zur Notification Number 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	DE
(b)	Notification number	B/DE/05/PEI35
(c)	Date of acknowledgement of notification	16/03/2005
(d)	Title of the project	A multicenter, randomized, double-blind, placebo-controlled study evaluating the efficacy of BIOBYPASS® (AdGVVEGF121.10NH) delivered by NOGA™-guided/MYOSTAR™ catheter in "no option" patients with Class II-IV stable angina
(e)	Proposed period of release	From /late 2005/ until 31/12/2006

2. Notifier

Name of institution or company: GenVec, Inc. (Sponsor)
Hesperion Ltd. (legal representative in the Community)

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 Adenoviridae

(b) Identity of the GMO (genus and species)
Adenovirus (recombinant Adenoviral vector)

(c) Genetic stability – according to Annex IIIa, II, A(10)
greater than 36 month at -70°C, up to 9 month at + 4°C, up to 4 month at + 23°C

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) AT, BE, DK, FI, GB

5. Has the same GMO been notified for release elsewhere in the Community by the same notifier?
Yes (.) No (.)
No information available
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 (.)
No information available

If yes:
- Member State of notification …
- Notification number B/../../…

7. Summary of the potential environmental impact of the release of the GMOs.
BIOBYPASS® is not expected to pose a direct environmental risk due to the nature of the GMO vector product construct, the route of administration, and its distribution profile in vivo as evidenced by the animal and human data to date. Extensive previous experience with this type of viral vector and delivery method has demonstrated that the risk of spread to other persons or the environment is minimal and that isolation of patients is unnecessary.

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) …
(ii) genus …
(iii) species …
(iv) subspecies …
(v) strain …
(vi) pathovar (biotype, ecotype, race, etc.) …
(vii) common name Adenovirus

3. Geographical distribution of the organism

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

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

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

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

(ii) No (.)
(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 animals, humans

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

5. (a) Detection techniques
Serology, antigen detection, PCR assays, virus isolation in cell culture

(b) Identification techniques
PCR assays, virus isolation in cell culture

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
Safety level 2

7. Is the recipient organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?
Yes (x) No () Not known (.)

If yes:

(a) to which of the following organisms:

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

(b) give the relevant information specified under Annex III A, point II. (A)(11)(d) of Directive 2001/18/EC
Adenoviruses can cause respiratory disease and inflammation of mucosa resulting e.g. in gastroenteritis, conjunctivitis or tonsillitis.

8. Information concerning reproduction

not applicable, recipient is a virus

(a) Generation time in natural ecosystems:
…
(b) Generation time in the ecosystem where the release will take place:
…
(c) Way of reproduction: Sexual .. Asexual ..

(c) Factors affecting reproduction:

…

9. Survivability

not applicable, recipient is a virus

(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 …	

(b) relevant factors affecting survivability:
…

10. (a) Ways of dissemination
shedding in body fluids, excretion (blood, saliva, urine, faeces)

(b) Factors affecting dissemination
Air temperature, host density

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/../../…

Has not been previously released.

C. **Information relating to the genetic modification**

1. Type of the genetic modification

(i)	insertion of genetic material	(x)
(ii)	deletion of genetic material	(x)
(iii)	base substitution	(.)
(iv)	cell fusion	(.)
(v)	others, specify …	

2. Intended outcome of the genetic modification
Replication deficient recombinant adenoviral vector containing the cDNA coding for the 121 amino acid isoform of human vascular endothelial growth factor ($VEGF_{121}$).

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 (.)

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

(b) Identity of the vector
Demonstrated by sequencing

(c) Host range of the vector
No host range, vector is plasmid…

(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
Ampicillin resistance

(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	transfection and recombination

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
121 amino acid isoform of human vascular endothelial growth factor ($VEGF_{121}$)

(b) Source of each constituent part of the insert
human (plasmid pUC121)

(c) Intended function of each constituent part of the insert in the GMO
promoting angiogenesis in coronary artery disease

(d) Location of the insert in the host organism

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

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

other, specify homo sapiens

2. Complete name

(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 …

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

(b) to which of the following organisms:

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

(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 (.) No (x)
If yes, specify …

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 (x) No () Not known (.)
Specify The GMO is unable to replicate

(b) is the GMO in any way different from the recipient as far as mode and/or rate of reproduction is concerned?
Yes (x) No () Unknown (.)
Specify Unable to reproduce

(c) is the GMO in any way different from the recipient as far as dissemination is concerned?
Yes (x) No (.) Not known (.)
Specify Unable to replicate

(d) is the GMO in any way different from the recipient as far as pathogenicity is concerned?
Yes (.) No (x) Not known (.)
Specify Apathogenic

2. Genetic stability of the genetically modified organism
The GMO is genetically stable as it is unable to replicate.

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
PCR, serology

(b) Techniques used to identify the GMO
PCR, serology

F. Information relating to the release

1. Purpose of the release (including any significant potential environmental benefits that may be expected)
BIOBYPASS®, which encodes human vascular endothelial growth factor isoform 121 (VEGF121), will be administered via the NOGA™-guided MYOSTAR™, a percutaneous injection catheter system. BIOBYPASS will be injected into the left ventricle of subjects with advanced CAD and moderate to severe angina pectoris who are not amenable to coronary bypass surgery or percutaneous coronary revascularization with the purpose of inducing new blood vessel growth at the site of disease.

