Growth of high-cell density microbial cultures in a single-use fermentor system

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Abstract
Here we show the performance of a single-use Xcellerex™
XDR-50 MO fermentor system
when used in high-cell density
cultivations of E. coli producing
a domain antibody (Dab) and
of modified Pseudomonas
fluorescens (P. fluorescens) producing a monoclonal
antibody (MAb) (Fig 1). Both the
achieved microbe densities and
product yield were shown to be
consistent with the performance
of conventional stainless steel
and glass bioreactor systems.

Introduction
Microbial processes are widely used for industrial
production of biopharmaceuticals. Due to the
historical limitations of single-use technologies,
bio-manufacturers have traditionally been referred
to the use of stainless steel equipment for these
processes. Bioreactors designed for mammalian
processes fall short of meeting the unique
requirements of production in microbial processes in
terms of, for example, oxygen transfer capacity and
temperature control. Xcellerex XDR-50 MO fermentor
system is purpose-designed and built to overcome the
mammalian single-use system limitations in
fulfilling the needs of a microbial process. The culture
vessel features a dimpled jacket heat transfer surface
for efficient cooling and heating of the culture. Robust
agitation is provided by a powerful magnetic drive
and a two-stage impeller, resulting in a high oxygen
transfer to the culture medium.

Cell growth and production in E. coli fed-batch cultures
A monoclonal antibody (MAb) was produced in parallel fed-batch
cultures of E. coli using XDR-50 fermentor and a reference
stainless steel system from Belach Bioteknik AB. Microbial
growth achieved in XDR-50 MO fermentor was comparable
with that of the reference bioreactor (Fig 7). Product titers were
also similar between the systems: 2 g/L for XDR-50 MO and
2.2 g/L for the reference bioreactor.

Discussion
The fermentor is designed to meet the unique requirements of
microbial cultures in terms of, for example, high oxygen transfer
capacity and high cooling capacity. As shown in applications with
E. coli and P. fluorescens, the XDR-50 MO fermentor is capable of
delivering both cell growth and protein production equivalent to
those of conventional stainless steel and glass microbial fermentor
systems. The improved features and benefits of this single-use
system eliminates the need for time-consuming cleaning-in-
place and sterilization-in-place operations and offers increased
operational flexibility for the biomanufacturer using microbial
processes.

Conclusions
• The single-use Xcellerex XDR-50 MO supports cell growth
  comparable with conventional fermentor systems
• A system design with a powerful drive enables high
  oxygen transfer rates > 500 mmole L⁻¹ h⁻¹
• The XDR-50 MO cooling capacity is sufficient to support
  high-density microbial cultures.