STRATEGIES FOR DEVELOPING A BIOTECHNOLOGICAL PLANT FOR L-ASPARAGINASE PRODUCTION

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ABSTRACT

The increasing importance of pharmaceutical biotechnology also highlights the challenges faced by industries in this sector, with an emphasis on the production of biopharmaceuticals. This article discusses the production of L-asparaginase, a key player in the treatment of Acute Lymphoblastic Leukemia (ALL), focusing on the evolution of regulations, both national and international, as well as highlighting the need to adhere to Good Manufacturing Practices (GMP) and obtain Certificates of Good Manufacturing Practices (CBPF) to ensure the quality and safety of biotechnology products. Economic aspects of biosimilars are explored, along with the challenges of the manufacturing process and the specifications for pharmaceutical products. Strategies for the development of a new biotechnology production plant are also addressed, with a focus on compliance with production process flows, environmental classifications and regulatory requirements, covering topics such as Active Pharmaceutical Ingredients (API), manufacturing processes, industrial projects and risk analysis, in a comprehensive manner of the field.

Keywords: Industrial Biotechnology, Biopharmaceuticals, Production Process Flows, L-asparaginase.

1 INTRODUCTION

Acute Lymphoblastic Leukemia (ALL) is a type of neoplasm that consists of mutated blood cells, compromising the function of cells of the myeloid or lymphoid lineage. Current therapeutic regimens use the biopharmaceutical L-asparaginase as one of the main options for treating ALL. This biosimilar, when administered in combination with other therapies, has shown success rates of 90% in treating patients.[1]

Unlike products derived from organic synthesis, biosimilars are drugs made up of complex chains, mainly amino acids. As such, this characteristic means that biopharmaceuticals have greater regulatory restrictions when it comes to obtaining production and marketing approval from health agencies.[2] As a result, factories need to have highly prepared and equipped facilities that comply with the regulatory requirements laid down in national and international legislation in order to guarantee the production of biotechnological Active Pharmaceutical Ingredients (APIs) in complete safety. [3]

The design of the buildings and the quality of the facilities at the drug production, storage and analysis sites must be designed to mitigate the risk of cross-contamination errors, guarantee the quality of the active pharmaceutical ingredients at all times, preserve the environment, provide easy access for maintenance and cleaning, and ensure the safety of employees. In order for the industry to be able to produce biotechnological drugs, there are a series of requirements and regulations that must be met. In the case of Brazil, these plants must comply with good manufacturing practice (GMP) requirements.[4]

These requirements can be modified depending on the country where the drug is to be manufactured or exported. Despite the similarity in GMP requirements, there is no harmony in the standards defined by the different global regulatory agencies, as each body responsible for certifying the product may present additional requirements. [5]

2 MATERIAL & METHODS

This work is qualitative and quantitative in nature and the method used is to propose a study of the strategies adopted to develop a new biotechnology plant dedicated to the production of the biopharmaceutical L-asparaginase.

In the development of this study, the research procedures were based on specialized literature on biopharmaceuticals and pharmaceutical inputs, guides to good manufacturing practices, both national and international, available to consolidate the entire database applied in this material.

Microsoft Visio® 2013 software was used to develop the layout proposals for the new plant. It is important to note that all the material presented in this work reinforces the consolidations that will be described in the data analysis and conclusions presented, emphasizing that the main objective is to address the strategies adopted in the design of the development process of a new biotechnology production plant dedicated to the production of the biopharmaceutical L-asparaginase and to discuss them.

3 RESULTS & DISCUSSION

One of the main weaknesses encountered in the development of layouts for pharmaceutical production plants is in relation to the flows of production processes, since at various stages of the process cross-flows must be avoided for both people and materials (production inputs, in-process materials, finished products, raw materials) and waste.

Cross-flows can occur, in principle, at almost any stage of the production process if they are not rigorously planned. However, it is worth noting that in a critical scenario, the most problematic crossing would be in the areas where there is the greatest exposure of the biomolecule to the environment, which generally occurs in places where people and waste pass through, due to the level of exposure of particles in the environment and the molecules of biopharmaceuticals being very susceptible to contamination during the manufacturing process.

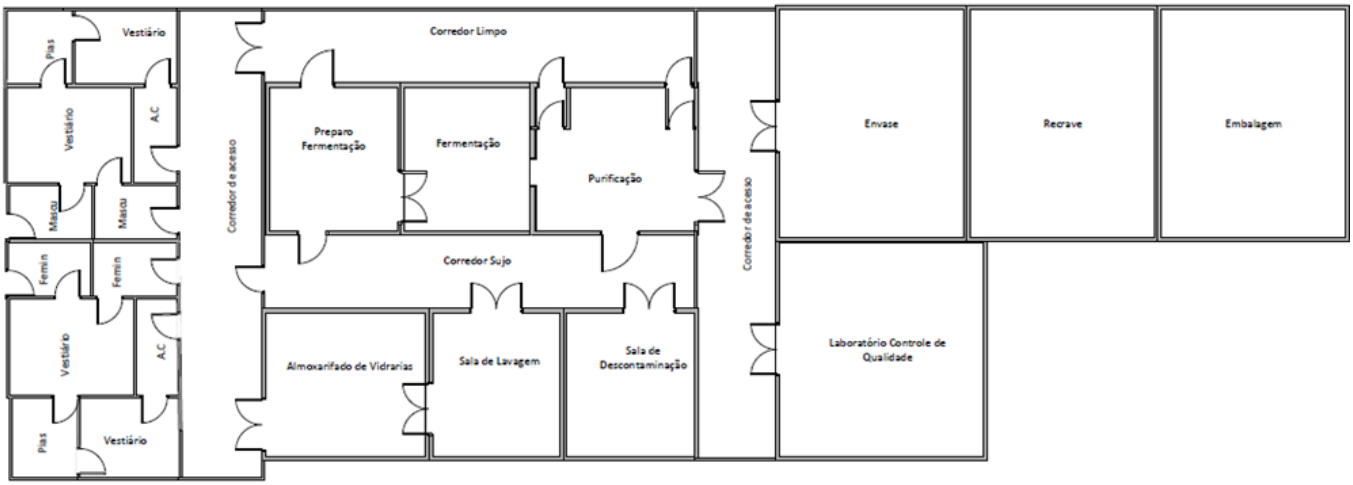

Figure 1 Layout proposal for an L-Asparaginase production plant.

The proposed layout shown in Figure 1 is divided into the following areas: entrances to the plant through the men's and women's changing rooms; an access corridor that connects the clean corridor which gives access to the process rooms; preparation of the culture media; fermentation and purification. The dirty corridor receives the materials used in the process and gives access to the decontamination room, washing room and glassware storeroom.

On the other side of the plant there is another access corridor for the purified product to be taken to the Quality Control Laboratory and the final formulation, filling, crimping and final product packaging area.

This layout proposal reduces the risk of crossing flows of materials in process and people with the waste outputs generated during the production process.

4 CONCLUSION

Based on the perceptions presented, it can be concluded that despite the wide access to standards, legislation and articles that provide guidance on the regulatory requirements necessary for new biopharmaceutical manufacturing facilities, it is still necessary to understand each item according to the needs of the process in order to ensure feasibility in the preparation of projects.

The assessment of multidisciplinary work made up of several highly qualified technical areas with knowledge of the processes involved in producing pharmaceuticals and biopharmaceuticals is fundamental in order to be able to proceed with the preparation of proposed layouts for developing a new biotechnology production unit.

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