biomega®

Technical and financial challenges in scaling up a bio-refinery using salmon waste

by

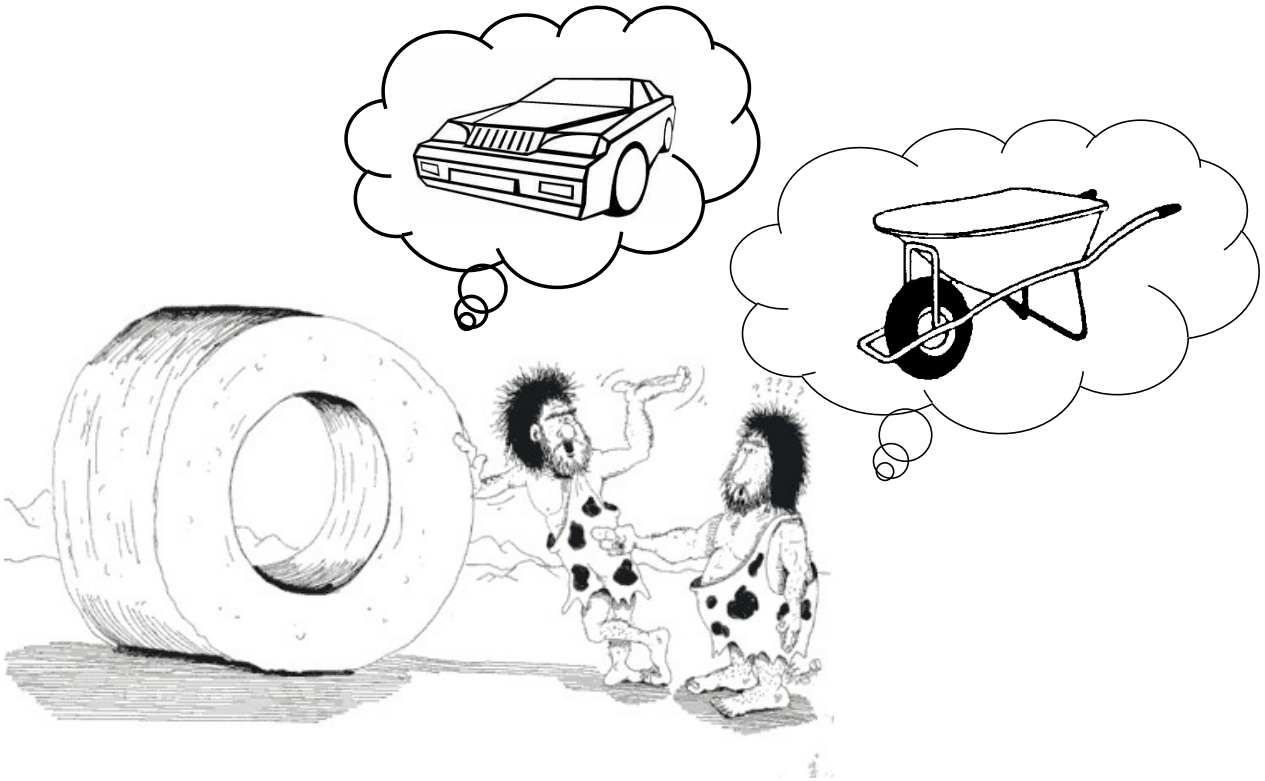
Kjartan Sandnes, Ph.d

Co-founder, member of the BOD, retired from management

Contents

- Idea
- **Technology**
- **Growth and financial issues**
- Present status

The ambition of the founders



Biorefining salmon co-products

Enzymatic hydrolysis

Water and enzymes

Exact time and temp

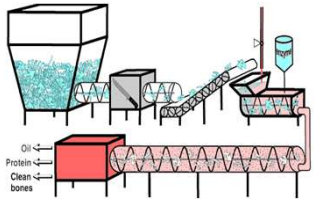
Oil

Water soluble protein

Sediment

The Biomega biorefining story

- 2000: Biomega AS established
- 2002: Production established with patented continuous enzymatic hydrolysis process.
- 2007: New site acquired for new factory.
- 2011: 30.000 tons raw materials processed.
- 2012: New plant with a capacity of 40.000 tons annually
- 2017: Aquired by Amerra Capital Management LCC, N.Y.

