DESIGNING QUALITY INTO THERAPEUTIC PEPTIDE MANUFACTURING

Quality cannot be tested into products; it has to be built and designed - *FDA Guidelines and General Principles of Process Validation, May 1987.*

Quality by Design has noticeable advantages over traditional strategies and the regulatory authorities are recommending the use this approach. The ultimate goal is the discovery, development, manufacture and approval of safer, affordable and more effective treatments for the growing population. The PolyPeptide Group has embraced Quality by Design and uses a risk based approach to develop, manufacture and commercialize peptide based therapeutics.

Quality by Design (QbD) is a culture that incorporates quality principles, strong compliance function, risk assessment and management. Only recently has the United States Food and Drug Administration embraced QbD as a vehicle for the transformation of how drugs (including small molecules, peptides and proteins) are discovered, developed, and commercially manufactured. On January 27, 2011 the FDA released the "*Guidance for Industry: Process Validation: General Principles and Practices*". The guidance aligns process validation activities with a product lifecycle concept, existing FDA guidance, and the ICH guidance for industry, which includes Q8(R2) Pharmaceutical Development, Q9 Quality Risk Management, and Q10 Pharmaceutical Quality System.

The long-standing approach to submission focused on developing a manufacturing process that had emphasis on mainly on chemistry and the specifications, and less on manufacturing science. This strategy failed to truly challenge the parameters of

the manufacturing process and lacked an understanding of the variability in raw materials. It was not representative of routine operations, created a "do not rock the boat" mindset, and made it difficult to implement continuous improvements into the manufacturing process, locking in low efficiency. From a regulatory stand point, submission documentation contained insufficient development information, and the information that was captured, was voluminous but not comprehensive. High number of supplements would have to be filed because changes made after submission would be considered critical.

Rather than focusing on fixed parameters and ranges, QbD encourages the creation of a design space by using a risk-based approach to the manufacturing process. The design space will allow the manufacturing process to be optimized and continuously improved as long as the critical parameters stay within the established ranges. The model allows for an increased understanding of the manufacturing process which ultimately will help in reducing raw material costs, product inventory costs and enable the creation of a more efficient manufacturing process. There will be increased predictability of the manufacturing output and quality, resulting in fewer failures and deviation investigations, which in the long-term will lower operating costs. The regulatory documentation will be more comprehensive and less voluminous allowing for faster review and approval by the regulatory bodies.

QbD enables closer links between research, manufacturing and marketing and it will help expedite the time to market of new therapeutics, while reducing costs. QbD is essential for pharmaceutical quality in discovery, development and commercialization.

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