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Manufacturing Equipment Trends

Advanced therapies, COVID-19 pandemic and vaccine production significantly impact equipment needs.

As pharma and biopharma pipelines trend toward biologics, complex oncology therapies, rare and orphan diseases, and with increasingly stringent FDA requirements, the impact on manufacturing equipment necessitates even greater flexibility. Additionally, the COVID-19 pandemic and vaccine production have significantly impacted equipment needs.

As batches and regimens trend shorter and more customized, the need for flexible equipment to accomplish more than one task is paramount. The latest trends impacting pharmaceutical manufacturing equipment include flexibility in product and container types, digitalization in pharma production, and processing of Advanced Therapy Medicinal Products (ATMPs). Additionally, a shortage of trained operators is advancing automation efforts.

This roundtable includes perspectives from top equipment suppliers across drug manufacturing, processing and packing of both large and small molecules, and provides insight into today's manufacturing equipment market trends, some of the latest advances, where the industry stands with adopting production innovations, new technologies and growth in automation.

PHARMA AND BIOPHARMA TRENDS IMPACTING MANUFACTURING EQUIPMENT

Andreas Mattern, Vice President Strategy & Global Product Management Pharma, Syntegon

"According to the World Health Organization, 4.9 billion people, or 61.6 percent of the world population have received at least one dose of a COVID-19 vaccine, gradually decreasing the pathogen's virulence. Despite these first successes, the virus' threat remains persistent, as new variants like Omicron are changing the game. This requires leading vaccine manufacturers to continu-

ously adapt existing vaccines and keep up global supply. Besides the vaccines themselves, their packaging and administration is also changing—from vials to pre-filled syringes. They contain a single dose and can be administered even more quickly. We are already experiencing this changing demand. While we supported drug producers with new vial lines and modernizations of existing equipment during the first years of the pandemic, we now see a rising demand for high-performance and highly accurate syringe filling machines. According to our analysis, about half of the global COVID production sites listed on the UNICEF COVID dashboard have processing or packaging equipment from Syntegon installed."

Jan Deininger, Group Communications Manager, OPTIMA packaging group GmbH

"Customers look to a comprehensive turnkey supplier who can take care of the complete filling line with isolator and freeze-dryer—from the conception phase through to the life cycle management. Complex filling lines with isolator and freeze-drying equipment are in demand. In order to bring these lines fast and safely into production we support our customers with our Comprehensive Scientific Process Engineering (CSPE) approach for a short time-to-market of turnkey projects. Digital engineering methods and integrated Factory Acceptance Tests of the entire equipment enable our customers to go into production as quickly as possible. Work that has typically taken place at the customer's site to date will already be performed to an even greater extent at one of our CSPE centers. In many cases, on-site tests do not have to be repeated, which significantly shortens the time-to-market.

"Digitalization in pharma production continues to be a great trend. For Optima Pharma, a broad portfolio of digital solutions was developed and these solutions are being used successfully in the first lines. Optima also massively upgraded in terms of cybersecurity and implemented a particularly secure VPN solution. Digital technologies not only help in engineering, but also in operating the systems: For example, during changeovers for format changes or when converting the line to a new pharmaceutical product. All the work to be carried out by the operating personnel can be called up via augmented reality glasses and can be visually fed into the filling line reality. The operator implements this information directly on the system."

Deborah Smook, Vice President of Marketing & Business Development, TurboFil Packaging Machines

"One trend is the need for flexible equipment that can accomplish more than one task. From our vantage point, we're seeing the pre-filled syringes market continue to expand, with syringes used for drug-device combination products seeing significant growth. Syringes are an example of a mission-critical device with a wide array of shapes, sizes and formats—exemplifying the need for flexibility.

"Importantly, a shortage of trained operators is advancing automation efforts. Staff shortages have also become an issue. In an industry that was already trending toward automation, COVID continued to push the boundaries of that trend for reasons of both personnel absenteeism and, of course, social distancing and safety. Now, the manpower shortage has expedited automation's growth toward permanence, with everything from production to inspection moving decisively in that direction."

Digital format change assistant from Optima Pharma

Raffaele Pace, Engineering Vice President of Operations, Stevanato Group

"Most of all, increasingly sophisticated treatments and medications are requiring equally sophisticated manufacturing equipment solutions. With complex, smaller-batch medications and niche therapies comprising a larger share of overall new drug launches, equipment now needs to be more flexible than ever to meet manufacturing needs will justifying cost of ownership/ROI.

"Further complicating matters is that, notably, this shift toward more specialized therapies hasn't meant a more limited range of devices and delivery system—but rather the opposite. Product customization is coming with a broader array of injection and inhaler devices, presenting significantly different designs in terms of size, material and shape. Each demands its own manufacturing processes—another reason machine flexibility and modular line configurations has become paramount."

