Mind the gap: Ensure successful scale-up of single-use processes

The increasing distance between new molecular entities output and pharmaceutical spending is often referred to as the Innovation Gap. Parker domnick hunter examines the single-use explanation for this and reveals the considerations to ensure successful implementation of single-use automation from laboratory-scale to large-scale production.

Recent trends in the biopharmaceutical market have shown a reduction in the number of large companies which are spending their entire R & D budget on developing new drugs[1]. Instead, start-up biotech companies are the major source of innovation within the biopharm industry and of new molecular entities (NMEs). The main goal of these start-ups with new products or interesting therapeutics is to survive. Survival in this case means getting far enough into the Food and Drug Administration (FDA) approval process to be bought or licensed by a large company.

Once a target is identified, speed is the key

The faster a process can be scaled-up, the faster the results can be gathered from animal models and eventually clinical trials. Speed to market is critical for most biomanufacturers, especially for small biotech companies with limited resources. After all, small biotech companies must demonstrate clinical success before venture funding runs out.

There are many pitfalls which can delay progress. One example is the need to redesign operations at the manufacturing-scale, having failed to integrate operating protocols from the laboratory scale. Start-up companies are now beginning to see the benefits of single-use technology (Infographic), such as low costs, reduced cleaning requirements, improved consistency, decreased asset inventories, and scalability of single-use technologies.

Thinking ahead to commercial production

Start-up biotech companies need to focus on the end goal, which is ultimately a validated, approved commercial manufacturing process. Ideally the supply chain is locked down and the procedures are in place to repeatedly produce the product safely. The process should run from start to finish in a very similar or identical fashion as the day the FDA approved it.

But what about process improvement? Once the drug master file is submitted, most of the procedures are locked in place. Changing a component or procedure requires, at least, a risk assessment and a round of change control. It is probable that some of the largest drug manufacturers in the world settle for sub-optimal yields to avoid re-submission.

In a stainless steel processing facility it may be difficult or impossible to make more material with the same equipment when market success leads to the need for additional capacity or facility throughput. A new facility may need to be built just

to accommodate the additional demand, which could lead to delays and shortages. Mobile, single-use, and completely contained processing units or systems with closed flowpaths, on the other hand, take up less permanent space and can be set up very quickly.

Facilitating scale-up from laboratory to production

The benefits of single-use technology to start-up biotechs at both laboratory and production scales are clear. However, what mindset must be adopted to make the transition from one to the other as seamless as possible?

First of all, start-up biotechs shouldn't wait to adopt single-use automated technology at the pilot level, as scaling up issues may arise at the R & D stage. When the pilot process supervisor is given a process from R & D their first question is, "How am I going to make this happen at pilot scale?"

In addition, material qualification can take a long time to conduct, and can sometimes preclude the use of a desired material at much later stages. Biotechs should make sure that the materials being used in R & D are the same technology that can be used aseptically with automated technology at pilot and process scales.

Keep strategies consistent

While single-use technology is more widely adopted in commercial manufacturing environments, R & D departments are also beginning to realize the benefits of adopting single-use technology.

Successful scale-up can be ensured by utilizing the same automated single-use equipment and strategies in R & D through to manufacturing scale, and relying on the expertise of scale-up specialists. With this strategy, a significant reduction in rework and inefficiencies can be expected in processes that would otherwise be extremely difficult to change once approved. ■

[References]

1. *Discoverymanagementsolutions.com, (2015). NME Output versus R & D Expense – Perhaps there is an explanation Discovery Management Solutions. [online] Available at: http://www.discoverymanagementsolutions.com/the-organization-of-biopharmaceutical-rd/common-goals-between-discovery-and-development/innovation/nme-output-versus-rd-expense-perhaps-there-is-an-explanation/ [Accessed 17 Feb. 2015].*

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Bridge the gap

in automated single-use technology between

R & D & MANUFACTURING

Benefits of using single-use technology

- Components are inexpensive while durable enough for multiple uses.
- Separation of capital and disposable equipment budgetsallows more time to make the final decision on single-use configuration.
- Changing out configured single-use components often does not require modification to capital equipment.
- No need for cleaning or regeneration of components which decreases turnaround times.
- Single-use components can be supplied pre-sterilized and ready to use.
- Using pre-made disposable manifolds rather than building a flow path for each different processing run gives more consistent results.
- Single-use technology can provide increased capacity as needed without requiring a second piece of equipment.

Benefits of consistency in R & D and Manufacturing

- Materials are pre-qualified at the R & D stage and approved for use in the application.
- Terminology is consistent between R & D and manufacturing.
- Vendors are pre-qualified, audited and already in the supply chain.
- Awareness of potential pitfalls in the large-scale process means future manufacturing problems can be prevented.
- Operator training time is reduced and user confidence with technology is increased.
- All steps can be performed aseptically so a cleaner process will be developed.
- Using scaleable automation solutions and single-use components increases the likelihood that control parameters developed on small scale systems are available on a larger system.
- All stages of the process can be developed and perfected in conditions that do not require overhead of special facilities and areas that require constant maintenance.