famhp
federal agency for medicines and health products

Research and Development

Federal agency for medicines and health products
Eurostation II - Place Victor Horta 40/40
1060 Bruxelles
www.afmps.be

Anne Lenaers
Tel. : +32 (0)2 524 81 03
Fax : +32 (0)2 524 80 01
e-mail : anne.lenaers@fagg-afmps.be

Ms Christine Jacobs
Harrison Clinical Research Benelux
Keiser Karellaan, PO Box 4
1082 Brussel

Your letter from	Your reference	Our reference	Annex	Date
		FAGG/R&D/LSA		

Onderwerp
Titre de l'objet
Subject

Goedkeuring van een klinische proef op 30/04/2013
Approbation d'un essai clinique le 30/04/2013
Authorisation of a clinical trial dated 30/04/2013

A Phase 2b, Double-Blind, Placebo-Controlled, Multinational, Multicenter, Randomized Study Evaluating the Safety and Efficacy of Intracoronary Administration of MYDICAR® (AAV1/SERCA2a) in Subjects with Heart Failure

EudraCT: 2012-001700-37

Chère Madame, Cher Monsieur,

Conformément à l'article 12 de la Loi du 7 mai 2004 relative aux expérimentations sur la personne humaine, j'ai décidé d'autoriser l'essai clinique ci-dessus mentionné.

Cependant, un suivi doit être apporté aux points mentionnés en annexe.

Salutations sincères,

Pour la Vice-Première Ministre et Ministre des Affaires sociales et de la Santé publique

Geachte Mevrouw, Geachte Heer,

In overeenstemming met artikel 12 van de wet van 7 mei 2004 inzake experimenten op de menselijke persoon, heb ik besloten de hierboven vermelde proef goed te keuren.

Niettemin moet er gevolg gegeven worden aan de opmerkingen vermeld in bijlage.

Met de meeste hoogachting,

Voor de Vice-Eerste Minister en Minister van Sociale Zaken en Volksgezondheid

Dr. Greet Musch

Unofficial translation

In accordance with article 12 of the Law of 7 May 2004 concerning experiments on the human person, I have decided to authorise the above mentioned clinical trial. However, the points as mentioned in annex are to be followed up.

Annex

QUALITY

An adequate answer has been presented to the grounds for non-acceptance arising from the quality assessment of the investigational medicinal product. Therefore, we have no objections against the start of the Clinical Trial.

However, the sponsor is recommended to take into consideration the following recommendation given in annex during further development of the product. It may be readdressed at the time of assessment of future applications related to this investigational medicinal product.

Similar to other non-integrating viruses, it was demonstrated that recombinant AAV are present as circular episomes (monomers and high-molecular weight concatemers) and assimilate into a chromatin-like structure where nucleosomes are regularly assembled along the viral genome in a pattern similar to cellular chromatin. This chromatinization may contribute to the stability of rAAV DNA in quiescent tissues, but could also lead to epigenetic-mediated modulation of transgene expression. Therefore, although the CMV-promoter DNA is not subject to silencing by cytosine methylation in this case, histone modifications (i.e. by methylation and/or deacethylation) can be involved in this regulation and became an issue in the long term. The applicant is advised to take into account this possible scenario that may trigger loss of efficacy in the long term follow up, assuming that the rAAV DNA is kept stable in the post-mitotic cells during the follow up of efficacy.

afmps
agence fédérale des médicaments et des produits de santé

Agence fédérale des médicaments et des produits de santé
Eurostation II - Place Victor Horta 40/40
1060 Bruxelles
www.afmps.be

DG Pré/R&D

Anne Lenaers
Tél. : 02/524.81.03
Fax : 02/524 80 01
e-mail : anne.lenaers@afmps.be

Ms Christine Jacobs

Harrison Clinical Research Benelux

Keiser Karellaan, PO Box 4

1082 Brussel

Votre lettre du	Vos références	Nos références R&D/LSA	Annexe(s)	Date

Objet : Dossier OGM B/BE/12/BVW2: A Phase 2b, Double-Blind, Placebo-Controlled, Multinational, Multicenter, Randomized Study Evaluating the Safety and Efficacy of Intracoronary Administration of MYDICAR® (AAV1/SERCA2a) in Subjects with Heart Failure

Chère Madame Jacobs,

Par la présente, nous vous informons que l'autorisation imposée en vertu de l'arrêté royal du 21 février 2005 règlementant la dissémination volontaire dans l'environnement ainsi que la mise sur le marché d'organismes génétiquement modifiés ou de produits en contenant vous est accordée sur base de l'avis favorable du Conseil de Biosécurité daté du 23 janvier 2013, et ce, aux conditions reprises dans la conclusion de l'avis précité, c'est-à-dire :

- The notifier and the investigators must strictly apply the trial protocol, and all the safety instructions as described in the dossier also taking into account the suggestions from the Biosafety Advisory Council for improvement of the personnel instructions and its synopsis.
- Any protocol amendment has to be previously approved by the Competent Authority.
- The notifier is responsible to verify that each study center 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 2 weeks when the first patient starts the treatment and the last subject receives the last treatment.

- 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 Council a report with details concerning the biosafety aspects of the project. This report will at least contain:
    - The total number of patients included in the trial and the number of patients included in Belgium
    - A summary of all adverse events marked by the investigators as probably or definitely related to the study medication
    - A report on the accidental releases, if any, of the recombinant AAV.

Laurette Onkelinx	Sabine Laruelle	Melchior Wathelet
Ministre des Affaires Sociales et de la Santé publique	Ministre des Classes moyennes, des PME, des Indépendants et de l'Agriculture	Secrétaire d'Etat à l'Environnement, à l'Energie et à la Mobilité