

This guidance provides Process Validation Sampling guidelines for non-sterile solid dose 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 solid dosage forms. It is not intended to provide definitive validation sampling plans for use in every circumstance.

1. Validation Sampling of Granulations and Powder Blends:

There are many concerns regarding blend uniformity sampling, for example:

- Inappropriate sample thief technology;
- Powder segregation of samples may occur after sampling;
- Difficulty in proving that the blender sample plan will be representative of worst-case locations;
- Segregation of blend that can occur during discharge, storage, and transport prior to final processing.

Sampling concerns can be overcome if the sampling method is known and demonstrated to be capable. Refer to Appendix A for validation sampling guidelines for this category of product.

2. Validation Sampling of Solid Dosage Forms (Tablets, Capsules):

Solid dosage forms typically provide many opportunities for applying appropriate and scientifically sound sampling approaches.

Refer to Appendix B for validation sampling guidelines for this category of product.

The Product Quality Research Institute (PQRI) Blend Uniformity Group has developed an approach to demonstrating blend uniformity by combining blend testing with in-process dosage unit compendial testing. This approach postulates that the analysis of finished tablets/capsules can support or provide statistical evidence that a failing blend result was due to poor sampling or handling technique.

The PQRI approach was adopted in the FDA, Draft Guidance for Industry: Powder Blends and Finished Dosage Units – Stratified In-Process Dosage Unit Sampling and Assessment of October 2003. The sampling recommendations in this guidance are based on this document. Refer to Appendix C for validation sampling guidelines and flow chart. Other sampling approaches and acceptance criteria may be used if they are scientifically and statistically justified.