Maintenance and Life Cycle Analysis of Biomedical Devices in the Pharmaceutical Industry

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Abstract— The global population growth, as well as the increasing longevity of people's lives allied with the mobility between Countries, is necessarily linked to an increasing number of pathologies and other associated comorbidities. In this way, health sciences, and particularly the pharmaceutical industry, play a fundamental role in responding to these challenges caused by the high number of illnesses affecting the human condition, in place and expected.

Within the pharmaceutical industry, chromatography is an analytical technique with a very importance in terms of quality, safety and compliance with the most demanding international standards of pharmaceutical products and compounds, in addition to being able to be a determining factor in terms of economical differentiation from other companies inside the market.

Failure Mode and Effects Analysis (FMEA) is a structured approach to discovering potential failures that may exist within the design of a product or process. Failure mode (FM) refers to the way in which something might break down. It includes potential errors that might occur, especially errors that could affect the customer. Effective analysis (EA) involves deciphering the consequences of those breakdowns. It does this by ensuring all failures can be detected, by determining how frequently a failure might occur and by identifying which potential failures should be prioritized. Business analysts typically use FMEA templates to assist them in the completion of analyses.

The case study in the present paper applies the chromatography knowledge and the FMEA technique to the pharmaceutical industry. This paper was carried out at the pharmaceutical company Hovione, more specifically in the Engineering and Maintenance department, and aims to analyze the life cycle of biomedical devices in the pharmaceutical industry, particularly those involving the chromatography technique. It was possible to identify the importance of this study in this type of industries.

Keywords- Chromatography; Biomedical devices; Pharmaceutical industry; Life cycle analyses; Maintenance.

I. State of Art

According to Ali T. et al. maintenance is a manufacturing program whose objective is to maximize the effectiveness of equipment throughout its useful life, through the participation and motivation of the entire workforce.

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The three main objectives of a maintenance program are trying to achieve zero accidents, zero defects and zero breakdowns. These goals can be achieved by implementing planned activities to improve equipment efficiency, creating an autonomous maintenance program, establishing a planned maintenance system, organizing training courses for workers, and designing a system factory management. The critical factors that affect the overall efficiency of pharmaceutical industry equipment are loading time, downtime, standard cycle time, current cycle time, unit produced and unit defective. Overall equipment efficiency is an indication of several major equipment-related losses, like set-up and adjustment, equipment failure, minor stoppage and idling, defect and rework, equipment shutdown, speed, minor stoppage, and idling. Implementation of maintenance is required to make the production process efficient and smooth. The current business field is becoming more challenging due to facilitating the inevitability of increasing productivity, maintaining global standards and cost-effectiveness. To achieve this, the main focus of manufacturers today is on the maintenance program to bring the entire production system to a zero-defect level. The implementation of a maintenance program can facilitate the production organization's quest to obtain a better production performance, leading to advantage from the remaining competition in the market. (Ali, Allama & Parvez, 2010).

Continuous manufacturing is an emerging technology in the pharmaceutical industry and has the potential to increase the agility and efficiency of pharmaceutical manufacturing processes. According to Ganesh, S. et al. to realize these potential benefits from ongoing operations, it is essential to manage, equipment, analyzers, data, and materials effectively. Developments for continuous pharmaceutical manufacturing have led to new technologies and approaches for processing materials, designing, and configuring individual equipment and process analyzers, as well as implementing strategies for active process control. Maintenance benefits from unified efforts for continuous verification and operational excellence, leveraging process knowledge and real-time data availability.

Maintenance can be a strategy for important assets or for those assets that have substantial repair and replacement costs or that notably impact the process when they collapse, as identified through reliability-centered maintenance analysis. Maintenance tasks might also involve methods of continuous or periodic assessment of system conditions to trigger a failure condition based on a measured parameter threshold and

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further react to fails with subsequent maintenance activities. With the ascent of continuous manufacturing implementations, maintenance, enabled by process knowledge and real-time data availability, can directly support an operational excellence. Manufacturing operations in the pharmaceutical industry can effectively develop the proactive use of process data and modern maintenance practices (Ganesh, Su, Vo, Pepk, Rentz, Vann, Yazdanpanah, O'Connor, Nagy & Reklaiti, 2020).

