HAKOBIO

SIMOGGA™
THE FACTORY DESIGN TOOL

Computational design of process and operator flows to optimize cell therapy production environment and its ergonomics

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Background

Emergence of T-Cell therapies creates new requirements for the design of facilities. This leads manufacturers to develop more flexible biomanufacturing production environments. They aim to streamline transition from R&D to production and implement automation and closed systems as much as possible. In order to do that, they need to think early in the design phase about the product platform and its footprint as well as the process flow. Innovative technologies such as 3D visualization tools and layout design software offer predictive models for cell culture applications and enable the design of the bioproduction environment.

Through this study, we tested those new solutions to determine to which extent closed systems and automation improved an allogeneic T-Cell therapy factory producing 200 batches a year to treat 5000 patients through a 17-day process. It also established which process (classic or closed system) implied less steps and could be performed in the most simplified facility. In order to compare both processes, we created two representations of lean cell therapy plants. The first one relied on operators and open systems. The second one relied on automated machines and closed systems.

Conclusion

Results show that equipment availability enables an increase in the yearly production.

The difference between the two processes is that closed system factory operators have more time that can be allocated to respond to a higher demand than classic factory operators who would be overwhelmed by order augmentation because of their less flexible work schedule. A switch to closed systems decreases the cost and the contamination risks and leads to a higher potential number of batches produced yearly. By testing the ergonomics with our VR solution, we were able to find the optimal space utilization. It highlighted the superiority of the one-room architecture when compared to the classic architecture.

Altogether, the results we obtained show that automation and the use of closed systems can lead T-Cell Therapy to a more agile and flexible environment.

Experimental Approach

Models

We used a layout design and a flow simulation software to generate predictive models of bioproduction environments and optimize their configuration. The process we represented is divided into 8 major steps: Thawing, Selection/Activation, Washing/Concentration/Transduction, Expansion, Transfer, Selection/Depletion, Fill & Finish and Freezing. The first model is the classic factory where every step is performed in a dedicated room. The process is performed with open systems in A or B-Grade room under Laminar Flow Hood. The second model is a closed system automated process where every step is performed in just one room. With new equipment such as Lovo (for Thawing, Selection/Activation, Washing/Concentration/Transduction) CliniMACS Prodigy® (Selection/Depletion), Control Rate Freezer (Freezing) or Crystal® L1 Robot Line (Fill & Finish), the time an operator is needed to actually handle the products is eliminated. Operators are still required to set up machines, load and unload the cells and monitor the process.

Process Development and Design with HakoBio

OUAT! developed HakoBio, a web-application that allows to easily design a bioprocess facility and enter it by using virtual reality. We used this platform to design a cell therapy process and the facility in which we added the required equipment.

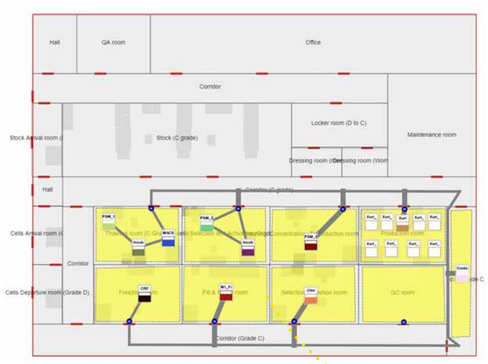
Process Simulation with SIMOGGA

AMIA Systems developed SIMOGGA, a software that quantifies and optimizes operations, simulates flows and production capacity. Once the facility layout, the process, the number of batches and the timing of each step have been established, we tested the models with SIMOGGA's planner algorithm software to identify the number of operators needed and the quantity of machines required to reach the requested yield.

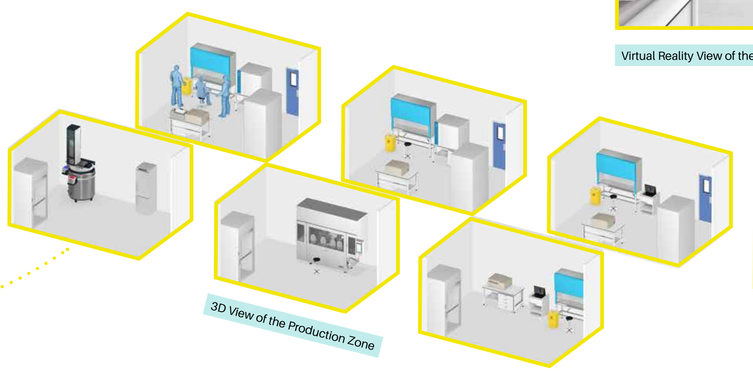
Layout Ergonomics on HakoBio

We then sent the data generated with SIMOGGA to HakoBio to obtain 3D models of both factories. We used HakoBio's Virtual Reality tool to assess ergonomics of the cleanroom filled with the necessary equipment and minimize its size.

