

## TIGHT CONTROLLED SCALABLE PERFUSION-SUBS FROM 250 ML AND UP

Per Stobbe, PerfuseCell A/S, Denmark  
per.stobbe@perfusecell.com

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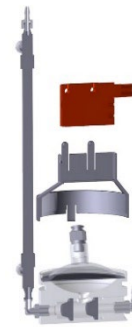
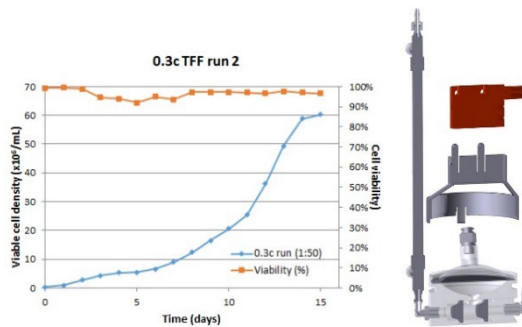
Equipment market for continuous cultivation of mammalian cells for expression of Mabs is dominated by just a few suppliers. Quite surprising only one supplier offer ready to use Perfusion-Single-Use-Bioreactor (**P-SUB**) in one size - as of writing. The latest **innovative solution for continuous processing** 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. Even introduction of SUBs into the marked almost 10 years ago have not established ready-to-use P-SUB packages. The important diaphragm pump has not changed over the last 100 year. Needed innovative input must be improved functionality, in particular accurate operation, highly wanted ability to measure mass flow and reliable data acquisition.

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

- Pre-assembled, customized as to process need, incl all hoses and connectors
- Scalable working volume within the limits of rigid plastics SUB sizes
- Pre-installed Single-Use-Sensor's 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)
- Control-System for SUP performance for dynamic precision control of mass flow and pressure
- Preinstalled membrane filter or Hollow-Fibre-Filter modules as required
- Fully assembled and ready to use (including abbreviations like **SUBs**, **SUSs**, **SUPs**, **HFFs**)
- Adaption to existing Process-Control-Systems (**PCS**) at end-user site

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 dingle 3.2 liter P-SUB incl **SUSs**, **SUPs**, **HFFs** and SUP control and air pumps. We are allowed to show photo (and data) from the Merck Darmstadt facility (# 2 from left). The dual setup is a combination of PerfuseCell P-SUB and DasGip/Eppendorf PCS operating 150 ml P-SUBs in parallel. Third photo show viability and cell growth performed at well-known lab in MA, USA. Fourth photo illustrates the fully controlled diaphragm SUP with the red laser sensor for on-line diaphragm position reading.

Merck Darmstadt do run up to 8 customized **P-SUBs** in parallel manufactured by PerfuseCell for the DasBox **PCS**. The **SUP** is controlled by the PerfuseCell **SUP** tower via OPC from DASware. Can the advanced **SUP** control be integrated with other **PCSs** – yes, easy if such PCS run Lucillus. This new P-SUB technology package covers both ATF and TFF processes and are so far scalable up to 30 litre. Integrated Single-Use-Sensor's (**SUS**) for process control, data acquisition is based on current advances in SUS. Do we need wider variety of **SUS** – yes, we and others are involved in such important development.