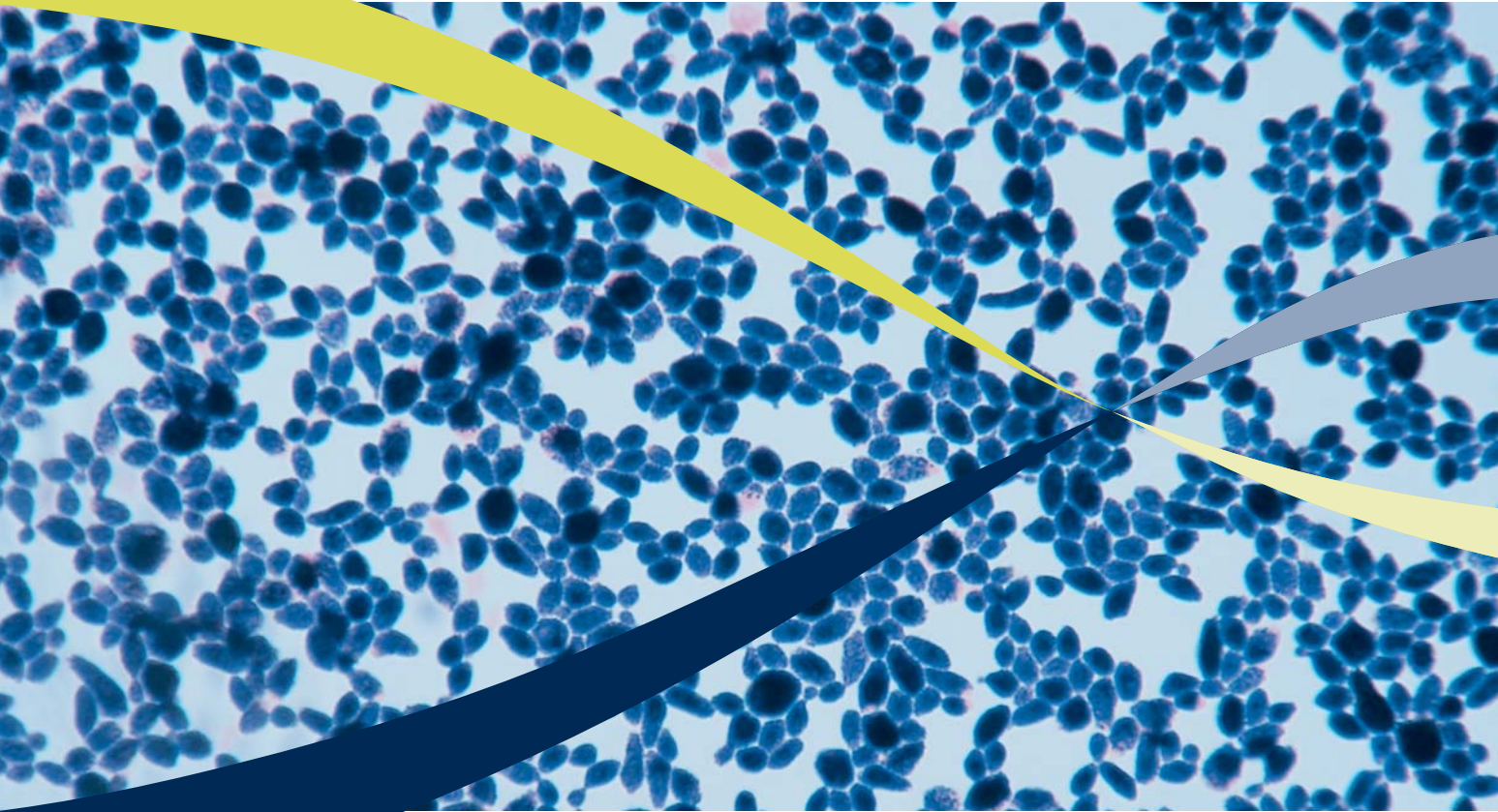


# The Yeast Experts



Industry leading expertise in developing  
yeast biomanufacturing processes

Avecia

The expression of proteins in yeast can offer a number of advantages over other systems. Avecia's experience in developing manufacturing processes over more than 10 years in both *Pichia* and *Saccharomyces* has given us an enviable track record from early phase clinical through to late phase and process validation.