Classic Factory



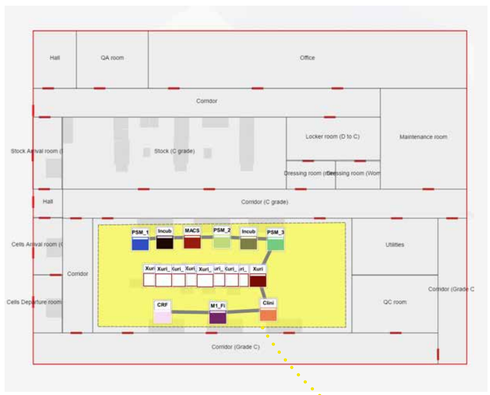
2D view of the Classic Factory



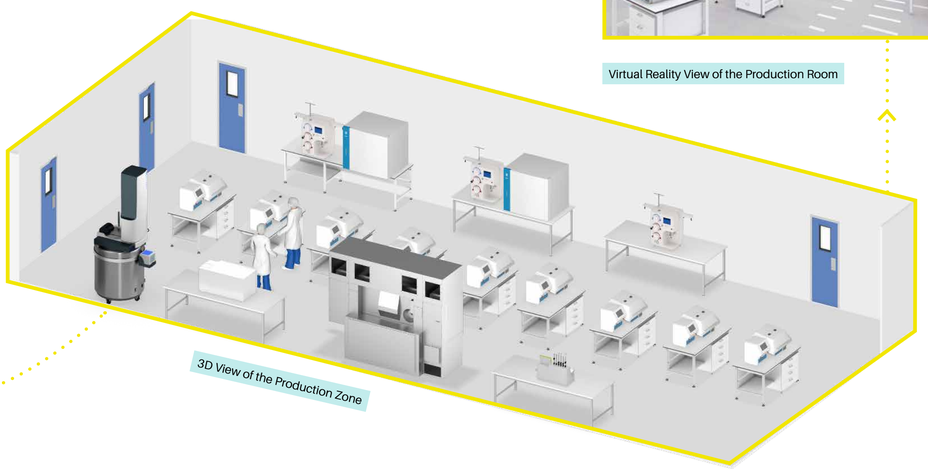
3D View of the Production Zone

Virtual Reality View of the Production Room

Closed System Factory



2D view of the Closed System factory



3D View of the Production Zone

Virtual Reality View of the Production Room

Results

Flow simplification

We first noticed that the flows of the closed systems factory were much simpler. This is due to the use of closed systems that allows the entire process to be performed in one big production room rather than in different small cleanrooms. This eliminates several constraints, such as crossflows, and decreases dressing time.

Operating Time

While equipment set-up and batch (un)load times remain the same, the operating time is down to zero in the closed system factory. If this does not impact the equipment availability, it strongly increases operators' availability.

Operators Number

Reduced operating time and elimination of dressing constraint lead operators number to slightly decrease in the closed system factory in comparison with the classic factory.

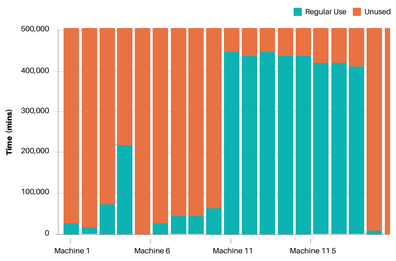
Overall costs

We estimated the impact on the cost by extrapolating the previous results. The decreased number of operators and the use of a C grade production room rather than multiple small A or B grade cleanrooms reduce the cost of the closed system process.

Equipment occupation
Classic Factory

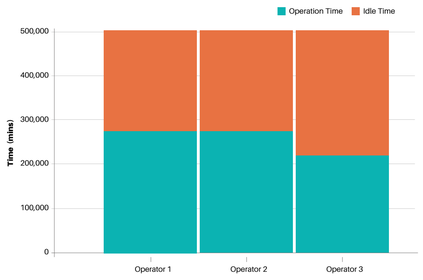
The graph shows the occupation of the equipment required for the process. Globally, machines are under-exploited except for the expansion equipment.

Equipment occupation
Closed System Factory



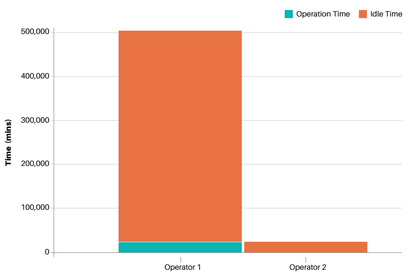
The graph shows a roughly similar equipment occupation than for the classic factory with an under-exploitation of the equipment except for the expansion equipment.

Operators Time occupation
Classic Factory



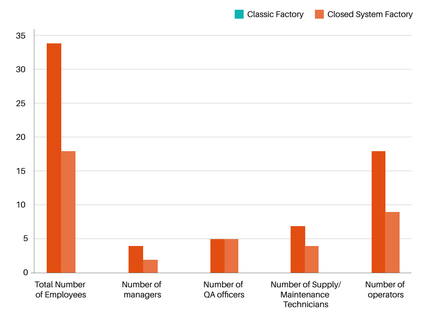
The graph shows the occupation of the team of three people that is needed to lead the process (two operators, one quality control officer).

Operators Time occupation
Closed System Factory



The graph shows the occupation of the team of two people that will be needed to lead the process (one operator, one quality control officer who will be only required for a couple of steps).

Number of employees



This graphs shows an estimation of the number of employees required for the different functions essential for the factories.

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