (baby hamster kidney cell line), CEF (primary chicken embryo fibroblasts), DF-1 (chicken embryo fibroblast cell line).

(b) Way of reproduction: Sexual .. Asexual (X)..

(c) Factors affecting reproduction: The growth adaptation of the virus to chicken cells resulted in the deletion of >30kb genetic information and a strong host range restriction determined mainly by the loss of viral genes regulating host functions; MVA is replication deficient in cells of human and mammalian origin partially due to the absence of the host-range gene K1L (Meyer H et al., 1991).

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	as it is well known for all poxviruses, cell-bound MVA is expected to show a high environmental stability with high resistance to drying; purified MVA, as present in vaccine preparations, is less resistant in the general environment.

(b) relevant factors affecting survivability: temperature, humidity, UV light

10. (a) Ways of dissemination
The only conceivable way of dissemination of MVA-MERS-S into the environment is by spillage from an open and intact vial or a damaged vial, needle sting accident, leakage from the injection site or exposure to contaminated waste. is through direct contact/inoculation through skin lesion with highly concentrated MVA-MERS-S material, e.g. such as needle stick injury, spillage from injection site;

(b) Factors affecting dissemination
MVA-MERS-S is replication incompetent and thus an infection with the GMO remains self-limiting. In case of accidental spilling, disinfection of the contaminated surface with 70% ethanol solution and readily commercially available disinfectant formulations is fully sufficient to inactivate the virus.

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/DE/11/PEI 1332: Phase I clinical trial using recombinant MVA encoding Hepatitis C virus non-structural proteins NS3, NS4 and NS5B.

B/NL/12/001: The identical recipient MVA (clonal isolate F6 sfMR) was released/tested as parental organism and as genetically modified virus to express the hemagglutinin H5 sequences of avian influenza virus H5N1 (A/VN/1194/04) which has been released/tested in clinical studies in the Netherlands (Dutch Trial Register (www.trialregister.nl) (NTR registration number: NTR3401; Kreijtz et al. 2014 Lancet Infect Dis).

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
Insertion of a synthetic promoter (PmH5) and the coding sequence of MERS-CoV S-glycoprotein (GenBank accession no. JX869059) into deletion site III of the MVA genome. Upon infection of a cell by the recombinant MVA the MERS-CoV S gene is expressed and the S protein is produced, thus affording MVA with antigenic properties relevant to MERS-CoV (active immunization principle). Vaccination with the recombinant MVA-MERS-S will result in the induction of S-specific antibodies and T cells that can protect against infection with MERS-CoV.

3. (a) Has a vector been used in the process of modification?
Yes (X) No (.)

If no, go straight to question 5.

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

4. If the answer to 3(b) is yes, supply the following information

(a) Type of vector

plasmid (X)
bacteriophage (.)
virus (.)
cosmid (.)
transposable element (.)
other, specify …

(b) Identity of the vector
pIIIH5red-S (Song et al. 2013)
(c) Host range of the vector
Escherichia coli…

(d) Presence in the vector of sequences giving a selectable or identifiable phenotype
Yes (X.) No (.)

antibiotic resistance (X)
other, specify …

Indication of which antibiotic resistance gene is inserted
Ampicilline resistance (AmpR) gene. However, the AmpR sequence is finally not contained in the DNA fragment which is inserted in the recipient MVA.

(e) Constituent fragments of the vector

The vector plasmid pIIIH5red-S is used a template for homologous recombination into the MVA genome. It contains DNA sequences for the MERS-CoV S gene, the red fluorescent marker protein mCherry, transcriptional regulation sequences (promoters) and sequences of flanking MVA genomic regions that direct homologous recombination into the site of deletion III of the MVA genome. See Song et al., 2013 for details of construction of MVA-MERS-S.

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

(i)	transformation	(.)
(ii)	electroporation	(.)
(iii)	macroinjection	(.)
(iv)	microinjection	(.)
(v)	infection	(.)
(vi)	other, specify	…Homologous recombination between MVA and pIIIH5red-S in CEF.

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 contains the donor gene sequences encoding the S protein of MERS-CoV (GenBank accession no. JX869059; for details of modification of coding sequence see Song et al., 2013; modifications pertain to nucleotide sequence alterations (silent mutations) suppressing vaccinia virus transcription termination signals). The insert also contains vaccinia virus promoter sequences, i.e. PmH5, for the transcriptional regulation of the S gene expression.

(b) Source of each constituent part of the insert

Full coding sequence of MERS-CoV S-glycoprotein derived from GenBank entry JX869059.2 (van Boheemen et al., 2012; PMID 23170002). PmH5 is a vaccinia virus-specific sequence element activating vaccinia viral early-late transcription (Wyatt et al. 1996 Vaccine 14:1451).

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

Intended function as expression template for full-length S-glycoprotein as antigen in active immunization principle (induction of MERS-CoV specific antibodies and T cells).

(b) Location of the insert in the host organism

-	on a free plasmid	(.)
-	integrated in the chromosome	(X) integrated in MVA genome
-	other, specify …	(.)