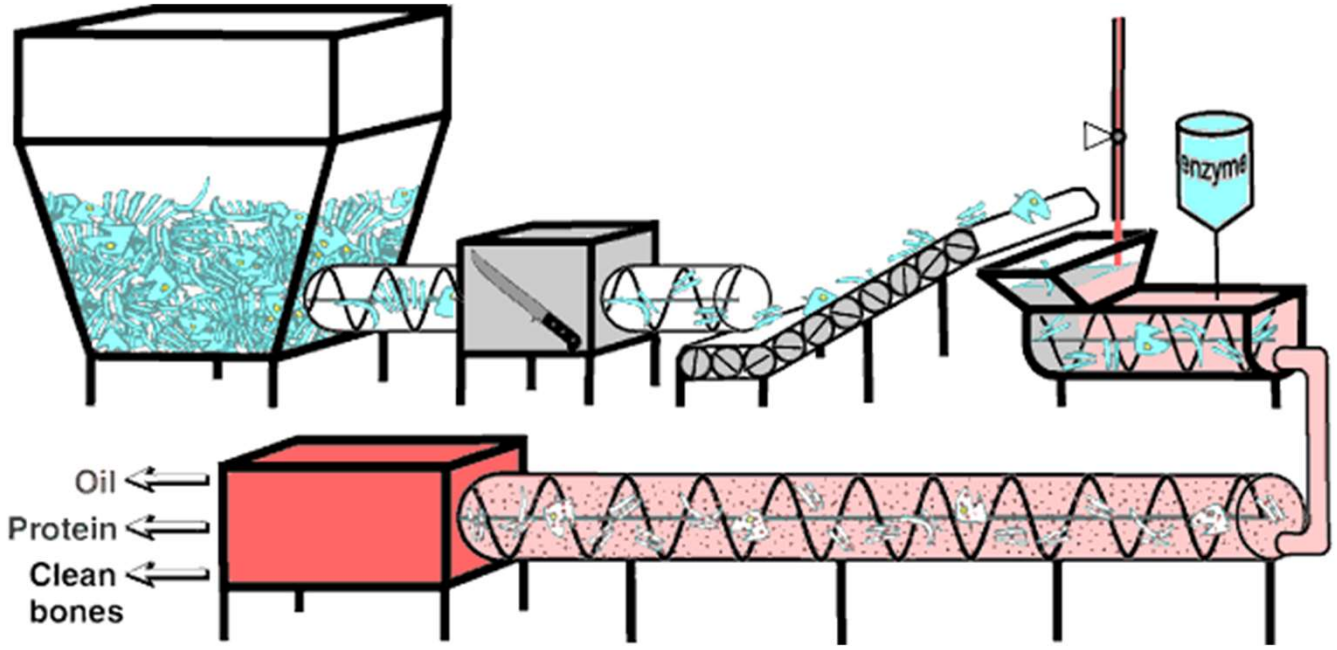


BIOMEGA

Norway plant – new reception area

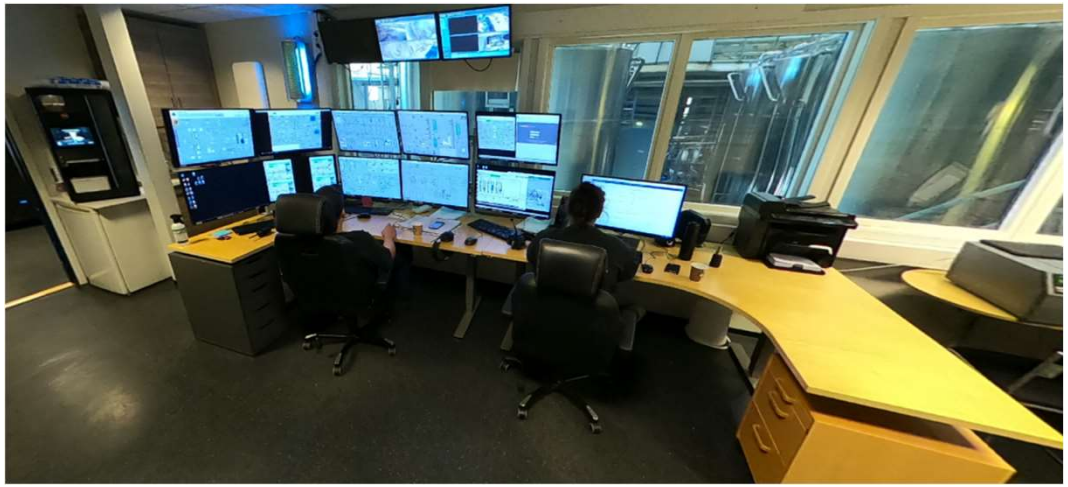
New reception area with no break in the cooling chain improves raw material quality and secures higher oil quality from the plant

The Biomega continous hydrolysis process - technical challenges



Biomega Norway

Control room



- Software developed in-house
- Fully controlled process

Plant overview

- The proprietary continuous Screw reactor to the right.
- Tanks for CIP liquids, oil and hydrolysate
- Raw material reception, separation room and dryer section not shown

