

This guidance provides Process Validation Sampling guidelines for non-sterile liquid (solutions and suspensions) and semi-solid (ointments, creams, pastes, gels and lotions) drug product dosage forms.

The purpose of this guidance is to provide the general principles and approaches that should be considered for sampling non-sterile liquid/semi-solid dosage forms. It is not intended to provide definitive validation sampling plans for use in every circumstance.

1. Validation of Non-Sterile Liquid Dosage Forms -Solutions and Suspensions  
Sampling of solutions pose few special concerns as all materials are in solution and each sample is the same as every other sample if homogenous.

For solutions the key aspects that should be addressed during validation include assurance that the drug substance and preservatives are dissolved and that the solution has been adequately mixed.

Suspensions on the other hand, by the nature of their formulation, are prone to separation or settling and pose special concerns for sampling and testing. For oral suspensions, there is the additional concern with uniformity, particularly because of the potential for segregation during manufacture and storage of the bulk suspension, during transfer to the filling line and during filling. Depending upon the viscosity, many suspensions require continuous or periodic agitation during the filling process. If delivery lines are used between the bulk storage tank and the filling equipment, some segregation may occur, particularly if the product is not viscous. During each process step in which separation or settling could occur, comprehensive sampling and testing should be performed to ensure that the process is performing as designed.

Refer to the Appendix for validation sampling guidelines for these categories of products.

2. Validation of Non-Sterile Semi-Solid Dosage Forms -Creams, Ointments, Pastes Gels, and Lotions

Ointments, Creams, Pastes, Gels and Lotions are often prone to separation or settling and may pose special concerns for sampling.

In formulations where the active pharmaceutical ingredient (API) is soluble in the base or vehicle, API uniformity would be expected to present less of a problem than those formulations where the API is insoluble and is suspended, as may be the case with certain semi-solid dosage forms. In the latter case, API uniformity would depend upon control of particle size, and the use of a validated mixing process.

A concern is mixer design and the presence of "dead spots" where quantities of the formula are stationary and not subject to mixing. Sampling points should include these points as part of the sampling plan.