(c) 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	Coronaviridae
(iii)	genus	Betacoronavirus
(iv)	species	MERS-CoV
(v)	subspecies	…
(vi)	strain	hCoV-EMC/2012
(vii)	cultivar/breeding line	…
(viii)	pathovar	…
(ix)	common name	…

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:

(b) to which of the following organisms:

humans (X)
animals (X)
plants (.)
other ..

MERS CoV was first described in September 2012 and continues to cause disease in humans in the fifth year after its first appearance. At present, WHO reports a total of 1,806 laboratory confirmed cases including 643 deaths (http://www.who.int/emergencies/mers-cov/en/). Dromedary camels are generally accepted to be the critical animal reservoir responsible for

spreading the virus to humans. The primary zoonotic infections can result in interfamilial or health care related secondary transmissions in human populations.

(b) are the donated sequences involved in any way to the pathogenic or harmful properties of the organism
Yes () No (X) Not known (.)

If yes, give the relevant information under Annex III A, point II(A)(11)(d)

4. Is the donor organism classified under existing Community rules relating to the protection of human health and the environment, such as Directive 90/679/EEC on the protection of workers from risks to exposure to biological agents at work?
Yes (X) No (.)
If yes, specify: MERS-CoV is classified BVL-ZKBS as BSL3[2] (Risikogruppe 3)

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 This has been investigated by Song et al. in a head-to-head comparison of plaque-forming units obtained after cultivation on chicken embryonic fibroblast cells and found to be identical (Song et al., 2013).

(c) is the GMO in any way different from the recipient as far as dissemination is concerned?
Yes (.) No (X) Not known (.)
Specify based on our preclinical studies in mice, where 1X10E8 PFU of MVA-MERS-S or MVA-GFP-mCherry (control) were administered by intramuscular injection, the GMO behaves essentially as described for the recipient, i.e. non-spreading.

[2] http://www.bvl.bund.de/DE/06_Gentechnik/03_Antragsteller/06_Institutionen_fuer_biologische_Sicherheit/01_ZKBS/03_Organismenliste/gentechnik_zkbs_organismenliste_node.html;jsessionid=3D9A3A7184219C26A328428747A599F1.2_cid340

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

Yes (.) No (X) Not known (.)

Specify Based on our preclinical studies in rat, where Full Human Doses of MVA-MERS-S were administered by intramuscular injection in a n+1 dosing scheme, the GMO behaves essentially as described for the recipient, i.e. non-toxic.

2. Genetic stability of the genetically modified organism

A genetic stability program was designed with testing of the recombinant gene expression, characterization of the genetic inserts as well as immunoplaquing assays. GMO demonstrated stable three passages beyond the passage intended for the production of a clinical lot (Song et al., 2013; Volz et al., 2015)

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)

There are no pathological and ecological traits of the insert, i.e. S protein of MERS-CoV. The S protein is the target of antibodies and T cells associated with viral clearance (Volz et al. 2015).

Non clinical studies (in mice and rats) performed with the GMO have shown no major toxic effect which could be related to the GMO. …

4. Description of identification and detection methods

(a) Techniques used to detect the GMO in the environment

GMO (MVA genome or MVA gene products i.e. RNA) can be specifically detected by PCR or RT-PCR.

(b) Techniques used to identify the GMO

GMO is identified by specific PCR analyses and sequencing of genomic DNA or cDNA from viral RNA

F. Information relating to the release

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

Purpose of release is vaccination of approx. 24 study subjects with the objective to establish the safety, tolerability and immunogenicity of the MVA-MERS-S vaccine candidate. There are no foreseen problems with this release.

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 Controlled release in phase I unit ~ hospital ward; in addition, the GMO and the recipient MVA are not naturally found in the environment.

3. Information concerning the release and the surrounding area

(a) Geographical location (administrative region and where appropriate grid reference):
University Hospital Hamburg Eppendorf
Clinical Trial Center North (CTC North GmbH & Co. KG)

(b) Size of the site (m^2): 413,46 m^2
(i) actual release site (m^2): … m^2
(ii) wider release site (m^2): … m^2

(c) Proximity to internationally recognised biotopes or protected areas (including drinking water reservoirs), which could be affected:
None.

(d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO
None.

4. Method and amount of release

(a) Quantities of GMOs to be released:
A total of approx. 5×10^9 plaque forming units.

(b) Duration of the operation:
The vaccination scheme follows a prime-boost schedule with a 28d interval between injections. Including waiting and holding periods for dose escalation the overall duration of release will be approximately 3 months.

(c) Methods and procedures to avoid and/or minimise the spread of the GMOs beyond the site of the release
Several as per study protocol, among: dressing of infection site, 70% ethanol wash of surfaces, autoclaving of contaminated items, confinement of study subjects for 24hours following administration. Personal safety protection by study personnel.

5. Short description of average environmental conditions (weather, temperature, etc.)
Not applicable, release within hospital ward.

