

Case study:**Batch mixing of Pharmaceuticals****Application :**

One of the most critical operations in the production of medicines is the process of mixing base materials with active ingredients or antibiotics. For this application the Vrieco-Nauta® conical mixer is often used to prepare the final mixture and for feeding the product into the tableting machine.

**Critical parameters in this process are:**

- Mixing accuracy, every tablet has to contain a similar amount of active ingredient.
- Sensitivity of fragile "agglomerated" products.
- Differences in bulk density and flow characteristics of the different ingredients.
- Segregation during discharge to tablet machine.
- Batch integrity of the mixture
- Cleanability of the mixer

Process:

The requested production capacity is 1.700 liter per day which includes all operations Like charging, mixing, tablet pressing , cleaning and drying of the complete system.



- The basic receipt contains:
- Micro crystalline cellulose 69 W %,
- Density 0.42
- Particle size 0.12 mm.
- Spray dried granules with active ingredient 29 W %
- Density 0.80
- Particle size 0.75 mm
- Lubricant 0.25 W %
- Density 0.20
- Particle size 25 mU

The differences in particle size, bulk density, fragile nature and quantity in the batch results in a challenging mixing operation.

- Distortion of spray dried granules might cause the release of active ingredient and can give trouble charging the tablet press.
- Differences in bulk density and size of the individual components increase the risk of segregation during mixing.
- Mixing the lubricant in homogeneously is necessary for the quality of the tablets.



Solution:

The selected mixer type is a Vrieco-Nauta® mixer type 20 MDC-43 in Pharmaceutical execution with an effective working volume of 1.700 litres. The mixer including controls is designed and validated in accordance with the URS and FDA standards

The central outlet in combination with the conical vessel guarantee a mass flow out of the mixer without the risk of segregation. During the design and manufacturing full attention is given to the internal and external cleanability of the mixer

Cleaning:

Due to batch integrity and the change of formulations, cleanability of the blender is of vital importance. Special cleaning facilities including fully automatic CIP system is available. The CIP system will be supplied in compliance with Gamp IV and is adapted for 21 CFR part 11.

Conclusion:

The lubricant has a cohesive nature, this often results in the need of mixing energy to realize a homogeneous mixture. Additional mixing energy often results in product distortion and the creation of fines.

The Vrieco-Nauta® Conical Agitated Blender has **proven** to be the technology for mixing of primary and secondary pharmaceuticals for many applications. Hosokawa offers you a record of more than 1.000 successful references in the pharmaceutical industry.

