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SOLUTIONS

Application Note

The Critical Role of Recirculating Chillers in Biopharmaceutical Manufacturing

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Introduction

Modern biotechnology hinges on the precise operation and performance of bioreactors, sophisticated vessels where cells are cultivated to produce life-altering vaccines, critical enzymes, and revolutionary protein-based therapeutics, including insulin and monoclonal antibodies (mAbs). Within these controlled ecosystems, every parameter – temperature, pH levels, nutrient concentrations, and gas flow rates – must be meticulously calibrated to achieve optimal cell growth, productivity, and product quality. The slightest deviations from these precisely defined conditions can have detrimental effects, leading to decreased cell viability, reduced yields, and compromised therapeutic efficacy.

Among these critical parameters, temperature stands out as a tier one requirement, as even minor fluctuations significantly impact enzymatic activities, metabolic rates, and overall cell viability. Excessively high temperatures can induce cellular stress and apoptosis, while temperatures that are too low can significantly slow down cellular metabolism, hindering the production process. Addressing this challenge, recirculating chillers have emerged as the behind-the-scenes enablers of bioprocessing, providing precise and reliable cooling solutions that ensure the consistent and optimal performance of bioreactors across a wide range of applications. These advanced systems effectively dissipate metabolic heat, maintain ideal temperature conditions, and ensure batch-to-batch consistency, from small scale laboratory experiments to large-scale industrial production runs. Compared to traditional cooling methods, recirculating chillers offer enhanced efficiency, reduced operational costs, and significantly improved production yields. In the biopharmaceutical field, where precision and reliability are paramount, recirculating chillers are essential components that contribute to the perfection of bioprocessing workflows.

The Critical Importance of Temperature Control in Bioreactors

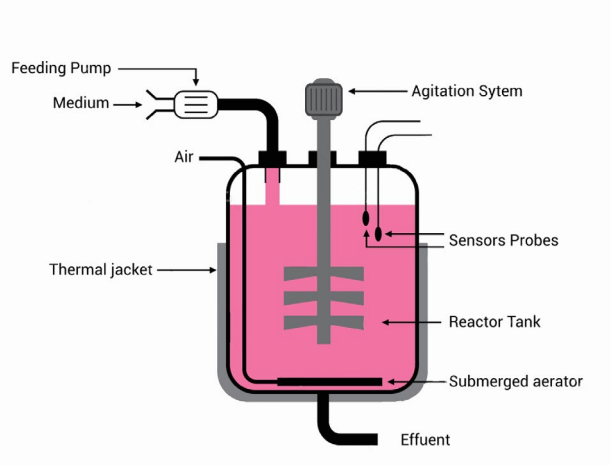
Temperature fluctuations within bioreactors can have profound and multifaceted impacts on cell growth, metabolic rates, and protein expression. Consistent and precise temperature control is crucial for supporting a healthy cellular environment and maximizing production output, ensuring repeatable temperature conditions across multiple production batches for consistent process and product quality and predictable yields, and adhering to stringent cGMP (Current Good Manufacturing Practice) and FDA (Food and Drug Administration) guidelines. Recirculating chillers provide the stability needed for reliable and reproducible results, and facilitate compliance by providing accurate and reliable temperature regulation. The main type of thermoelectric coolers used in optical packages are multistage micro TECs.

Optimizing Insulin Production with Recirculating Chillers

In the biopharmaceutical industry, producing recombinant insulin using Escherichia coli is a cornerstone of modern medicine, demanding meticulous control over every process parameter to ensure high yields and consistent product quality. A typical large-scale setup features a 1000-liter stainless steel bioreactor, engineered to maximize yield and product quality.

The bioreactor, constructed from durable stainless steel with glass observation windows, is equipped with a jacketed vessel that acts as a heat exchanger for the reactor tank. These systems work in tandem to regulate the culture medium's temperature, maintaining the optimal 37°C required for E. coli growth and insulin expression. Temperature sensors, wired to a PID controller, provide real-time feedback, ensuring stability even as metabolic heat from the rapidly growing bacteria threatens to push conditions off target.

Here, the role of recirculating chillers is critical. Connected to the bioreactor's jacket, a high-performance chiller circulates a precisely cooled mixture of water and glycol, efficiently dissipating excess heat. During critical fermentation phases, when oxygen sparging and propeller agitation drive up thermal loads, the chiller's rapid response helps maintain a consistent process. Post-fermentation, the chiller supports a controlled cool-down to preserve insulin integrity before downstream processing. Ultimately, the recirculating chiller's consistent and reliable temperature control ensures high yields and batch-to-batch reproducibility, minimizing thermal stress on the E. coli cells.



