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.

The rate of moisture removal is rapid during the first phase of drying, with mostly unbound, free water being removed. The product temperature changes very little during this phase because of evaporative cooling. The second phase removes free moisture from the surfaces of particles, and the rate of evaporation during this phase is relatively constant. This phase exhibits a gradual, relatively small increase in product temperature. In the third and final drying phase, moisture migrates from the inner interstices of particles to the outer surface, and this becomes the limiting factor that reduces the drying rate during this period. The drying rate declines during this phase, and product temperature increases as evaporative cooling has little effect on the particles.

Excessive moisture remaining in the product mix results in an inconsistent tablet dissolution profile, so moisture of the dried granulated mixture has been identified as a critical quality attribute (CQA). Over-drying the product results in some erosion of particle size and adversely affects the compression of the product mix into tablets, so too low a moisture level is also detrimental.

Product drying for a fixed period of time results in undesired variability in moisture levels.

Monitoring of temperatures (product temperature within the dryer and external temperature of the exhaust air) results in less variability in moisture levels, but requires sampling and measurement with a moisture analyzer to verify that the expected moisture level is obtained.

With temperature monitoring, additional drying may occasionally be required to meet the Loss on Drying (LOD) requirement of 1.5 to 2.5%. This LOD requirement is closely correlated with the moisture level for the dried mixture.

Continuous monitoring of the drying operation with near infrared (NIR) spectrometry for moisture content provides better knowledge of the progress of the drying operation.

While air flow, and temperature are considered potential critical process parameters (CPPs) for this operation, monitoring with NIR provides superior control and permits relaxation of time and temperature limits. Air flow and drying temperature must still be controlled within reasonable limits to reduce process variability in terms of the time needed for the drying operation. However, continuous monitoring with NIR, while not itself an operating parameter, is identified as the critical process control necessary to insure consistently meeting the product's moisture CQA. Table 1 summarizes the potential CPPs and controls for this step of the process.