According to Parr & Schmidt (2017) the application of life cycle management concepts to analytical procedures in the pharmaceutical industry offers a chance to use information gained from the application of scientific and quality risk management for continuous improvement and data quality assurance. Analytical method lifecycle management combines analytical method development, improvement, qualification, validation, transfer, and maintenance activities related to Current Good Manufacturing Practice (CGMP) production. Also, the extinction of a process must follow the quality management principles. This information that has been stored needs to be considered especially if the method was used in a regulated environment (like in the pharmaceutical industry). If the data indicates that the method is not operating as expected (producing results out-of-specification), an identification of the root cause of the variation should be evaluated. The result of the investigation might result in a change of the method and thus in the improvement of the performance of the method. The type of the change determines the action required, like a change in the method. But even if a new method is based on the retired method, some parts of the previous lifecycle can be used to start the new one (Parr & Schmidt, 2017).

II. CROMATOGRAPHY

Chromatography is an important biophysical technique that allows the separation, identification and purification of the components of a mixture for qualitative and quantitative analysis. Components can be purified based on characteristics such as size and shape, total charge, hydrophobic groups present on the surface, and ability to bind to the stationary phase (Coskun, 2016).

On this way, that chromatography is often used to confirm the presence or absence of a compound in a sample, and this is done by comparing the chromatogram (chromatography curve) of the pure substance with the one that represents the unknown substance, when carried out under identical conditions. The chromatography operator must be certain that a substance detected in a sample is, in fact, actually present (for example, a banned substance in an athlete's urine) and, equally important, that a substance not detected is not actually present, and that means, above a defined detection limit (for example, pesticides in a food).

In recent decades, chromatography has been increasingly used significantly for quantitative purposes in the fine chemical, biotechnological and pharmaceutical industries. Quantitative data is widely used in industry for quality control, in clinical chemistry for analyzing body fluids, and in environmental science for monitoring water, air and soil samples. (Ryan & Robards, 2021)

This technique has three different types, and inside the field of analytical chemistry, HPLC and GC chromatography are the most used methods (Ryan & Robards, 2021).

III. PRODUCT VALIDATION

Validation is one of the important steps to achieve and maintain the quality of the final product. If each stage of the production process is validated, we can guarantee that the final product is made with the best quality. Validation is the art of planning and developing the steps outlined in accordance with established standards. Validation and quality assurance are thus interconnected, guaranteeing the complete quality of products. Process validation emphasizes process design elements and maintaining control of that process during product marketing, asserting itself as a continuous program that aligns process validation activities with the product life cycle.

Validation of pharmaceutical processes is the most important and recognized parameter of CGMP. The requirement for process validation appears as the regulation of the quality system. The goal of a quality system is to consistently produce products suitable for their intended use. Process validation is a key element in ensuring these principles and objectives are met.

The concept of validation was first proposed by officials at the Food and Drug Administration in 1970 with the aim of improving the quality of pharmaceutical products. Process validation is to ensure and document the process within the specified and designed criteria, so that the manufactured product meets pre-determined quality criteria and attributes with a reproducible and constant result. Assuring product quality derives from a careful attention to several factors, including the selection of quality parts and materials, appropriate design of products and processes, process control, and testing both in-process and on the final product. Due to the complexity of today's medical products, routine end-product testing is often not sufficient to ensure product quality for a variety of reasons, as some end-product testing has limited sensitivity. The main objective of a pharmaceutical industry project is to achieve a predictable therapeutic response from a medicine included in a formulation that is capable of a large-scale manufacturing with a reproducible quality. Process validation is one of the important steps to achieve and maintain the quality of the final product. It is the "key element" to guarantee the identity, purity, safety, effectiveness and maintain the quality of the final product. The basic principle of quality assurance is that a medicine must be produced in a form suitable for its intended use. To meet this principle, a good understanding of the processes and its performance is important. Quality cannot be adequately guaranteed by inspecting and testing the product during and at the end of the process but must first be incorporated into the manufacturing processes. These processes must be controlled so that the final product meets all quality specifications. Process validation aims to establish that the proposed manufacturing process is suitable and consistently produces a product with the desired quality, that is, that the process is

suitable and under control. (Jain, Agarwal, & Bharkatiya, 2018).

IV. Maintenance

One of the main objectives of LCA is to provide a framework for the design of an ideal maintenance policy, that is, to define a program of interventions that maximizes the profit derived from the existence of the project, ensuring its safety and availability. Maintenance activities are understood as all physical processes that aim to increase the useful life of the system. These activities may be initiated because the system is experiencing some type of failure (generally referred to as reactive or corrective maintenance), or they may be initiated before a failure is observed (generally referred to as preventative maintenance).