Financial challenges

- Financial history

- Family x (from start)
- Local capital fund (2011-2017)
- Amerra (2017)
- Eversource (Mirova)

- Present ownership

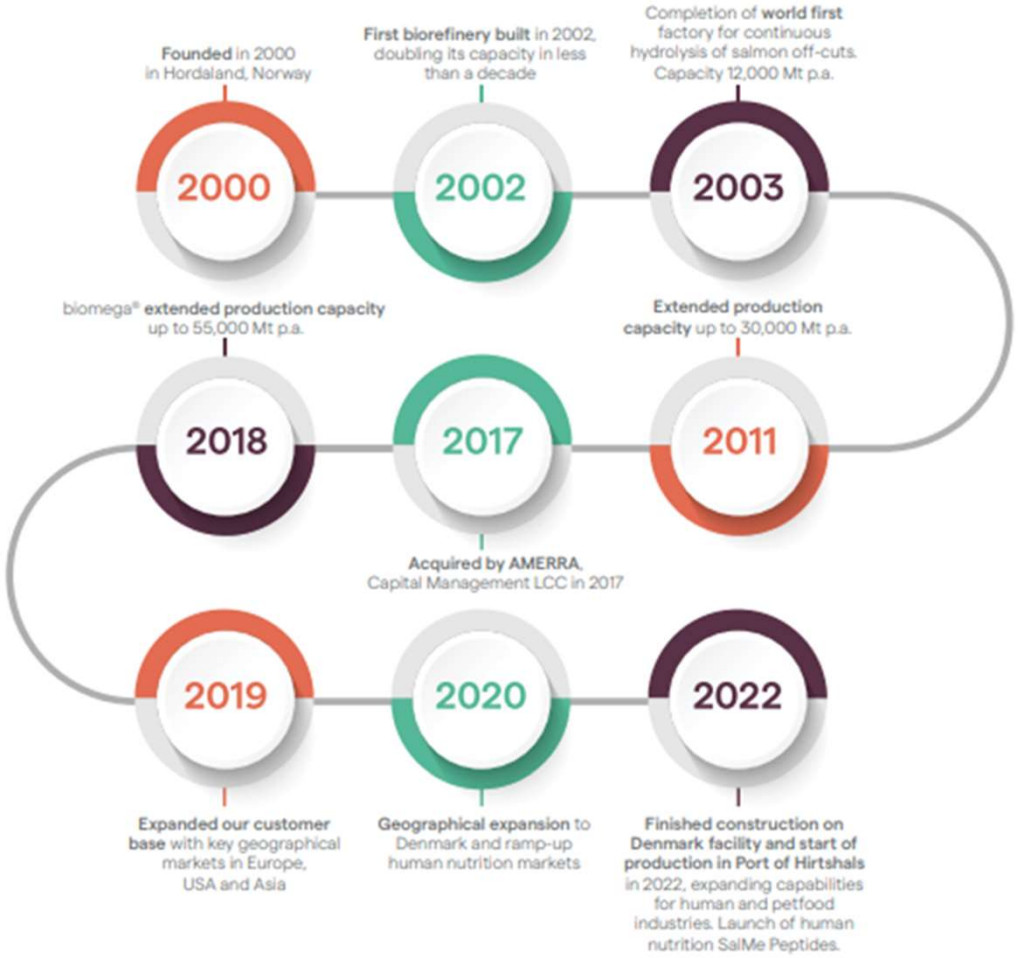
• Amerra Magni LCC	54,5 %
• Althelia Sustainable Ocean Fund Sic	15,6 %
• Amerra Magni II Lic	13,5 %
• Eversource Retirement Plan Master T	7,4 %
• Remaining (founders, management etc)	9 %

