Even if no change of formulation, process, or site of manufacture is contemplated, there may be other reasons for additional stability studies. Unfortunately, it is not unknown for a new product that we believe to have been fully validated with respect to all quality attributes (including stability) to exhibit unexpected stability problems. These problems may progressively develop in a most insidious way, affecting all batches or, in some instances, only some batches intermittently. In either event, troubleshooting directed at identifying the cause and then taking appropriate remedial action is necessary.

Similarly, if complaints from patients, health professionals, or others involve stability problems, it is obviously important that stability group personnel should be involved in the evaluation of the problem and be consulted when it is decided if remedial action is required.

3.6. Product in the Channel of Distribution

It is not sufficient to restrict our concerns about drug product stability to the quality of the pristine, freshly manufactured material that we regard with justifiable pride as it waits in our warehouse for distribution after it has been cleared from quarantine by our QC/QA (Quality Control/Quality Assurance) department. Of course, it is normal to store some stability samples in our stability storage areas (retained samples). However, the evaluation of samples that have been stored under the utopian conditions in the manufacturer's stability storage areas is of limited value. Samples retained for stability testing are not dropped off the back of a truck; they are not left on a loading dock in the blazing sun; nor are they left in the freezing cold. Thus it is somewhat unrealistic to expect retained stability samples to reflect accurately the stability status range of products that are in the channel of distribution. As is discussed in Chapter 18, there is now increased concern about the stability status of products in the channel of distribution.

3.7. Product Under the Control of the Patient

There is good reason to believe that, in many instances, the conditions under which patients store their drug products is far removed from optimal. At one time some regulatory authorities were considering the possibility of requiring shelf lives that could be guaranteed right through to the time when the patient used the last dose of the product. It is now probably generally appreciated that this idea is not feasible. It certainly is, however, most appropriate that pharmacists should take time and trouble to counsel patients on the appropriate ways to store drug products.

3.8. *In Vivo* Stability

The final stability concern is the degradation of the drug *in vivo*. In particular, the hydrolysis of drug at the low pH conditions of the stomach can be particularly serious. The traditional answer to this particular problem is to enteric coat a tablet. In the past, the materials used as enteric coats were not always effective. The polymers now available for enteric coating are much more reliable (11).