Frederick Murray, President, KORSCH America

"The emphasis on OEE (Overall Equipment Effectiveness) continues to be a major consideration for most manufacturers. Tracking machine uptime, output, and yields in addition to key quality attributes—and gearing improvement efforts around reducing changeover times or permitting a single operator to monitor multiple machines—is a key focus. Most products have been validated across a defined speed range of the tablet press, but often, there is the potential to run at the maximum validated speed if the right steps are taken with optimizing the press setup.

"In addition to the focus on equipment utilization, the industry continues to move toward an increased requirement for medium (OEB 3) and high-containment (OEB 4/5) systems for tablet compression applications—driven by both safety and process efficiency considerations. A fully wash-in-place (WIP) tablet compression system will include the press, deduster, metal check, tablet tester, contained feeding system, and contained air-handling system—all tied together with a single SCADA system that controls both the process as well as the automated WIP sequence. Eliminating full-time PPE requirements is also an ob-

Syntegon Versynta microBatch

jective of many EHS groups—and the latest technology permits the operation of medium and high-containment systems without any PPE requirement."

LATEST ADVANCES IN MANUFACTURING EQUIPMENT

Andreas Mattern, Syntegon

"In the wake of the biopharmaceutical and specialized treatments surge, equipment manufacturers like Syntegon have started developing solutions for small and micro batch filling that meet several requirements at once. For high-priced biotech drugs, it's all about low output and high product yield. Syntegon's small batch solution Versynta Flexible Filling Platform (FFP) with an integratable isolator, which was launched last year, ensures maximum flexibility and product safety. Versynta FFP consists of pre-tested modules that can be selected individually, including different filling systems and Syntegon's four axis handling robot specifically developed for aseptic operation. For even smaller batch sizes of only several hundred containers per hour, the fully automated, gloveless production cell Versynta microBatch is currently being developed. Typical use cases are fill/finish of drugs for clinical trials or production of gene and cell therapies."

Sabri Demirel, Managing Director, Romaco North America

"The extensive automation of entire manufacturing processes and the implementation of smart technologies are among the most innovative advances in pharmaceutical processing. An example of this new generation of machines is our TP R Optima Tablet Coater from Romaco Tecpharm, which uses automation to make manual intervention in parameter setting virtually unnecessary, thus creating absolutely reproducible coating results and on top of this, offering a unique batch size variability of true 10 to 100 percent in a single drum.

"This is achieved on the one hand by very accurate parameter monitoring, and on the other by the technological tools to respond to changes and conduct the necessary adjustments: The TP R Optima uses, among other things, sonar technology to continuously measure the batch volume and tablet bed inclination as well as an intelligent spray arm and individually controllable exhaust air flaps to adapt to parameter alterations."

Mandar Dixit, Head of Value Chain Solutions, Bioprocess Solutions, Sartorius

"There is increased adoption of single-use equipment to replace traditional stainless-steel systems to reduce drug manufacturing costs by eliminating the need for cleaning and associated cleaning validation. Single-use technologies also help reduce capital costs, new facility construction time-frames as well as their energy consumption.

"Both larger and smaller scale single-use stirred tanks as well as rocking motion bioreactors are available from multiple suppliers to cover the gamut of applications from mAb's and recombinant proteins through mRNA and cell therapies. Chromatography and TFF systems for downstream processing with fully single-use flow paths are being increasingly implemented for obvious reasons.

"Also, specialized equipment that supports intensified or continuous bioprocessing such as scalable multi-column chromatography (MCC) BioSMB systems from Sartorius are available. Integration of two or more-unit operations on to a single skid is also being evaluated. Increased automation through in-line or at-line measurements of key process parameters and their easy integration into the centralized DCS or MES systems in the plant is another key trend that we observe."

Debbie Bowers, Vice President of Commercial Development, Picoliter Dispensing Technologies for BioDot, an ATS Company

"Major advancements include machine learning for self-tuning of various instrument parameters, including fluidics, positional dispensing and speed of movements. Other enhancements include digital connectivity for preventative maintenance and early warning of potential future break/fix needs—a trend aiming to meet higher equipment uptime needs."

Marie Jourdan, Vice President Marketing & Product Management, Univercells Technologies

"We are purposely designing manufacturing platforms for advanced therapies, re-thinking process architecture to amplify the

benefits of process intensification and integration. The use of automated, closed platforms reduces manual operations, increasing process reliability and batch-to-batch consistency by minimizing risks of errors, deviations, and lost batches from human operators.

