Regulatory Expectation of Investigational New Drug Application (IND) in Cell and Gene Therapy Products

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Cell therapy is the prevention or treatment of human disease by administration of cells that have been selected, multiplied and pharmacologically treated or altered outside the body. The aim of cell therapy is to replace, repair or enhance the function of damaged tissues or organs. The cells used can originate from the patient (autologous) or from a donor (allogeneic) or from another species (xenogeneic). The cells used in cell therapy include myoblasts, cardiomyocytes, chondrocytes, dendritic cells, various lymphocytes, fetal neural tissue, fibroblasts, hepatocytes, islet cells, keratinocytes and stem cells. As the cell therapy application grows, regulatory issues become important consideration.

Human gene therapy is the use of normal genes or genetic material to replace or cancel out the "bad" or defective genes in a person's body that are responsible for a disease or medical problem. And we define that gene therapy is the administration of genetic material in order to modify or manipulate the expression of a gene product or to alter the biological properties of living cells for therapeutic use. Scientific progress over the past decade has led to the development of novel methods for the transfer of genetic material to cells. Gene therapies has greatly being developed from academia and industry, therefore regulatory authorities confronted by providing the necessary guidance documents to ensure quality, safety and efficacy, and by providing rapid review of the application.

Safety, efficacy and quality is an essential consideration of any new therapy and regulatory considerations for cell therapy are those for biological preparations. KFDA concerns a range of cell therapy products, relevant manipulation procedure, and products to be administered is of acceptable quality and standard, and free from contamination. All necessary control measures should be considered in order to ensure appropriate sourcing and control of all materials, minimizing the risks of damage and ensuring integrity, desirable characteristics and function of the therapeutic product, and compliance with high quality and safety standards of establishments and processes involved in the manipulation of cell products. Also, preclinical studies are intended to define the pharmacologic

and toxicological effects predictive of the human response. Due to the unique and diverse nature of the products employed in cell therapies, conventional pharmacology and toxicity testing may not always be appropriate to determine the safety and biologic activity of this therapeutics. Available animal models mimicking the disease indication may be useful in obtaining both sufficient safety and efficacy data prior to entry of cell therapy products into clinical trials. It is recommended that plans for preclinical studies be discussed with KFDA before initiation.

Vectors used in gene therapy clinical trials are mainly retrovirus, adenovirus, naked plasmid, pox, vaccinia virus vector, etc. and around 1,000 cases of clinical trial are performed to assess the efficacy in the world. The International Conference on Harmonisation of technical requirement for registration of pharmaceuticals for human use (ICH) has provided standardization and flexibility in design of toxicity study, and proposed uniformity in content and format. The validation and acceptance of alternative methods, use of non-traditional animal models, development of noninvasive and minimally invasive technologies, are all expected to not only improve the predictive value of preclinical studies but also increase the safety knowledge base. Also, manufacturers of gene therapy products must test their products extensively and meet requirements for safety, purity and potency. The design, evaluation and regulation of gene therapies have demanded state-of-the art knowledge of the latest biotechnology to anticipate risks and devise methods to address them. Science-based regulations are satisfied with not only requirements for expert regulators, applicable laws, regulation and policy but also needs of manufacturers.