mother liquor based impurity carry over to 0.4% of that in a saturated cake. Whilst this rule of thumb is useful the eventual outcome is highly dominated by the particle properties.

13.8.5 Drying

A number of processes may accompany the desired process of solvent removal. Frequently a dryer also functions as an agglomerator/granulator. In all instances where the product has solubility in the solvent(s) removed during drying the dryer functions as an evaporative crystallizer. The mass of material deposited during drying corresponds broadly to the solubility of the product in the mass of solvent removed at the drying temperature. However, this deposition is not uniform throughout the process volume as drying is a surface phenomenon, thus the migration of solvent to the evaporative surface provides a mass transport mechanism for dissolved product and impurities. Whilst the consequences of this uneven deposition can be mitigated by agitation during drying, an agitated drier also operates as a crystal breaker, especially for needle-like particles.

It is useful both to tray-dry some material from laboratory experiments and to subject a subsample of the same batch to intense agitated drying. These two materials typically represent the extremes of the attainable product attributes, thus evaluating the differences in performance between these two materials is very informative. It is recommended to think holistically across the whole process and identify the important parameters which should be investigated.

13.8.6 Further Troubleshooting Strategies

When addressing an isolation problem it is obvious that a researcher should start with filtration, washing and drying but it is important to be aware that this may point back to the crystallization step, for example, a change in filtration rate, cake bulk density, drying time and product assay may be linked to a change in CSD from the crystallization process for example linked to the presence of additional fines. It is important to be able to distinguish between this and for example issues arising from incomplete washing of a cracked filter cake.

Dealing with chemical impurities it is essential to both identify and quantify impurities. The identity may suggest the source and may possibly indicate a mechanism of incorporation. The quantity is useful in understanding the magnitude of the challenge, a stoichiometric quantity of a by-product is a different challenge to a smaller quantity of a structurally similar impurity.