In that way, maintenance can be defined as a set of actions taken to keep a system (e.g. machine, building, infrastructure) operating at or above a pre-specified service level.

Maintenance differs from reconstruction because it is planned and executed during the operational phase of the system, before the planned complete replacement (Sánchez-Silva & Klutke, 2016).

Industrial maintenance is essential to extend the useful life of assets and prevent breakdowns that could compromise performance and ultimately lead to the suspension of its activity. When the asset or machine has a malfunction, this problem can affect various sectors of the industry or even the customer, resulting in losses. However, it is possible to minimize the damage caused by failure if repairs are carried out periodically, thus prolonging the functioning of the asset and even preventing the emergence of failures. As industries normally deal with high-cost assets, the lack of maintenance can be even more expensive, as the need to completely replace equipment is also expensive.

Also, if there is a need to suspend, even temporarily, operations to exchange equipment or components, there are expenses with employees and losses due to the absence or delay in the delivery of products or services provided. Therefore, constant maintenance translates into savings and prevention of inconvenience caused by the interruption of activities. To maintenance be effective, it is necessary to analyze which type of maintenance is most appropriate for the situation of the company in question (Willich, 2022).

To draw up a maintenance plan, you need to identify the most appropriate type of maintenance for each situation. To understand which, there are some points to pay attention:

- Criticality: the level of criticality is high in case equipment failure has a major impact on the company or service. For example, in the case of agricultural equipment which, if it fails to function correctly, harms the harvest. Equipment such as cell phones, which are normally used individually and can be replaced by other devices, have a low degree of criticality;
- Lifespan: an asset with a short lifespan has different maintenance needs than equipment that is expected to operate for a long period of time, such as elevators (long lifespan) and lamps (short lifespan);
- Budget: some maintenance is more expensive than others, so the company's budget must be taken into account when preparing a maintenance plan;
- Frequency: maintenance frequency is related to the needs of each asset. Some equipment requires periodic maintenance, while others do not.

The decision on the most appropriate type of maintenance must be analyzed by a qualified technician, however the recommendation from the asset manufacturer must also be considered (Willich, 2022).

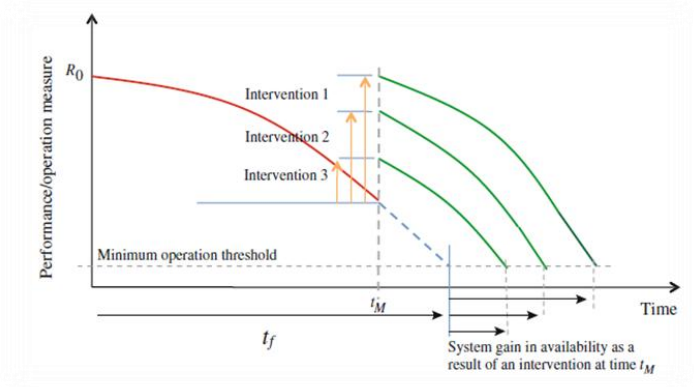

Fig. 1 - Effect of various intervention measures on expected time to failure (Sánchez-Silva & Klutke, 2016)

Maintenance comprises the associated technical and administrative actions intended to preserve a system or restore it to a level at which it can perform its required function.

The long-term benefits of preventive and reactive maintenance include improving availability and extending system life, as seen in figure 2, reducing replacement cost, decreasing system downtime and improving inventory management (Sánchez-Silva & Klutke, 2016).

There are several ways to divide the types of maintenance. The three main types of maintenance generally accepted are corrective maintenance (CM), preventive maintenance (PM) and predictive maintenance (PdM) (Infraspeak Team, 2023).

Corrective maintenance is one of the maintenance policies which actions, such as repair or replacement of components, are performed on a system to restore it back to normal operation after a failure (Kamaruddin, 2017). Because this technique is carried out after the failure has occurred, it is also called reactive maintenance. Its advantages over other types of maintenance are the fact that it is the ideal type for low priority equipment (without which the company's operations can continue to function normally) or low value equipment (its constant maintenance or monitoring could be more expensive than replacement or repair when the failure occurs) and the little planning required for this approach, making its implementation cost lower. The major disadvantage of CM is that with this approach the lifespan of equipment will end up being reduced, since there are no preventive actions, and therefore it should not be implemented on medium/high

priority assets, having the risk of unexpected downtime and huge repair costs (Infraspeak Team, 2022).

