PRESENTATION OF THE FINAL RESULTS OF DELIBERATE RELEASE INTO THE ENVIRONMENT OF GENETICALLY MODIFIED ORGANISMS

IN ACCORDANCE WITH ARTICLE 10 OF DIRECTIVE 2001/18/EC

The final report format shall be completed by the notifier.

- The notifier shall fill in the report format according to the proposed form.
- The notifier shall illustrate as much as possible the reported data by means of diagrams, figures and tables.
- Statistical data could also be provided where relevant.
- In the case of multi-sites and/or multi-events release(s) the notifier shall provide a general overview of the measures taken and effects observed for the full duration of the consent.
- The space provided after each item is not indicative of the depth of the information required for the purposes of this report.
- The information provided in this report is not considered confidential in accordance with Article 25 of Directive 2001/18/EC.

1. General information

1.1. European notification number: *Number can be found on the corresponding SNIF form (i.e. year and number, B/NL/xx/xxx)*	B/NL/08/003
1.2. Member State of notification:	The Netherlands
1.3. Date of consent: *Date of issue of permit*	20/08/2008
1.4. Title of the project:	Intradermal vaccination with naked DNA encoding the fusion protein domain1 of tetanus toxin fragment C and MART-1(aa 26-35) for the induction of MART-1-specific T cell immunity in stage IV melanoma patients
1.5. Name of institution or company: *i.e. legal entity = notifier*	Stichting Het Nederlands Kanker Instituut Plesmanlaan 121 1066 CX Amsterdam PO Box 90203 1006 BE Amsterdam The Netherlands
1.6. Duration of release:	From 01/11/2008 until 31/12/2012
1.7. Period of release:	49 months

2. Characteristics of the release

2.1 Scientific name of the recipient organism:	The medicinal product is not a GMO per se. It is an investigational gene therapy medicinal product consisting of a purified plasmid DNA (pDNA) drug substance.
2.2 Transformation event(s) (acronym(s)) or vectors used: *Describe the GMO(s) and/or vector(s) and insert(s) used for the modification*	The vector is a naked plasmid DNA vaccine
2.3 Unique identifier, if available: *i.e. product name or GMO name*	pDERMATT
2.4 Geographical location(s) (administrative region):	The Netherlands
2.5 Number of test subjects:	9 metastatic melanoma patients
2.6 Amount of GMO administered to each test subject:	Three patients, 0.5mg plasmid DNA, 6 doses Three patients, 1 mg plasmid DNA, 6 doses Three patients, 4 mg plasmid DNA, 6 doses
2.7 Number of administrations per test subject:	6 vaccinations per patient (on day 0,3,6 and day 28,31,34)

3. Risk management measure(s)

Please report the risk-management measures used to avoid or minimize the spread of the GMO(s) outside the site(s) of release, and in particular those measures

- *not originally notified in the application,*
- *applied in addition to the conditions in the consent.*
- *required by the consent only under certain conditions,*
- *that the consent allowed the notifier a choice of measures.*

Answer: Risk management was executed according to the application. Patients were treated in a dedicated, closed room according to the protocol in the original application. Waste was disposed in airtight and break-proof specific hospital waste containers, which were transported by a dedicated company to a waste management plant (ZAVIN) for immediate incineration.

4. Post-release monitoring measures

Please describe here any monitoring strategies.

Answer: No post-release monitoring was applied, due the negligible risk of the application of naked DNA on the skin.

5. Results of the foreseen and unforeseen release(s)

Consider in the following questions 5.1 through 5.4 all results of the foreseen and unforeseen release(s) in respect of any risk for human health or the environment, without prejudice to whether the results indicate that any risk is increased, reduced or remains unchanged.

5.1 Results of the study

Provide a summary of the study results in respect of any risk for human health or the environment. Include also the results of the monitoring measures (if applicable).

Answer: The study showed that DNA vaccination with this vaccine was safe and feasible.
The DNA vaccination appeared safe as there were no treatment-related deaths.
One patient had grade 4 toxicity, but this was most likely related to tumor-progression. The most common adverse events were dermatologic reactions to the vaccination site such as; bleeding, rash, erythema and pain. Fatigue, nausea and/or vomiting and myalgia were other often seen grade 1-2 toxicities.
One patient achieved a stable disease, which lasted for 353 days.

5.2 Unexpected effect(s) and adverse effects

'Unexpected effects' refer to effects on human health or the environment, which were not foreseen or identified in the environmental risk assessment of the notification. This part of the report should contain any information with regard to unexpected effects or observations relevant for the initial environmental risk assessment. In case of any observed unexpected effects or observations, this section should be as detailed as possible to allow a proper interpretation of the data.

Answer: No unexpected effects were observed.

The most common adverse events were dermatologic reactions to the vaccination site such as; bleeding, rash, erythema and pain. Fatigue, nausea and/or vomiting and myalgia were other often seen grade 1-2 toxicities.

5.3 Unintended release of the GMO

'Unintended releases' refer to any incidents or spills with regard to the GMO that occurred during the study, where possible effect(s) on human health and/or the environment cannot be excluded. Describe these effects, including actions taken to manage the risks.

Answer: not applicable, the plasmid does not result in any survival advantage for micro-organisms, so release to does result in survival and spreading. No unintended release events occurred during the study.

5.4 Other information

Notifiers are encouraged to supply information, which is outside the scope of the notification but which might be relevant to the trial(s) in question. This may also include observations of beneficial effects.

Answer: not applicable.

6 Assessment of risk following completion of release

Please provide a reflection of the risk assessment and risk management strategies carried out prior to the release in relation to the obtained results and findings of for instance monitoring and samples taken from the test subjects. Do the results of the study justify the performed environmental risk assessment and conclusion?

Answer: No additional risk was observed in this study. The performed environmental risk assessment was suitable for this study.

7 Conclusion

Here the notifier should elaborate on the efficacy and efficiency of all measures taken, and elaborate on the insights gained during this release. Also, specify how the gain in experience can benefit further (future) releases with respect to risk management.

Answer:

No risk or release was observed. The performed environmental risk measures were suitable for this study.