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Chemical Drug Substance Characterization

Characterization is integral to the theatrical experience.

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8.1 Introduction

Lead drug substances might be derived from three sources: chemical, biological, and botanical (including minerals). These compounds (or a mixture of compounds) may be delivered to the preformulation team at a myriad of characterization stages. Although the drug discovery group has, by this time, established the pharmacological activity, the synthesis or extraction group has, by this time, not necessarily fully characterized the lead compound. There is also a proposal on the table regarding the prospective drug delivery systems and their routes of administration. The task of the preformulation group therefore starts with the development of a detailed plan for the complete characterization of the lead compound. The depth and breadth of the characterization would depend on the type and source of the compound as well as its destination—the dosage form. Although the formulation part is yet to come, the preformulation group must provide lead suggestions on the choice of the excipients through preliminary interaction trials. These studies must be conducted using analytical methods that are established, though not necessarily fully validated at this stage.

The regulatory impact of preformulation studies is very significant, as in one format or another, the key component of all regulatory filings involves the complete characterization of the drug substance. These details are provided in the guidance provided by the U.S. Food and Drug Administration (FDA) on the preparation of the chemistry, manufacturing, and control package or in the Common Technical Document package, as required by the European Agency for Evaluation of Medicinal Products. Although the full scope of these documents covers the drug substance and the drug product, the studies conducted at the drug substance level are pivotal to further development. The aim of pharmaceutical development is to design a quality product and a manufacturing process to deliver the product in a reproducible manner. The information and knowledge gained from pharmaceutical development studies provide scientific understanding to support the establishment of specifications and manufacturing controls. Of greatest importance in the development of pharmaceutical studies are the sections devoted to the characterization of drug substances.

The physicochemical and biological properties of the drug substance that can influence the performance of the drug product and its manufacturability, or those that