

## PRODUCT DEVELOPMENT

Scale-up, technology transfer, and PPQ are performed toward the terminal phase of the development cycle of generic products. However, the performance and success of these phases is affected by “upstream” activities such as formulation design and process characterization, in-process controls, finished product acceptance criteria, and test methodology. Because many of these are established at early stages of product development, it is imperative to address formulation and process development issues that can have pronounced effect on the manufacturing process, scale-up, and PPQ. Once a product is identified for generic development, various activities are initiated and a stepwise but parallel approach is taken in the development work, to include the following:

1. Preformulation studies
2. Formulation design and process development optimization
3. Scale-up characterization of manufacturing process
4. Process demonstration and technology transfer
5. PPQ
6. Documentation, registration, approval, and launch

### PREFORMULATION STUDIES

The manufacturing process utilized is affected by the variability in physical properties of the active pharmaceutical ingredient (API) and the excipients [1]. If the API component comprises the predominant portion of the dosage form, its physicochemical properties and variability, if not controlled, would influence mixing, granulation, flow, compression, and coating. Typically, the composition of the branded product is used as a guide in selecting excipients for the corresponding generic product. The formulation scientist needs to perform extensive work to identify the particular type or grade of excipient suitable for the product. The type of excipient can affect the manufacturing process and performance of the product and quality attributes of the finished dosage form. Excipient selection must be made, keeping in mind the final manufacturing process [2] intended for commercial production. This important consideration is often ignored in the early stages of product development, and often, improper selection of excipients and their inadequate characterization and control contribute to significant scale-up challenges during technology transfer and PPQ [3]. Table 5.1 provides a list of common excipients and their effect on manufacturing process and scale-up.

The formulation scientist must carefully review various physicochemical properties of the excipients and the resulting dosage form in selecting excipients and the manufacturing process. Excipients not only help in achieving target quality attributes, but proper excipient selection and control also influences the manufacturing process, ease of scale-up, and successful PPQ. In many instances, various excipient grades are available, differing in particle shape, size, degree of crystallinity, moisture content, flowability, and compressibility. Careful evaluation of the excipient properties in light of manufacturing process to be utilized is important. For example,