

Communication Paper

Second Workshop on Gene Therapy

Osaka 12th November 2003

Satellite session to the ICH 6 conference

The International Conference on Harmonization (ICH) Steering Committee confirmed that in the area of gene therapy medicinal products, there is a need to exchange information with the following objectives:

- Monitoring emerging scientific issues
- Developing new ways of communication to ensure that the outcomes of ICH are well understood and widely disseminated
- Proactively setting out principles that may have a beneficial impact on harmonizing regulations of gene therapy products

Within this framework, the second ICH open workshop on gene therapy was convened in Osaka on 12th September 2003. The program addressed the following topics:

- Mandate and goals of the ICH gene therapy discussion group
- Experience gathered with the use of the Adenovirus Type 5 Reference Material
- Potential for inadvertent germline integration
- Insertional mutagenesis and oncogenesis
- Scientific principles for quality and design of Lentiviral vectors
- A new gene therapy delivery system using Sendai virus vectors

The workshop format consisted of presentations made on scientific and regulatory developments in the field of Gene Therapy followed by general panel discussions.

Representatives and experts from the six parties – the three ICH regions (including regulatory authorities and industries), Health Canada, WHO, and the European Free Trade Association (EFTA)- contributed in this public workshop. Overall about 450 participants attended this workshop.

The following topics were presented at the workshop:

Mandate and goals of the ICH gene therapy discussion group

- Address priority topics and emerging issues (e.g. insertional oncogenesis, novel vectors) in a rolling work- program.
- Implement new ICH working methods such as: e-mails, teleconferences, direct contacts, regional workshops and other activities as relevant preparation to ICH meetings.

- Convene public workshops and consensus conferences under the ICH umbrella to produce consensus principles documents.

Updates on gene therapy issues

Representative gave updates from Japan, EU and Canada.

Standard reference material.

The Adenovirus Type 5 Reference Material (Ad5) is being used in 13 countries world wide for validation of in-house developed standard materials. This would allow useful comparison of experimental results from different studies with respect to measurements of viral particles and the infectious titers. The experts discussed their experience with the use of this reference material.

Lentiviral vectors

The presentation centered on manufacturing principles and strategies to ensure quality and safe use of Lentiviral Vectors (LV). The discussion included consideration on the following aspects:

- The nature of parental lentiviruses and impact on LV development
- Characterization and control testing of LV
- Potential generation of replication competent lentiviruses
- Potential for insertional mutagenesis

Germline Transmission

The presentation centered on the following:

- FDA's recommendations for performing animal biodistribution studies
- Summary of previous discussions at public meetings regarding inadvertent germline transmission
- FDA's Current approach for patient follow-up

Insertional Mutagenesis and oncogenesis by retroviral vectors

The presentation discussed the report of leukemia's in two study subjects enrolled in a gene therapy trial for the treatment of SCID-X1. It was stated that the cases of leukemia's were most likely to be caused by retroviral vector integration in LMO-2, with possible contributions of the γ c chain gene transferred, the SCID-X1 disease, and the very young age of the patients treated.

Cytoplasmic Gene Therapy: A new concept using Sendai virus vectors

The presentation was made on cytoplasmic gene therapy using Sendai virus vectors. These vectors show high gene expression and theoretically lack the risk of insertional mutagenesis.