REPORTING OF THE FINAL RESULTS OF DELIBERATE RELEASE INTO THE ENVIRONMENT OF GENETICALLY MODIFIED ORGANISMS USED IN INVESTIGATIONAL MEDICINAL PRODUCTS

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

A final report on the results of the deliberate release shall be delivered by the notifier to [name of Competent Authority] after the deliberate release has terminated, at a date specified in the consent issued by the Competent Authority or otherwise communicated by the Competent Authority. To this end, the present template can be used.

Note: The information given in this template does not describe the requirements to pass the peer review process. It should only be viewed/considered as a guide for preparation of the reports, which would allow thorough evaluation. Filling in this form does not prevent the competent authorities from requiring additional information from the notifier, both confidential and non-confidential.

The final report template shall be completed by the notifier.

- The notifier shall fill in the report template according to the proposed form.
- This form must be filled with respect to any risk to human health or the environment, and not with respect to the clinical results.
- Where appropriate, the notifier shall illustrate as much as possible the reported data by means of diagrams, figures and tables provided in high quality.
- The notifier is encouraged to provide statistical data when relevant, supported by the justification of the choice of the statistical test.
- The final report will be sent to the European Commission and uploaded to the public GMO register of the EU Commission on the deliberate release and placing on the EU Market of GMOs (https://gmoinfo.jrc.ec.europa.eu). It should therefore not contain confidential information unless required by Article 25 of Directive 2001/18/EC. In the case of confidential data, it should be provided in an Annex to the reporting template, with a non-confidential summary or general description of these data, which will be made available to the public.
- List of abbreviation (or explanation in the text) should be provided.

1. General information

1.1. European notification number: **B/IE/18/01…..**
Number can be found on the corresponding SNIF form (i.e. member state (yy), year and number, B/yy/xx/xxx)

1.2. Member State of notification: …Ireland ……..

1.3. Date of issue of consent: ……13/11/2018…..
Date of issue of permit

1.4. Title of the project: CT-AMT-061-02 Uniqure Study …….

1.5. Purpose and expected outcome of the release (provide short summary or link to the relevant section in the SNIF):	Recombinant serotype 5 adeno-associated virus (AAV) based vector containing the Padua variant of a codon-optimised human coagulation factor IX gene (AAV5-hFIXco-Padua). The gene encoding a normal human clotting FIX will be expressed in the hepatocytes of patients with severe or moderately severe haemophilia B. The gene is codon optimised to enhance hFIX expression and clotting activity and thus enable sustained levels of plasma FIX activity. To test whether a single administration of AAV5-hFIXco-Padua is efficacious (i.e. that it has the ability to produce the desired or intended result) and that it is safe in patients with haemophilia B. ……..
1.6. Name of the notifier: *i.e. legal entity = notifier*	Uniqure Biopharma BV Paasheuvelweg 25A 1105 BP Amsterdam The Netherlands.
1.7. Start and end date of the release:	Started release 26 th Feb 2020 Last release was 21stMarch 2020……..
1.8. Site(s) where the project was conducted (e.g. hospital(s) or care unit(s)):	Wellcome –HRB Clinical Research acility at St James's Hospital ……..

2. Characteristics of the release

2.1 Scientific name of the recipient organism:	…AAV5-hFIXco-Padua(serotype adenoassociated viral vector containing a codon optimized human factor 9 padua gene.
2.2 Transfer event(s) (acronym(s)) or vectors used: *Describe the GMO(s) and/or vector(s) and insert(s) used for the modification*	…AAV-5 Padua Uniqure ……..
2.3 Name of the investigational medicinal product and the clinical trial number, if available:	CT -AMT -061-02……..
2.4 Number of clinical trial subjects that received the investigational medicinal product:	……3…..

2.5 Dosing and administration schedule (in case of repeated dosing) of the investigational medicinal product administered to each clinical trial subject:	Single weight based dosing to each individual adult, administered by intravenous infusion on 26th Feb 2020, 11th March 2020 21th March 2020…..

3. Risk management measure(s)

Where applicable, please report the risk-management measures used to avoid or minimize potential negative impacts to humans, animals and the environment arising from the spread outside the site(s) of release or the shedding of the GMO(s) from the clinical trial subject not originally notified in the notification,

- *applied in addition to the conditions in the consent,*
- *required by the consent only under certain conditions,*
- *where the consent allowed the notifier a choice of measures.*

Answer: ……No deviation from the risk management as notified ……

4. Post-release monitoring measures

Please describe any deviation from the notified monitoring strategies and methods aiming at detecting shedding, spread or transmission of the GMO and the frequencies with which monitoring was carried out to detect the effects of the release.

Answer: ……No deviation from post release monitoring measures……

5. Results and effects of the foreseen and unforeseen spread or shedding

Consider in the following questions 5.1 through 5.4 all results of the foreseen and unforeseen spread or shedding and possible interactions 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 spread or shedding studies

To the extent that the clinical trial collected information on the spread of shedding of the GMO contained in the investigational medicinal product, please provide a summary of the results in respect of any risk for human health or the environment.

Answer: … In addition to regular procedures to manage spreading and shedding the study protocol made provision for the collection of semen samples from the treated individuals at monthly intervals until 3 vector negative samples are received. This continues for all three individuals. In the interim PI educates partcipants in relation to barrier protection.

5.2 Observed effect(s) relevant to ERA[1]

5.2.1 Expected effects (if applicable[2])

Answer: Shedding through semen was expected and the study is ongoing in this regard. ……

5.2.2 Unexpected 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 ……

5.3 Unintended release[3] 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: ……No Unintended releases took place……

5.4 Other information

Notifiers are encouraged to supply any further information, such as deviations from the original release plan*, which was not included in the original notification but which might be relevant to the ERA*.

6 Assessment of risk for human health and the environment following completion of release

Please provide conclusions on 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 clinical trial subjects.

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[1] Section 5.2 does not have to be filled-in in cases where the clinical trial concerned by the submission has not collected any data on shedding or spreading of the investigational medicinal product into the environment.

[2] Section 5.2.1 does not have to be filled-in when the investigational medicinal product is covered by a specific environmental risk assessment as described in the "Good Practice on the assessment of GMO-related aspects in the context of clinical trials with human cells genetically modified by means of retro/lentiviral vectors" (https://ec.europa.eu/health/sites/health/files/files/advtherapies/2018_gmcells_gp_en.pdf) and in the "Good Practice on the assessment of GMO related aspects in the context of clinical trials with AAV clinical vectors" (ref.).

[3] Any events of abnormal release of the investigational medicinal products containing the GMO. For example: via leakage or breakage.

Answer: The risk assessment and risk management strategies were appropriate for the study and maintained throughout there was no unintentional or unforeseen events and no additional risk strategies or hazards identified

Date: 31/03/2021