Biomega at present

- Two processing plants

Skaganeset, Norway

Hirtshals, Denmark



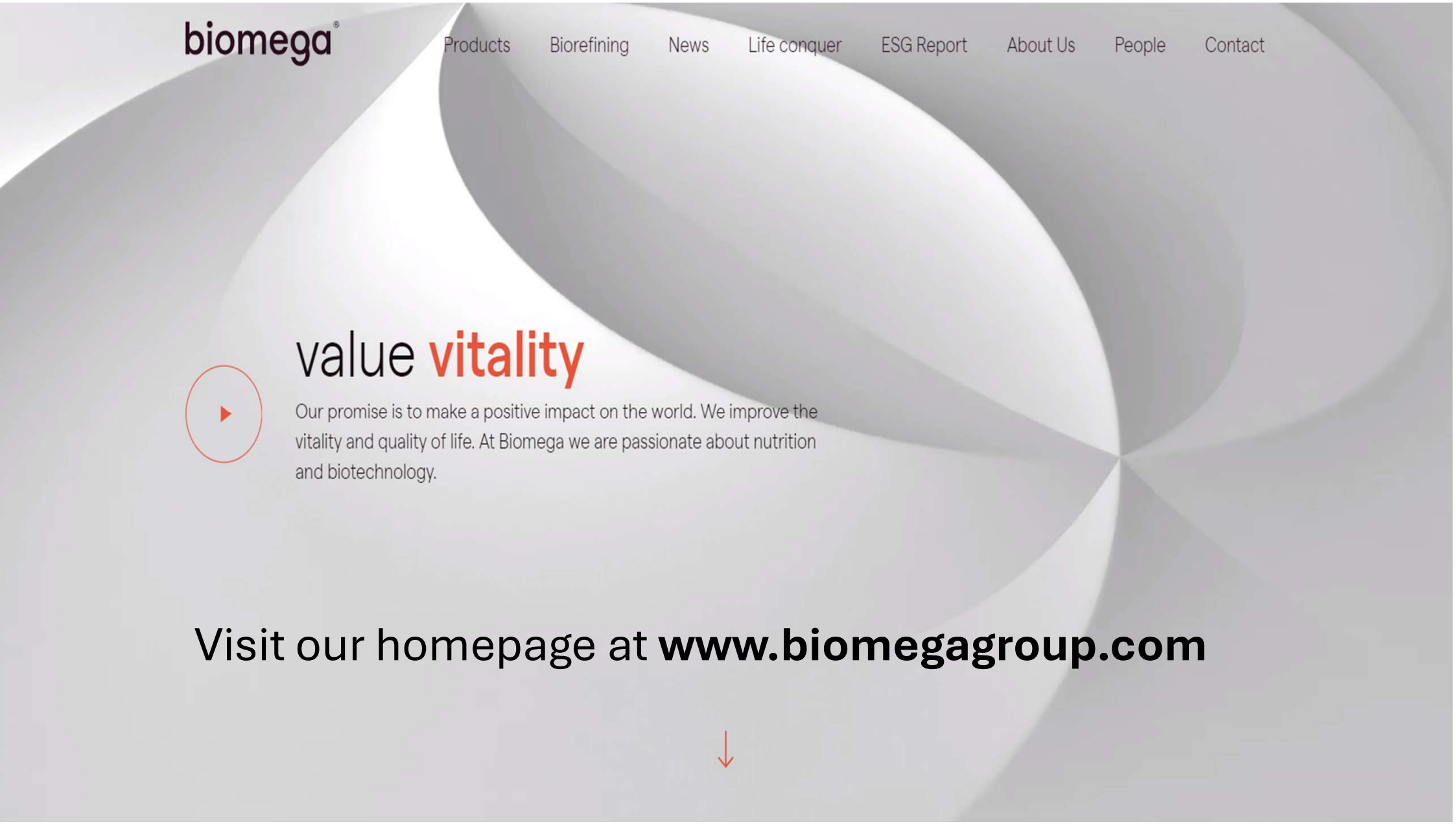
Some present key info

- CEO Stig Petersen

- +70 employees
- Processing ~50.000 MT
- Turnover ~500 MNOK
- 2023 EBITDA ~50 MNOK (11 %)

