P035 Unconventional ultra scale-down techniques for active pharmaceutical ingredient filtration and size reduction

E.O. Ojo[1,2], **A. Rayat**[2], **C.J. Price**[1], **C.J. Brown**[1], **M. Hoare**[2], **A. Johnston**[1], **A.J. Florence**[1]

[1] EPSRC CMAC-Future Manufacturing Research Hub, Technology and Innovation Centre, University of Strathclyde, 99 George Street, Glasgow, G1 1RD, UK

[2] The Advanced Centre for Biochemical Engineering, Department of Biochemical Engineering, University College London, Gordon Street, London, WC1H 0AH, UK

The use of scale down devices for early-stage process development enables early availability of experimental data, indicative of large-scale processes. In this work, an automated ultra scale-down (USD) filtration and a shear device which when used together allow the study of the recovery of active pharmaceutical ingredients (API) of different crystal particle size distributions at 10s of milligram-scale. For an early understanding of the process interactions based on a simple DoE design, a pressure difference of 70 kPa was observed to be significant for the filtration process when the 5 m filter pore size is used. At all other conditions investigated, the outcomes of the USD filtration were compared with established laboratory-scale filters operating at 10-fold scale based on total working mass. Good comparability was obtained for samples with narrow PSD, while samples with larger PSD had reduced predictive capability. API of narrower PSD was achieved by using a USD shear device and applied mechanical force. For the shear stressed crystals using USD shear device, crystals were found to be robust to shear stress with a small amount of fines produced, and the impact of fines on filtration was not remarkable. Mechanically size reduced crystals produced a substantial amount of fines, which resulted in a considerable reduction of the filtrate flux and approximately ten-fold rise in specific cake resistance when compared with shear stressed crystals. In general, the PSD of the crystals were found to be critical to determining the filtration conditions such as pressure difference and filter pore size. As concluded in this study, PSD is directly related to filter pore size and inversely related to the pressure difference, as would be expected. The implementation of the automated USD filtration platform enables rapid-process understanding and reduces cost and time due to a reduced amount of materials. The data obtained shows similar process trends and are primarily indicative of process performance at a larger scale.