Perfusion-SUBs

Tight controlled and scalable – from 250 ml and up

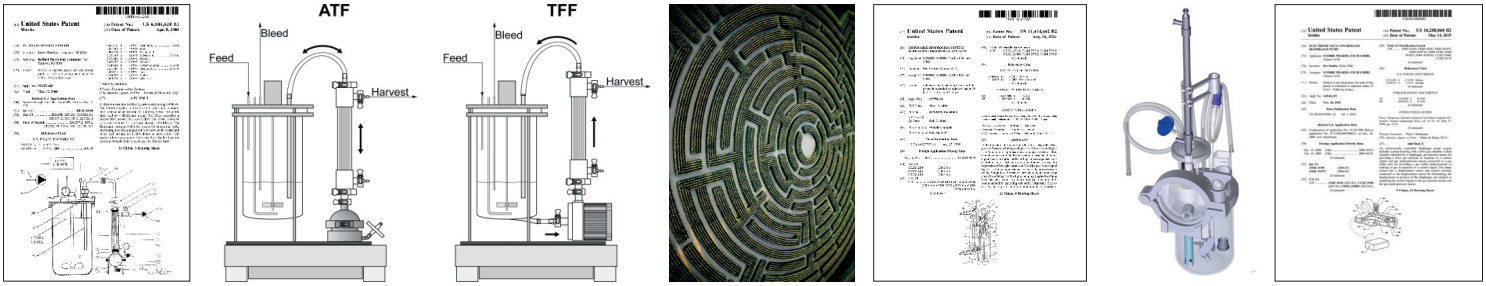
Keywords: Perfusion, Continuous, Single-Use-Bioreactor, customized, scalability

Author: Per Stobbe, email: per.stobbe@perfusecell.com - 2022-25-08 – ver 1.4

Equipment market for continuous cultivation of mammalian cells for expression of Mabs is dominated by just a few suppliers. Quite surprising only one supplier offers ready to use Perfusion-Single-Use-Bioreactor (P-SUB) in 250 ml size - as of writing. The latest innovative solution for continuous processing is described here.

Speeding up process development and small-scale manufacturing benefit from ready-to-use P-SUB solutions minimising facility space and capital investment in sterilization equipment.

Even continuous processing is known for decades an important innovative step forward was Jerry Shevitz input in year 2000 with what became known as the ATF system. Since then, this now more than 20-year-old ATF technology package lack innovative input - until recently. Even introduction of SUBs into the marked almost 10 years ago since then lacked ready-to-use P-SUB packages. The important diaphragm pump has not changed over the last 100 years. Needed innovative input must be improved functionality, in particular accurate operation, highly wanted ability to measure mass flow and reliable data acquisition.

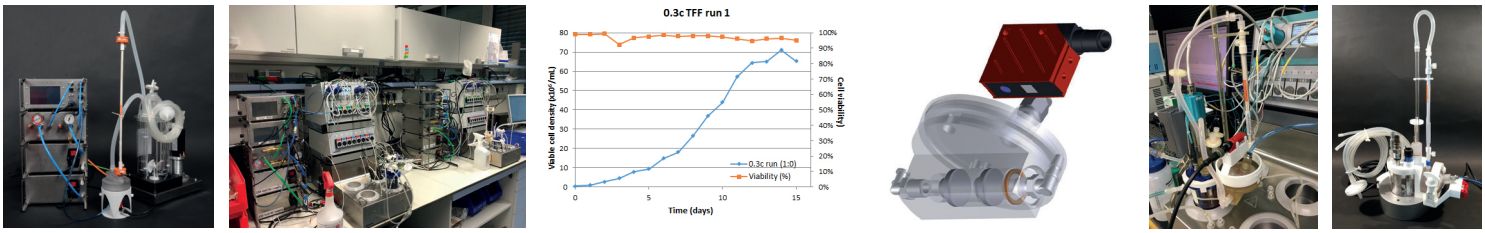


IPR (Intellectual-Property-Rights) is like a labyrinth which though most important support new development, and gives Freedom-to-Operate if one is visionary enough. Above some respect to Jerry, sketch of the two most used system principles, how I see the IPR labyrinth, one of several of my perfusion IPR input and rendered CAD drawing with the highly innovative diaphragm Single-Use-Pump (SUP) in front, and to the most right the important IPR of the diaphragm SUP.