life conquer

Co-funded by the European Union



Visit our homepage at **www.biomegagroup.com**

Fermented Products: Design-for-manufacture

Andy Ellis

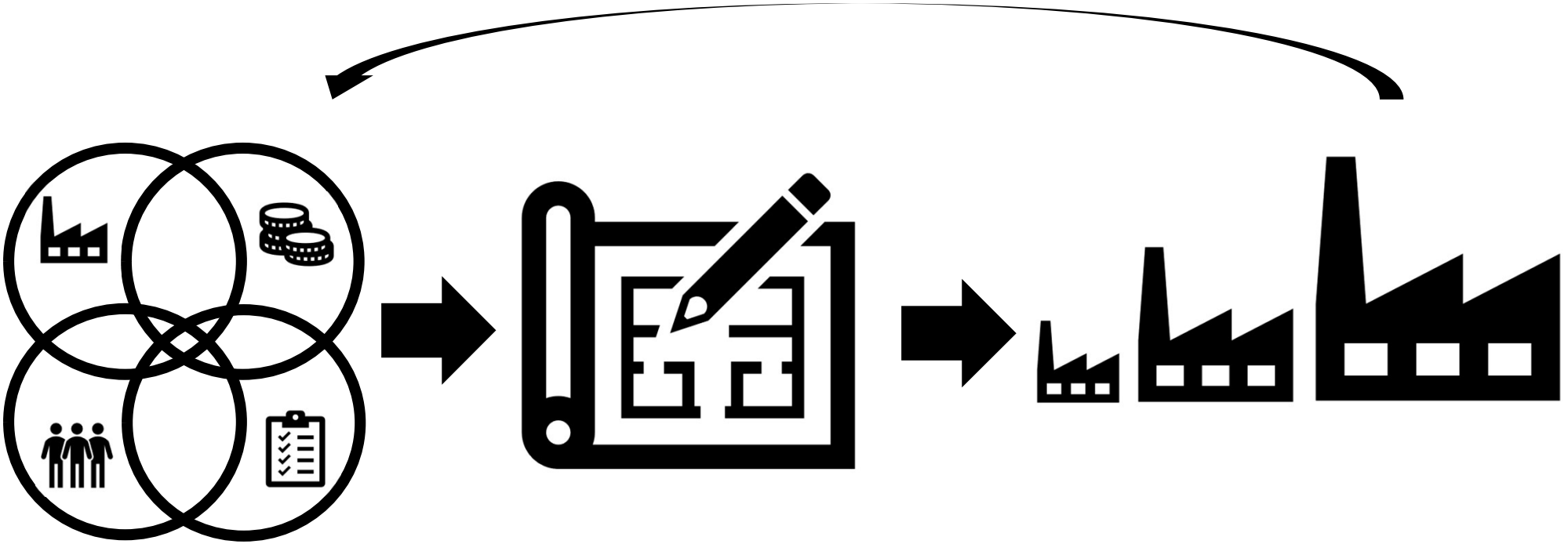
VP Fermentation BU & Technical Director

11th April 2024

Biocatalysts Ltd

- Customer-exclusive and market enzymes and proteins
- >300 enzymes scaled up to 750L scale
- >50 enzymes scaled up to 10m3 scale
- >25 enzymes scaled up to 20-65m3 scale
- Food enzymes, enzymes for API, clinical diagnostic enzymes, enzyme for speciality chemicals, food proteins
- Fed-batch fermentation process using Saccharomyces spp., Pichia pastoris, E.coli, Yarrowia liploytica, Pseudomonas spp., Bacillus spp.

DFM = First, Think Last



Design for manufacturing (DFM) is the **engineering practice of designing products to optimize their manufacturing ease and production cost**. DFM involves considering the assembly process, testing, and potential factory constraints in early design stages. DFM aims to simplify, optimize, and refine the product design. DFM is applicable to almost all engineering disciplines, but the implementation varies depending on the manufacturing technology.

DFM – TECHNO-OPERATIONAL CONSIDERATIONS

Obvious

Fermentation-
S.T.Y
Feeding regime
Kla/OTR – aeration, agitation, +P
Cooling capacity
Materials availability and spec

DSP -
Protein PI and stability (concn/temp)
Separation and clarification for purity
Temperature control

Less-obvious

Fermentation-
Protein toxicity (foaming)
Plant capacity

DSP -
Biomass and CIP waste
Water/energy
Drying or liquid stabilisation

SPOT-LIGHT:
Do you need/Can you afford that purity?

Request –
2 stage chromatography purification at 17m3 fermentation scale.

Estimated cost –
Cost +>75%

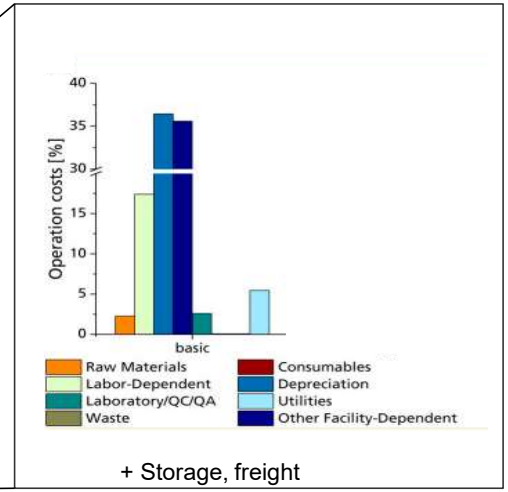
Solution –
Heat-treatment during early DSP to precipitate contaminating proteins
Cost +10%

DFM – ECONOMIC CONSIDERATIONS

Price target – price per unit of X?

Value Chain

Fermented product = market benchmarks or value add
Enzyme = expected cost contribution for biocatalysis reaction product e.g. pharma API, food ingredient



Process productivity?

Productivity assumptions

U or g/L from fermentation
% recovery of g or U during DSP
(compounded losses!)

