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Commissioning-based analysis of heating, ventilation, and air conditioning systems in biopharmaceutical cleanrooms: enhancing energy efficiency and reducing cost

Análise de sistemas de aquecimento, ventilação e ar condicionado em salas limpas biofarmacêuticas: melhorando a eficiência energética e reduzindo custos

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ABSTRACT

Cost reduction through improvement in energy efficiency is a determining factor for the optimization of operational processes and the economic sustainability of organizations. One opportunity for achieving significant levels is by designing energy-efficient heating, ventilation, and air conditioning systems for new industrial facilities. Cleanrooms, used in biopharmaceutical companies, require high air change rates to maintain cleanliness, which are particularly energy intensive. This paper analyzed data collected from third-party sources, demonstrating a method used in a biopharmaceutical facility in Ireland. The study's objective was to compute the parameters related to energy efficiency before and after fresh air volume control implementation, aiming to ascertain the effectiveness of this approach in optimizing energy consumption and ventilation performance. This case study analyzed 185 cleanrooms of different sizes and classifications; it was observed that all rooms exceeded the recommended air change per hour. The data indicated that rooms with higher volumes had greater energy waste, underscoring the importance of optimizing airflow management in large cleanroom environments. The implementation of fresh air volume control showed a reduction of 8.87% in fan energy consumption, equivalent to a decrease of 46,666 units of air change per hour annually. This decrease in units was accompanied by a substantial reduction in fan waste, amounting to 203,399.1 kWh, and saving more than €49,055.8 per year using pressure gradient control strategies in the ventilation system. Overall, the present work provides insights into improving energy efficiency

RESUMO

A redução de custos por meio da melhoria na eficiência energética é um fator determinante para a otimização dos processos operacionais e a sustentabilidade econômica de organizações. Uma forma de se alcançar níveis significativos de eficiência energética é utilizando sistemas de aquecimento, ventilação e ar condicionado, energeticamente eficientes, para novas instalações industriais. As salas limpas, utilizadas em empresas biofarmacêuticas, exigem altas taxas de troca de ar para manter a higienização, o que consome muita energia elétrica. Esse artigo analisou dados coletados de fontes terceirizadas, demonstrando um método usado em uma instalação biofarmacêutica na Irlanda. O objetivo do estudo foi calcular os parâmetros relativos à eficiência energética antes e depois da implementação do controle do volume de ar fresco, visando verificar a eficácia desta abordagem na otimização do consumo de energia e do desempenho da ventilação. O estudo de caso analisou 185 salas limpas de diferentes tamanhos e classificações, observou-se que todas as salas excederam a troca de ar por hora recomendada. Os dados indicaram que salas com volumes mais elevados apresentavam maior desperdício de energia, destacando a importância de otimizar a gestão do fluxo de ar em grandes ambientes de salas limpas. A implementação de controle de volume de ar apresentou uma redução de 8,87% no consumo de energia dos ventiladores, equivalente a uma diminuição de 46.666 unidades de troca de ar por hora, anualmente. Essa diminuição das unidades foi acompanhada por uma redução substancial de desperdício nos ventiladores, totalizando 203.399,1 kWh, economizando mais de €49.055,81 por ano usando estratégias de controle de gradiente de pressão no sistema de ventilação. Em geral, o presente trabalho fornece uma estratégia para melhoria de eficiência

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in the biopharmaceutical industry and highlights the economic and energy-saving benefits associated with implementing the proposed method. Furthermore, it offers a practical solution to reduce operational costs and environmental impact while maintaining stringent cleanliness standards, essential for cleanroom operations.

Keywords: economic benefit; recirculation airflow control; fan waste.

energética em indústria biofarmacêutica e destaca os benefícios econômicos e a economia de energia associados à implementação do método proposto. Dessa forma, oferece uma solução prática para reduzir custos operacionais e impacto ambiental, enquanto mantém os padrões de limpeza rigorosos, essenciais para operações em salas limpas.

Palavras-chave: benefício econômico; controle de recirculação de ar; desperdício nos ventiladores.

