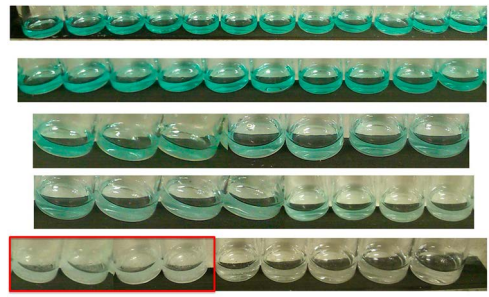

Figure 13.10 Sequence of 10 drop aliquots of mother liquor/wash solvent displaced during filter cake washing 4 of the 46 samples (numbers 38 to 41) contain suspended crystals. (Data collected by Chris Price & Sara Ottoboni University of Strathclyde).

saturated until all the wash has been added. The outlet of the filter is connected to a fraction collector which allows sequential small aliquots, *e.g.* 10 or 20 drops of filtrate/wash solution, to be collected and checked for product/impurity crystallization by visual inspection and the product loss in washing to be quantified by analysis. An example of the resulting aliquots is shown in Figure 13.10.

The appearance of crystals in aliquots 38 to 41 indicates that there is a point in this washing procedure where the combination of mother liquor and wash solvent results in material being forced out of solution. If the washing process had been slower, for example using a thicker cake or targeting a longer contact time between the wash solvent and mother liquors, some of this crystallization could have taken place in the filter cake resulting in the crystalline bridges forming between particles resulting in granules forming in the product. An alternative wash solvent or solvent composition should be sought to avoid this.

13.4.5 Washing to Avoid Granule Formation During Drying

As well as the mechanism of granule formation due to product being forced out of solution during filter cake washing described in the preceding text it also very common to form granules during drying. The reason for this is the solubility of the API in the solvent which is to be removed during drying. Any solvent not removed during the final deliquoring stage of filtration is removed by evaporation and whatever material was dissolved in that solvent is deposited in the filter cake as additional solid. Knowing the solubility of the API in the final wash solvent and the loss of mass on drying allows the mass of material deposited to be estimated. Clearly it is desirable to leave the crystals wet with a non-solvent to avoid this undesired effect. Hydrocarbons, in particular *n*-heptane, are used to achieve this objective since the solubility of typical drug molecules in hydrocarbons is negligible. However, this requires an additional washing step to displace