Cost per unit (X) of fermented product?

Margin model

Price target = £200/kg
Total COGS = £45/kg
Margin = 78%; 5mt p.a revenue of £1m; profit of £750k)
(10%; ~~5 mt p.a. revenue of £1m; profit £100k~~)

Project £ feasibility – ROI, NPV

+ development costs: R&D, regulatory

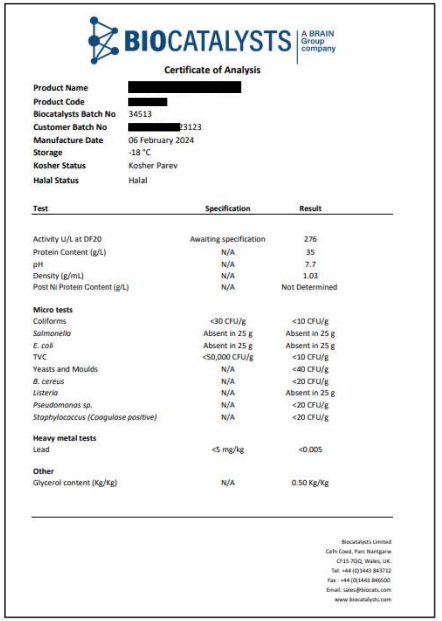
Enzyme X

WACC	5.7%															
	Year	cash out (project)	sales in	net profit (60%)	Net cash	present value	cumulative	Kg	Price/Kg		Working vol	SP £	Cost £	GM	OH	NP
2023	0	-	100,000	-	-	-	100,000	-	100,000		0	£ -	200			
2024	1	-	[redacted]								50m3		200	[redacted]		
2025	2	-														
2026	3															
2027	4															
2028	5															
					NPV (Yr5)		933,186									

DFM – REGULATORY CONSIDERATIONS

SPOTLIGHT: The problem with recombinant DNA? - Regulation (EC) No 1331/2008 “…….the applicant should investigate whether the target DNA is detected in analyses having a LoD of 10 ng of DNA per g or mL of enzyme product or lower”

SPOTLIGHT: The problem with phosphates? - gov. uk: ….”The fines published today cover the 2020/21 financial year, with more than £27 million of fines issued to 33 companies for emissions breaches”



BIOCATALYSTS | A BRAIN Group company

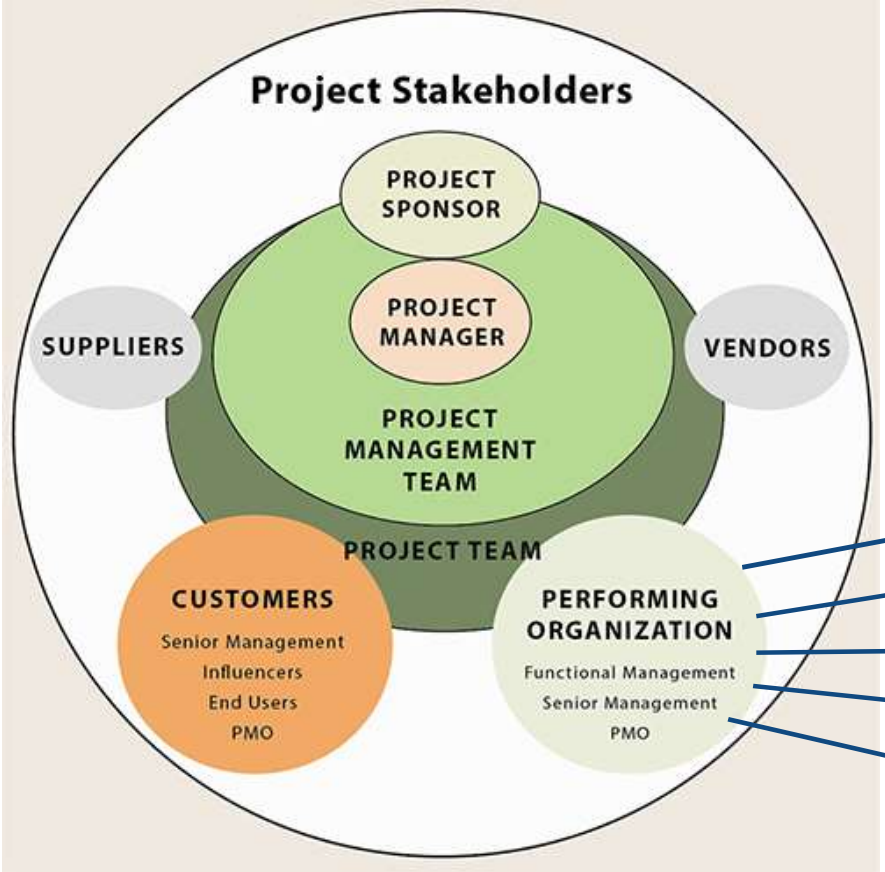
Certificate of Analysis

Product Name	[redacted]
Product Code	[redacted]
Biocatalysts Batch No	34513
Customer Batch No	[redacted]3123
Manufacture Date	06 February 2024
Storage	-18 °C
Kosher Status	Kosher Parev
Halal Status	Halal