## Why Yeast?

- Yeasts are able to secrete correctly folded protein into the culture supernatant
- Yeasts have the cellular machinery to accurately fold more complicated proteins than prokaryotic systems
- *Pichia* can use the methanol-inducible alcohol oxidase 1 gene (AOX1) which can result in tight control of heterologous expression
- Post-translational modifications are possible eg. glycosylation

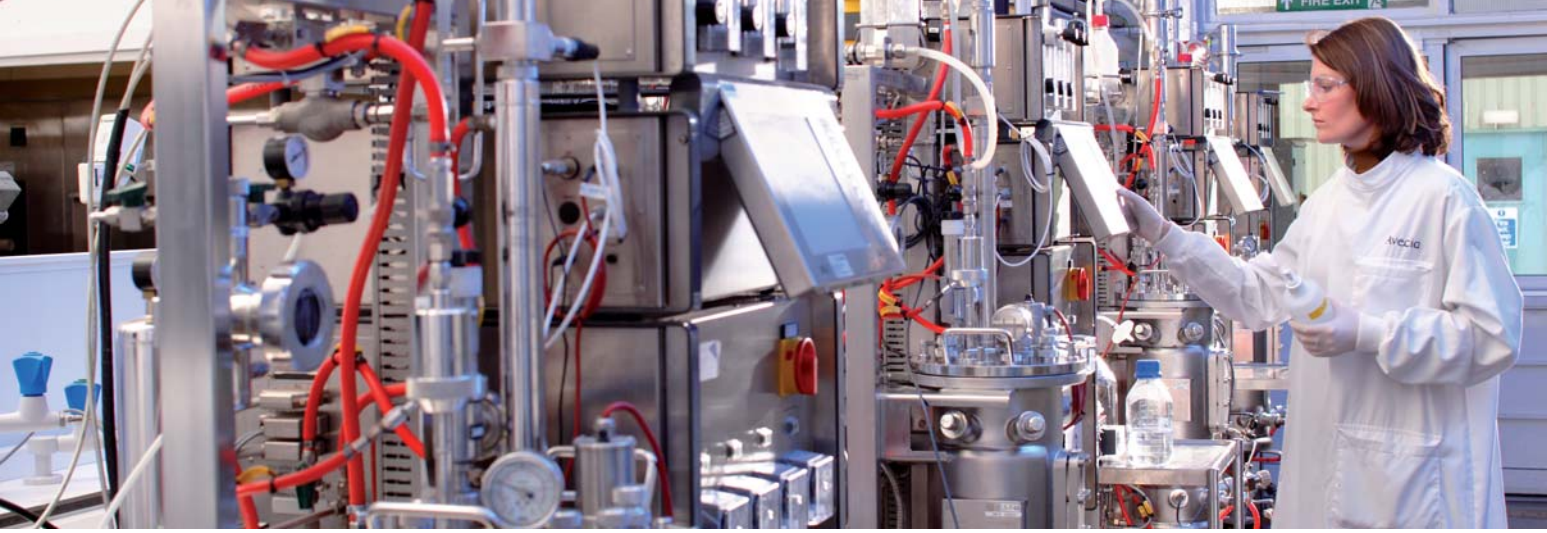
## Avecia's Track Record Spans >10 years' Experience



## Avecia's R&D Capabilities

- 30 modern laboratory bioreactors capable of operating high cell density yeast processes with methanol and O<sub>2</sub> supplementation
- Experience using FMEA methods to define Laboratory Process Characterisation (LPC) studies ahead of validation
- LPC studies carried out using statistical experimental design, allowing rapid and robust process characterisation
- Experience of scaling fermentation processes from 15L laboratory to 3000L production scale
- Developed yeast processes from phase I through Phase II/III/Validation to NDA
- Experience of scaling expanded bed chromatography from 2.5cm to 100cm production scale





