**Regulatory Basis:**
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

**General Discussion**

This document provides an example of documentation to support the use of Continuous Quality Verification (CQV) for demonstrating that a manufacturing process is in a validated state.

CQV is an alternative approach to process validation. This document includes example documentation for when the CQV approach is used in lieu of a more traditional validation approach.

This document provides an example of key information to include in documentation that will contribute to the overall CQV package. Documentation for a process may include some or all of the content described here, depending on the nature of the process. Other documentation may also be needed to support a CQV approach. No particular format has been defined for documenting this information and the necessary information may appear in a single report or multiple reports.

The types of documentation described here are categorized by the main elements into which CQV is divided. See document on 'Documentation to Support CQV' for more detailed information about each element.

**Example: A drying process**
**The process:** A granulated drug product mixture is dried using a fluid bed dryer. Air is passed through the mixture to remove moisture, providing a mixture for compression into tablets.

**1. Process Understanding documentation** for this process includes a brief description of a process to dry a granulated drug product mixture, such as that described below.
The product is dried with a fluid bed dryer, which uses a through-the-bed flow pattern with air passing through a distribution plate and into the drying chamber, where it lifts the granular product and maintains the granules in a fluidized state. This bed of granulate particles displays fluid-like properties like that of a liquid. This fluidization provides intimate contact between particles and the warm (about 40 $^{o}$C) air stream, providing an efficient means of transferring moisture away from the product particles. The fluidized mixture enters the expansion chamber, where the velocity of the air is reduced, allowing entrained particles to fall out of suspension and back into the bed. Exhaust air is passed through filter socks to capture smaller particles.

 

2. **Continuous Quality Monitoring and Control** for this process uses a probe linked to a nearby NIR spectrometer with a fiber optic probe fitted into the dryer with a compression fitting (see Figure 2). Digital output sent from the dryer control system governs software acquisition of data during processing of a product batch. NIR spectra are obtained every 3 seconds for the duration of drying. For equipment and software information, see Table 2.

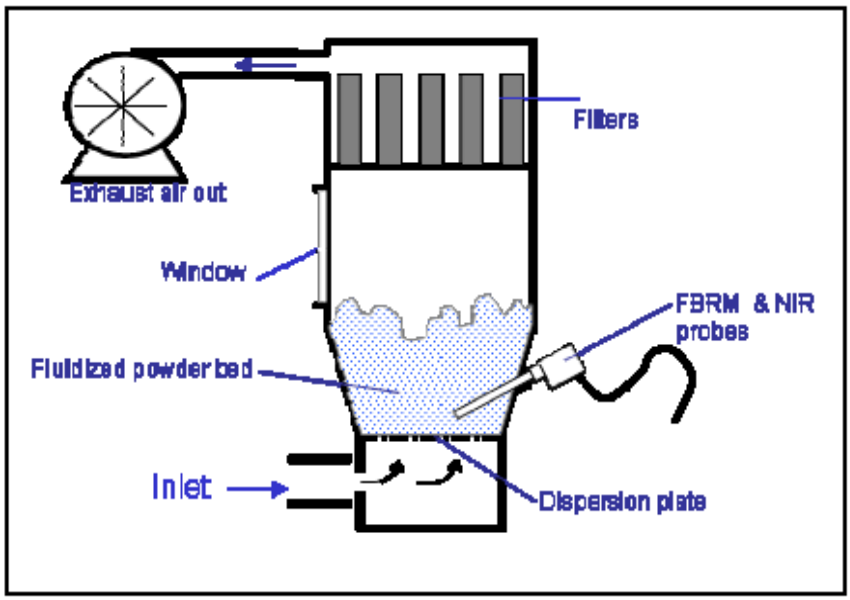


**Figure 2. Schematic Representation of Fluid Bed Dryer PAT installation**

 

**4. Continuous Process Improvement**

A plan should be established for the analysis of process trends. This plan should include a recommendation for the appropriate frequency for evaluation of process trends and what data should be reviewed. For this drying step, an appropriate plan for assessing process trends would be a post-campaign review after each production campaign to verify that the expected moisture results are consistently being obtained. Alternatively, the review of process trends and knowledge acquired from deviation investigations could be performed as part of the Periodic Review or Annual Product Review work processes.

Data from monitoring of the CPPs and critical controls should be included in the trend evaluation. For this process, the evaluation should include trending of data for the drying air temperature and the NIR in-process monitoring of the drying endpoint. A Right First Time study of the results could provide effective tools for the on-going analysis of the process.

 