Test	Specification	Result
Activity U/L at DF20	Awaiting specification	276
Protein Content (g/L)	N/A	35
pH	N/A	7.7
Density (g/mL)	N/A	1.03
Post Ni Protein Content (g/L)	N/A	Not Determined
Micro tests		
Coliforms	<30 CFU/g	<10 CFU/g
Salmonella	Absent in 25 g	Absent in 25 g
E. coli	Absent in 25 g	Absent in 25 g
TVC	<50,000 CFU/g	<10 CFU/g
Yeasts and Moulds	N/A	<40 CFU/g
B. cereus	N/A	<20 CFU/g
Listeria	N/A	Absent in 25 g
Pseudomonas sp.	N/A	<20 CFU/g
Staphylococcus (Coagulase positive)	N/A	<20 CFU/g
Heavy metal tests		
Lead	<5 mg/kg	<0.005
Other		
Glycerol content (Kg/Kg)	N/A	0.50 Kg/Kg

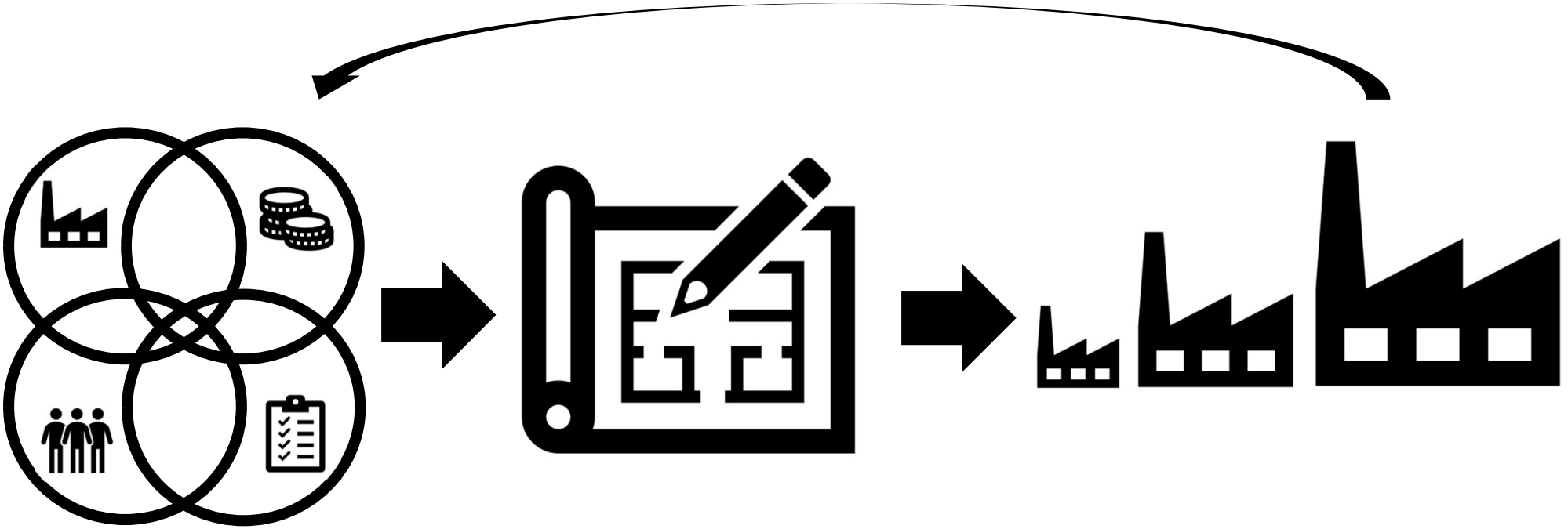
DFM – STAKEHOLDER CONSIDERATIONS

SPOT-LIGHT:
Customer contacts can change mid project; ensure expectations/accountabilities are clear and documented throughout!

