Continuous Manufacturing: Strategies for Solid Processing in Synthesis, Workup and Formulation using Process Intensification.

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The petrochemical industry switched to continuous processing in the sixties and seventies of the last century, which generates a great boost in the process economy. The fundamental idea behind this is based on a different mind-set in development. The plant design is based on the needs of the chemical reaction and not on the capabilities of a batch reactor. Now the pharmaceutical and fine chemical companies try to benefit from continuous manufacturing. Researchers and companies in the field of flow chemistry, micro reactors and process intensification have developed excellent solutions to fulfil the needs of the continuous manufacturing.

While the first applications of flow chemistry and micro reactors have addressed fast highly exothermic reactions. The main focus today is much broader and more on complex applications dealing for example with solids. Melted educt materials are processed by means of continuous systems as well as continuous crystallizations are executed. Suspensions of reactants or catalysts are continuously formed and will be directly used in the chemical process. This enables the reduction of mass and heat transfer distances by a magnitude. Downstream processing as well as formulation manufacturing open up a wide range of new application fields of continuous manufacturing.

Economic strategies will be discussed in the presentation. For example BASF has studied recently the main factors to get the costs per kg down. The outcome No.1 was to work with intensified processes. The reduction of mass transfer distances from meters in batch vessels to centimetres has a significant impact on the realization concept. Heat transfer time can be reduced by a factor of 10 or more for chemical synthesis, which need certain temperature conditions. Filling, emptying and cleaning are procedures, which do not create value. These can be avoided in continuous setups. Continuous operating units do not need much staff for operation. Flexibility know from batch technology can be provided in other ways. These strategies will be presented and their important impact on the manufacturing costs will be demonstrated.

Three case studies will be presented. The first one in a propoxylation reaction, where the necessary reaction time is switched from 12 hours to 1 minute. This means that the process has been intensified by a factor of 700. The exhaust gas has been reduced to zero. The second case study demonstrates how a solid is continuously dosed into a API manufacturing plant, dissolved and reacted under precise cryogenic condition. The third case study is pilot plant executing complex crystallization processes. This plant is equipped with PAT technology supervising the crystal growth. An outlook will be given for continuous manufacturing of liquid and paste formulations.