If, in practice, it has been demonstrated that they are not formed in the confirmatory studies, these degradation products need not be examined further. Confirmatory studies should then be undertaken to provide the information necessary for handling, packaging, and labeling. Normally, only one batch of drug substance is tested during the development phase, and then, the photostability characteristics should be confirmed on a single batch selected, as described in the parent guideline, if the drug is clearly photostable or photolabile. If the results of the confirmatory study are equivocal, testing of up to two additional batches should be conducted. Samples should be selected as described in the parent guideline.

Care should be taken to ensure that the physical characteristics of the samples under test are taken into account and efforts, such as cooling and/or placing the samples in sealed containers, should be made to ensure that the effects of the changes in physical states, such as sublimation, evaporation, and melting, are minimized. All such precautions should be chosen to provide minimal interference with the exposure of samples under test. Possible interactions between the samples and any material used for containers or for general protection of the sample should also be considered and eliminated wherever not relevant to the test being carried out.

As a direct challenge for samples of solid drug substances, an appropriate amount of sample should be taken and placed in a suitable glass or plastic dish and protected with a suitable transparent cover, if considered necessary. Solid drug substances should be spread across the container to give a thickness of typically not more than 3 mL. Drug substances that are liquids should be exposed in chemically inert and transparent containers.

At the end of the exposure period, the samples should be examined for any changes in physical properties (e.g., appearance, clarity, or color of the solution) and for assay and degradants by a method suitably validated for products likely to arise from photochemical degradation processes. Where solid drug substance samples are involved, sampling should ensure that a representative portion is used in individual tests. Similar sampling considerations, such as homogenization of the entire sample, apply to other materials that may not be homogeneous after exposure. The analysis of the exposed sample should be performed concomitantly with that of any protected samples used as dark control if these are used in the test.

The forced degradation studies should be designed to provide suitable information to develop and validate test methods for the confirmatory studies. These test methods should be capable of resolving and detecting photolytic degradants that appear during the confirmatory studies. When evaluating the results of these studies, it is important to recognize that they form part of the stress testing and are not therefore designed to establish qualitative or quantitative limits for change.

The confirmatory studies should identify precautionary measures needed in the manufacturing or formulation of the drug product and whether light-resistant packaging is needed. When evaluating the results of confirmatory studies to determine whether change due to exposure to light is acceptable, it is important to consider the results from other formal stability studies in order to ensure that the drug will be within the justified limits at the time of use.

8.2.5.7.2 Bracketing

For the study of drug substances, matrixing is of limited utility, and bracketing is generally not applicable.