The CMAC Future Manufacturing Research Hub team has demonstrated a holistic digital-first approach for the design and manufacture of mefenamic acid particles with the required quality attributes.

Digital-first refers to computational modelling to design the required particle attributes and subsequent manufacturing process in a more resource efficient, faster way.

It is a significant shift away from the traditional experience-driven approaches relying on empirical methods and tacit knowledge.
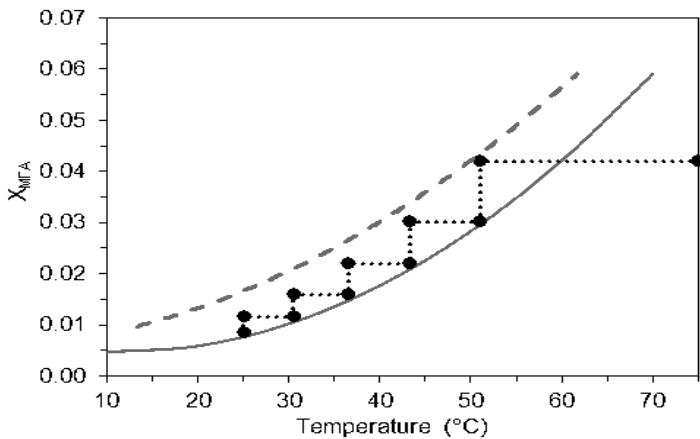
Model predicted conditions successfully implemented to make the larger particle size of mefenamic acid
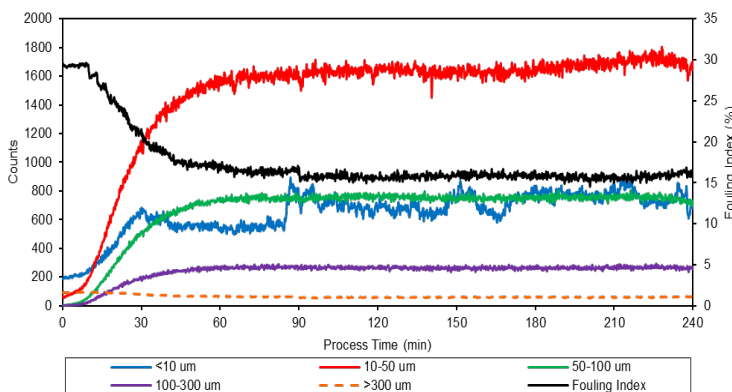
In-process monitoring of particle size for 2-stage MSMPR model verification experiment (using focused beam reflectance measurement (FBRM))
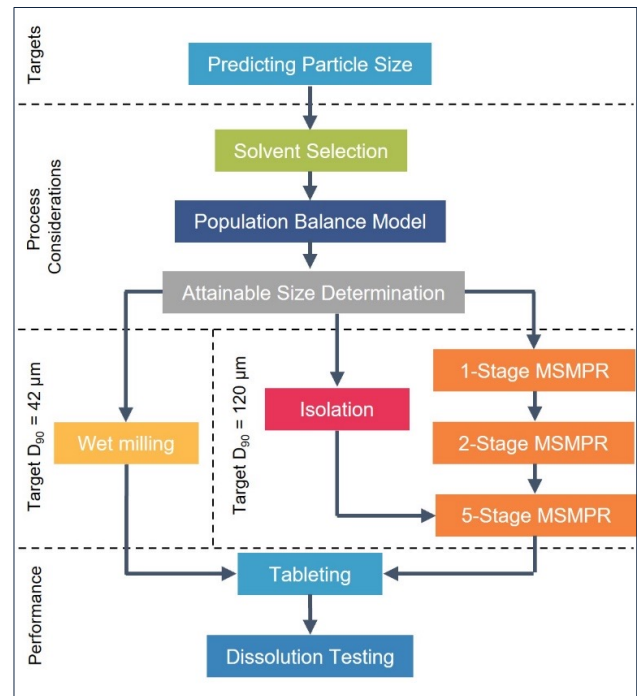
The "Digital First" Workflow

This modelling work informed two independent manufacturing runs with both of them producing the active pharmaceutical fully meeting all required quality targets. The work has been published: https://doi.org/10.1016/j.cherd.2023.07.003

Modeling was used for:

✔ Selection of quality targets

✔ Screening solvents and crystallisation optimisation

✔ Wet milling to make the smaller particle size

✔ Cooling seeded crystallisation for a larger particle size with accompanying isolation procedure

✔ Predicting product performance through dissolution models

Experimentation is still required for parameterizing and verifying the models and identifying physical phenomena not covered in the models.

The interdisciplinary team from the University of Strathclyde and Loughborough decreased the raw materials required for development by an order of magnitude.
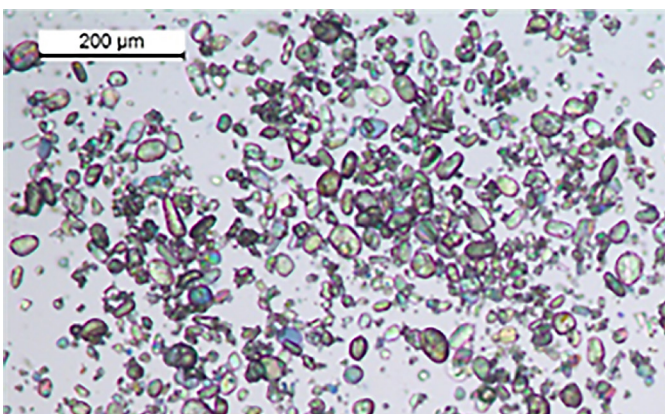
Smaller sized mefenamic acid particles made by wet milling
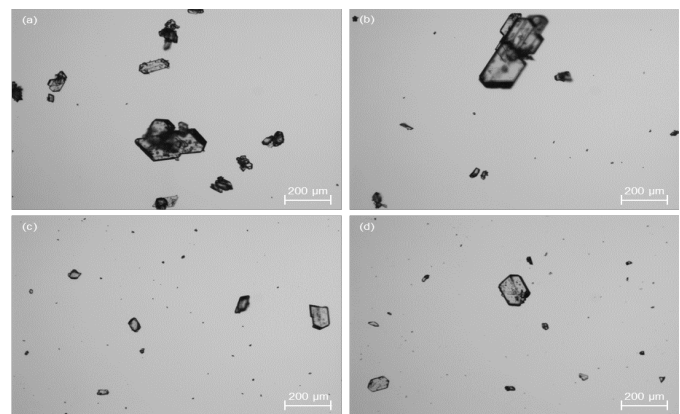
Larger mefenamic acid particles (images on top show agglomeration, those on bottom are high energy dispersion measurements breaking the agglomerates)

Benefits of Digital-first:

✔ Digital-first will reduce development time, cost, and resource requirements.

✔ Enables the design of robust manufacturing processes, enhancing flexibility in design space operation through "Quality by Digital Design".

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