Preventive maintenance is planned and executed after a specific period, or after a specific system is used, with the purpose of reducing the probability of failure, being a proactive maintenance (acts before failure) (Kamaruddin, 2017). The advantages of PM are increased asset life, fewer unplanned stops, greater equipment reliability, lower long-term costs, better safety and happier potential customers. As for the disadvantages, these are the bigger planning requirement, the need to readjust routines, it is not applicable to any equipment, it can generate unnecessary actions and requires more outsourcing (Infraspeak Team, 2023).

Predictive maintenanceinvolves monitoring systems for the system's condition (Kamaruddin, 2017) and comprising all types of maintenance it is the most recent and the one that requires the biggest investment in technology. The objective of PdM is trying to predict as much as possible when a failure will occur. When certain undesirable conditions are detected, a repair is scheduled before the actual equipment breakdown occurs, thus eliminating the need for more expensive or unnecessary CM. Monitoring systems used such as vibration analysis, acoustics or infrared or thermal imaging tests are essential to obtain the physical and operational condition of the equipment. The great advantage of this form of maintenance is that it will always be better informed, since the equipment will only be subject to maintenance when a breakdown is expected, reducing costs and labor time spent in maintenance (Infraspeak Team, 2022).

Other types of maintenance are emergency maintenance (EM), reliability-focused maintenance and condition-based maintenance, thus accounting for six types of maintenance (Infraspeak Team, 2022).

EM is a similar type to CM, however it occurs at different stages of a failure: CM is carried out when certain physical damage or disturbance in the normal functioning of the equipment is visible, however it is operational, whereas EM occurs after a complete equipment failure, thus requiring urgent maintenance and therefore having high costs (Infraspeak Team, 2022).

Reliability-focused maintenance aims to increase equipment availability, being similar to PM (Infraspeak Team, 2022). It can be said that it focuses on the reliability of each asset and not on the functionality of each. In this type of maintenance, it is essential to carry out personalized maintenance plans, ensure that assets are available at any time and improve the cost-efficiency relationship.

Therefore, instead of maintenance actions being planned based on the function of each asset, the important thing is to ensure that each asset is reliable (number and frequency of breakdowns). An asset is as reliable the greater its availability to perform its function (Infraspeak Team, 2019).

Condition-based maintenance focuses on well-defined analyzes and parameters. Therefore, if after a visual inspection something abnormal is detected, an intervention is carried out. If the output of the equipment has declined, then there has been an obvious change in the condition of the equipment and maintenance must be performed. PdM is sometimes defined with condition-based maintenance, however it goes a little further by trying to detect faults at an even earlier stage (Infraspeak Team, 2022).

E-maintenance has emerged since the early 2000s and is now a very common term in maintenance-related literature. The concept of e-maintenance today widespread in the industry refers to the integration of information and communication technologies (ICT) in the strategy and/or maintenance plan to meet new emerging needs for innovative forms of production support (e-manufacturing) or business (e-business).

E-maintenance can be simply defined as a maintenance strategy where tasks are coordinated electronically using equipment data obtained in real time thanks to digital technologies (i.e. mobile devices, remote sensors, telecommunications and online technologies). From this point of view, e-maintenance is interpreted as a maintenance management process, which deals with expanding the volume of available data.

E-maintenance can also be seen as a maintenance plan, which meets the future needs of the world of manufacturing automation, in exploring the approaches of maintenance, proactive maintenance, collaborative maintenance, remote maintenance and support service, provision for access to information in real time and integration of production with maintenance. The implementation of an e-maintenance plan requires a proactive e-maintenance scheme, that is, an interdisciplinary approach that includes monitoring, diagnosis, prognosis, decision and control processes.

Generally speaking, e-maintenance is the symbol of the gradual replacement of traditional types of maintenance with more predictive/proactive types. Regular periodic maintenance must be innovated and changed to the intelligent maintenance philosophy to satisfy the manufacturer's high reliability requirements. Thus, e-maintenance would be like predictive maintenance, which will only provide monitoring and predictive prognosis functions.

Finally, e-maintenance can be called supporting maintenance, that is, a combination of web service technology and equipment action technology, which provides a way to carry out more intelligent maintenance plans in a maintenance system. E-maintenance can also be seen as a distributed artificial intelligence environment, which includes information processing capabilities, decision support and communication tools (Muller, Marquez, & Iung, 2008).

