where β_0, β_1, and β_2 are the parameters of the second-degree polynomial, and t is the time. The degradation rate is a function of time, which is not constant in this case.

$$\delta = \beta_1 + \beta_2 t \tag{8.24}$$

Degradation at the storage temperature can be predicted from the degradation at elevated temperatures as:

$$D = \beta_0 + (\beta_1 + \beta_2 t)t\lambda \tag{8.25}$$

The acceleration factor, λ, is based on the Arrhenius equation. Statistical tests indicated that the use of this equation was appropriate in this case. Shelf life predictions were also verified by real-time stability testing results.

8.2.4.2.2 Similar Products

When most of the assumptions required to use the Arrhenius equation are not satisfied, comparisons with a product of a known stability are performed to assess shelf life. This approach requires having a similar product with a known shelf life to be used as a control. The new or test product is expected to demonstrate a similar behavior to the control, as they belong to the same family and have the same kinetics of degradation. Side-by-side testing of the control and test products at different elevated temperatures is then performed. It is necessary to assume that the same model can represent the degradation pattern at each elevated and storage temperature.

If the degradation patterns of the test and control samples at the same elevated temperatures are not statistically different, it can be assumed that they will degrade similarly at the storage temperatures. The closer the elevated temperatures are to the storage temperatures, the more confident we can be in making this statement. The experimental protocols used are similar to the protocols used with the Arrhenius equation. Degradation patterns of a family of products at certain elevated temperatures can be modeled and used to check the behavior of a new product that belongs to the family.

The complications in calculations arise mainly because of the degradation models that are usually nonlinear mixed models, where a lot-to-lot variability is the random component. Estimation of the parameters of the models is important for the accuracy of shelf life predictions. It is recommended to use the maximum likelihood (ML) approach to estimate these parameters. As no closed-form solutions for ML estimates exist, an iterative procedure is performed, starting with some initial values for the parameters and updating them until differences between consecutive iterations are minimal and the estimates converge to their final value. Initial values are usually chosen by experience. The closer these values are to the final values, the faster the model will converge. A suitable program is nonlinear mixed model procedure of statistical analysis system for data analysis (3). Values of the real-time stability model converge relatively quickly, while several initial values for the parameters of the accelerated model are tried before they converge. Statistical theory and the applicability of ML estimation are common in the literature, and many computer routines are available to facilitate data analysis. However, experience with the modeling and estimation