XPURE
innovative continuous chromatography

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Are You Ready for the Future of API Manufacturing and Continuous Chromatography?

Continuous processing is the best path forward for developing sustainable manufacturing platforms, which enable maximum utilization of raw materials, produce minimum waste, and enhance process efficiency to obtain a high-value product at the lowest cost. During this time of growth and transition in Active Pharmaceutical Ingredient (API) manufacturing, it is critical to rethink and innovate API production.

The global demand for both innovative fermentation-based and generic synthetic APIs has been continuously growing over the past decade. The global market size is estimated to grow from about $180 billion in 2019 to about $250 billion by 2024 with an average growth rate of > 6%. This scenario is further strengthened by the increase of new infections and growing cases of lifestyle-induced health conditions.

Therefore, the dynamic market sets the field for API manufactures to improve patient health and safety by focusing on:

1. **Robust and secure supply chain from raw materials to finished products**
2. **Innovative, stable, safe, specific, and effective products**
3. **Efficient manufacturing platforms to meet capacity, purity, and price targets**
4. **Compliant, accessible, and affordable drugs**

Purification technologies based on filtration, chromatography, and evaporation principles have been an integral part of API manufacturing platforms. These technologies define the final product purity, stability, and efficacy. Chromatographic purification using ion exchange, affinity, hydrophobic interaction, size-exclusion, and adsorption principles has been widely applied mainly due to its high selectivity, reliability, robustness, easy scalability, GMP compliance, operability, and mild operating conditions maintaining product stability. However, batch mode of operation has labeled chromatography as an expensive and less efficient technology. In order to overcome this problem, several technology providers have investigated simulated moving bed (SMB) mode of continuous chromatography.

The challenge in implementing SMB for API manufacturing is that GMP compliance requires a clean mechanical design with minimum product contamination risks. Further, continuous processing in GMP manufacturing requires implementation of reliable process

analytical technologies (PAT) that can control and enable a stable process and resulting product quality profile.

XPure Innovative Continuous Chromatography aims at implementing the well-known SMB principle on a highly flexible and modular valve platform, which is specifically designed for implementation in cGMP processes. The hardware setup, together with its automation built for robust control based on process-specific PAT philosophy can efficiently address the process productivity, purity, and yield requirements without deviating from compliance.

XPure has implemented continuous chromatography for purification of both synthetic and fermentation-based APIs. The technology is being used at different stages of purification including product capture from fermentation or reaction mixtures, product recovery from waste streams or mother liquors, and product polishing. The major advantage of utilizing an XPure system is that the technology is nimble! It can be designed and built to match the process in terms of techno-economic value of the purification stage and critical process requirement in terms of productivity and purity.

For example, continuous ion exchange process for removal of salt impurities from an API product stream has a lower process economic value and complexity compared to selective API product capture from a complex fermentation-based stream. XPure focuses on this essential difference to develop a techno-economically feasible solution. Below are two cases explaining the outcome of such a process implementation at multi-ton scale of API production.

In case of Cephalosporin C (CPC) when produced by fermentation route, the main impurities desacetyl cephalosporin (DCPC) and desacetyloxy cephalosporin (DOCPC) are difficult to separate. Therefore, a chromatography step with selective adsorbent and multiple operating zones including feed, wash, gradient elution, and regeneration is required to obtain the target product purity. Since the chromatography step defines the final process outcome in this scenario, it has high process economic value. This further translates into the economic potential of implementing continuous chromatography to reduce buffer and resin consumption. Comparing batch vs continuous chromatography in this case, XPure designed a continuous chromatography system with 40% lower operating expenditure (OPEX) by investing an additional 30% as capital expenditure (CAPEX). The final process not only ensured product quality at lower costs but also met the process compliance requirements.

In another case, XPure developed a process with 4 columns per step for removing salts from an API (sugar) stream using commercial cation and anion exchange resins. This process required a simple process facilitating only 2 input streams per step for feed and regeneration. In this case, the benefit from increasing the productivity outcompetes the costs saved from reducing buffer and resin requirement. Therefore, a marginal 15 % increase in CAPEX to implement XPure innovative continuous chromatography philosophy reduced the OPEX resulting from the desalting step by 40%. This mainly was due to increase in productivity by about 2-fold and reduction in the water, acid, and base regenerant consumption by more than 30%.

XPure, with its experience in implementing continuous chromatography at different stages of API manufacturing, provides the best fitting solution to meet the client

requirements. As part of ProPharma Group, XPure streamlines its technology to the applicable regulatory standards for a smooth implementation at industrial scale.