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	…
(iv)	species	…
(v)	subspecies	…
(vi)	strain	…
(vii)	cultivar/breeding line	…
(viii)	pathovar	…
(ix)	common name	human beings, Phase I study subjects

2. Anticipated mechanism and result of interaction between the released GMOs and the target organism (if applicable)
Transient expression of the transgene in fibroblast and muscle cells and phagocytes/dendritic cells to elicit innate and adaptive immune responses. No virus replication or propagation due to profound replication deficiency of recombinant MVAs.

3. Any other potentially significant interactions with other organisms in the environment
None.

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 selective advantage or disadvantage has been conferred to MVA-MERS-S; there is no known mechanism through which competitiveness could be acquired by the GMO.

5. Types of ecosystems to which the GMO could be disseminated from the site of release and in which it could become established
GMO is not anticipated to interact with non-target organisms due to its severely restricted host tropism. Given hospital environment the only mode of dissemination conceivable would be to medical personnel and/or other study participants. Due to the replication deficiency further spread would be highly unlikely.

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.

7. Likelihood of genetic exchange in vivo

   (a) from the GMO to other organisms in the release ecosystem:
   Extremely unlikely to impossible: Gene transfer by recombination with environmental orthopoxviruses (cowpox viruses) is extremely unlikely (probability equal to or less than 10^{-13}, based on frequency of cowpox reportings for human population) and tissue barrier function of skeletal muscle to which MVA-MERS-S will be administered.

   (b) from other organisms to the GMO:
   Extremely unlikely to impossible: Gene transfer by recombination with environmental orthopoxviruses (cowpox viruses) is extremely unlikely (probability equal to or less than 10^{-13}, based on frequency of cowpox reportings for human population) and tissue barrier function of skeletal muscle to which MVA-MERS-S will be administered.

   (c) likely consequences of gene transfer:
   No data are available.

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.):
   Not known – there are no data available regarding the behavior and characteristics of MVA-MERS-S in the mentioned environments.

9. Possible environmentally significant interactions with biogeochemical processes (if different from the recipient or parental organism)
   Not applicable.

H. Information relating to monitoring

1. Methods for monitoring the GMOs
   Based on the non-spreading character of the GMO no specific viral detection relative to MVA-MERS-S is planned in the present proposal.
   Monitoring of the direct and indirect effects of the GMO in patients will be achieved using the following clinical assessments: physical examinations, adverse event reporting, clinical laboratory assessments throughout the clinical study for all patients.

2. Methods for monitoring ecosystem effects
   None planned as the GMO and the parental MVA virus are not naturally found in the environment.

3. Methods for detecting transfer of the donated genetic material from the GMO to other organisms
   None planned as the methods are not available - The probability for a transfer of the donated genetic material to other organisms (human beings) is unlikely since GMO has no nuclear localization and there is no known human endemic virus able to complement, to recombine or to exchange genetic material with the MVA genome.

4. Size of the monitoring area (m^2)
Not applicable: the GMO will be administered to patients by intramuscular injections in conventional hospital or clinic rooms.

5. Duration of the monitoring
Safety assessments will be performed all along the patient's participation in the clinical trial.

6. Frequency of the monitoring
Monitoring visits, during which safety will be assessed, will be performed at each GMO injection and during the follow-up period.

I. Information on post-release and waste treatment

1. Post-release treatment of the site
General hospital hygiene. The place where the product will be prepared for injection will be decontaminated before and after the manipulation with a standard disinfectant based solution. Following the patient's discharge home, the clinic or hospital room (surfaces and floor) and the toilets will be cleaned in a standard way using an active disinfectant based solution.

2. Post-release treatment of the GMOs
Autoclaved.

3. (a) Type and amount of waste generated
Limited amount of waste containing or potentially containing GMO, i.e. syringe with needle, vaccine vial, gloves, surgery sheets, band aids.

3. (b) Treatment of waste
The waste will be disposed in a biosafety container and will be treated as hospital waste being autoclaved.

J. Information on emergency response plans

1. Methods and procedures for controlling the dissemination of the GMO(s) in case of unexpected spread

Protocols, for stick and cut accidents and in case a spill has occurred, are in place. In case of spillage on clothing the textile will be disinfected with 70% ethanol (if spillage occurred in the size of droplets) before it will be washed.
In case of spillage on a surface it will be disinfected with 70% ethanol. Also when all handlings with the GMO have finished the surfaces that were used to work on (chairs, sinks and tables) will be disinfected and cleaned with 70% ethanol.
..

2. Methods for removal of the GMO(s) of the areas potentially affected
Potentially contaminated areas/Surfaces will be disinfected with 70% ethanol solution..

3. Methods for disposal or sanitation of plants, animals, soils, etc. that could be exposed during or after the spread
None planned.

4. Plans for protecting human health and the environment in the event of an undesirable effect

MVA and recombinant MVA-MERS-S are non-pathogenic and have a strong host-range restriction. If, at all, the virus could spread after the proposed release to other humans or animal species, the infections will be self-limiting and thus will not result in an environmental impact. Undesirable effects thus are not to be expected. But in case changes in risk management occur, procedures will be adapted accordingly. A possible change is the occurrence of allergic reactions although the risk is low.