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: B/NL/14-004

1.2. Member State of notification: The Netherlands

1.3. Date of consent: September 9, 2014

1.4. Title of the project: A randomized, placebo-controlled, multi-center, multi-country, Phase 3 efficacy trial of PROSTVAC-V/F in men with asymptomatic or minimally symptomatic, metastatic, castration-resistant prostate cancer.

1.5. Name of institution or company: Stichting VU medisch centrum,

1.6. Duration of release: November 2014 up to September 2017.

1.7. **Period of release:** November 2014 up to September 2017.

2. Characteristics of the release

2.1. Scientific name of the recipient organism: *Homo sapiens*.

2.2. Transformation event(s) (acronym(s)) or vectors used: PROSTVAC-V and PROSTVAC-F. PROSTVAC-V/F is a live, attenuated vaccine that consists of two components (PROSTVAC-V and PROSTVAC-F). PROSTVAC-V is a recombinant Vaccinia virus expressing a modified human prostate specific antigen (PSA) gene and three genes encoding human immunological stimulating molecules, namely B7.1, a cell-surface glycoprotein associated with antigen independent T-cell activation and proliferation, ICAM-1, intercellular adhesion molecule 1, and LFA-1, lymphocyte function associated antigen-3, which together are known as TRICOM. PROSTVAC-F is a recombinant Fowl pox virus that co-expresses the same four genes as PROSTVAC-V.

2.3. Unique identifier, if available*:* PROSTVAC V/F.

2.4. Geographical location(s) (administrative region): Amsterdam, The Netherlands.

2.5. Number of test subjects: 3 patients.

2.6. Amount of GMO administered to each test subject: 0.5 ml containing at least 2 x 10^8 Infectious Units (Inf.U) PROSTVAC-V, 0.5 ml containing at least 1 x 10^9 Inf.U PROSTVAC-F.

2.7. Number of administrations per test subject: 7 injections per subject.

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.*

During this human vaccine study the risk management measures stated in the license have been applied. No additional controls were necessary. During the study no deviations occurred that might have changed the potential environmental impact as described in the risk assessment.

4. Post-release monitoring measures

According to the risk assessment and the license no post-monitoring measures were deemed necessary.

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).

No adverse effects to human health or the environment were expected and none have been noticed.

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.
No unexpected effects or adverse events were observed.

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.

During the study no deviations occurred that might have impacted human health or the environment.

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.

No additional information.

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?

According to the risk assessment the potential risk to human health and the environment were considered to be negligible. In hindsight, the study results and operational experience give no indication for a different outcome of the assessment.

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.

In September 2017 the third intermediate study evaluation indicated that the study did meet the “criteria for futility”, which made the DMC to advise to end the trial. As a result the study was aborted worldwide. No health or environmental issues were reported.

Created: November 7, 2018.
Reviewed: November 20, 2018.