18.3 DISCUSSION

When drugs are applied topically, a pharmacologically active agent must be released from its carrier (vehicle) before it can contact the epidermal surface and be available for penetration in the stratum corneum and lower layers of the skin. A topical formulation is a complex drug delivery system, and the dynamics of drug release from a vehicle have been a subject of debate and investigation for many years. A simple and reproducible method, generally applicable to all topical dermatological dosage forms, has been developed to measure in vitro drug release from the dosage form using a VDC and a synthetic membrane, as described in SUPAC-SS guidance (1).

The IVR test is gaining importance as a product performance and quality control test. Scientific workshops on scale-up of a semisolid disperse system (2) and on the value of in vitro drug release (3) have resulted in recommendations on the use of IVR tests as a measure of in-process control and also as a finished product specification for creams, ointments, and gels. In addition, the cited workshop report recommends the use of an IVR test for monitoring product reproducibility during component and compositional changes, manufacturing equipment and process changes, scale-up, and/or transfer to another manufacturing site (2, 3). These recommendations (use of IVR test) are the basis of assuring product sameness after SUPAC (1).

18.4 PRODUCT PERFORMANCE TEST

Following regulatory approval of a drug product by the regulatory authority, e.g., FDA, the product performance test becomes the sole means of directly monitoring the ongoing performance of the dosage form. Two categories of tests are performed with drug products: (1) product quality tests and (2) product performance tests. Product quality tests are intended to assess attributes of the dosage form such as identification, assay (strength), impurities, physicochemical properties, uniformity of dosage units, pH, apparent viscosity, microbial limits, antimicrobial preservative content, antioxidant content, sterility (if applicable), and other tests that may be product specific that are part of a compendial monograph. Product performance tests are designed to assess the performance of the dosage form that in many cases is related to drug release from the finished drug product.

USP General Chapter <1724> provides procedures for determining product performance test/drug release from semisolid dosage forms (4). The product performance tests do not directly measure bioavailability and relative bioavailability (bioequivalence), although they can detect product changes that may correspond to altered in vivo performance of the dosage form. These changes may arise from changes in physicochemical characteristics of the drug substance and/or excipients or to the formulation itself, changes in the manufacturing process, shipping and storage effects, aging effects, and other formulation and/or process factors.

The VDC system is the most common in vitro drug release system. It is a reliable and reproducible means of measuring drug release from semisolid dosage forms. In addition to the VDC system, an immersion cell and modified flow-through cell system can be used to assess drug release from semisolid dosage forms.

18.5 APPLICATIONS OF THE IN VITRO RELEASE TEST

Application of IVR testing in drug development and its value in topical drug products quality assurance was discussed extensively in scientific workshop entitled “Assessment of Value and Applications of In Vitro Testing of Dermatological Drug Products” (3). The report indicates that the IVR methodology is based on sound scientific principles and is of value in assessing product quality. It also indicates that the IVR should not be used to compare fundamentally different types of topical formulations such as creams, ointments, and gels. IVR testing may find a future use as a quality control tool to assure batch-to-batch uniformity, just as the dissolution test is used to assure quality and performance of solid oral dosage forms.