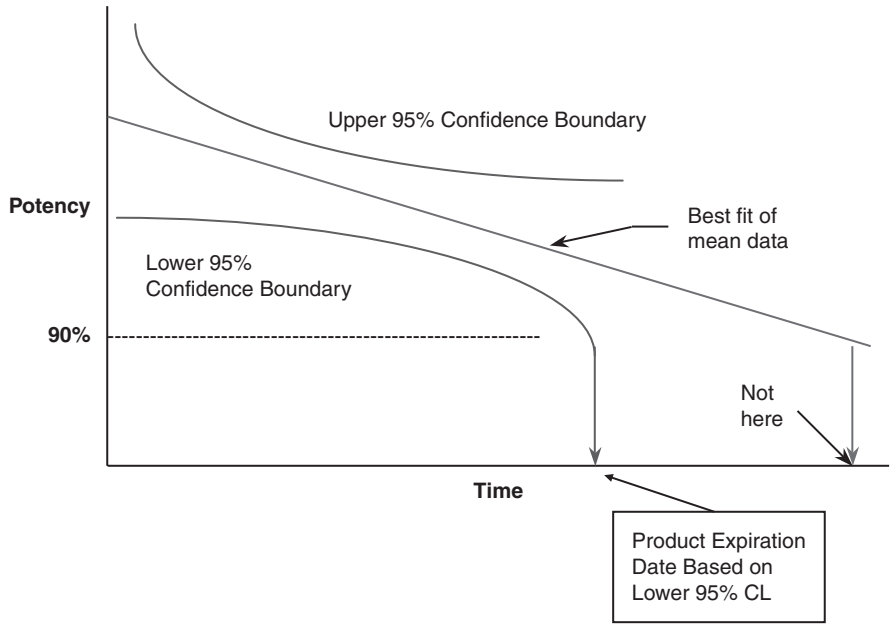

Figure 24-1 Regression analysis of stability data.

microbiological issue than chemical/physical stability issue. In fact, European guidelines (13) require immediate usage (not more than three hours after reconstitution) if the product is not preserved with antimicrobial preservatives or to use within 28 days if the product is preserved.

Many drugs are sensitive to light and are protected from excessive light exposure via packaging (e.g., amber glass, amber bags, always maintaining drug product in its secondary package) and storage in dark conditions. Data on light stability should be an integral part of *stress* testing and should be conducted on at least one primary batch of the drug product (5,6). The unprotected bulk drug, fully exposed drug product, & drug product in marketed package are all to be stress tested for light stability. It must be demonstrated that the product is adequately protected from exposure to light if it is unstable in the presence of light. The light source can be any source with output similar to D65 (outdoor daylight) or ID65 (indoor daylight) standards defined in ISO 10977 (1993). Typical light sources include the following:

- Cool, white fluorescent lamp
- Xenon or metal halide lamp
- Near-UV fluorescent lamp.

The exposure requirements are an overall illumination of >1.2 million lux hours and integrated and a near-UV energy of >200 watt hr/m2. Such exposure conditions are approximately equal to a five-month exposure period under normal room light (800 lux) for 10 hr/day.

After a product has been approved for commercial use, the first three commercial lots are stability tested. Afterwards, a minimum of one lot per year of each dosage form and each container-closure system of the product is placed on long-term stability testing. Special stability testing must be conducted whenever changes or deviations occur unless it is determined that stability testing not required (14).

Inherent in all aspects of design of appropriate stability studies, including sampling, sample times, number of replicates, defining validation of analytical methods, and evaluation of all data is the use of valid statistical procedures (15). Regression analysis is considered an appropriate approach by the FDA in evaluating stability data for any quantitative attribute and establishing a retest period or shelf life (16). Other examples of statistical methods employed in stability testing include poolability tests (17, 18) and statistical modeling (19).