2. Is the site of the release different from the natural habitat or from the ecosystem in which the recipient or parental organism is regularly used, kept or found?

Yes (.) No (x)

If yes, specify …

3. Information concerning the release and the surrounding area

(a) Geographical location (administrative region and where appropriate grid reference):
It is anticipated that only two German clinical sites will participate in the proposed clinical study, namely:
St. Georg Hospital
Dept. of Cell Biology
Lohmuehlenstr. 5
20099 Hamburg
Germany
Medizinische Klinik C, Universitatsklinik Münster
Albert-Schweitzer-Str. 33
48149 Münster
Germany
Münster is a small city (population 267,000). Hamburg (population 1,689,000) is a large city located in flat territory surrounded by mountains with the River Elbe flowing through it. Neither clinical site is located near a farm, livestock, protected areas, or water supplies. Both cities' flora includes trees, grass and flowers. Neither target nor non-target ecosystems are likely to be affected; likewise, neither city's climatic characteristics are likely to be affected by the GMP vector product construct.

(b) Size of the site (m^2): … m^2
The treatment procedure will be carried out in a standard operating room, equipped for catheter deliveries.
(i) actual release site (m^2): … m^2
(ii) wider release site (m^2): … m^2

Not applicable

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

Not applicable

4. Method and amount of release

(a) Quantities of GMOs to be released:
BIOBYPASS® will be administered once as 12 intramyocardial injections (200 µL each) at 4 x 10^{10} PU

(b) Duration of the operation:
It is anticipated that the proposed clinical trial will begin in late 2005, lasting through 2006. BIOBYPASS® will be administered once, as 12 intramyocardial injections (200 µL each, total volume of 2.4 mL) at 4 x 10^{10} PU

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

Wastes containing the GMO vector product construct should be properly contained, labeled, stored and disposed of as biohazardous waste consistent with the US NIH Guidelines for handling of Biosafety Level 2 (BSL2) agents, are recommended for this protocol, however, all local and national laws governing the handling of similar biologic agents must take precedence over these recommended guidelines. All contaminated waste products should be placed in a box and autoclaved before disposal. Labels should be used on the container with the wording 'WARNING – HAZARDOUS WASTE – CONTAGIOUS'. Inactivation of AdGVVEGF121.10NH occurs by autoclaving at 121ºC for a minimum of 15 minutes, giving effective kill. Using a higher temperature or a longer time is permissible.

Puncturing – Cutting waste should be put in a special box marked externally with labels: 'WARNING – HAZARDOUS WASTE – PUNCTURING, CUTTING, CONTAGIOUS'.

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

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.
No previous release.

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) Homo sapiens

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

2. Anticipated mechanism and result of interaction between the released GMOs and the target organism (if applicable)
GMO can enter human cells and transfer the gene for the human vascular endothelial growth factor.

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

4. Is post-release selection such as increased competitiveness, increased invasiveness for the GMO likely to occur?
Yes (.) No (x) Not known (.)
GMO is replication deficient.

…

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 vector product construct will be released into cardiac tissue (cardiac fibroblasts, cardiomyocytes, endothelial cells).

GenVec, Inc. has evaluated the distribution of AdVEGF protein and vector DNA (in porcine, rabbit and rat models) using 4 routes of delivery (intramyocardial, intramuscular, intravenous, and interstitial delivery to the fat pad).

The intramyocardial distribution study in pigs is the most relevant for the proposed clinical study. Following intracardiac injection of 4.1×10^{10} PU AdVEGF121.10NH (identical to the clinical dose), small amounts of vector DNA, generally near the limits of reliability for the assay can be detected in the injection site and splenic tissue at day 92 post administration. Following intracardiac injection of 4.1×10^{11} PU (10 fold higher than clinical dose) AdVEGF121.10NH, vector is detected at similar low levels at the injection site, and in the spleen. The presence of trace vector DNA was not associated with detectable VEGF expression or histological abnormalities or angiogenesis in distant tissues. It is not known if this DNA represents intact vector or a degraded fragment of the vector DNA.

