AsahiKASEI BIOPROCESS

Increasing Biopharmaceutical Manufacturing Downstream Process Efficiencies

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Tristan holds a Bachelor of Science (B.S.) degree in Biochemistry from Rutgers University. He brings a wide range of experience in sales and business development, including expertise in fluid management, contract research and manufacturing, as well as instrumentation. In addition, he has a background as a research biochemist and analytical chemist.

Large-scale biopharmaceutical manufacturers consistently focus on increasing efficiency in their downstream processes to optimize the use of resources, create a higher-quality product, and increase yield. Downstream processing can be as high as "80% of the total production cost."[1] At scale, one simple tweak to the operation can equate to potentially thousands of hours and millions of dollars. The top considerations for increasing process efficiencies are: optimization of space by way of advancements in machinery, innovations in biomaterial processing methodology, automation, and operator productivity.

Large-scale facilities require more space, not only because of the relative scale-up in size but also because it is often more cost-effective to have massive quantities of solutions housed and prepared on-site. By implementing innovative technologies, operators can now utilize their space more efficiently by increasing production capacity for their large batches, or they can diversify their production output by using versatility-enabling equipment to produce smaller batches of a potentially bespoke order. This process is particularly beneficial for cases such as those where the increasing demand for biologics, biosimilars, and novel biopharmaceuticals in varying batch sizes continues to increase. The most notable examples of space-efficient machinery include column packing, inline buffer formulation, and inline conditioning machinery. Essentially, optimizing available space will increase overall output and potentially the diversity of products being produced.

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Advancements in biomaterial methodology utilized in the downstream process for purification are often overlooked when considering increasing overall factory efficiency. A major reason to highlight this area is the bottleneck created by the incredible growth of upstream titers. A "more than tenfold increase in titers has been seen over the past 30 years with an average of 3 g/L, while several new products are reported to reach more than 10 g/L."[2] This increase directly impacts the costs associated with the downstream process because there is a

[1] https://doi.org/10.3389/fmicb.2021.700863
[2] https://www.sciencedirect.com/science/article/abs/pii/S1742706119301813

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significant rise in purification capacity. While there are several different methods for chromatography, affinity chromatography is currently the most used capture method for purification at a larger scale.[3] Affinity chromatography requires two phases: a mobile phase as well as a stationary phase in order to purify molecules in a mixture. The drawbacks of this method are its high media cost and limited loading capacity. Fortunately, manufacturers can evaluate alternative "non-chromatographic methods, including membrane separations, magnetic separations, and precipitation/phase separations"[4] to see which solution is right for their use case, optimizing for cost, time, and the reduction of waste.

Although potentially challenging in terms of integration, factory digitalization plays a beneficial role in continuously increasing plant efficiency. Operators are able to see a complete system overview via the compilation of data from sensors, log data, clickstream, social network, geolocation, CRM and ERP, as well as real-time and historical data compilation and analysis.[5] Developing the artificial intelligence side of production saves processing time with, at minimum, the same amount of output, achieving greater accuracy with reduced errors and executing overall better quality control. An important factor to note is that the digitalization of manufacturing facilities does not require implementation overnight. Traditional manufacturers who are looking to digitize can do so in stages so that installation costs can be spread out over time instead of incurring them all at once. With the step-by-step approach, employees will also have thorough and reasonably paced training, allowing for an increase in adoption/utilization.

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[3,4] https://www.sciencedirect.com/science/article/abs/pii/S1742706119301813
[5] https://doi.org/10.1002/jctb.6792

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Human operators play a key role in increasing production capacity and can work together with automated equipment to make ongoing improvements to operational processes. There are sys-tems that can keep track of productivity, so management can ensure that time is used effectively, and waste is reduced. Additionally, improving mental health has been a major focus in the workplace. Researchers in Great Britain found that "more than [70 million] working days are lost each year to mental illness in the UK,"[6] and manufacturers that have implemented positive changes focused on improving mental health at work can "boost worker productivity by up to 10% (and as much as 17% in one study)."[7] A major factor that encourages employee satisfaction is curating a good working culture and environment. This has a positive correlation with higher output volume and reduced turnover, which, in turn, lowers costs significantly. Essentially, manufacturers have the opportunity to increase overall output for a relatively low cost by combining the use of technology to track and maintain accountability for employee work as well as increasing workplace morale for personnel.

With all of this in consideration, more stepwise optimizations in equipment may be more suitable than a complete overhaul.

With all the emerging technologies, companies are now empowered with additional processing options to meet the latest market demands. It is important to note that not all options are right for all manufacturers. For large-scale manufacturers especially, it is recommended to implement any decided change in a calculated and incremental way. In an evaluation, it may be discovered that the traditionally practiced method is still the most efficient–particularly when examining the potential costs of change to equipment, energy expenditure, the time horizon of production, and retraining of employees. With all of this in consideration, more stepwise optimizations in equip-ment may be more suitable than a complete overhaul. Overall, long-term success for large-scale biopharmaceutical manufacturers is especially found in aptly improving efficiency in the down-stream process through concentrated evaluation and investment in a dual-focused landscape of both data and processes.

Questions?

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[6, 7] https://www.nass.org.uk/Publications/Publication4432/EEF-Unlocking-employee-productivity-report.pdf