Products/Services Highlights

• Reinventing Biopharmaceutical Manufacturing with Single-use Disposable Systems p.310
Advancements in biotechnology and bioprocessing are driving the rapid development, commercialization, and availability of biopharmaceuticals globally. The US Department of Commerce reports in 2003 that there are more than 370 biotech drugs and vaccines in clinical trials in the US. Additionally, of the 155 biotechnology drugs and vaccines that have received regulatory approval from the Food and Drug Administration (FDA) to date, 70% of these have been in the last six years.1

Technological breakthroughs have resulted in an unprecedented number of drugs and biologics currently in research and development phases. Biopharmaceutical manufacturers face increased pressure to commercialize new and unique therapies faster and at lower cost. As a result, production demand is outpacing available manufacturing capacity. To meet existing and future demand and maintain a competitive advantage, many manufacturers are striving to develop increased efficiencies within their manufacturing processes.

Opportunities exist to streamline traditional biopharmaceutical manufacturing processes. Today, many of the leading drug companies spend more than twice as much on manufacturing as on R&D. Product quality is always the top concern of biopharmaceutical manufacturers. Existing manufacturing facilities can produce up to 10% discrepant product primarily due to antiquated equipment or process failure.

It is clear that the advancements in the industry demand new and robust manufacturing equipment and processes. The introduction of single-use disposable components and systems are key in meeting new, emerging standards in biopharmaceutical manufacturing. Rapidly gaining acceptance worldwide, single-use, high quality plastic components and systems speed the manufacture of drugs and can significantly reduce production costs.

Disposable components minimize labor-intensive connections, lengthy clean-in-place (CIP) steps and cleaning validation, and reduce opportunities for contamination.

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Reinventing Biopharmaceutical Manufacturing with Single-use Disposable Systems

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Steam-Thru™ Connection.
Single-use components developed specifically for biopharmaceutical manufacturing applications signify higher quality, more reliability, and greater efficiencies. Today’s disposable components work in concert with existing laboratory and manufacturing equipment to form an integrated solution that includes capsule filters, tubing, clamps, adaptors, and connection devices.

Disposable technology can play an important role in each processing step of a biopharmaceutical product. Single-use components securely deliver the sterile transfer of fluids and cells to and from a bioreactor before, during and after production. Disposables are extensively used in the storage and transport of biological solutions in process. Working in concert with traditional methods, disposable components improve the speed of drug development and delivery.

Advantage of the Disposable

Biopharmaceutical manufacturers achieve significant gains by utilizing single-use disposable technology. Traditional stainless steel, hard-piped and glass systems are expensive to clean and sterilize on a batch-by-batch basis. Single-use disposable products eliminate the need for cleaning since they are discarded after use, saving time and valuable operator resources.

Regulatory agencies require proper cleaning and cleaning validation every time a hard-piped system is used in biopharmaceutical applications. Single-use disposable systems eliminate the time required during drug development for validation documentation of cleaning, maintenance and sterilization. These cleaning and validation processes add greatly to the time and cost needed to develop drugs and introduce opportunities for non-compliance with regulatory agencies.

What is “Bioprocessing”? It is a technique that produces a biological material, such as a genetically engineered microbial strain, for commercial use; production of a commercially useful chemical or fuel by a biological process, such as microbial fermentation or degradation.
**Significant Time Savings**

Disposable systems significantly reduce the time required to perform core biopharmaceutical manufacturing processes. Establishing sterile connections is a primary activity in bioprocessing. Connections are used throughout drug development to link key bioprocesses together. Sterile connections ensure the integrity of biopharmaceutical processes and are fundamental to the quality and safety of manufactured medicines.

In comparison to stainless steel re-usable connection devices, disposable connection devices significantly reduce the amount of time it takes to establish a sterile connection. Establishing a sterile connection typically requires use of heavy, cumbersome capital equipment, such as a laminar flow hood and a tubing welder that demands significant operator time. Traditional re-usable connection devices require cleaning and cleaning process validation before a media bag can be coupled to a bioreactor. A disposable connection device can initiate a sterile connection in a matter of minutes without the need for additional steps or equipment before or after the connection process.

**Cost Effective Connection**

Table 1 contrasts the cost of establishing a sterile steam-in-place (SIP) connection using traditional stainless valves and fittings versus the new disposable connection. The cost per connection utilizing a single-use, steam through connection is approximately one-fourth that of the traditional stainless equipment. Labor costs are dramatically reduced using disposable connections.

