

the preceding wash solvent, since washing the primary filter cake directly with a hydrocarbon almost invariably results in both product and impurity deposition leading to the formation of agglomerates and a failure to meet the target purity. The approach described in the previous section can be used to identify solvent ratios at which product or impurity deposition is minimised or eliminated.

In summary, the essential characteristics of a wash solvent are:

- Full miscibility with the primary solvent at the isolation temperature.
- The product should exhibit appropriately low solubility in the wash solvent and declining solubility in mixtures of the primary solvent and wash solvent as the proportion of wash solvent increases.
- Product should not be precipitated when contacting a saturated solvent with the proposed wash solvent.
- Solvents used in the later stages of API manufacturing are usually selected from category 3 in ICH guideline Q3C (R6).³
- It may be necessary to displace a good wash solvent with a suitable non-solvent to avoid granule formation and to facilitate drying.

13.4.6 Deliquoring the Washed Cake Prior to Drying

The final processing step prior to drying is deliquoring. Obviously it is desirable to minimise the drying duty by removing as much solvent as possible from the wet cake prior to drying. In traditional batch filtration this is achieved by blowing nitrogen through the wet cake. This is an area where a centrifuge offers some advantages over conventional pressure filtration.

13.5 Drying

From a process engineer's perspective drying is dominated by the evaporative mass transfer through which the solvent is removed and the associated heat transfer required to drive this process. From a material scientist's perspective, the focus is on the changes drying brings about in the API particle properties. These two perspectives need to be combined to achieve the desired goal of efficient drying to deliver a solvent free non-granulated API with good powder flow properties.

The key step in understanding the impact of drying on API particle attributes is to realise that most evaporation takes place at the surface of the wet cake. The simplest way to illustrate this is to take a sample of solvent wet filter cake which contains a low level of a soluble coloured impurity and leave it to dry without agitation. During drying the vast majority of the coloured impurity is transported to the surface of the wet powder resulting in a highly coloured lump of material which when broken apart reveals a much lighter core. The impurity is transported with the solvent to the surface through capillary forces acting on the film of residual liquid covering