Manufacture of Individualized Dosing:

Dropwise Additive Manufacturing of Pharmaceutical Products (DAMPP)

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In accordance with the changes observed in health care systems towards more innovative personalized therapies, we present a novel technology for small scale, distributed manufacturing of individualized dosing. A dropwise additive manufacturing process for melt-based solid oral drug production is developed, which utilizes the drop-on-demand (DoD) printing technology for predictable and highly controllable deposition of active pharmaceutical ingredients (API) onto an edible substrate, such as a polymeric film or placebo tablet. This manufacturing method has tremendous potential in individualized dosing because through a combination of drop size and number of drops, the dosage can be precisely and reliably controlled to match the prescribed amount for a patient. The DAMPP process is a viable method for on-demand production of various formulations including solvent based systems, i.e. solvent-polymer-API solutions, and melt based systems, i.e. polymer-API melts.

A real-time process management strategy is developed for the dropwise additive manufacturing of pharmaceutical products. The automation program assures synchronous operation of process units, while monitoring process parameters and maintaining process control. For the dropwise additive manufacturing system, the critical process parameters (CPP) are controlled to achieve the desired critical quality attributes (CQA) of the dosage forms. The effect of the CPPs on the final drug property is investigated and it is shown that implementation of a supervisory control system on the process is essential for producing individual dosage forms with the desired CQAs. A polynomial chaos expansion based surrogate model is developed to predict the dissolution profile of the solidified drug deposition given the temperature profile applied on the substrate. Using this model, a hierarchical control system is implemented by monitoring the drop size on-line and predicting a temperature profile to achieve the desired dissolution profile for the dosage forms created. The process control strategy effectively mitigates variations in the dissolution profiles due to variable dosage amounts, hence enabling the application of the DoD system for the production of individualized dosage regimens. The prototype system offers great promise as a tool for advancing personalized medicine by allowing the precise production of convenient solid oral dosages tailored to the patient on site at hospitals, clinics and even pharmacies.