

Analysis of operational cost savings for various cell culture processing approaches

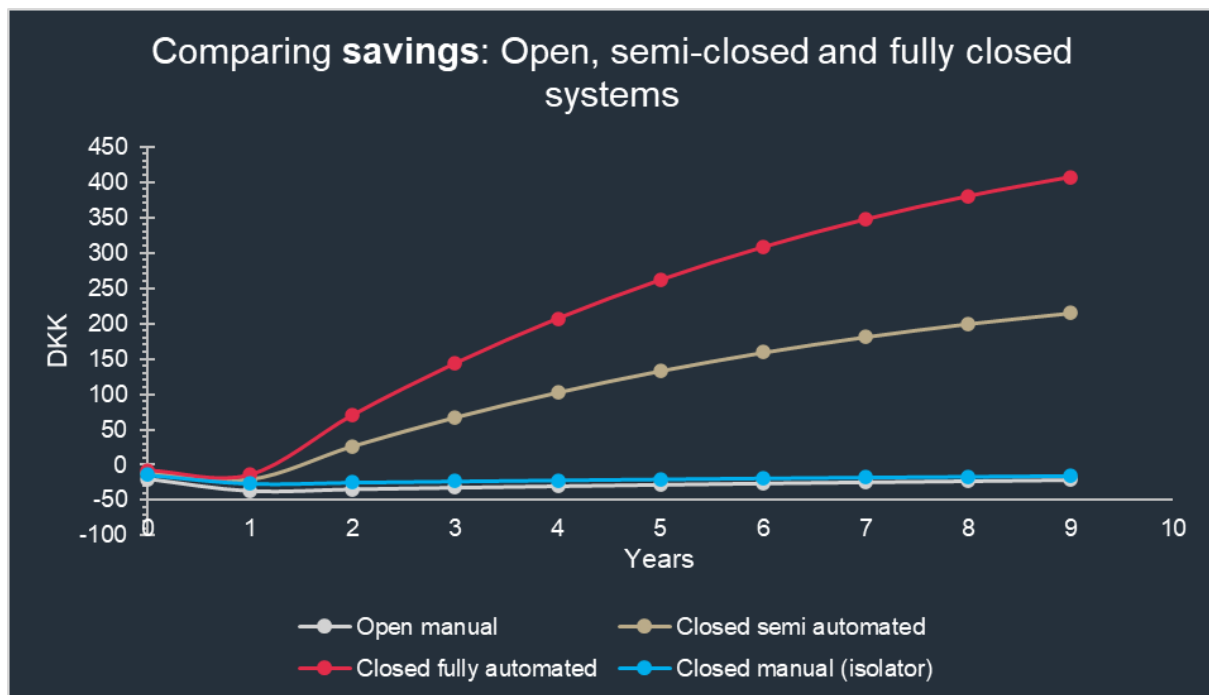


Figure 1: Comparison of different cell culture processing approaches. In the longer run, closed fully automated operations will result in significant savings due to the facility footprint, HVAC cost and FTE cost. The scenario calculations are based on processing 2000 Batches of autologous product per year, and are partially inspired by the scenarios in James, D., 2017. How short-term gain can lead to long-term pain. Cell & Gene Therapy Insights and typical data from suppliers, as well as internal NNE cost data.

NNE conducted an overview analysis on the operational cost regarding the different approaches associated with cell production, with a focus on clean room cost (Facility / HVAC) and Full Time Employees (FTEs).

An open manual operation is typically conducted in a class B cleanroom under class A processing area(s). This requires tedious handling and is generally resource heavy in terms of the running cost of the facility HVAC and FTEs. For example, classical manufacturing in this setting requires approximately 3 times the employees to process 1 batch of product vs. a fully automated and closed process approach. This is due to manual handling of the manufacturing process and manual handling of cleanroom monitoring.

Moving the manufacturing process to a closed barrier system such as an isolator reduces environmental monitoring requirements and the cleanroom classification to C which thereby reduces HVAC capacity. In addition, fewer FTEs are needed as the cleanroom doesn't have the same monitoring requirements as an open manual setting.

However, in terms of area footprint and operational cost of the isolator, one does not see significant savings. So, although isolators enable operation to be conducted in a lower classified cleanroom while keeping a sterile barrier, the cost and energy consumption of the isolators are a vast downside.