Introduction

In recent years, the biopharmaceutical market has experienced significant growth. Many pharmaceutical companies were established to accelerate the development of new products, especially after the COVID-19 pandemic. In 2020, more than €39,600 million was invested in research and development in Europe in this sector. According to the European Federation of Pharmaceutical Industries and Associations (EFPIA), Ireland was responsible for €19,395 million of pharmaceutical production in 2020 (EFPIA, 2022). This substantial investment highlights the importance of efficient manufacturing processes in the biopharmaceutical industry.

Biopharmaceutical cleanrooms are utilized for the manufacturing of therapeutic recombinant proteins acquired via biotechnological methodologies and sourced from living organisms. Biopharmaceuticals exhibit heightened specificity and targeting capabilities, thereby providing sophisticated therapeutic modalities for intricate ailments such as cancer, autoimmune disorders, and genetic disorders (Jozala et al., 2016).

According to the International Organization for Standardization (ISO) 14644-1:2015, biopharmaceutical cleanrooms are defined as rooms that have strict requirements for cleanliness and control parameters such as differential pressure, temperature, humidity, and airflow pattern. Cleanrooms are designed in a way to minimize the introduction, generation, and retention of particles inside them. The ISO standard includes the cleanroom classes quantified by the number of particles in every cubic meter, in which ISO Class 1 has the lowest level of contaminants while ISO Class 9 has the highest (ISO, 2015). The volume of the room and air change per hour (ACH) are two important factors that impact air quality and cleanliness in the cleanroom. The volume of a room is crucial because it determines the amount of air needed to be circulated to achieve the desired level of cleanliness (Tan et al., 2022).

Cleanrooms are very energy intensive due to the high air change rate required to maintain a high cleanliness level (Cetin et al., 2019; Loomans et al., 2019). Cleanrooms are designed with different pressures to prevent the entry of contaminated air from outside areas. It is common for a pharmaceutical area to be subdivided into multiple rooms, each with a distinct level of cleanliness (Cheng et al., 2022). The ventilation of the rooms is facilitated by what is known as an air handling unit system, which is designed to accommodate varying air volumes tailored to the specific needs of the building (Noussan et al., 2017).

Heating, ventilation, and air conditioning (HVAC) systems contribute significantly to energy consumption in buildings, representing between 30 and 80% of the total energy usage (Simpeh et al., 2022). Often, the air-conditioning system does not operate consistently, and the air change rate is frequently an unknown parameter. This typically leads to oversized designs of the air handling unit in the HVAC system to ensure compliance with cleanliness standards, resulting in excessively high energy consumption. This presents multiple opportunities for energy savings on-site, ultimately contributing to improved energy efficiency (Bahrens et al., 2022).

Some studies demonstrated improved energy efficiency when fresh air volume management was applied. In a related study, experiments using electronic frequency conversion on the air-supply fan unit were conducted to measure cleanliness, ventilation rate, and pressure gradient. This research developed an energy-saving operation strategy for multi-cleanrooms, which was proven to be feasible and reliable. The experiments demonstrated a reduction in energy consumption of approximately 24.5% (Wang et al., 2015).

Lyu et al. (2023) proposed an energy-efficient fresh air system utilizing pressure-independent dampers to balance system resistance and accurately control fresh air volume. Laboratory and on-site tests revealed annual savings of up to 29.3%, although the energy consumption of the dampers slightly reduced overall efficiency. Wang (2024) affirmed that fresh air systems contribute significantly to HVAC energy consumption. The study showed an occupancy position-oriented fresh air (OPFA) system that uses a stereo camera-based indoor occupancy positioning system to accurately and efficiently direct fresh air to occupied areas. Over eight months of classroom monitoring, the OFPA system identified occupancy patterns, reducing fresh air volume by 60.2% and energy consumption by 67.7%, showing casing a strategy for optimizing ventilation.

Energy efficiency plays a crucial role in the development of environmentally-friendly and sustainable buildings. According to the International Energy Agency, which focuses on achieving the global targets outlined in the Paris Climate Agreement, energy efficiency has the potential to contribute 44.0% of the required emissions reductions by 2040 (Zhunag et al., 2021; Paramati et al., 2022). In this way, energy efficiency represents a rapid and effective solution to mitigating environmental impacts in enterprises (IEA, 2018; Hafez et al., 2023).