Scaling Up Monoclonal Antibody Production with Reliable Cooling

Monoclonal antibodies (mAbs) have revolutionized healthcare, offering effective treatments for a wide range of diseases, from cancer immunotherapy to autoimmune disease management. The production of these complex biologics relies on bioreactors that culture mammalian cells, such as Chinese Hamster Ovary (CHO) cells. Precise temperature control is crucial in this process. A typical setup, using a 500-liter stainless steel bioreactor, illustrates how recirculating chillers empower mAb production.

The bioreactor maintains the culture at an optimal 36.5°C, balancing cell growth and antibody production. CHO cells are particularly sensitive to temperature fluctuations; even a slight deviation can reduce cell viability or alter glycosylation patterns, which can significantly impact the efficacy of the resulting antibodies. As the culture scales and metabolic heat increases, amplified by impeller agitation and oxygen sparging, the recirculating chiller is used to circulate a steady stream of cooled fluid through the jacket, effectively counteracting thermal spikes throughout the 10–14 day production run. After production, the chiller gently lowers the temperature to 4–10°C for harvesting, and safeguarding product stability.

In R&D labs, multi-reactor arrays for example, eight 2-liter units, test process parameters in parallel. A single chiller can ensure each reactor holds steady, delivering data that bridges lab-scale insights to commercial success. Whether supporting one bioreactor or many, recirculating chillers provide the precision and adaptability that mAb production demands. The precise temperature control ensures consistent glycosylation, which is crucial for the antibody's ability to bind to its target

Recirculating Chillers – Essential for Today's Bioreactors

TRecirculating chillers are essential for maintaining optimal performance in various types of bioreactors, particularly those used in pharmaceutical, food, and chemical industries. Compared to tap water cooling or simple ice baths, recirculating chillers are crucial for:

- Bioreactors larger than 10 liters where chillers with cooling capacities up to 2900 watts are recommended
- Exothermic bioprocesses, where depending on the scale and intensity of the biological fermentation, reactions can generate significant heat requiring cooling capacities from 1 – 3 kW, even up to 150 kW, to maintain stable temperatures.
- Temperature-sensitive applications where bioreactors cultivating bacteria and yeast for pharmaceutical, antibody, and vaccine production can require 2 – 10 kW cooling capacity chillers.
- Continuous operation systems where lab scale bioreactors require chillers that can manage temperatures from -10°C to 40°C with cooling capacities from 0.25 to 1.2 kW.
- Industrial scale bioreactors which may need chillers with cooling capacities up to 265 kW

Recirculating chillers are preferred for bioreactors because they provide more consistent and precise temperature control (±0.1°C stability) and more capable of responding to fluctuating heat loads compared to tap water cooling as well as reducing operating costs and wastewater. They are energy efficient, designed for continuous operation, offer a compact and easy-to-operate solution for temperature management, and can maintain temperatures across a wide range, typically from -20°C to 40°C, depending on the model.

Tark Thermal Solutions' EFC Series of natural refrigerant recirculating chillers, NRC Series of performance chillers and VRC Series of value chillers provide a wide range of cooling capacity solutions for bioprocesses from 400 W to 4900 W. These next generation recirculating chillers feature a high coefficient of performance (COP) and low-noise operation in a smaller and lighter package. The chillers use compressor-based or thermoelectric technology to cool well below ambient and manage heat in today's bioreactors.

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Conclusion

Recirculating chillers are essential components in modern biopharmaceutical manufacturing. Their ability to provide precise, stable, and reliable cooling is critical for optimizing cell growth, maximizing product yields, and ensuring consistent product quality. From insulin production to monoclonal antibody manufacturing, recirculating chillers empower biopharmaceutical companies to develop and produce life-saving therapies with greater efficiency and precision. As the biopharmaceutical industry continues to evolve to require even more precision and repeatability, the role of recirculating chillers will only become more critical, driving innovation and enabling the production of the next generation of advanced therapies. The ability to maintain optimal temperatures in bioreactors ensures the consistency and efficacy of biopharmaceutical products, ultimately benefiting patients worldwide. By using recirculating chillers, researchers and manufacturers can ensure optimal growth conditions for microorganisms, maximize yield in bioproduction processes, and maintain the reliability and consistency of their experimental or production results.

About Tark Thermal Solutions

Tark Thermal Solutions develops thermal management solutions for demanding applications across global medical, industrial, transportation, and telecommunications markets. We manufacture one of the most diverse product portfolios in the industry, ranging from active thermoelectric coolers and assemblies to temperature controllers and liquid cooling systems. Our engineers use advanced thermal modeling and management techniques to solve complex heat and temperature control problems. By offering a broad range of design, prototyping, and in-house testing capabilities, we partner closely with our customers across the entire product development lifecycle to reduce risk and accelerate their time-to-market. Our global manufacturing and support resources help customers maximize productivity, uptime, performance and product quality. Tark Thermal Solutions is the optimum choice for standard or custom thermal solutions.

Have a question or need more information about us?
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