V. Sustainability and LCA in the Pharmaceutical Industry

The industrial sector in general plays a vital role in the world economy. Industry is responsible for more than a third of all types of energy used in the world. Industries have a variety of highly energy intensive systems for process heating (like steam) and engine driven equipment such as air compressors, pumps and fans. Industries have many high

energy consumption parts that cause various impacts on the environment. Thus, electricity and energy demands are very high in the market. Most of the energy that the industry uses is supplied by the conventional electricity generation system (coal, oil and gas). Therefore, reducing electricity consumption and impacts on the environment are very essential. There are different ways and techniques to solve these problems, such as life cycle assessment (LCA – life cycle analysis) and industry optimization. These techniques include maximizing production with the same inputs, minimizing costs, reducing the handling and transportation of materials, using equipment to control pollution, reducing emissions into the environment and the use of waste.

The quantities of emissions are not exactly important, but rather how much volume of air and water are needed to dilute the emissions. Also, reuse is better than recycling, which is better than single use. LCA and energy management are therefore essential tools for generally improving the efficiency of industries, in this case as an important and comprehensive method for analyzing the environmental impact of products and services.

Life cycle management are the management practices and organizational arrangements that are applied to manage the entire life cycle of a product, from its conception to its final disposal. Industry energy management is a way of effectively using energy to minimize its cost, where efficient optimization of the system has potential economic improvements in energy costs, in addition to reducing CO2 emissions, and understanding that the energy use and energy waste can help identify areas with high energy intensity and improve their efficiency (Chauhan, Varun, & Suneel Kumar, 2011).

LCA is a very useful tool for analyzing interactions between human activities and the environment. It is also a technique for evaluating various aspects related to the development of a product. It also acts as a tool to assess the potential impacts throughout the life of a product (from the "cradle" to the "grave"), from raw material acquisition, processing, production, use and, finally, disposal (like shown in Figure 1). It is also used for comparison between several alternatives. The objective, scope, assumptions, description of data quality, methodologies, and results of the LCA analysis must be transparent. The LCA of any product includes four steps which are:

- definition of objective and scope;
- inventory analysis;
- impact assessment;
- interpretation of results (Chauhan, Varun, & Suneel Kumar, 2011).

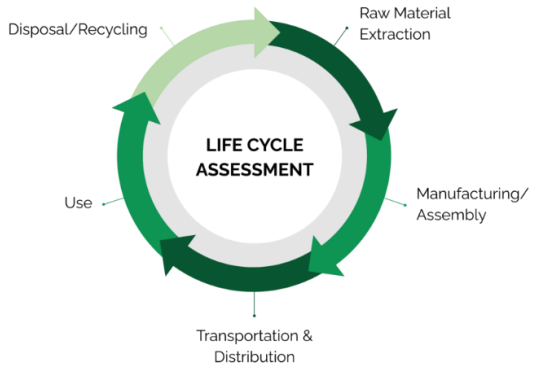

Fig. 2 - Life cycle analysis (Eckelman, Nunberg, & Kundu, 2023)

LCA is a process for evaluating the environmental effects associated with a product, process or service throughout its entire life cycle. Before LCA was known as LCA, it was described as "ecobalances," resource analysis, comprehensive environmental analysis, and environmental profiles. It has had a long journey since the 1960s, where its roots took shape because of the need to optimize energy in industry (Chauhan, Varun, & Suneel Kumar, 2011).

The pharmaceutical industry sector is characterized by a dynamic focused on research and development (R&D), industrial production and marketing with high investments and a competition strategy focused on product differentiation.

The challenges of pharmaceutical industries, such as sustainable management, merger and acquisition of other companies (used as a form of external growth and combating competition), efficient R&D, which have as key issues: how to speed up product placement time in the market, incorporating health studies into clinical experiences in a way that is safe and effective in reducing the patient's time in hospital or on sick leave and how to manage and organize scientists spread across the globe. The ability to redesign the business in times of turbulence requires professionals with multidisciplinary training. With all this, we can say that pharmaceutical industries take care of the human factor in their actions, encouraging diversity of academic knowledge, even if it is as a business strategy.

The discourse of managers in the pharmaceutical industries about sustainability is directed at their employees and seeks to guide environmental, economic and social management practices to a positive image of the company.

Regarding the content related to sustainability published by the organization, the environmental variable stands out, both for managers and employees, followed by the social and finally the economic one.

We can also state that the human factor is considered part of the environmental dimension, as it influences and is influenced by environmental conditions (Salomão, 2013).

