to 35 °C, while the nucleation temperature was supplied as 40 °C. The generation of supersaturation rates was tested by applying different cooling rates and trouble free crystallisation was running for twice the residence time but encrustation was then observed initially in zone 1, later zone 2.

On the examination of the operational conditions, all the appropriate procedures and protocols were followed; would connecting the exit stream back to the feed tank have any influence on encrustation? It turned out that this was the main factor causing the encrustation and when the exit stream was fed to a separate tank, the encrustation issue was resolved. What were the explanations? Crystallisation is a purification process and the solid after crystallisation would be purer than that at the start. Directing the exit stream back to the feed tank acted effectively to alter the purity of the starting materials, even though the temperature of the feed tank was sufficiently high to dissolve the incoming colder stream. It is known that purer materials nucleate later than less pure materials as impurity drives heterogeneous primary nucleation. This means that some would be nucleated at higher temperatures, others at lower ones; the range of nucleation temperatures observed supports this line of thinking. The further postulation, following this line of inquiry, was that nuclei generated at higher temperatures would not be sufficient in mass to complete the nucleation, leading to encrustation, in comparison to nuclei generated at the same temperature in the earlier residence time.

3.5.4.6 Case 6 – Due to Oil out

A cooling crystallisation of an organic compound was undertaken in a NiTech DN15 crystalliser at a lab of a chemical company in Europe; the starting temperature was 75 °C and was cooled to 15 °C. The nucleation temperature was given as about 55 °C from lab batch experiments. Two temperature zones were set up: 75 to 55 °C and 55 to 15 °C at a cooling rate of 5 and 1 °C min^{-1} respectively. Just before reaching the nucleation temperature, the solution became cloudy and the formation of a second liquid phase, *i.e.* oiling out, was noticed. Nucleation took place after oiling out and some oil was stuck on the crystal solids, leading to some encrustation in DN15 and lower crystal purity. Generally, the larger the oil droplet size, the smaller the crystal size. Oscillation conditions seemed to control the crystal size. The trend of crystal size changing with mixing was similar to the work by Takasuga and Ooshima (2014)[212] who explained that the generation of small crystals was due to the fact that the primary and secondary nucleation frequencies increased with the droplet size, while the generation of large crystals was due to the growth of a small amount of crystals generated in small droplets through the consumption of API in the remaining crystal-vacant droplets.

Oiling out has been observed during cooling crystallisation of complex molecules like pharmaceuticals,[213] proteins[214–216] or polymers from