Obviously, if a product is not stored in accordance with label instructions, the expiration date cannot necessarily be relied on.

8. SOME POSSIBLE STRATEGIES TO IMPROVE SHELF LIFE

It is fortunate that many drug substances and products are inherently stable; thus, with little difficulty, we can justify a shelf life of 3 years or more. However, there are drug substances that are very much more liable to degradation, and it may require much skill and hard work to develop a product with a shelf life that is commercially acceptable. Since this book is not focused on formulation *per se*, this section only outlines some of the general approaches that might be considered in efforts to improve shelf life.

8.1. Sampling and Analytical

Examination of Fig. 1 reveals that the more scatter that we have on a stability plot the wider the 90% zone of confidence will be. If we were somehow able to obtain experimental points that all fitted exactly on the regression line, then both the upper and lower 90% confidence bounds would also be on the mean regression line; thus our estimate of the conformance period would be given by the intersection of the regression line and the 90% potency line. Clearly, this would substantially extend the shelf life that we could legitimately claim. Of course, it is impossible to obtain such perfect data that the 90% confidence zone has no width whatsoever. However, anything that we can do to reduce its thickness will improve our shelf life.

There are two main causes for the fact that stability plots, such as that shown in Fig. 1, show scatter, *viz.*, sampling error and analytical error. Anything that we can do to reduce either or both of these errors will improve our shelf life without our having made any change to the formulation or process used for our product.

It is not often easy to see how sampling error could be reduced. Possibly the use of near-infrared spectroscopy for single-tablet assay (see Chapter 18) of the same known, individual tablets throughout the shelf life testing period, and averaging the data so obtained at each time point, might be a practicable method to reduce error due to content uniformity variation (14). Perhaps reduction of sampling error is one of the incentives that we have in making sure that all samples are tested on time.

In terms of analytical error, if we can improve precision and reproducibility we will slim the 90% confidence envelope and improve our shelf life. In some cases, it has been shown that the extra cost of a more sophisticated assay may be justified by the improvement in shelf life that results.

8.2. Statistical

If testing of samples is continued beyond the point at which degradation has reached the 90% confidence of the label claim value, we move the narrow "waist" of the 90% confidence zone to later times and thus improve our shelf life. This valid statistical approach was specifically mentioned in the 1984 FDA Stability Guidelines.