Table 26-8 Current Paradigm Compared to Quality by Design Paradigm

Current paradigm	Quality by design paradigm
• Quality is tested into the product • Product specifications are based on batch testing results • Validation "freezes" the process • Process improvements require preapproval	• Quality is designed into the product • Employs real-time quality control based on process analytical technology • Product specifications are based on "fitness for use" and process capability • Process changes within the established design space do not require preapproval • Process validation is redundant

performance criteria based on analysis of experimental data. Table 26-8 briefly contrasts the QbD paradigm with the current regulatory environment.

A key element of QbD is the concept of design space (Fig. 26-2), which is a multidimensional space encompassing combinations of product design and processing variables that provides assurance of suitable product performance. The QbD approach is intended to provide regulatory relief throughout the lifetime of a product by allowing product and process changes that fall within the design space to be implemented without prior approval. Design space is proposed by the applicant and is subject to regulatory review and approval.

While the principle of QbD is simple and appealing, the actual development, scale-up, and commercialization of pharmaceutical products present a significant challenge to pharmaceutical scientists and engineers. Establishing a meaningful design space requires aggressive experimentation on a small scale, particularly since the supply of active pharmaceutical ingredient (API) is generally limited. In order for these small-scale experiments to be meaningful, scale-up must be understood at a very sophisticated level.

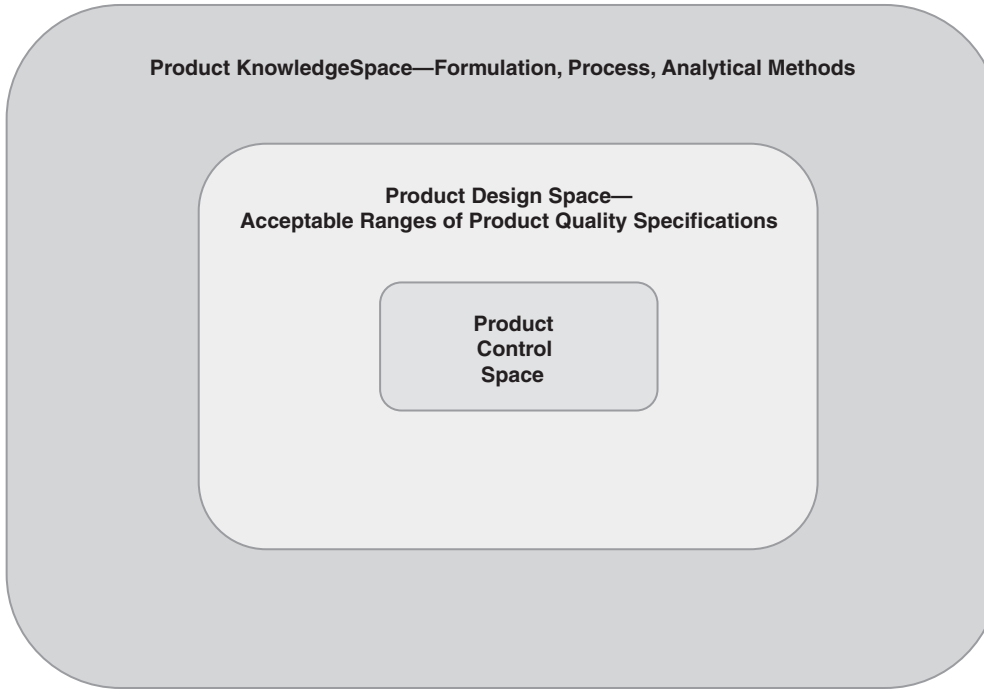

Figure 26-2 Illustration of quality by design.