Pharma Europe 2019: Biomanufacturing of Biopharmaceuticals - Ganapathy Sivakumar -University of Houston

Ganapathy Sivakumar,

University of Houston, USA

Abstract

Biomanufacturing has become an emerging industry of strategic importance worldwide and is one among the key technology areas identified by the US Advanced Manufacturing Partnership (AMP) as an appropriate target for public-private investment to support advances in manufacturing and U.S. competitiveness. the event of advanced biomanufacturing technologies consortium will foster and support the fast growing biomanufacturing industry and establish sustained leadership of the US within the area. This session organized by the Biomanufacturing Science and Technology Consortium (BSTC) team will feature experts from government, academia and industry and seek to: 1) discuss the challenges and drivers of biomanufacturing in upstream, downstream and drug product processing, 2) identify the main scientific/technological, operational and regulatory barriers within the biopharmaceutical industry, and 3) define a pre-collaborative work space for companies, academia and regulatory authorities. Biomanufacturing produces a good range of biobased products for the emerging global bioeconomy. Biomanufacturing begins with bioprospecting – the invention and commercialization of latest products supported biologic resources.

Biomanufacturing requires knowledge and methods from many scientific disciplines including biology, microbiology, biotechnology, chemistry, physics, engineering and technology. It includes gene-splicing and metabolic engineering plus various cell and tissue culture technologies. Bio manufactured products range from biopharmaceuticals to industrial enzymes, human tissues and replacement organs, biofuels, 'green' chemicals and green products to exchange those derived from petroleum. the appliance of biotechnology to industrial manufacturing isn't only transforming how we develop and produce products, it is also generating new ideas - like using microalgae to wash power station effluent gases and process water while making biofuels to assist run the facility plant at an equivalent time. Another example is anaerobically turning manure and other wastes into gases to form electricity. Every job during a biomanufacturing enterprise must combine during a unified effort to create quality into each phase of creating the merchandise . Everyone involved shares an equivalent goal: achieve the very best quality product on a uniform basis. Commonly held skill standards and protocols establish and maintain this state of thorough control. The Food and Drug Administration's current Good Manufacturing Practices (cGMP), outlined in CFR 210 and 211, are wont to create repeatable standard operating procedures (SOPs) which will be validated to form sure manufactured products always have consistent quality. Teams develop methods for effectively monitoring production performance. Together, they analyse samples to guage each step and continually improve goal attainment.

There are a number of challenges facing the biomanufacturing industry, from both the contract manufacturing organisation (CMO) and industry perspectives. Biomanufacturing is a complex, labour-intensive and expensive process and therefore it is extremely important to understand and balance capacity versus demand and staffing level. Identifying, hiring, training and retaining properly qualified personnel are very critical to the successful operation of a facility, since biomanufacturing requires a very specialised and experienced workforce. Staff must have technical expertise in specific areas including upstream or downstream current Good Manufacturing Practice (cGMP) manufacturing operations, process development, project management, process engineering, quality assurance, analytical development, quality control, regulatory compliance, and many other highly specialised functions. Once on board, new employees must be trained on facility, process and testing standard operating procedures (SOPs) in order to be qualified to perform their job functions. Training and qualification in some aseptic operations can be quite complex, taking several months to complete, and can involve on-the-job training and, in some cases, qualification testing using established procedures such as media fills.

Global manufacturing of biopharmaceuticals has increased significantly over the last decade due to several factors. A major industry driver has been the expansion of the market for biopharmaceutical products. Biopharmaceuticals can be highly effective and potent, can have fewer side effects and can cure diseases rather than merely treat the symptoms. These advantages, combined with the increasing number of new diseases treatable with biopharmaceuticals, are driving demand for these drugs worldwide. In 2005, biotechnology revenues worldwide were forecast to reach more than US$45 billion, or almost 10% of total global drug sales. The therapeutic antibody market represents over US$8 billion. More than 100 biotechnology drugs have been approved since 1997 and, today, at least seven of the top biotechnology drugs bring in more than US$1 billion annually. It is estimated that 300 biopharmaceutical products are in clinical trials, with another 600–700 in pre-clinical or early clinical development. Large pharmaceutical

