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Your letter from	Your reference	Our reference	Annex	Date
		FAGG/DGPRE/R&D/MMN 1137778		

Dossier GMO : B/BE/18/BVW6

2017-004087-35: A Global Study of a Single, One-Time Dose of AVXS-101 Delivered to Infants with Genetically Diagnosed and Pre-symptomatic Spinal Muscular Atrophy with Multiple Copies of SMN2

2017-000266-29: Phase 3, Open Label, Single Arm, Single Dose Gene Replacement Therapy Clinical Trial for Patients with Spinal Muscular Atrophy Type 1 with One or Two SMN2 Copies Delivering AVXS 101 by Intravenous Infusion

Geachte Mevrouw Nobels,

Hierbij informeren wij u dat de vergunningsplicht krachtens het Koninklijk besluit van 21 februari 2005 tot reglementering van de doelbewuste introductie in het leefmilieu evenals van het in de handel brengen van genetisch gemodificeerde organismen of van producten die er bevatten u wordt toegekend op basis van het gunstig advies van de Adviesraad voor Bioveiligheid daterend van 7 januari 2019 en dit volgens de voorwaarden hernomen in de conclusie van bovenvermeld advies, dat wil zeggen:

"- *The notifier and the investigators must strictly apply the clinical trial protocol, and all the safety instructions as described in the dossier.*

- Any protocol amendment has to be previously approved by the Competent Authority.

- The notifier is responsible to verify that each study centre has qualified personnel experienced in handling infectious material and that the investigator has the required authorizations to perform the clinical trial activities inside the hospital (laboratory, pharmacy, hospital room, consultation room...) according to the Regional Decrees transposing Directive 2009/41/EC on Contained use of genetically modified micro-organisms.

- The Biosafety Advisory Council should be informed within two weeks when the first patient starts the treatment and the last patient receives the last treatment.

- The notifier has to deliver to Sciensano - Transversal activities in applied genomics a control sample the latest 15 days after the approval and the start of the trial.

- At the latest six months after the last visit of the last patient included in the trial, the notifier must send to the competent authority at the attention of the Biosafety Advisory Council a report with

details concerning the biosafety aspects of the project. This report will at least contain:

- *o The total number of patients included in the trial and the number of patients included in Belgium;*
- *o A summary of all adverse events marked by the investigators as probably or definitely related to the study medication;*
- *o A report on the accidental releases, if any, of AVXS-101."*

Met hoogachting,

Maggie De Block

Minister van Sociale Zaken, Volksgezondheid, Asiel en Migratie

Marie Christine Marghem

Minister van Energie, Leefmilieu en Duurzame Ontwikkeling