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.

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.

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

II. Dosage Form: SUSPENSIONS

<table>
<tr><th>Manufacturing Stage</th><th>Process Validation Sampling Guideline</th></tr>
<tr><td>Mixing</td><td>Manufacturing Vessel Samples:
Samples should be taken from the manufacturing vessel after the completion of the final mix step. Samples are taken and tested for potency and preservative content (if applicable) to prove product uniformity of API and preservatives (if applicable) at the end of bulk manufacture.

A possible sampling scheme would be as follows:

<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>
<tr><td>10. Bottom (from drain if possible)</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.

Note 2: Take samples from Top, Middle and Bottom of the tank for viscosity testing.</td></tr>
<tr><td>Holding</td><td>If packaging of the lot is delayed and the suspension is transferred to a Holding Storage Tank, Refer to Holding time sampling guidance</td></tr>
<tr><td>Filling/Packaging</td><td>Take 3 samples at 10 sampling points (including the end of the batch/lot) distributed throughout the packaging process. Samples are taken to prove product uniformity of API and preservatives (if applicable).
Also refer to the Semisolids Filling section (below).</td></tr>
</table>