When intramuscular routes of injection were examined in rabbits, low levels of vector DNA was detected in the injection sites and draining lymph nodes following administration of 4×10^{9} PU AdVEGF121.10NH (equivalent to the clinical dose). After administration of a ten fold increase in dose (4×10^{10} PU AdVEGF121.10NH), low levels of viral DNA could be also be detected in inguinal lymph nodes, injection site, as well as in the spleen and liver. Angiogenesis outside the sites of injection was not observed.

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

Not 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	…

7. Likelihood of genetic exchange in vivo

(a) from the GMO to other organisms in the release ecosystem:

Findings from preclinical studies show that the VEGF gene is expressed predominantly in the target site; expression levels are highest in the target cells, with very low, to undetectable levels in the surrounding and draining tissues respectively. Further, the expressed gene is not detected in the reproductive organs when administered by intramyocardial injection, thereby precluding any concern regarding vertical transmission of an exogenous DNA sequence to future generations.

(b) from other organisms to the GMO:

…

(c) likely consequences of gene transfer:

Not likely. The following evaluation provides the reviewer with an overview of the pre-clinical data generated with AdVEGF121.10NH (BIOBYPASS) with a view to address the potential gene-transfer to the germ line, and an overview of the clinical data generated to date.

GenVec Inc. has studied the biodistribution of AdVEGF in a Hanford pigs (Report #745-03409, GLP) whereby the animals received either AdVEGF121.10NH or vehicle at 4.1 x 10^{10} PU (equivalent to the dose proposed in this human study) or 4.1 x 10^{11} PU (10 times the proposed human dose) by intramyocardial injection. VEGF protein was detected on day 5 in heart and lungs and/or plasma. Biodistribution of vector DNA was examined on day 5, 29, and day 91. Viral DNA was detectable by PCR at the injection site, lungs and spleen on day 91. Vector was not detected in reproductive organs at any times examined. These findings are similar to a published study in mice involving injection of adenovirus vectors via intraventricular route, whereby no transmission of germ cells could be detected (Peters et al Molecular Therapy 2001, 4 (6) p 603-13).

GenVec Inc. also studied the biodistribution of AdVEGF121.10NH following a systemic injection into rabbits, a dose of 4 x 10^{10} PU (10 times the human dose scaled to rabbits) into the auricular vein ("Single Dose Toxicity Study of CI-1023 (AdGVVEGF121.10NH) in Male and Female Rabbits", Report #745-03160, GLP). Viral DNA was low level but measurable in reproductive organs (ovaries, testes) on days 5 and 29, but at day 92, low levels of viral DNA in testes and ovary were detected.

In Phase I clinical studies, GenVec also examined the risk of shedding of adenovirus vectors or replication-competent vectors from the target organ systemically or into the environment, blood, urine, pharyngeal, nasal, and rectal. Over 1685 samples were assessed in Phase I studies in cystic fibrosis, colon carcinoma, coronary artery disease, and peripheral vascular disease. Samples were obtained at baseline, days 1-3 (or days 2,4,7 depending on the protocol) and assessed for replication-deficient adenovirus (e.g. the vector) using 293 cells and for replication-competent adenovirus (e.g. from in vivo recombination) on A549 cells. Of these samples, none (0/1685) showed presence of replication competent adenovirus. There was a single positive pharyngeal culture in the cystic fibrosis study 2 days after nasal administration of virus (Harvey et al. Safety of Local Delivery of Low- and Intermediate-Dose Adenovirus Gene Transfer Vectors to Individuals with a Spectrum of Comorbid Conditions. Human Gene Therapy. 13:15-63, 2002).

In Phase II studies in coronary artery disease and in peripheral vascular disease, there were no samples that were positive for replication-deficient adenovirus or for replication-competent adenovirus in urine or throat cultures. Therefore, the risk of transfer of vector in body fluids is low. In addition, it is unlikely that vector DNA would be present in the gonadal tissue based on the preclinical studies cited above, with studies in pigs demonstrating an absence of vector in gonadal tissue following intracardiac injection in pigs of a dose 10 fold higher than proposed in the study. Additionally, following a systemic injection of a dose 10 fold higher dose in rabbits, levels in reproductive tissues were below the limit of detection.

Moreover, germ line transmission of the patients in BioByPass clinical studies is likely to be of little consequence as patients are not of prime reproductive age, and

importantly, anti-contraception is mandated by the protocol for a period of one year. In view of these findings, and the fact that adenovectors including AdGVVEGF121.10NH are non-integrating vectors, GenVec Inc. believes that the risk of vertical transmission is very low and highly unlikely.

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 applicable.

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
PCR, Serology

2. Methods for monitoring ecosystem effects
Not applicable.

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

4. Size of the monitoring area (m^2)
Patient's shed fluids.

5. Duration of the monitoring
Please refer to pages 46 through 48 of the Service of Biosafety and Biotechnology Form prepared for Belgium's Biosafety Council.