When looking at a semi-automated and closed approach, significant savings come from the reduction of area footprint, cleanroom classification, FTEs, and HVAC cost. Typically, the process approach will involve various types of process equipment that are closed to maintain sterility. The equipment might be connected using sterile welding or aseptic couplers which mitigate the risk of contamination seen in open process with manual handling. A semi-automated approach might involve 1-2 FTEs for the whole manufacturing process line.

Looking at a closed, fully-automated approach, most savings come from a reduction in cleanroom footprint, a lower cleanroom classification and lower operational costs and HVAC capacity. This is due to the technological advancement of this approach, as the equipment is typically fully integrated and can process more steps compared to the cases above. In theory, a fully automated closed system could be applied in a ball room setting, where each system processes an individual patient's product.

This scenario is ideal for autologous cell and gene therapy. Because the system comes fully closed, less environmental monitoring is required compared to the traditional class A/B approach and less HVAC and it requires a smaller facility footprint. In terms of FTEs, few staff resources are needed to run daily operations around the process as it is automated and fixed in lead time. Staff would only be necessary to monitor and change media and remove waste etc. when needed.

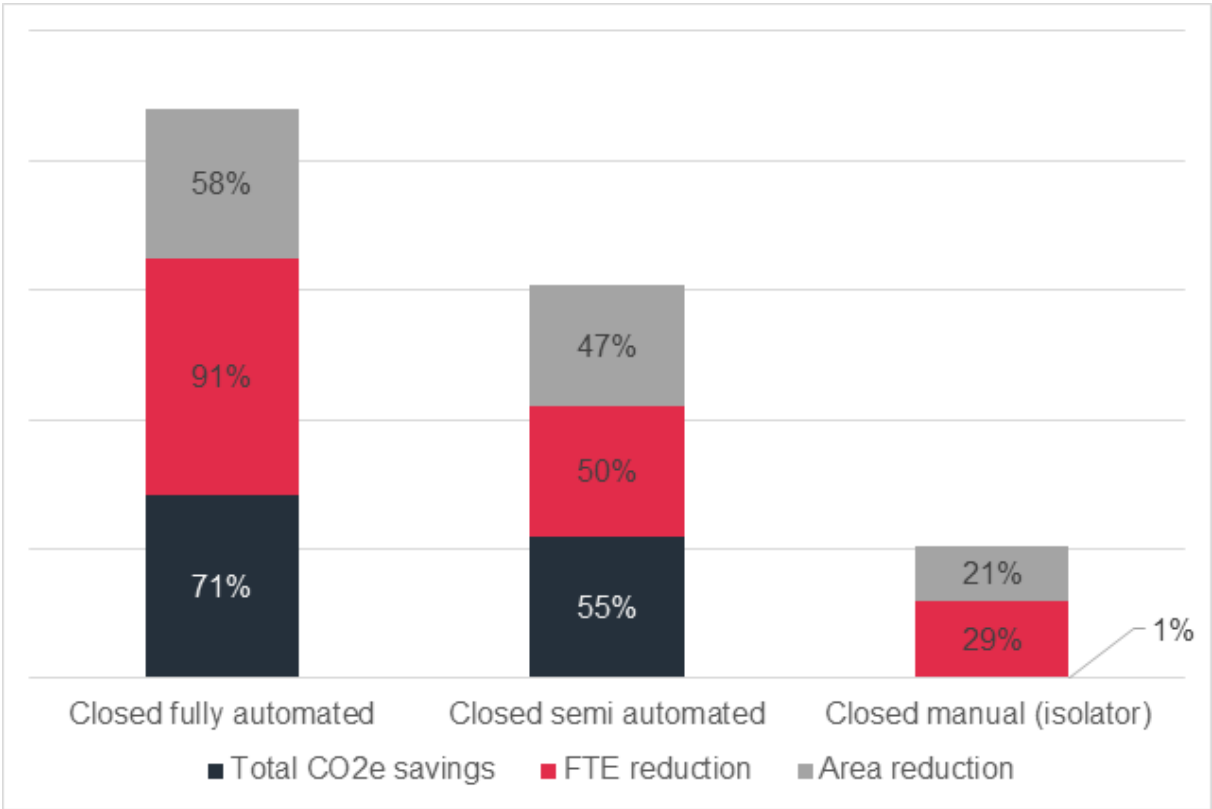


Figure 2: Illustration of estimated savings in total CO2e, FTE and Area compared to open manual process