A strategy for managing airflow including supervision of the pressure gradient inside the cleanroom and automatically controlling fans could provide a means to better optimize the airflow in a cleanroom and the energy efficiency of the HVAC system. In this context, the objective of this study was to analyze the economic impact and energy-saving potential following the implementation of fresh air volume management in a biopharmaceutical facility in Ireland and to present results that have been successfully utilized.

Methodology

The present study took place in a biopharmaceutical production facility situated in Ireland. This facility spans 2,000 sq. ft and is dedicated to the discovery, development, and manufacturing of biologics, including monoclonal antibodies and recombinant proteins, all in a single central location. The facility employs multiple 4,000-liter single-use bioreactors, achieving up to 48,000 liters of production capacity. The facility exemplifies the broader biopharmaceutical industry due to its extensive scale and wide range of biologics it produces.

The research universe encompasses the global biotechnology and pharmaceutical industry, particularly focusing on contract research, development, and manufacturing organizations (CRDMOs). This industry is crucial for the development of new biologics, including therapeutic proteins, antibodies, vaccines, and cell and gene therapies. The industry relies on companies that provide comprehensive services from drug discovery to commercial manufacturing. The company's relevance is underscored by its extensive service offering and global presence. The company has built a robust infrastructure, including current Good Manufacturing Practices (cGMP) facilities across Asia, North America, and Europe. These facilities enable the company to meet the diverse needs of its clients, from small biotech firms to large pharmaceutical companies. The overall Energy Usage Intensity (EUI) of buildings in the pharmaceutical sector is typically significantly higher. While the average EUI for a commercial office building constructed after 2000 is about 257 kWh/m^2, the average pharmaceutical plant has an EUI of approximately 3,816 kWh/m^2 (Boyd, 2011).

The study aimed to assess the energy and economic advantages arising from the utilization of fresh air volume control in fan supply systems. The controlled fresh air supply to the room was established and fixed, with the ACH being determined based on this specific air volume, ensuring accurate measurement and analysis of ventilation dynamics within the environment.

Sample selection

The case study was conducted in 185 cleanrooms in the building supplied by 28 air handling units, including non-classified and classified rooms, according to ISO 14644-1:2015. The cleanrooms were chosen to reflect a spectrum of operational conditions and cleanliness standards commonly found in the biopharmaceutical sector.

Data collection

Data on room volume (m^3), air volume supply (m^3/h), and fan energy waste (kw/h) were collected from commissioning documents provided by the facility. These documents are standard in the industry and provide reliable information on HVAC system performance.

Energy efficiency analysis

Using the data collected, a series of calculations were conducted to assess the energy efficiency, incorporating various factors and metrics to provide a comprehensive analysis.

The term ACH was used to quantify ventilation dynamics within the cleanrooms and refers to the amount of air, expressed as volume per unit time in hours. It was calculated using the formula (CDC, 2003) as described below (Equation 1):

$$ACH = \frac{Q}{V} \quad (1)$$

Where:
Q: represents the air volume (m^3/h); and
V: represents the total volume of the cleanroom (m^3).

ACH is derived from the hourly volume of air exchanged relative to the room's total volume, highlighting the importance of quantifying and optimizing ventilation dynamics (Cheng et al., 2023; Permana and Wang, 2024; Zhang et al., 2024). ACH serves as a crucial metric for assessing ventilation efficiency in this context.

The lost airflow, denoted as Q_{waste}, was determined using the expression (Equation 2):

$$Q_{waste} = \Delta ACH \ x \ V \quad (2)$$

The airflow waste (m^3/h), also referred to as the energy-saving opportunity, was calculated using the following expression in the cleanroom (Equation 3):

$$\Delta ACH = ACH_{measured} - ACH_{designed} \quad (3)$$

The energy savings of the fan (kW.m^3) were calculated as (Equation 4):

$$Q_{fan\ saving} = E_{fan} \ x \ Q_{waste} \quad (4)$$

Where:
E_{fan}: represents the energy consumed by the fan (kWh).

In 2022, the average cost of energy to commercial buildings in Ireland was €0.24/kWh (SEAI, 2022), and this value was considered in this study.