## Avecia's Manufacturing Capabilities

### Upstream

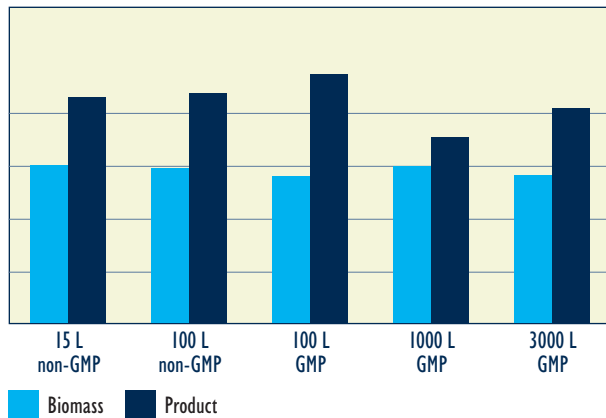
Avecia's manufacturing capabilities are designed to enable:

- The high oxygen transfer rates and cooling capacities required for high cell density culture
- Reproducible and robust scale up from 15L laboratory scale to 3000L manufacturing scale
- Delivery of consistent performance at all scales

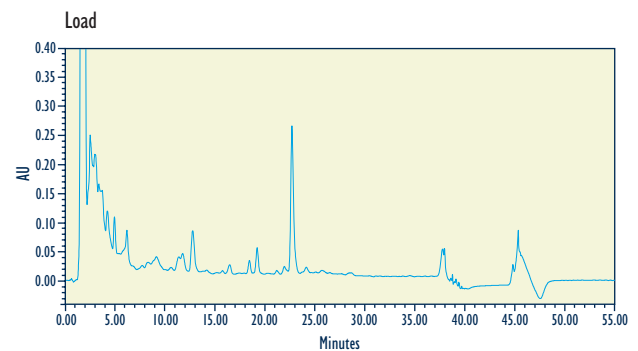
### Downstream

- Able to apply the full range of separation and purification options including the use of expanded bed chromatography (EBC)
- Extensive experience of EBC capture/purification:
  - Provides rapid and efficient scalable primary capture combined with initial purification
  - Excellent scale-up data from a 2.5cm expanded bed up to 100cm
  - Taken through process validation

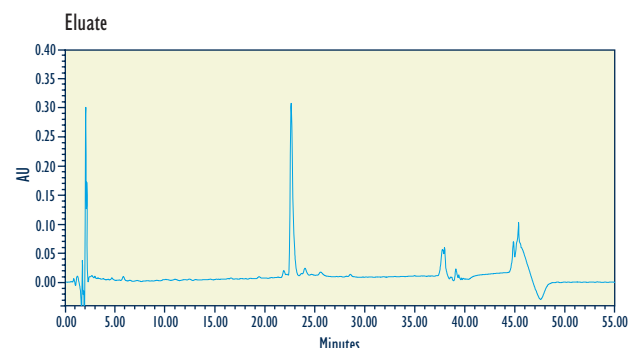
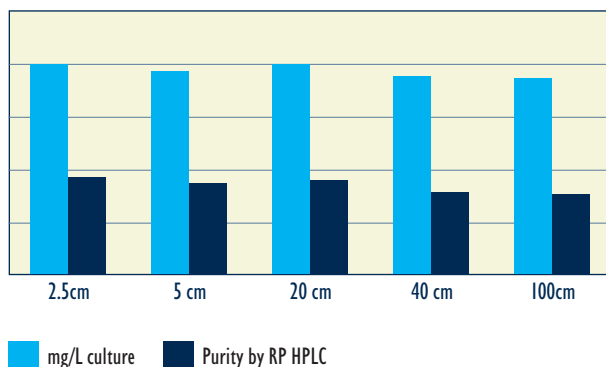
### Final Biomass and Product Titres