Many pharmaceutical compounds pass through the human and animal body, and these substances and their metabolites are increasingly frequently found in the environment where they can have harmful effects. In contrast, the production of pharmaceutical compounds has not been properly analyzed. There are few studies and detailed production data on

pharmaceutical products are not publicly available, as their production parameters are generally confidential. Pharmaceuticals are among the most complex chemicals produced, and available data on the production of fine chemicals is very scarce in general. The reasons for this are, in addition to confidentiality issues, the specialized processes involved in the production of pharmaceuticals and other fine chemicals. They are produced not in continuous processes, but in discrete batches, which can vary in size from batch to batch. They are commonly produced in multi-use production zones, sharing equipment and facilities between production lines. This makes energy inventories extremely difficult to obtain, as steam and electricity usage is often only measured at the building level.

Furthermore, pharmaceuticals may be difficult to synthesize, but their benefits justify the unusual costs and efforts of producing them. The chemistry of pharmaceutical production is therefore often specialized and "resource-intensive".

The large number of process steps can introduce large uncertainties due to the propagation of errors throughout production. This means that process models that result in acceptable errors in two or three process steps may not be applicable in fine chemical inventories, as the total error would make the result meaningless.

The generally small production quantities in pharmaceutical production also mean that little effort is often made to optimize production. Because production costs are generally exceeded by R&D or marketing costs (which often require up to 80% of total development costs), the economic incentive to optimize production is lower than in the production of other chemicals. Additionally, there is less time to increase process efficiency as time to market is crucial for pharmaceutical products.

For these reasons, processes can consume more resources and be less efficient than other fully optimized processes. An additional factor is that pharmaceutical products often undergo formulation and purification processes after production to ensure product purity and that pharmacological function is maximized. These steps can also be very energy and resource intensive. As resource-intensive productions are also often environmentally problematic, this raises the question of the impacts of pharmaceutical production. Mass intensity analyzes are sometimes performed in the pharmaceutical industry. However, energy use and emissions are not commonly assessed from a life cycle perspective (Wernet, Conradt, Isenring, Jiménez-González, & Hungerbühler, 2010).

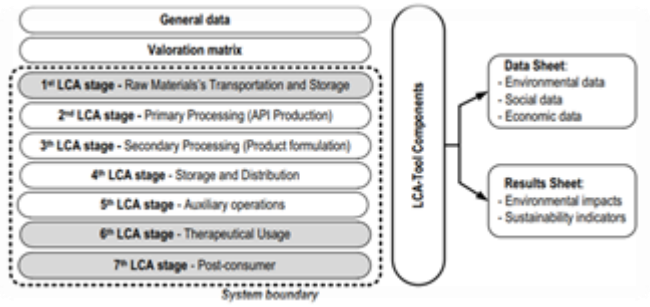

Fig. 3 - LCA in the pharmaceutical industry (Mata, et al., 2012)

In order to define the periods of the useful life cycle of a biomedical device, graphs such as the one in figure 4 are used. This graph assumes the lifespan of a device starting from the moment of its manufacture until the end of its life, which is defined by its disposal. For example, from the point of view of a company within the healthcare sector, this life cycle is vital to indicate with a good certainty which are the most critical periods of the device in terms of its number of failures, and therefore better define which the times when it will be most important to invest in maintenance activities. From this graph it is possible to adjust preventive and corrective intervention activities to adapt to the phase of the life cycle where the equipment is located to best apply economic resources (Reis, 2019).

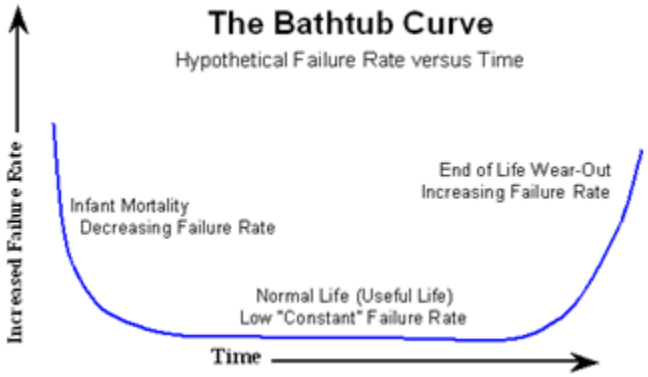

Fig. 4 - "Bathtub curve" graph (UpKeek, 2024)

To develop a device, an entire process of research and adjacent tests is necessary. It is very important to ensure that this equipment allows an acceptable activity in terms of safety, so we try to ensure that criteria such as robustness are correctly considered during this phase. It is considered that this equipment must adapt to a specific and real need or add a different functionality that is intended for a certain function. The tests carried out throughout this research stage must ensure that it is equipment that can adapt to the operator as well as the environmental factors that are involved. At the end of this phase and even before the company purchases the equipment, it must be produced and subject to regulatory authorities that will ensure its functionality in the environment of its use.

