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Safety evaluation of gene therapy - a case study of naked DNA product

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Gene therapy is a medical intervention based on modification of the genetic material of living cells. Gene transfer usually conducted using bacterial plasmid DNA and/or virus vector to express a specific protein. Gene transfer medicinal products classified as naked nucleic acid, complexed nucleic acid or non-viral vectors, viral vector, and genetically modified cells according to biological origin. Plasmid DNA may be administrated either in a simple salt solution (as "naked" DNA) or complexed with a carrier or an adjuvant. To facilitate the initiation of clinical trials of gene therapy, the US FDA developed a "Points to Consider" document in 1996 describing how the manufacture and safety of DNA vaccines planned for clinical use would be evaluated. In Europe, the EMEA published a "Note for Guidance on the Quality, Preclinical and Clinical Aspects of Gene Transfer Medicinal Products" in 2001 describing preclinical pharmacological and toxicological evaluation of gene transfer products.

Recently, as more drug manufactures, Bioventures, and other research organization in Korea take part in the development of gene transfer-based medicinal products, the need for guidelines increases tremendously. To achieve this goal, we would like to share our preclinical evaluation experience for the following two naked DNA products.

VMDA 3601, a naked DNA for the treatment of peripheral artery occlusive disease, was developed by Dong-A Pharmaceutical Company and ViroMed Co. Ltd. It was the first naked DNA had entered the clinical study and successfully finished phase I study. The other naked DNA vaccine, GX-12, is a naked DNA vaccine for the treatment of HIV infection, consists of four separate plasmids which encode the HIV gag, env, pol, and regulatory genes. It is preparing for an Investigational New Drug (IND) application.

This presentation will discuss the safety issue of gene transfer-based products and the case studies for the IND application process. With more knowledge accumulated on how to deal with the safety of gene transfer-based products, it will be helpful to establish safety guideline for gene therapy.