Existing heating, ventilation, and air-conditioning systems and retrofit implementation

The collected data were analyzed using the previously shown calculations to compare energy consumption before and after the retrofit. The analysis involved calculating ACH for each cleanroom, determining airflow waste, and estimating potential energy savings.

The effectiveness of the retrofit was verified through field measurements by comparing energy consumption data.

Energy efficiency improvements were verified by comparing the energy consumption of the HVAC system before and after the retrofit. This included assessing pressure gradients stability, airflow waste reduction, and overall energy savings. The results demonstrated significant energy savings and validated the effectiveness of fresh air volume management.

Results and Discussions

In this study, 185 cleanrooms were subjected to analysis. These cleanrooms had minimum requirements for ACH according to international standards outlined in ISO 14644-1. By comparing the recommended ACH with the actual measurements taken in the cleanrooms, it was observed that all rooms exceeded the recommended ACH, reaching 100% of the total. This indicates that the minimum ACH requirement for the rooms was surpassed, resulting in energy wastage. This finding highlights the inefficiencies in current cleanroom ventilation practices and the urgent need for optimized air change rates. The implications of this finding for cleanroom energy management are substantial. Excessive ACH not only increases energy consumption but also inflates operational costs and contributes to unnecessary environmental impact. By reducing ACH to recommended levels, cleanrooms can achieve substantial cost savings and improve energy efficiency without compromising cleanliness standards. Implementing advanced control systems that dynamically adjust ACH based on real-time environmental conditions and particulate levels can further enhance these savings, ensuring that energy use is aligned with actual cleanroom requirements.

Figure 1 shows the relative frequency of rooms and the amount of ACH exceeded. Specifically, 32.98% of rooms exceeded the recommended ACH up to 1, and 30.81% of the rooms exhibited an excess of 2.01 to 5 ACH. Additionally, 23.78% of the rooms had an excess of 1.01 to 2, while 12.43% of the rooms exceeded 5.01 to 25 ACH. Among the 12.43% of rooms with the highest excess ACH, it was observed that nine exceeded the recommended level by more than 10. This suggests that there is excessive energy consumption in several rooms. Higher ACH requires increased ventilation, leading to higher energy usage.

Other studies considered the ACH for energy demand assessment. Bahrens et al. (2022) investigated ACH determination for a pharmaceutical cleanroom ISO Class 8, aiming to ensure compliance with particle concentration limits. The study involved testing four different ACH rates (10, 12, 15, 20) and types of operator garments. The results indicated that 10 ACH rate was sufficient to meet the requirements of this cleanroom class. Notably, reducing the ACH by 50.0% resulted in approximately 25–30% less energy consumption by the HVAC system. The authors found that reducing the ACH rate to 10 can meet cleanroom requirements and significantly lower energy consumption. Our study supports this by showing that all analyzed rooms exceeded the recommended ACH, suggesting potential for energy savings by reducing ACH.

Among the 185 cleanroom analyses, 70.0% had energy waste from fans up to 1,000 kWh/year, 14.0% wasted between 1,001–2,000 kWh/year, 6.5% between 2,001–3,000 kWh/year, and the remaining 8.6% wasted between 3,001–16,000 kWh/year (Figure 2).

The rooms with the most energy waste were numbered 5, 13, 23, 43, 45, 78, 85, 100, 106, and 128. Among the top ten energy-consuming rooms, eight (128, 106, 100, 23, 45, 43, 13, and 5) belonged to the classified part, while the remaining two (85 and 78) were situated in the clean non-classified (CNC) area of the manufacturing. The CNC is characterized by uncontrolled levels of airborne particles, where the design does not adhere to the formal classification criteria for cleanliness grade (Fernandez, 2019). Specifically, room 10 accounted for 7.4% of the total energy waste, whereas room 78 contributed to 6.7% (Figure 3).

