

although they are probably rare, when it will be worthwhile to continue stability testing on an R&D formulation that we know will never be marketed just because we are interested in the stability of a new excipient that we have included in the formulation.

5. MODES OF DEGRADATION

5.1. Chemical

Chemical degradation (solvolysis, oxidation, etc.) is common and is described in subsequent chapters of this book. Our knowledge of kinetics can be of material assistance in dealing with chemical degradation.

5.2. Physical

Physical degradation can be caused by a range of factors (e.g., impact, vibration, abrasion, and temperature fluctuations such as freezing, thawing, or shearing). Physical testing is described in Chapter 10.

Unfortunately, in many instances, our knowledge of the exact mechanisms involved in physical degradation is incomplete. It is also unfortunate that a number of the physical test methods that could be used in evaluation of physical stability (e.g., tablet friability, tablet impact resistance, suspension redispersibility, or injection syringeability) are still nonofficial and variable. It is noteworthy that it was not until 1997 that official standardized test methods for the quantification of bulk and tap density were introduced into the USP, although such tests have value in helping to evaluate compressibility.

5.3. Biological (Especially Microbiological)

In North America, Japan, and Western Europe it is microbiological factors that are most likely to be involved in biological stability problems. However, in some parts of the world rats, roaches, ants, and other nonmicrobiological organisms can be responsible for stability problems.

5.4. Limitations of This Classification

Useful though the above tripartite classification of degradation mechanisms may be, there is a danger that its use may overcompartmentalize our approach to drug product stability. This can be dangerous. In fact, many stability problems involve more than one mechanism. For example, insufficient antioxidant in a rubber condom may result in oxidation of the device by a chemical mode. However, the effect that may be detected is loss of tensile strength, which is, of course, a physical parameter.

6. THE ESSENTIAL ELEMENTS OF A HIGH-QUALITY, COST-EFFECTIVE STABILITY PROGRAM

6.1. Commitment of the Organization to Quality

It is essential that throughout the organization responsible for the development and production of pharmaceutical products there be a *true* commitment to quality.