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Trends & Developments in BioProcess Technology

A Production of BioProcess Technology Network

From the Editor-in-Chief

Call me jaded. One of the latest fads in the production of biologics is "continuous processing." While I won't argue that this does sound avant-garde, and is possibly the industry's long-lost solution for lowering production costs, I'm not sure we should start popping the champagne corks.

I've seen a lot in my 30+ years as a process engineer, including continuous processing for petrochemicals and waste treatment, plus batch processing for pulp and paper manufacturing. And the more I dig into the articles, as well as the meetings on continuous processing, the more dubious I become. What I'm seeing are techniques that have always been available, but no one was brave enough, or had the political capital, to make them happen. Far more simplistic processes have been shut down zillions of times by the "FDA would never allow that" argument, so how in the world are we going to implement a stem to stern continuous process for biologics? And then, how do we know that it would cut production costs and cross-contamination risks, plus make batches more reproducible?

Let's start with "upstream" technology where perfusion has been available forever, or at least since the early '80s at any realistic scale. We had hollow-fiber ultrafilters, OptiCell ceramic cores, multi-plate Cell Cubes, fluidized beds, packed beds, and of course, stirred-tank bioreactor systems with a number of cell retention devices that made them perfusion systems. But guess what? Very few companies have adopted perfusion technology since they felt it was too difficult or too risky. What if a tube broke in a peristaltic pump head, or a tube popped off a hose-barb fitting? There is an endless litany of nightmares about coming into work the next morning and finding millions of dollars worth of product all over the floor.

But one of the earliest blockbuster biologics, Remicade, was made with a good old-fashioned spin filter in a stirred tank, and a process that lasted for weeks. Still, those "in the know" said that only batch processes would be accepted by regulators.

So let's concede that the upstream realm can lend itself to continuous processing, but the really hard stuff was always on the downstream side. Here we've had to deal with product clarification and purification, which typically involve cross-flow (tangential) filtration and chromatography run in a batch mode, with regeneration steps in between whatever was considered a batch.

But leave it to this industry to create another cause célèbre which is no more than cycling banks of batch systems and adding far more complexity and risk than was ever conceived of with perfusion. Let's see how things go.

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