The innovative solution for continuous processing by Perfusion-SUBs will benefit form:

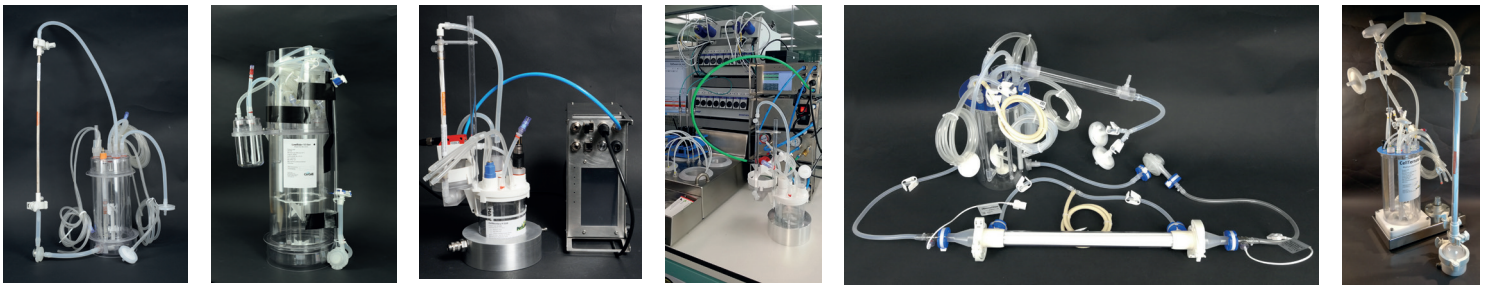
- Fully pre-assembled P-SUB, customized as to process need, incl all hoses and connectors
- Scalable working volume (WV) within the limits of rigid plastics SUB sizes
- Pre-installed Single-Use-Sensors (SUS) as to end-user needs
- Integrated electronically controlled positive displacement diaphragm Single-Use-Pump (SUP) operating like the mammalian heart with selectable operation parameters (0-100 % mass flow, selectable pulse width and pulse sequences)
- Preinstalled membrane filter or Hollow-Fibre-Filter modules as required
- Fully assembled and ready to use (including abbreviations like SUBs, SUSs, SUPs, HFFs)
- Either combining existing Process-Control-Systems (PCS) with PCS-SUP or a complete customizable PCS package running appropriate software – like Lucullus.

Fulfilling the above reasonable requirements is the innovative solution for continuous processing and the missing giant step ahead supporting the market requirement for continuous cultivation of mammalian cell lines.



*First photo (at left) shows a 3.2 liter **P-SUB** incl **SUSs**, **SUPs**, **HFFs** and **SUP** control units incl air pumps units. We are allowed to show photo from the Merck Darmstadt facility (second photo from left). The dual setup is the combination of PerfuseCell **P-SUB** IPR controlled by combining DasGip PCS and Cronus-PCS units operating 2 x 4 **P-SUBs** in size 150 ml WV in parallel. Third photo show viability and cell growth performed at Eppendorf lab in MA, USA. Fourth photo illustrates the fully controlled diaphragm **SUP** with the red laser sensor for on-line diaphragm position reading. Photo fifth is a model CellMembra combined setup with Eppendorfand sixth photo a 250 ml WV PerfuseCell model CellRetention ATF.*

Merck Darmstadt do run 8 in parallel Eppendorf bioBLU customized to P-SUBs by PerfuseCell for the DasBox. The **SUP** is controlled by the Cronus-PCS tower via OPC-UA to-and-from DASware. Can the advanced **P-SUP** control be integrated with other **PCSs** – yes, Cronus-PCS offer a complete PCS package running Lucullus. This new **P-SUB** technology package covers both ATF and TFF processes and so far, scalable up to 25 litre WV. Integrated Single-Use-Sensors (**SUS**) for process control, data acquisition is based on current advances in **SUS** from Hamilton, ABER and CerCell.



Various examples of end-user customized P-SUBs -from left: 4 liter LowRider-1 integrating a Levitronix centrifugal SUP, a 10 litre Working-Volume LowRider-10 with bottom outlet for the Levitronix SUP, a 250 ml P-SUB with various SUS and the tightly controlled diaphragm SUP, similar 250 ml P-SUB as in use at Catalyst/UK, somewhat advanced Ready-to-Use pre-assembled 3.2 litre LowRider-2 a Levitronix SUP, gas cooler, huge membrane filter, even a couple of PendoTech sensors, last CellTernate-2 all single-use ATF ready to use.

CerCell www.cercell.com

PumpCell www.pumpcell.com

PerfuseCell www.perfusecell.com

Cronus-PCS www.cronus-pcs.com

ProlifeCell www.prolifecell.com