Sometimes, every lot of clinical supplies may be on stability. There is a periodic evaluation of data by direct comparison of the data to established specifications or by statistical evaluation (e.g., regression analysis), to assure the continued suitability of the clinical supplies in the field.

IV. PROPOSED PRODUCT

The proposed product stage covers the period from selection of the final formulation to NDA filing; it roughly corresponds to the period during which Phase III clinical studies are conducted. At this point in the development process, a substantial amount of fundamental stability information will be available. Any inherent sensitivities of the active ingredient have been determined, significant degradation products identified, and major stability-limiting characteristics of the various experimental formulations have been detailed.

The objectives of this stage are (1) to assess the stability performance of the selected formulation for the purpose of defining storage conditions and stability-limiting factors; (2) to confirm degradation pathways in the selected formulation; and (3) to establish the initial expiration dating period for the container–closure system in which the product is to be marketed.

A greater variety of test data can be collected during this phase to establish the stability-limiting factor(s). Both short-term accelerated studies and long-term studies at proposed label storage conditions are conducted. The tests and assays to be conducted should be essentially the same as those given in Section III.C. Many of the tests and assays included in the stability protocols utilized during this stage will not be included in the protocols in later stages because they will be deemed redundant or unnecessary. In general, at least three lots of the proposed formulations are placed on test in the proposed container–closure systems. These lots are usually produced in production-scale equipment (Table 5).

There are cases when scale testing may not be scientifically necessary. If a stable, noncomplex formulation (formulation defined as a fixed ratio of active ingredient(s)/excipients) is being developed in several strengths or concentrations, full testing should be conducted on *the highest and lowest strength or concentration*. The data from this testing regimen will provide information to fully characterize the stability performance profile of formulations *at all intermediate strengths*. For example, the lowest concentration would test the case for which the package surface area per milligram of active ingredient is at a maximum, whereas the highest concentration would test the case for which the probability of nucleation and crystal growth (solutions) or agglomeration (suspensions) is maximized.