companies continue to outsource manufacturing and filling of selected products, but the real growth is from the many biotechnology companies that elect to outsource pre-clinical to commercial development to avoid the cost and risk of establishing in-house manufacturing. Outsourcing Biomanufacturing Certainly a key advantage of outsourcing biomanufacturing pertains to capital utilisation requirements. Not all companies have the capital, internal expertise or time to invest in constructing a cGMP-complaint facility for manufacture of their biopharmaceutical product. Outsourcing to an experienced CMO can lower production costs, improve manufacturing efficiency and have a positive impact on the balance sheet. Companies can buy and make capacity at the same time, accessing external technology and expertise early in the clinical development of the drug and maintaining flexibility until internal manufacturing capability becomes strategically important. Companies are finding that certain operations, such as lyophilisation and aseptic processing, that are not core competencies are not economical to run in-house. They are looking to outsource more of these activities. Outsourcing biomanufacturing also reduces time-to-market as constructing a new, fully validated facility takes several years. Outsourcing manufacturing gives companies an opportunity to place greater focus on their own core competencies.

When selecting a contract manufacturer, a company needs to evaluate the contractor's capacity, capability and track record. The two businesses should also be aligned behind common scientific standards. A CMO's ability to take over the manufacturing process and its experience making similar products with similar production processes needs to be considered. The CMO's capacity and flexibility to handle current volumes and its ability to expand operations if needed down the line is another critical factor. The company also needs to assess the CMO's 'corporate culture' – that is, how well the contractor's management team will work with the sponsor and how smoothly the project is likely to go. Other factors that could affect the outsourcing decision are the goals and scope of the outsourcing initiative: which products will be manufactured in what volumes and on what timeline? Which functions will be handed over to the contractor and which will be retained by the sponsor or outsourced to another third party service provider? Careful planning and wellthought-out execution can eliminate any obstacles to successful technology transfer.

Abstract

Plant-based drugs to treat human lethal diseases have been elicited with cutting-edge clinical research. Colchicine is an important alkaloid-based drug used to treat gout, cardiovascular disease, etc. However, plant-based biopharmaceuticals and industrial-scale development pose several challenges in biomanufacturing. Biorhizome is a new technology to enhance the colchicine biomanufacturing. Nevertheless, the biochemical pathways and regulatory networks in the biorhizomes that control colchicine biosynthesis are yet to be characterized, leaving a significant barrier to improving colchicine biomanufacturing. The presentation will emphasize the biomanufacturing of biopharmaceuticals and improving the commercial-scale biorhizome-based colchicine.

Recent Publications

1.Sivakumar G (2017). Upstream biomanufacturing of pharmaceutical colchicine. Critical Reviews in Biotechnology, DOI: 10.1080/07388551.2017.1312269.

2.Sivakumar G, Kamran A, Phillips GC (2017). Biorhizome: A biosynthetic platform for colchicine biomanufacturing. Frontiers in Plant Science, 8: 1137.

3.Gentile L, Uccella NA, Sivakumar G (2017). Soft-MS and computational mapping of oleuropein. International Journal of Molecular Sciences, 18: 992.

4.Gentile L, Uccella NA, Sivakumar G (2017). Oleuropein: Molecular dynamics and computation. Current Medicinal Chemistry, DOI: 10.2174/0929867324666170912102623

Biography

Sivakumar's research is primarily focused on biomanufacturing and biotech implications of biopharmaceuticals. He has extensively studied the plant-based small molecules pathway biochemistry, synthetic biotechnology and metabolic & bioprocess engineering. He is internationally recognized in the field of biopharmaceuticals and a pioneer in biomanufacturing of biorhizome-based colchicine. He has over 50 publications. He is also on the editorial board of several journals. He serves as an expert of grant proposals as well as numerous scientific journals. His laboratory focuses on metabolic and bioprocess engineering of colchicine pathway and developing potential anticancer medicine.

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