"The NevoLine Upstream platform offers a total solution by chaining the fixed-bed scale-X bioreactor with in-line clarification and concentration steps to deliver concentrated bulk harvest within a 3 m^2 automated footprint. Continuous manufacturing principles were deployed to combine upstream (cell culture and virus production) and midstream unit operations (clarification, in-line concentration) steps into an automated, closed environment.

"Within the NevoLine platform, or in benchtop systems, scale-X bioreactors are available from R&D to commercial scale to ensure streamlined scale up and tech transfer from process development to market. A structured fixed-bed design promotes homogeneity with low-shear to increase specific viral productivity. Scaling is based on bioreactor height and diameter with constant compaction for linear volume/surface ratio. Simpler process transfer is achieved with three step optimizations compared to traditional technologies that have complicated, multi-step processes that are costly to scale."

INDUSTRY ADOPTION OF PRODUCTION INNOVATIONS AND NEW TECHNOLOGIES

Andreas Mattern, Syntegon

"The pharmaceutical industry is not known for its fast adoption of new technologies or processes, mainly due to the strict regulatory guidelines in place to ensure maximum product and patient safety. In many cases, working on pilot projects or in strategic partnerships has shown to speed up innovation significantly.

"Artificial intelligence is the most prominent example. Deep Learning vision tools, which only require moderate software modifications, have been available for a while. It took a machine manufacturer (Syntegon) with sound software, process, and validation expertise, and a pharmaceutical producer (Amgen) with the wish to make processes even safer and more reliable to implement the first fully validated visual inspection system utilizing AI.

"Partnerships have also been driving innovations in small batch liquid fill-finish operations. Versynta microBatch, the highly flexible and fully automated production cell with a gloveless isolator, is a joint development of Vetter and Syntegon. Together, both companies are addressing the need for ever more flexible platforms that process smallest batches of highly effective drugs."

Raffaele Pace, Stevanato

"In our business, the integration of artificial intelligence into visual inspection systems is moving toward systems capable of detecting, measuring and quantifying essentially every particle in a vial, syringe or other container. This ability for machines to 'learn' will pay dividends in the longer term. Tapping this potential also aligns with the niche, smaller-batch direction of the greater pharma and biopharma landscapes. Such nimbleness and agility can be key drivers in accommodating rapid, cost-effective production of this sort, as it would deliver batch-level defect detection capabilities."

Michael Healy, Vice President Applications Engineering, Systems Engineering and Innovation, ATS Automation – Life Sciences

"Companies are looking for ways to take advantage of new technologies to give them a competitive advantage. There is also a shortage of trained people to operate the equipment and new technologies are being looked at as potential ways to bridge the gap, and build the smarts into the equipment, not relying as much on people. In summary, the desire to adopt new technologies is high, but the actual rate of adoption and incorporation is low.

"The barriers to adoption that I see are a) capability and specifically the shortage of knowledgeable people, b) regulatory requirements and compliance to same, c) clear problem statements and therefore appropriate solution implementation, and d) perceived risk and hesitancy to change. For example, there are a lot of software companies that claim cloud integration experience and application of AI to the collected data. The problem you find is these companies do not understand the basics, i.e. what it takes to run a machine, to make a machine go from 92% to 93% OEE.

"With the aggressive pace of new projects, new product introductions, ramp-up plans, etc. making a change can be seen as risky. To me, a partner who understands technology adoption, is dedicated to it, has a track record of success, and can provide the necessary service/support mitigates the adoption risk and solves this hesitancy problem."

Sabri Demirel, Managing Director, Romaco North America

"The pharmaceutical industry is very open to innovations, provided they really improve the production processes, also in the long term, and thus justify the investment in new technologies. Let's take the example of digitalization: Romaco has developed the Remote Assist service concept, which provides customers with digital tools that reduce downtime and therefore increase the OEE. These tools include remote maintenance, in which a remote diagnosis can be made via secure online connections and faults can be rectified immediately at best, as well as real-time support via data glasses worn by the machine operator in the customer's facility. These enable our service technicians to see through the operator's eyes, so to speak, and provide guidance during the ramp-up phase or during format changes and repairs. These offers are very well received, also because they allow flexibility in exceptional situations."

Phil Vanek, Chief Technology Officer, Gamma Biosciences

"We're seeing considerable interest in next generation technologies in the advanced therapy space, as it has long been recognized that first generation bioproduction technologies could not fully address the manufacturing complexity of these new modalities. The rate of adoption has been driven forward by the underlying needs of better, faster, and cheaper manufacturing, but tempered by the caution of a regulated industry that is working tirelessly to get safe and effective medicines to market. As these Industry 4.0 abstractions continue to translate into practical, real-world manufacturing technologies, there is no shortage of enthusiasm to adopt them if product quality and safety can be assured." **CP**

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