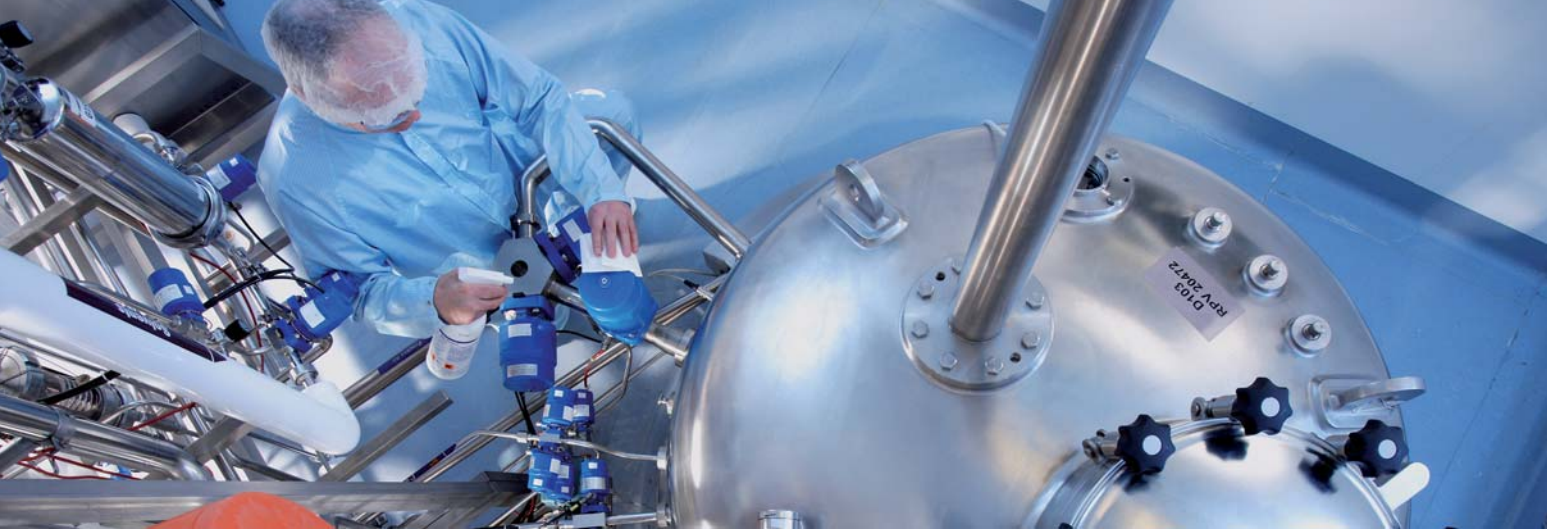


### Analytical RP-HPLC of EBC Load and Eluate from 5000L Run



### EBC - Yield and Purity

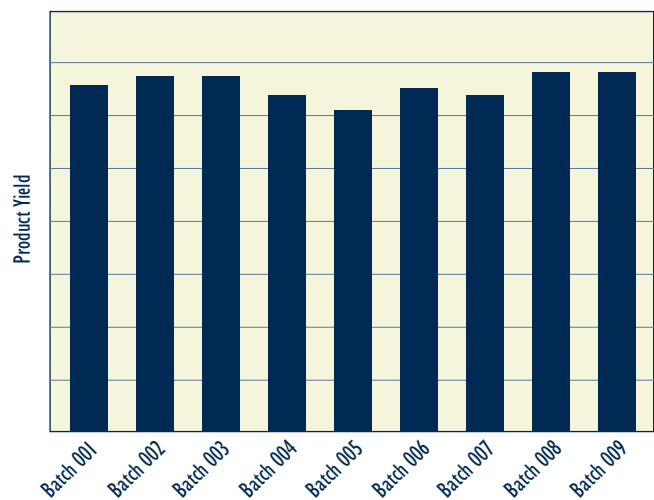




## Avecia - The Yeast Experts

- Avecia's capability in process development and biomanufacturing have been shown to result in robust reproducible yeast-based processes
- More than 10 years' experience in producing clinical therapeutic proteins using yeast systems
- Successful track record in taking processes from early phase clinical through to late phase and process validation
- Able to demonstrate consistent cGMP performance and output
- Strategic investment in technology advances to deliver further improvements in performance, output and cost-of-goods

### Yeast Process (*Pichia*) Consistency at 1000L GMP Scale



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# Avecia