Quality Evaluation of Biotechnological Products

Yeowon Sohn

Biotechnological Division, Biologics Evaluation Department, KFDA

Biotechnology has evolved significantly over the past twenty years since the development of early recombinant DNA-derived products, such as interferon and insulin. Production and testing techniques for these molecules have evolved and matured, particularly in areas involving protein biotechnology. As a result, many new and important medicines are now available to improve public health. These include products such as therapeutics, vaccines and diagnostics.

Manufacturing is a key element in maintaining the quality and safety of biotechnology products. As with traditional biological products, it is important to look at the entire manufacturing scheme and have control over this process. This includes production, characterization, process validation, testing and specifications. In evaluating biotechnology-derived products, it is important to review from the source material, e.g. the master cell banks and working cell banks, fermentation procedures, harvesting, isolation and purification, through the formulation, filling and labelling. In addition, in-process controls are necessary, as well as validation, to ensure product quality, safety, potency and efficacy.

Over the past fifteen years, a number of scientific issues have been raised with respect to proteins produced by biotechnology. The source of the materials is extremely important, i.e. the cell source used in manufacturing the product and the source of the gene DNA/RNA that was cloned. Post-translational modifications, and particularly glycosylation, may be of importance. This is particularly important with eukaryotic systems. There are also process-related changes. As one is purifying and isolating the protein, one needs to be concerned about oligomers, proteolytic activities that truncate these molecules, deamination, oxidation, and other key chemical reactions. Formulation may also have an impact on the product. The conformation is important, particularly with prokaryotic systems, where one has to use fairly harsh conditions in order to solubilize the protein. Because these molecules come from living sources, there is concern with adventitious agents. Contaminants from the manufacturing process can be introduced at any point including during purification. Finally, we are concerned with the stability of these molecules.

As for all biologicals, the standards for licensure for products derived from biotechnology are dependent on their safety, purity, potency, identity, and efficacy. These should be made consistently and under current good manufacturing practices (GMPs) and be stable for the designated dating period. In addition, there should be appropriate and effective process validation, in process controls, analytical and functional testing, and the establishment of key specifications.