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Artificial intelligence driving inventory management for improved single-use systems manufacturing

EXPANSION OF SINGLE-USE SYSTEMS

The use of single-use (SU) technology for pharmaceutical and biopharmaceutical manufacturing is one of the most important and transformative trends in the industry.[1] It is expected that the adoption of this technology will continue to expand, encompassing more and more applications in both upstream and downstream processes.

It is estimated that the global market for single-use technologies in biopharmaceutical manufacturing will grow from $4.3 billion in 2021 to $7.3 billion by 2026 with a compound annual growth rate (CAGR) of 11.3% for the period of 2021-2026.[2]

Factors driving this growth:

- SU systems support faster startup to commercialization for new biopharma industry entrants. For a company ready to build a new facility, production processes centered on SU technology both reduce the capital expenditure for the startup and can shorten the time to production.
- SU technology is an important tool to mitigate and reduce contamination risks by eliminating the need for in-place cleaning and sterilization of fluid pathways and systems. This is impactful for CMOs (contract manufacturing organizations) because it reduces cross contamination between drug products.
- There has been a marked increase in the number of approved drugs using SU technologies; this gives manufacturers growing confidence that they can use SU products without complicating the FDA approval process.

Most significantly, SU technology provides a powerfully efficient tool as biopharma manufacturers continue to innovate and advance their production processes. SU products offer improved flexibility for single and multiproduct facilities by being able to adjust and/or customize the types of SU products they use according to different monoclonal antibody (mAb) or mRNA drug production requirements.

IMPROVING SU FLEXIBILITY AND ADAPTABILITY

Biopharmaceutical manufacturing continues to undergo rapid changes in approaches to production processes, to increase yields and improve productivity. This, along with the rapid growth of new kinds of biopharmaceutical therapies, such as mRNA vaccines and cell and gene therapies, is driving constant demand for SU products that can be rapidly customized to the unique challenges associated with these workflows.

For example, the expanded use of intensified processes such as perfusion, as well as the introduction of new filtration technology, is leading to greater cell densities in upstream production; in turn, this is driving efforts to explore how SU products can be applied to optimize downstream processes.

SU manufacturers are now challenged to be more agile and flexible in their design, customization and production processes — including assuring that their supply chains are sufficiently secure and globally diversified to meet their end users' demands.

SU manufacturers, sometimes referred to as SU integrators, draw from a broad range of raw material suppliers to create these unique customized fluid handling pathways and systems. At Avantor, our single-use raw material portfolio (also referred to as our "library") features multiple types of tubing, filters, connectors, sensors and other components. This library is constantly being augmented to include new suppliers based upon new or emerging end-user requirements.

In addition to the actual components used in a SU assembly, there are critical, parallel production supply requirements that also require effective supply management. SU products are intended to be used for drug production and used in regulated controlled environments. They are manufactured in environmentally controlled clean room conditions; therefore, clean room supplies and personal protective equipment (PPE) must be fully stocked and managed to ensure production and delivery commitments are sustained.

Equally important to the manufacturing process of SU products is ensuring the proper inventory of the associated packaging, including primary packaging bags, labels and boxes.

Single-use manufacturers need powerful inventory management, production forecasting and control tools that will support the flexibility and certainty they need to be agile and responsive suppliers for biopharma customers with needs that are constantly evolving.

BUILDING AND PROVIDING VALUE WITH THE LARGEST "LIBRARY"

SU manufacturers are true systems integrators; the final SU product or assembly is designed for a specific customer's use, built from the specified connectors, tubing, bottles and other raw material components designed for their unique upstream or downstream process function. All raw materials that go into the production of the final assembly are part of the raw material "library." Every part that is included in the library has been carefully selected and evaluated for its regulatory requirements and specifications. These specifications include (but are not limited to) USP Class VI, gamma stability, ADCF, chemical compatibility, supply assurance, etc.

Growing Raw Materials Libraries

- Connectors
- Filters
- Film
- Tubing
- Conical Tubes

Finished Assemblies

- Tubesets
- Bottle Assemblies
- Bioprocess Bags
- Sampling Assemblies

Fig. 1: Examples of SU libraries of material and examples of the assemblies they produce.