Reliance on traditional equipment also increases the space needed to create sterile connections. By switching to disposable technology, a facility can operate more efficiently by reducing capital and maintenance costs.

<table>
<thead>
<tr>
<th>Current Application</th>
<th>Cost per Stainless Connection (US$)</th>
<th>Cost per Disposable Connection (US$)</th>
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</thead>
<tbody>
<tr>
<td>Valve System</td>
<td>$600 per connection, 2,000 uses = 30 cents per use</td>
<td>Disposable connector $40 (estimated)</td>
</tr>
<tr>
<td>Replacement Pieces</td>
<td>$50 for replacement piece with 50 uses = $1 per use</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>Labor Costs</td>
<td>$2½ hours @ $110 per hour = $275</td>
<td>¼ hour @ $110 per hour = $28</td>
</tr>
<tr>
<td>Total Costs</td>
<td>$276</td>
<td>$68</td>
</tr>
</tbody>
</table>

**Reduced Contamination Risk**

As such, single-use disposable systems deliver an immediate return on investment measured in terms of time and cost savings. However, disposable technology provides arguably an even greater benefit. By providing a more robust manufacturing process, the likelihood of contamination or a failed process is minimized. A contaminated or failed process results in the total loss of a production batch, which can range from US$100s to US$100,000s.
In bioprocessing, there is a significant risk of damaging or delaying a development due to contamination occurring during or within the process. Contamination can occur from product to product or batch to batch. It often takes months to develop and grow vaccines and move them through the process. If the process is contaminated at any stage, then the time and costs associated with the months of development is lost.

Opportunities to expose a process to contamination are numerous. Contamination can come from several sources including:

- improperly cleaned, reusable equipment or components; and
- dead-legs or bug-traps within connections points.

In existing SIP processes, for example, establishing a sterile connection relies on multi-connection points, increasing the risk for contamination. Single-use disposable greatly reduces these contamination risks. The unique design of certain disposable connections also eliminates the possibility of “dead legs”, reducing the potential for contamination.

Single-use disposable systems improve the safety of operators by eliminating the use of CIP processes. The handling of often hazardous or toxic material is no longer required.

The Future

The 1967 movie, The Graduate, declared “There’s a great future in plastics”. Almost 40 years later, nowhere is this more true than in bioprocessing. Biopharmaceutical companies are shifting from stainless steel and glass systems to plastic single-use disposable technology. Increasingly, single use systems are being adopted by the biopharmaceutical industry to eliminate risks of batch-to-batch cross contamination, to reduce costs of cleaning and sterilizing and to enhance speed to market.

The future will include widespread use of plastics in biopharmaceutical production as well as disposable production equipment within facilities. Today it’s possible to build a system from high quality plastic, disposable parts ranging from media bags to storage and shipping containers. New development facilities are being designed and built with single-use plastic components and systems. Existing manufacturing facilities are integrating disposable plastic components with traditional stainless steel and glass equipment. Single-use bioreactors are already available.

While all companies are benefiting, biotech start-ups perhaps stand to gain the most from disposable processing systems. Disposable processing is very cost-effective for start-ups who do not have hard-piped processing systems in place. Biotech start-ups will be able to pursue developments more cost-effectively with less capital expenditure tied to the purchase and maintenance of expensive capital equipment. Faster progress in drug development will undoubtedly occur. In this way, single-use disposable systems are in fact helping to fuel the very innovation that made their existence in the biopharmaceutical market so very important.
About the Author

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About Colder Products Company

CPC is the leading provider of controlled performance connections for Biopharmaceutical, Biotech, Chemical, and Medical markets. For 25 Years, CPC (a world leader in the design of plastic quick disconnects for flexible tubing) has combined innovative engineering with leading edge manufacturing to provide a diverse range of fluid management solutions worldwide. Today CPC components are found in ultra high purity chemical dispensing equipment, life-saving kidney transplant systems and controlled biological environments aboard the International Space Station.

Headquartered in St. Paul, Minnesota, USA, CPC has an Asian regional office in Hong Kong, covering countries such as South Korea, China, Taiwan, Hong Kong, Australia, New Zealand, Thailand, Malaysia, Singapore, Vietnam, Indonesia, Philippines, India, Pakistan and Sri Lanka.

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