Novel fluid-dynamics variables for the optimization of nanoparticles manufacturing

Marco Bellotti¹*, Alessia Giglio², Bice Conti², Nur-E-Hasnat², Ferdinando Auricchio¹, Ida Genta², Enrica Chiesa², Alessandro Caimi¹

¹ Department of Civil Engineering and Architecture; Via Ferrata 3, Pavia, Italy

² Department of Drug Sciences, University of Pavia, V.le Taramelli 12, Pavia, Italy.

* Email: <u>marco.bellotti01@universitadipavia.it</u>

Conventional approaches for the production of nanoparticles (NPs) present high variability and low repeatability of the experimental results obtaining NPs with different characteristic with the same experimental set-up. In recent years, microfluidic mixers were developed to overcome this limitation, exploiting the laminarity of the flow and therefore the repeatability of the process with the consequent production of NPs with always the desired morphological features.

Nevertheless, the approach to translate old formulation or develop new ones is long and expensive since the necessity to design a set of experiments aimed at the characterization of the process parameters effect on the final NP produces. Furthermore, so far the numerical approach do not encompass the different phases of the NPs formation giving only information about the mixing performances of the microfluidic cartridge.

In this work a microfluidic-based manufacturing process for Eudragit[®] L100 NPs is optimized using a combined experimental and computational approach.

The polymer precipitation curve for a specific binary mixture is obtained through experimental means and further processed to extract thresholds used in the numerical post processing phase to calculate process specific parameters such as the Volume of Precipitation (VoP).

The trends highlighted by those parameters are then validated through the production of NPs at the same BCs adopted for the numerical simulation.

The results obtained show how this approach can help to improve efficiency and cost-effectiveness of NPs production and how the combination of DoE and numerical simulations can optimize production parameters and refine manufacturing processes for advanced drug delivery systems.