In figure 4, the first phase defined as the period of infant

mortality corresponds to the highest rate of failures, which tends to decrease until the most stable period, the device's useful life phase. This first period includes a greater number of PM to repair gaps in its manufacturing and hence the reduced quality of the devices. During the most stable period defined as the useful life period, normal life, it will be the moment where maintenance activities will be mainly of the preventive type, a period in which there are no frequent breakdowns in terms of quantity and severity, and it is only necessary to certify the normal operation of the device. The end of life of the device comprises a period of wear and tear where the device will be subjected to frequent wear and tear that will result in its disposal, therefore being a phase in which the failure rate will increase again. According to the "bathtub curve" scheme, the relationship between failure rate and device age is applicable, with age being the reason for the equipment degradation (Reis, 2019).

VI. The Pharmaceutical Laboratory

Hovione is a Portuguese company founded in 1959 by Ivan Villax, a chemical researcher interested in the development of anti-inflammatory corticosteroids and tetracyclines, specializing in the area of health science. In the most recent decades, Hovione has responded to the emerging needs of pharmaceutical industries worldwide, investing in research and development of the chemical process and industrial production of new drugs and medical devices for the global pharmaceutical industry, mainly with active substances for inhalation, formulations for inhalation, dry powder inhalers and particles engineering. It asserts itself as a company with a sense of innovating and maintaining a leading position on a international level in the field of pharmaceutical chemistry.

To guarantee a long-term sustainable business model, Hovione contributes positively to environmental, social and economic sustainability. These concerns are embedded their core values and purpose. Sustainability is integrated into the business strategy and makes the best use of science, innovative technologies, systems and business conduct to ensure it strives to protect the environment. The idea is to give back to society while conducting business in a responsibly way (Hovione, 2023).

VII. Conclusions

To conclude, this work represents a bibliographical review of the wide variety of topics that we find within the subject of maintenance and life cycle analysis of biomedical devices. Chromatography, a technique with the highest potential for failure situations according to data obtained from Hovione, and which is why it is referred to in this article, represents a very important technique currently in several laboratories in the most different scientific areas, like environmental, health or industrial production. Maintenance encompasses various ways of keeping a system, equipment or parts of it, within a correct functioning threshold, and is therefore an essential part of any industry. With new developments, new technologies and increasingly fierce competition, maintenance techniques are constantly being updated and increasingly require highly qualified professionals to carry out these actions that essentially aim to maintain the safety of all parties involved in the processes. Validation is essential to maintain the quality of final products and aims to guarantee at each stage of a process that the best standards are followed in order to guarantee a final product or service of the highest quality. Sustainability and LCA are interconnected, with sustainability giving attention to the environmental, social and economic aspects, so that an industry can prosper without compromising the environment and society around it. LCA is an important tool that helps to analyze the different interactions between humans and their surroundings. To better understand how a piece of equipment will behave throughout its life, graphs such as "The bath curve", developed from previously obtained or predicted data, are created in order to understand its expected life cycle, creating a structured plan for that piece of equipment, in order to make correct use of it from its conception to its disposal, thus satisfying sustainability issues.

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References

[1] Ali, T., & Allama, M., & Parvez, M. (April 2010). A Total Productive Maintenance (TPM) Approach to Improve Production Efficiency and Development of Loss Structure in a Pharmaceutical Industry. *Global Journal of Management and Business Research*, Vol. 10 Issue 2

[2] Ganesh, S., & Su, Q., & Vo, L., & Pepka. N., & Rentz, B., & Vann, L., & Yazdanpanah, N., & O'Connor, T., & Nagy, Z., & Reklaiti, G. (4 July 2020). Design of Condition-based Maintenance Framework for Process Operations Management in Pharmaceutical Continuous Manufacturing, *International Journal of Pharmaceutics. International Journal of Pharmaceutics*, USA. https://doi.org/10.1016/j.ijpharm.2020.119621

[3] Parr, M., Schmidt, H. (2017). Life cycle management of analytical methods. *Journal of Pharmaceutical and Biomedical Analysis*, S0731708517312219–. doi:10.1016/j.jpba.2017.06.020 https://doi.org/10.1016/j.jpba.2017.06.020