Avantor has built and continues to expand their sophisticated library of SU raw material supplies, as well as direct, fast-moving items such as boxes, fasteners, PPE gowns and other materials, to enable efficient SU production. If an existing SU assembly needs to be modified to include a different filter (due to changes in upstream production or batch sizes), Avantor can access its library to modify the filtration without having to do extensive testing or validation of the entire design.

This library is also an agile production tool to ensure that high-moving clean room and packaging items are also stocked and available, based on the current and upcoming production schedules. This library approach provides a powerful foundation for true end-to-end SU manufacturing, covering the entire lifecycle of the product.

In addition, investing the time and resources to expand it and keep it up to date gives Avantor the ability to match the innovations and improvements its customers are making as they advance biologic production processes.

MAJOR SU INVENTORY AND SUPPLY CHAIN ISSUES

Building and sustaining the inventory and supply chain resources necessary for productive and agile SU manufacturing is forcing SU providers to solve several interrelated issues.

The first is common to many life sciences lab operations, as well as manufacturers in other industries: lack of complete, real-time visibility into inventory of both SU raw materials and production-related materials. There are many state-of-the-art inventory management platforms that can, if properly established and with proper inventory control, provide the inventory visibility SU manufacturers need to have, especially with the demands for regulatory compliance and customization called for with SU technology.

Secondly, single-use manufacturers continue to be challenged with unpredictable supply chains. The impact of COVID on global supply chains and lingering inefficiencies for critical components have led many manufacturers to adopt less efficient and expensive "just in case" overordering and supply hoarding practices.

While adding some elasticity to the supply chain instead of relying on extremely tight just-in-time ordering and inventory management practices makes sense, there are ways to make much more effective use of advanced inventory management and forecasting tools that use machine learning and artificial intelligence (AI) capabilities.

Ultimately, lack of visibility and unpredictable supply chains can limit a SU manufacturer's unique value to biopharma producers: the ability to rapidly create custom designs and fill orders for SU products that can help advance biopharma innovation and productivity.

SOLUTION: LEVERAGE AI FOR DATA-DRIVEN DECISION MAKING

Taken on a piecemeal basis, even the most robust inventory manager software can still have gaps in information that will inhibit the ability of SU manufacturers to be as agile and responsive as they need to be to help advance biopharma productivity.

There is a growing recognition that the use of AI and machine learning tools can begin the process of moving from predictive, human-driven inventory management and manufacturing processes to genuine, data-driven decision making that goes beyond predicting what is needed to determining, prescribing and essentially deciding how to leverage the supply chain and nearly perfectly match it with the SU product demand.

