**General Discussion**

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.

 

## APPENDIX A: SAMPLING OF NON-STERILE LIQUID AND SEMI-SOLID

### III. Dosage Form: SEMISOLIDS

<table>
<tr><th>Manufacturing Stage</th><th>Process Validation Sampling Guideline</th></tr>
<tr><td>Mixing</td><td>Sample from the manufacturing vessel from the top, middle and bottom of the container for homogeneity of the API by testing the samples for potency. The number of samples to be taken will depend on the vessel geometry. If satisfactory data are available on similar formulations, using the same/equivalent equipment and mixing process, less than nine samples can be justified (e.g. one sample from top, middle and bottom of the mixer).<br><br>Mixing vessel<br><table><tr><th>Sample Location</th></tr><tr><td>1. Top-Left Side</td></tr><tr><td>2. Top-Right Side</td></tr><tr><td>3. Top-Middle</td></tr><tr><td>4. Left 3-6" below surface (Middle)</td></tr><tr><td>5. Right 3-6" below surface -Middle</td></tr><tr><td>6. Middle-Middle</td></tr><tr><td>7. Left - Bottom</td></tr><tr><td>8. Right - Bottom</td></tr><tr><td>9. Middle- Bottom</td></tr></table>Note 1: Sufficient sample volume should be taken from each sampling location to allow for the defined testing, together with investigation of any OOS or unexpected results.</td></tr>
<tr><td>Holding</td><td>Refer to Holding time sampling guidance</td></tr>
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