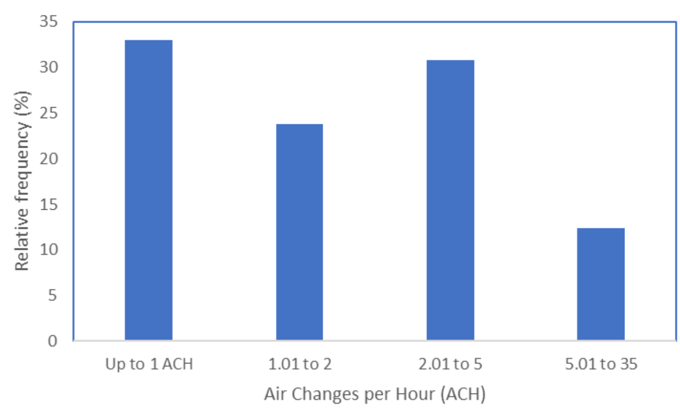

Figure 1 – Relative frequency of rooms and the amount of air changes per hour exceeded.

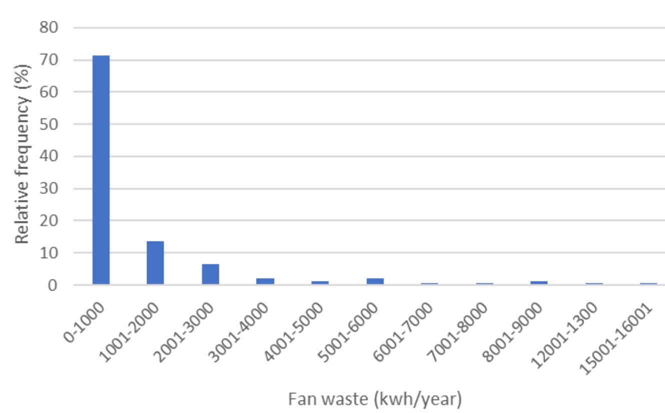

Figure 2 – Energy waste from fans (kWh/year) among the 185 rooms analyzed in the study.

There was a similarity among these ten rooms—the volume exceeding 4,000 m^3. Considering all the rooms studied, 16.0% had a magnitude greater than 4,000 m^3, and of these, 83.3% had energy waste surpassing 1,000 kWh/year. The energy wasted by the fans increased with the larger volume of air in the room, as shown in Figure 4. Although the correlation is weak (r=0.57), the graph shows that rooms with a smaller air volume exhibit lower energy losses.

This significant energy waste underscores the challenges associated with maintaining energy efficiency in large cleanroom environments. Managing energy consumption in large cleanrooms involves several specific challenges, such as maintaining consistent air change rates, controlling temperature and humidity, and ensuring the efficient operation of HVAC systems. Potential solutions include implementing advanced control systems that adjust ventilation rates based on real-time particle monitoring, optimizing HVAC system design to match the specific needs of different cleanroom zones, and employing energy recovery ventilators to reclaim and reuse energy from exhaust air. By addressing these challenges with targeted strategies, large cleanrooms can significantly reduce energy consumption and operational costs.

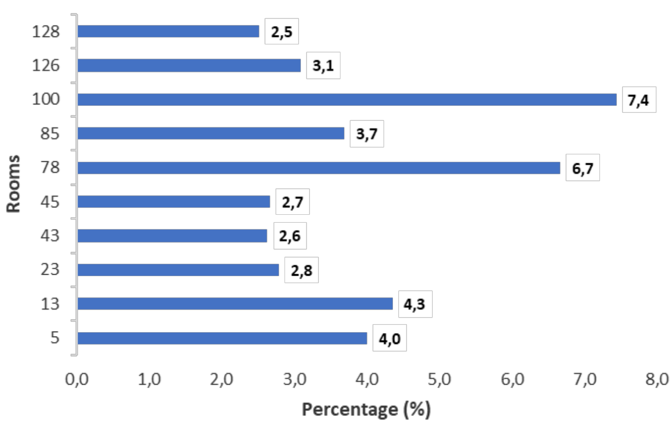

Figure 3 – Percentage of energy waste (kWh/year) between the less energy-efficient rooms.

