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Annual Report to the Environmental Protection Agency and Ministry of Primary Industries (NZ)

Application reference: APP202601

Client: SillaJen Inc.
Product: Pexa-Vec
Date: 09 June 2017
Page Count: 6
Version: 1.0

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1 List of Abbreviations

AE	Adverse Event
CNS	Clinical Network Services
EPA	Environmental Protection Agency
GMO	Genetically Modified Organism
MPI	Ministry of Primary Industries
NZ	New Zealand
OGTR	Office of the Gene Technology Regulator (Australia)
SAE	Serious Adverse Event
SIV	Site Initiation Visit
VIG	Vaccinia Immunoglobulin

2 Introduction

In accordance with Control 7 of the "EPA-MPI compliance expectations for APP202601 controls". *The New Zealand sponsor must submit a report that shows compliance with the above controls, to the EPA and MPI, six months after the commencement of the Phase 3 clinical trial, then on or before 30 June every year thereafter until the conclusion of the Phase 3 clinical trial*.

This is the first annual report to the Environmental Protection Agency (EPA) and Ministry of Primary Industries (MPI) regarding the Genetically Modified Organism (GMO) "Pexa-Vec", approved for use in a clinical trial on the 27th October 2015. This report outlines a summary of the evidence/information demonstrating compliance provided to the EPA and MPI, for the period of approximately 12 months after the first 6-month report submitted on the 19th June 2016.

3 Compliance Measures

The EPA approved the study on the 27th October 2015 until the conclusion of the Phase 3 trial. SillaJen is the Applicant and Clinical Network Services (CNS) Pty Ltd is the NZ Agent/Consultant. The first Site Initiation Visit (SIV) was conducted in New Zealand (NZ) on the 14th and 15th of December 2015 at the Auckland clinical trials unit.

The EPA was notified by CNS of the planned commencement of the study in Auckland on the 23rd December 2015, one month prior to the first patient being dosed (in the control cohort), in accordance with Control 2 of the EPA-MPI compliance expectations for APP202601 controls. An additional notification was sent on the 19th May 2016 to notify the EPA of an additional site in Christchurch. Although the patients at the Christchurch site will not receive Pexa-Vec (receiving the standard of care only, Sorafenib), they are part of the study group.

All appropriate personnel have been trained in the handling of this GMO product in accordance with Controls 1, 2 and 3 (records can be provided to the EPA on request). In addition, according to Control 1 (Note 1), the date(s) de-identified trial participants were intratumorally administered with Pexa-Vec, including the name of the practitioner who administered Pexa-Vec and where the administration occurred (trial site), has been recorded in a master checklist. The signed master checklist can be provided to the EPA and MPI on request. This is listed on each IT injection preparation and administration sheet and the master checklist will be the site delegation log which lists who is registered to perform the study and their roles/responsibilities.

All required documentation was provided to the EPA on the 19th August 2015 during the submission/approval period (see 6-month report to the EPA/MPI dated 19th July 2016).

In accordance with Control 5, there have been no occurrences of Pexa-Vec-induced adverse effects resulting from confirmed events of Pexa-Vec transmission from Pexa-Vec treated individuals to untreated individuals or animals, notifiable to the EPA/MPI. Standard safety blood samples as per the protocol are sent to a central lab in Singapore.

4 Adverse Events

During this reporting period (6th June 2016 to 5th May 2017), there have been nine (9) patients treated with Pexa-Vec.

There have been no reports of AEs/SAEs resulting from confirmed events of transmission to date and there is no requirement under the EPA controls to report AE/SAEs that do not result in transmission. Treatment-emergent treatment-related SAE listings are available on request.

No transmission to other persons or animals have been reported to date. All patients were given biohazard containers and trained on pustule management, In accordance with EPA-MPI controls. The development of pustules following Pexa-Vec administration is deemed expected. No other concerns have been noted.

In accordance with Control 6, adequate stocks (at least 2 doses) of Vaccinia Immunoglobulin (VIG) and cidofovir, within their expiry dates, are stored at the Auckland clinical trial site and will be for the duration of the trial. Practically speaking, this equates to 12 vials of VIG where 8.4 vials are needed for a 70 kg person. Therefore, 12 vials would cover one dose for a large or average person and 2 doses for small (up to 50 kg) patients. Two vials of cidofovir should equate to 2 doses.

Currently, as of 5th May 2017, 12 vials of VIG with an expiry of February 2022 and 2 vials of cidofovir with an expiry of March 2018 are in stock. Additional stock is held in Singapore to send as needed (26 hours' total delivery time). In addition, there are 9 Pexa-Vec kits available in stock with an expiry date of 30th June 2018.