6. Frequency of the monitoring
Please refer to pages 46 through 48 of the Service of Biosafety and Biotechnology Form prepared for Belgium's Biosafety Council.

I. Information on post-release and waste treatment

1. Post-release treatment of the site
Following treatment, the procedure room will be sanitized following methods consistent for spill clean up and disinfection procedures used to decontaminate the vector contained in bodily fluids.

2. Post-release treatment of the GMOs
Following treatment, the procedure room will be sanitized following methods consistent for spill clean up and disinfection procedures used to decontaminate the vector contained in bodily fluids.

All equipment (e.g. catheters, syringes, etc.) that comes into contact with the GMO vector product construct will be discarded and treated as biohazard waste. Reusable items will be autoclaved before cleaning.

3. (a) Type and amount of waste generated
All equipment (e.g. catheters, syringes, sheaths, etc.) that comes into contact with the GMO vector product construct should be discarded and treated as biohazard waste. Reusable items should be autoclaved before cleaning.
The expected amount of waste generated (e.g. catheters, syringes, sheaths, etc.) that will correlate with the number of subjects treated (approximately 20 to 30 in Germany).

3. (b) Treatment of waste
All equipment that comes into contact with the GMO vector product construct should be discarded and treated as biohazard waste. Reusable items should be autoclaved before cleaning.

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 an accidental spill, the spill area should be isolated. The spill solution should be absorbed with paper towels or other suitable disposable absorbents. The area should be treated with 5% bleach, 0.5% sodium hydroxide solution or a solution of virucidal disinfectant, such as Virkon. Using additional disposables and a suitable collection pan (e.g., dustpan), the spilled material should be collected and all contaminated clean-up materials placed into a sturdy plastic disposable bag or dedicated sharps bin. When all contaminated material has been collected, the area should be rinsed with clean water using additional disposable towels.
Upon completion of the clean up, all contaminated materials should be placed in a suitable properly labeled drum and discard as biohazardous waste.
Basic hospital infection control procedures, consistent with the US NIH Guidelines for handling of Biosafety Level 2 (BSL2) agents, are recommended for this protocol. However, all local and national laws governing the handling of similar biologic agents must take precedence over these recommended guidelines.

2. Methods for removal of the GMO(s) of the areas potentially affected
In the case that BIOBYPASS® is accidentally released into the environment, any surfaces that come into contact with it will be disinfected with 5% bleach, 0.5% sodium hydroxide solution or a virucidal disinfectant, such as Virkon, all of which provide 100% kill.

3. Methods for disposal or sanitation of plants, animals, soils, etc. that could be exposed during or after the spread
see **J**.1., above

4. Plans for protecting human health and the environment in the event of an undesirable effect
Extensive previous experience with this type of viral vector and delivery method has demonstrated that the risk of spread to other persons or the environment is minimal and that isolation of subjects is unnecessary. However, GenVec recommends the following precautions when conducting study procedures involving the GMO vector product construct:

Precautions concerning the staff

- All hospital staff involved in this study should be trained appropriately. Operational guidelines should be prepared and available in the preparation and treatment rooms at all times.
- Eating, drinking, smoking, applying cosmetics or storage of food for human consumption should be prohibited in the procedure room.
- There should be effective disinfectants and specified disinfection procedures available in case of spillages of the GMO. Washing and decontamination facilities should be provided for the personnel in the procedure room.
- Inhalation, ingestion and contact with skin, eyes or mucous membranes are to be avoided. The first aid measures to be taken in the case of accidental exposure to the GMO are provided below.

Exposure Controls/Personal Protection during handling and administration of the study medication

- Following intracoronary injection all intravenous lines, catheters and sheaths must be removed from the patient in the cath lab. All materials that came in contact with the study product must be disposed of as biohazardous waste.
- Eye Protection: Safety eye goggles should be worn.
- Respiratory Protection: A respirator mask (N95 grade) with high efficiency filter will be used in accordance with the manufacturers instructions.
- Skin Protection: Disposable, impermeable gloves, gown, mask and goggle should be used when handling the study medication.
- Engineering Controls: The study product should be prepared in enclosed or contained processes, or with effective local exhaust ventilation.

First Aid Measures

- INGESTION: If swallowed, seek medical attention immediately
- EYES: Immediately flush eyes with plenty of water for at least 15 minutes. Seek medical attention.
- SKIN: Immediately wash skin with plenty of soap and water. Remove contaminated clothing. Seek medical attention.
- INHALATION: Remove to fresh air. If not breathing, give artificial respiration. Seek medical attention.
- ACCIDENTAL INJECTION: Seek immediate medical attention. It is recommended that all materials involved in the injection be carefully placed in a clean puncture-proof, leak-proof container in case they are needed to establish how much material was actually injected.

Fire Precautions

Non-flammable. Use extinguisher that is appropriate for the class of the surrounding fire. The products of combustion have not been determined.