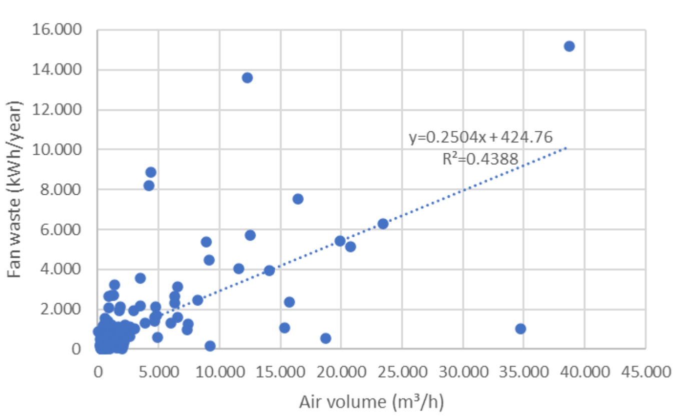

Figure 4 – Fan energy waste and air volume in the cleanrooms.

Some studies examined the influence of cleanroom size on energy consumption. They stated that large cleanrooms typically result in greater energy losses due to their large volume and higher air change requirements. Additionally, larger cleanrooms may require a more powerful HVAC system to ensure proper air distribution and control. These systems involve larger fans and more extensive ductwork (Xu, 2002; Bhatia, 2020). Our results align with these studies, showing that larger cleanrooms experience greater waste due to the increased ACH requirements. An open or spacious cleanroom configuration with fewer obstructions allows for smoother air circulation and higher ACH. The presence of equipment or other sources of heat or particulate generation can affect the ACH. These factors may require higher ventilation rates to ensure adequate air exchange (Holbrook, 2009).

The configuration and arrangements of a cleanroom, including the placement and quantity of air supply and exhaust vents, the organization of equipment and fixtures, and the presence of personnel or other factors that may disturb airflow, all have an impact on air circulation within the cleanroom (Bhattacharya et al., 2022).

Achieving a well-regulated air distribution pattern is crucial in cleanroom ventilation. This can be accomplished through careful room design, which involves considerations such as the type of ventilation system employed (Thatiparti et al., 2017).

Studies have shown that human occupants are a significant source of contamination in cleanrooms. The presence of personnel inside cleanrooms introduces particles, microorganisms, and other contaminants through activities such as movement, breathing, and the shedding of skin flakes. Hu et al. (2016) and Ljungqvist et al. (2020) emphasized the impact of human presence on cleanroom contamination in their researches. By recognizing the role of human occupants as a major contamination source accounting in cleanroom design and operation, it is possible to enhance the overall cleanliness and performance of cleanroom environments (Hu et al., 2016; Ljungqvist et al., 2020). While our study focused on ACH and energy consumption, Zhang et al. (2022) emphasized that the equivalent value of human particle emission rates should vary based on cleanroom cleanliness when designing ventilation systems. Addressing the uncertainty in human dynamic emission rates, the study combined its findings with others to determine suitable emission rates for Class B biopharmaceutical cleanrooms, revealing that current ventilation rates are excessively high. The adjustment could lead to over 50.0% energy savings, a conclusion supported by previous studies showing effective energy-saving and control strategies using simple occupant information.

Decreasing the pressure gradient between the rooms was the initial approach to reducing consumption. However, it is imperative to ensure that the pressure gradient does not fall below the designated level as specified in the design. Studies on cleanroom energy efficiency revealed that incorrect pressure differentials can emerge as a significant contributing factor to excessive energy consumption (Bhattacharya et al., 2022). The pressure gradient of each room is critical to achieving the goal of maintaining the room clean when operating the HVAC system in a biopharmaceutical plant.

The room pressure design relies on the cleanliness level required. Often due to passive factors, the volume of the air supplied can significantly change and the pressure gradient cannot adapt to the variable air volume supplied. When the volume in the cleanroom changes, the pressure gradient will be disturbed leading to cross-contamination (Li et al., 2021).

Out of the 185 rooms analyzed, 143 exhibited variations in measured room pressure compared to the intended design. In most rooms that exhibited variations, the range achieved fell within -1.5 Pa to 2 Pa of the designated room pressure, with only room 34 showing a difference of 5.6 Pa. The minimal difference observed between the design and measured pressure indicated that changing the pressure gradient would not effectively reduce fan ventilation energy waste, particularly because it would result in a pressure lower than what is defined by ISO 14644-1 (Wang et al., 2015). Wang et al. (2015) and Bhattacharya et al. (2022) discussed the role of pressure gradients in energy efficiency. Our results showed minimal differences between the design and measured pressure gradients, indicating that adjusting the pressure gradient alone may not be sufficient to reduce energy waste.

