(Re)Defining Process Intensiﬁcation

Sartorius shares its vision for better, faster, and cheaper bioprocessing.

What is process intensiﬁcation (PI)? There’s currently no straight answer. But, in this roundtable, three of the company’s ﬁnest lead us through Sartorius’ bold mission to deﬁne, reﬁne, and deliver PI to biopharma manufacturers across the globe.

Why has PI become such a hot topic for biopharmas in recent years? Martin Lobedann: Increasing cost pressures, diversiﬁcation of product portfolios, and an expanding number of molecules in the pipeline have pushed PI to the fore. Every player needs fast and safe changeovers, high eﬃciency, and, of course, low product costs. PI can help by producing more molecules with a smaller facility footprint and lower demand in utilities.

Why do deﬁnitions of PI vary? Martin Lobedann: There is little consensus on PI’s deﬁnition. According to the very general deﬁnition, it’s all about getting more by doing less. But divergencies in methods and steps mean that every vendor handles PI diﬀerently, and thus we have no common understanding. At Sartorius, we’re trying to deﬁne a general and applicable standard for PI.

Martin Lobedann: Quite simply, PI provides companies with a framework to increase productivity and reduce costs. At Sartorius, we use a four-tier system to help deﬁne how well PI is integrated into a business. From no PI at all to completely continuous systems, we can accurately deﬁne PI integration at all levels.

JB: That’s right. Our tiers help shed light on the use of PI within businesses. Level 0 is, per deﬁnition, our base case for reference without intensiﬁcation. Level 1 then includes consumable intensiﬁcation (RCC, high binding capacities), together with stand-alone system intensiﬁcation (ILD; ILC; MCC), or combinations thereof. Level 2 would be a connected process (Level 0 and/or Level 1 intensiﬁed) multi-step systems. Finally, Level 3 would comprise continuous processes.

KR: Sartorius is also considering intensiﬁed control strategies when designing automation for intensiﬁed systems – in other words, we will set up our systems using a standard conﬁguration with parameters that can be monitored and controlled from a supervisory control platform.

What factors and technologies can help drive PI? ML: From a technical point of view, PI is driven by combining or connecting several unit operations. The correct orchestration software must then be put in place to monitor and control every unit. Here, data analytics is key to keeping the process robust and catching deviations.

An open mindset also helps. Though PI is a powerful tool, it can’t work effectively without support from technical and management teams. Though these people often have many responsibilities to juggle, taking the time to understand how PI can lead to business improvements is important. Some may be hesitant to embrace the technology – PI can be costly after all – but the investment is sure to pay oﬀ.

JB: I’d add that, before embarking on any PI journey, the managers and technical teams need to understand and understand the parameters of the process. Here, a software platform is key to simulating, identifying, and facilitating process intensiﬁcation. It will also be crucial for controlling and analyzing the product quality in real time.

The pharmaceutical industry is relatively conservative in its adoption of new technologies, thus these companies need support in any decision they make. For instance, to switch from batch to multi-column processing will require a shift in mindset, and so a simulation tool that can highlight the main impacts and changes on the current process will help inform that decision.

Why do monoclonal antibodies lead the game when it comes to biopharma PI? JB: mAbs have been the leading therapeutic for decades, and thus mAb manufacturers are experts in developing and deﬁning mAb processes – and that opens the door for PI to remove and improve any remaining suboptimal operations.

KR: As Jean-Luc says, it’s because the platform processes are already available. We need to put more effort into the software orchestration is needed to guarantee a steady state ﬂow through all unit operations. At Level 3, residence times become predictable, and uniform characters and distributions are achieved. At this level, we also see long run times – at least three days for downstream puriﬁcation and closed processing.

Why do you think Siemens’ Biobrain is a game changer for PI? JB: As Jean-Luc says, it’s because the software supports our customers in predicting, running, and analyzing any unit operation in their process intensiﬁed suite. Our Biobrain control software platform should ideally ﬁll the gaps. There is also some alignment needed around the equipment platform to improve integration.

What is the one thing about PI that everyone should know? JB: For me, process intensiﬁcation is the bioprocessing term for “lean manufacturing.” It is about reducing waste in a production process. There are many types of waste in bioprocessing; from inventory to excess capacity – and depending on one’s process, diﬀerent strategies can be used to make the process more eﬃcient.

KR: Everyone should know that process intensiﬁcation makes life easier and can be implemented stepwise; for example, starting with automated buffer preparation and multi-column chromatography. It can then be extended to a level two or level three integrated process. An open mind may be the most important aspect – from both a technical perspective and in management.

JB: Lots of process industries – including the automotive, electronic, and food and beverage – use PI. It’s possible to plug the gaps at the unit operation level. Sartorius is working actively – using customer feedback and internal knowledge – to ascertain which gaps are the most important right now, and how they should be closed.

JB: As Martin says, to maximize the potential of Sartorius’ PI strategy, we need to be able to continuously support our customers in predicting, running, and analyzing any unit operation in their process intensiﬁed suite. Our Biobrain control software platform should ideally ﬁll the gaps. There is also some alignment needed around the equipment platform to improve integration.

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