[4] Hovione. (15 February 2023). *Quem somos*. From Hovione: https://www.hovione.pt/grupo-hovione/quem-somos

[5] Coskun, O. (11 November 2016). Separation techniques: Chromatography. *Northern Clinics of Istanbul* , pp. 156-160. https://doi.org/10.14744/nci.2016.32757

[6] Ryan, D., & Robards, K. (2021). *Principles and Practice of Modern Chromatographic Methods* (2ª ed.). Elsevier Science. https://doi.org/10.1016/B978-0-12-822096-2.00011-6

[7] Liew, W. T., Adhitya, A., & Srinivasan, R. (april 3rd 2014). Sustainability trends in the process industries: A text mining-based analysis. *Computers in Industry, 65*, pp. 393-400. https://doi.org/10.1016/j.compind.2014.01.004

[8] Chauhan, M. K., Varun, S., & Suneel Kumar, S. (2011). Life cycle assessment of sugar industry: A review. *Renewable and Sustainable Energy Reviews*, pp. 3445– 3453. https://doi.org/10.1016/j.rser.2011.04.033

[9] Eckelman, M., Nunberg, S., & Kundu, V. (2023). *Life Cycle Assessment Explained*. Accessed february 25 2023, from Sustainability tools in cultural heritage: https://stich.culturalheritage.org/life-cycle-assessment-explained/

[10] Jain, K., Agarwal, P., & Bharkatiya, M. (April/ June 2018). A review on pharmaceutical validation and its implications. *International Journal of Pharmacy and Biological Sciences, 8*, pp. 117-126.

[11] Sánchez-Silva, M., & Klutke, G.-A. (2016). *Reliability and Life-Cycle Analysis of Deteriorating Systems.* Springer. doi:10.1007/978-3-319-20946-3 https://doi.org/10.1007/978-3-319-20946-3

[12] Willich, J. (30 May 2022). *Tipos de manutenção: quais suas diferenças?* Accessed April 26 2023, From Produttivo: https://www.produttivo.com.br/blog/tipos-de-manutencao-quais-suas-diferencas/

[13] Infraspeak Team. (15 May 2023). *Diferenças entre manutenção preventiva e manutenção preditiva*. Accessed june 11 2023, from Infraspeak Blog: https://blog.infraspeak.com/pt-pt/manutencao-preventiva-vs-preditiva/

[14] Infraspeak Team. (1 December 2022). *Tipos de Manutenção: Conheça os 6 Principais*. Accessed june 11 2023, from Infraspeak Blog: https://blog.infraspeak.com/pt-pt/tipos-de-manutencao/

[15] Infraspeak Team. (20 March 2019). *Infraspeak Blog*. Accessed april 25 2023, from Manutenção Centrada na Fiabilidade: https://blog.infraspeak.com/pt-pt/manutencao-centrada-fiabilidade/

[16] Muller, A., Marquez, A. C., & Iung, B. (2008). On the concept of e-maintenance: Review and current research. *Reliability Engineering and System Safety*, pp. 1165–1187. https://doi.org/10.1016/j.ress.2007.08.006

[17] Salomão, D. (2013). *Sustentabilidade nas indústrias farmacêuticas: ajustes entre discursos e práticas gerenciais.* SOPCOM.

[18] Wernet , G., Conradt, S., Isenring , H., Jiménez-González, C., & Hungerbühler, K. (2010). Life cycle assessment of fine chemical production: a casestudy of pharmaceutical synthesis. *The International Journal of Life Cycle Assessment*. https://doi.org/10.1007/s11367-010-0151-z

[19] Mata, T., Martins, A., Neto, B., Martins, M., Salcedo, R., & Costa, C. (2012). LCA Tool for Sustainability Evaluations in the Pharmaceutical Industry. *Chemical Engineering Transactions, 26*, pp. 261-266. doi:10.3303/CET1226044

[20] Reis, J. (2019). *Procedimentos de manutenção aplicados a dispositivos médicos : estágio na PromeiCentro.* Master's internship, Instituto Superior de Engenharia de Coimbra, Engenharia Eletrotécnica, Coimbra. From http://hdl.handle.net/10400.26/40880

[21] UpKeep. (s.d.). *Bathtub Curve*. Accessed 10 february 2024, from https://www. https://upkeep.com/learning/bathtub-curve/