From predictive to prescriptive

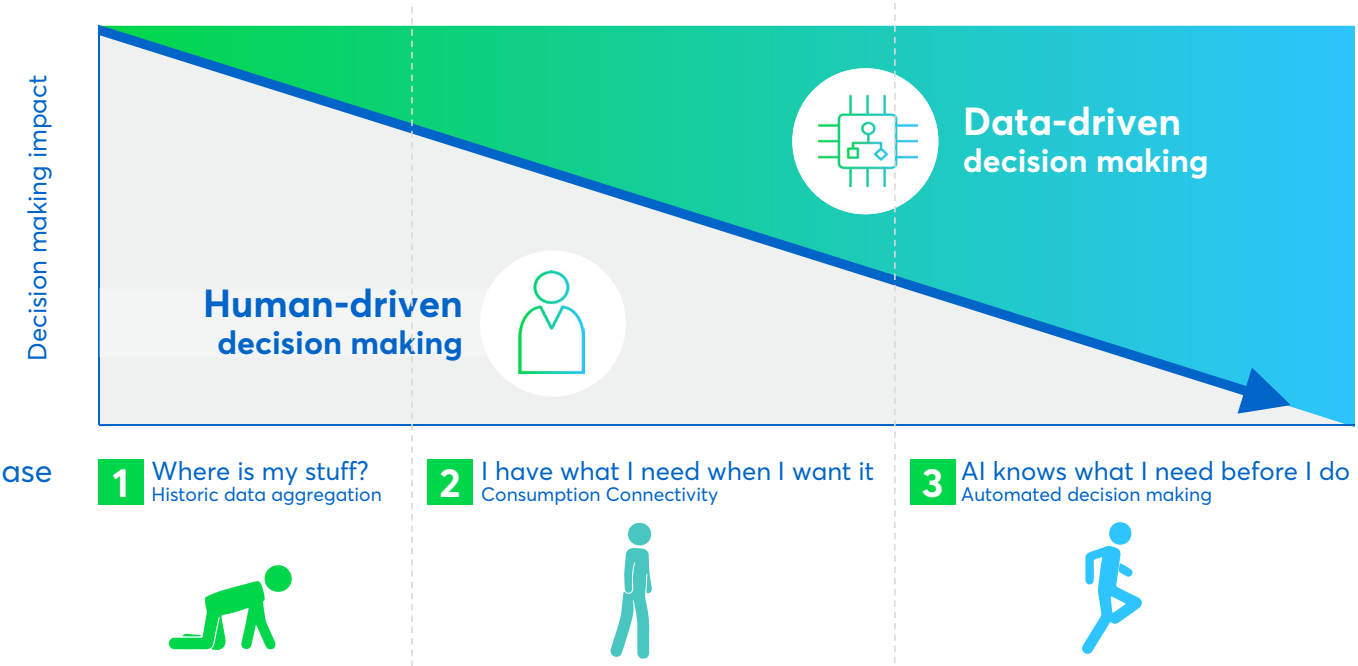

Fig. 2: Three key stages moving from predictive to AI-driven prescriptive decision making.

With AI and machine learning, SU manufacturers have stronger tools to automate and proactively identify deficits or roadblocks in both onsite inventories and supply chain resources. This can be done through the use of newly available inventory tracking tools like smart shelves that use Internet of Things technology to gather critical, real-time data.

This cuts down the time and effort required by sending personnel to manually scan shelves or double-check storage areas to track down materials that are supposed to be in stock. With AI learning and tracking what's available — and what isn't — production planning and inventory restocking becomes prescriptive; order replenishment can even be automated.

Biopharmaceutical manufacturers have launched significant investments in AI and advanced data mining capabilities. These companies are designing their own technology and partnering with AI platform developers for support in target identification, drug design and clinical trial analysis.[3]

It makes sense, then, with the expanded role SU technology is playing in biopharma, for SU manufacturers to consider making similar investments. The ultimate vision is to go from where many SU manufacturers are now — historic data aggregation, or "where is my stuff?" — to automated decision making, or "AI knows what I need before I do."

CASE STUDY: IMPLEMENTING AI IN SU MANUFACTURING

At Avantor Fluid Handling (AFH), expanding the role of AI technology to move from predictive to prescriptive decision making has been following the multistage model. AFH is building from existing historic data aggregation processes to a more advanced consumption connectivity operation with improved confidence in real-time inventory availability and operational efficiency, with the ultimate goal of automated data-driven decisions.

There are two factors that are key to helping move this implementation forward:

- **Collaboration with customers:** AFH has established close working relationships with drug manufacturers using SU technology. These relationships have been critical to helping AFH understand and respond to fast-emerging changes in SU product requirements.

  These close collaborations enable AFH to take maximum advantage of Avantor's best-in-class library approach to SU technology manufacturing. This approach lets SU end users choose from a wide selection of single-use raw materials from Avantor's brands or other vendors. To fully realize the agility this open architecture approach offers, AFH has to have the confidence that its inventory and supply chain can meet a request for a new assembly.
- **Expanding the use of IoT technology:** Data-driven decisions need as much data, in real time, to make effective choices that manufacturers trust. At AFH, a significant investment in a range of IoT systems is generating that data, not only to guide current decision making (not yet fully automated) but also to build up deep historic data that AI technology can mine to enable reaching the ultimate goals of automated decision making.

The technology has enabled AFH to develop a more sophisticated approach to managing its SU component inventory. Using a multitiered approach, components are identified and managed according to criticality: highly critical, moderate or low-level.