To address this issue, a method of managing airflow was implemented, incorporating the fixed air supplied to each room to maintain the desired differential pressure. Upon applying the method, it was possible to observe that the utilization of fan energy exceeded 204,399.2 kWh per year within the 185 rooms studied. However, by implementing the fresh air volume control outlined in this paper, a reduction of 8.84% in fan energy consumption and the amount of ACH per year was achieved, with a decrease of 46,666 units, leading to an energy saving of €49,055.8. This reduction in ACH was accompanied by a substantial decrease in fan waste totaling 203,399.1 kWh.

Implementing the fresh air volume control method led to a substantial reduction in fan consumption by 8.87% in the 185 cleanrooms selected for the study. This method optimized the amount of fresh air introduced into the cleanroom, ensuring that only the necessary volume was used to maintain cleanliness standards, thereby reducing the workload on the ventilation system. The potential for widespread implementation of this method is significant as it offers a straightforward yet effective approach to enhancing energy efficiency in the cleanroom. By adopting fresh air volume control, facilities can achieve considerable energy savings, reduce operational costs, and lower their environmental impact, all while maintaining the stringent cleanliness requirements essential for cleanroom operations. Table 1 presents the comparative results obtained before and after implementing the fresh air volume control.

By implementing a coordinated demand-controlled ventilation strategy to optimize the supply of cleanrooms, 63.3% of energy savings could be achieved, according to Zhunag et al. (2021). Hence, if the cleanroom air volume can be dynamically adjusted, it allows a reduction in operating air volume.

Various cost-effective and simple methods have the potential to enhance energy efficiency. For example, Wang et al. (2015) used a method for reducing fan energy excesses employed in cleanrooms called demand-controlled filtration and observed that during periods of low filtration demand, the night and weekend setback strategy achieved a remarkable 28.0% energy savings in comparison to continuous fan operation. Cheng et al. (2023) demonstrated that controlling the bidirectional switching of pressure gradients between standby and production modes in a biopharmaceutical cleanroom reduced the operational energy consumption of the facility. Hence, it is fundamental to implement HVAC strategies aimed at mitigating energy consumption in cleanroom environments.

Conclusion

This study emphasized the significance of improving energy efficiency to reduce costs, with a specific focus on heating, ventilation, and air conditioning system designed for new industrial facilities. Cleanrooms, which are known for their high energy consumption due to frequent air changes, present a significant opportunity for energy savings. The study introduced a method that involves controlling recirculation airflow using fresh air volume control to maintain the desired pressure gradient within the cleanroom. The implemented fresh air volume control method effectively reduced fan energy consumption and air change rates, maintaining the necessary differential pressure within cleanrooms. The results demonstrated a decrease in energy waste, achieving an 8.84% reduction in fan energy consumption and yielding significant cost savings.

These findings contribute to insights in the field of energy efficiency in the biopharmaceutical industry and to future initiatives in cleanroom design and operation. By adopting energy-saving strategies like the fresh air volume control method, industrial facilities can significantly decrease costs, and minimize their environmental impact while upholding the necessary cleanliness standards.

Future research may explore further optimization of airflow management systems and investigate the integration of advanced control technologies to enhance energy efficiency in cleanroom environments. These efforts will be crucial in advancing sustainable practices within the biopharmaceutical industry and other sectors reliant on cleanroom technology.

Table 1 – Comparative results obtained before and after implementing the fresh air volume control.

	Before study	After study	Difference	Savings (%)
ACH	525,710.3	479,043.7	46,666.6	8.88
Fan waste (kWh/year)	2,301,610.9	2,098,211.8	203,399.1	8.84
Energy cost (€)	552,626.4	503,570.6	49,055.8	8.88

ACH: air change per hour.

Authors' Contributions

Ozelame, K.: Conceptualization, data curation, formal analysis, writing – original draft. **Maffessoni**, D.: data curation, writing – review & editing.

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