Based on the data they have already accumulated, critical components are those with longer lead times and with fewer sources in the supply chain that provide that component. Using this approach, AFH is also able to work multiple layers of opportunity based on an end user's regulatory requirements. These efforts were expanded during the COVID pandemic and enabled the implementation of stronger supply chain assurance and improved business continuity capabilities.

The portfolio of IoT technologies developed by Avantor and deployed at AFH's Devens, Massachusetts, manufacturing facility is already having a major impact on the facility's efficiency, quality control and ability to meet customer requirements.

Smart buttons:

These simple devices support the digitization of clean room processes, enabling significant time savings. Located throughout the workspace, they can be used by personnel to request quality control (QC) or engineering support from outside the clean room. They have already contributed to improving throughput during assembly processes while increasing assurance that all critical QC inspections are conducted before an assembly can move to the next step in the process, either to complete assembly or send to packaging.

The smart buttons provide a single point of contact for onsite support teams, further standardizing the process. Equally important, better management of these kinds of technical requests is helping minimize the frequency with which personnel have to enter the controlled environment, helping reduce contamination risks.

Over the long term, machine learning can track when and why these requests were made and correlate with other data flows to identify ways to further streamline processes, potentially even automating support requests based on the long-term data captured.

Smart shelves:

These tools are crucial to transforming SU inventory management. The real-time data they provide contributes to building the critical insight AI needs to learn and ultimately prescribe order and replenishment cycles, guided by the AFH's criticality approach to component supplies combined with more enriched data from Avantor's global supply chain.

Smart shelves developed by Avantor and used in Devens are dramatically improving inventory visibility, helping minimize inventory discrepancies, reducing stockouts and generating detailed consumption data.

The data generated is fully integrated with ERP systems and is already supporting automated reordering. This includes more than just SU components: High-volume inventory items such as PPE products, as well as all the packaging materials needed for safe, aseptic shipping of complete SU assemblies, are tracked and managed through tools like smart shelves.

They are also generating significant labor savings by significantly reducing the need to have personnel inspect and scan shelved inventory to update and verify stock availability. This means the Devens team can assign personnel to more important, value-added SU production tasks, often saving hours of time each week previously dedicated to double-checking what's on hand.

AI-powered vision systems:

Implementing an array of vision systems, both in storage areas and in clean rooms where SU products are assembled, can significantly improve quality monitoring and control, especially related to the proper use of PPE materials, as well as critical QC monitoring of SU assembly steps.

In SU production, there is a significant amount of time embedded in product inspection and assembly verification — such as seal inspections — as well as verification that associates are properly gowned with the correct PPE before proceeding into the clean room. Through AI-driven vision systems, quality and specification assurance can provide critical backups through proactive deviation alerts if there has been an error in these steps.

Vision systems can combine with data from smart shelves to enhance inventory management, tracking and replenishment processes. They also can contribute to AI efforts to harness data to better understand when and how errors in assembly and gowning procedures occur and help fuel prescriptive end user, inventory and market forecasting.

MOVING SU MANUFACTURING FORWARD WITH AI

Demand for single-use systems and technology in biopharma will continue to grow, challenging SU manufacturers to be more productive as well as more agile, to satisfy the customization requirements that many drug producers will have as they continue to innovate their manufacturing processes.

AI-driven inventory management for the full range of SU products and manufacturing needs — components, PPE, packaging materials and other items — provides a powerful tool to enable SU manufacturers to meet this demand.

Advances in AI and machine learning systems, coupled with sophisticated IoT systems such as smart shelves and vision systems, can generate the data needed to move inventory management from predictive to prescriptive decision making.

At Avantor Fluid Handling, these tools and the investment in building AI-driven decision making are already generating tangible savings and greater efficiencies in production and quality control. Combined with Avantor's library approach to inventory management, there are significant advantages to investing in both the IoT technology Avantor offers and the implementation of AI capabilities to elevate SU manufacturing productivity.

With these tools, SU manufacturers will spend less time "checking the shelves" and devote more time and expert resources to the scientific and engineering challenges of developing innovative new SU solutions for bioprocess drug manufacturers.

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