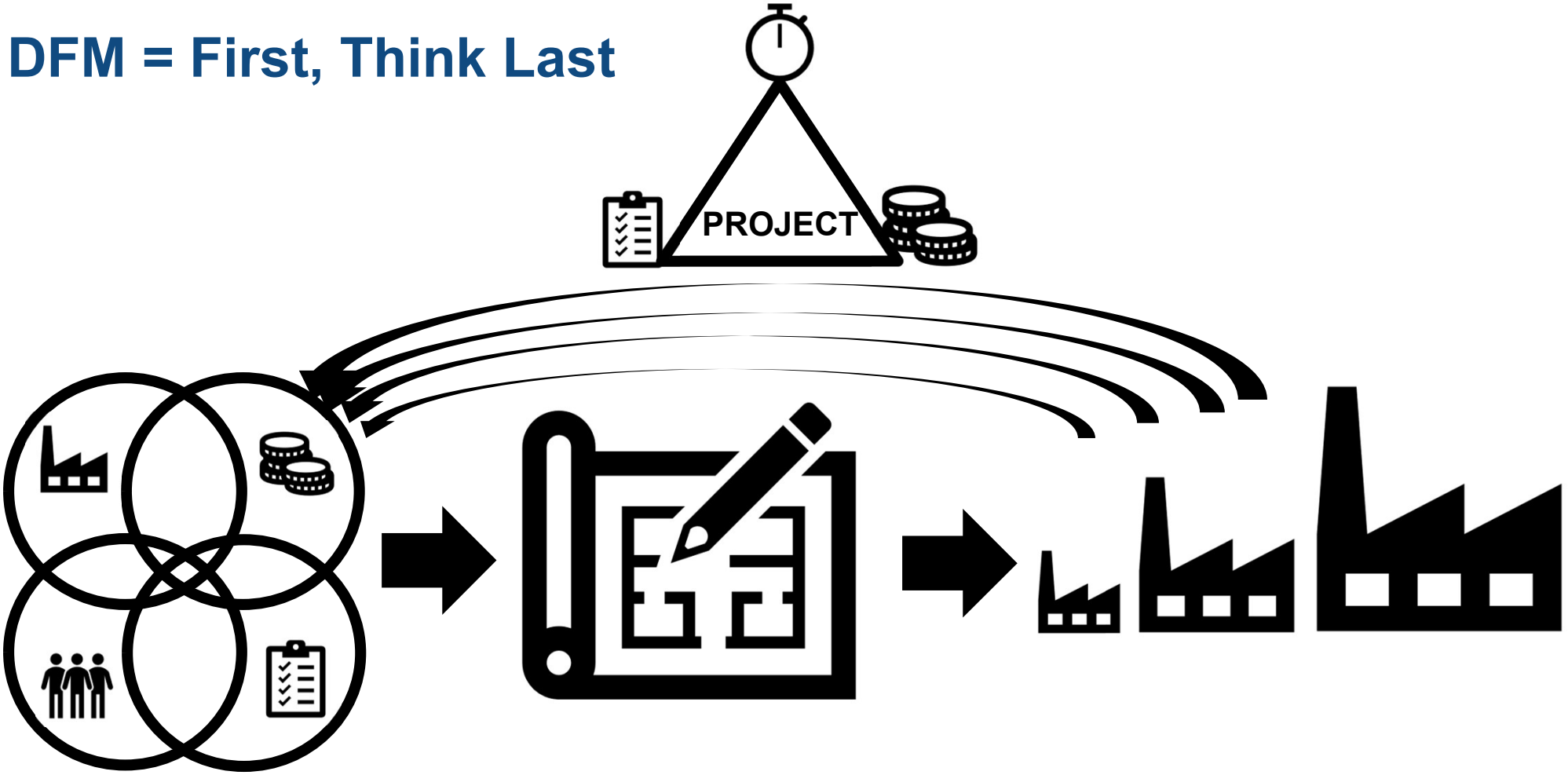


- Finance
- Sales/Marketing
- Quality
- Regulatory
- Operations

DFM = First, Think Last

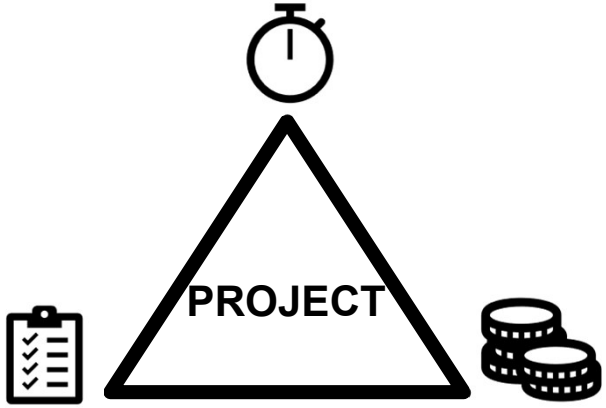


DFM = First, Think Last



Project management

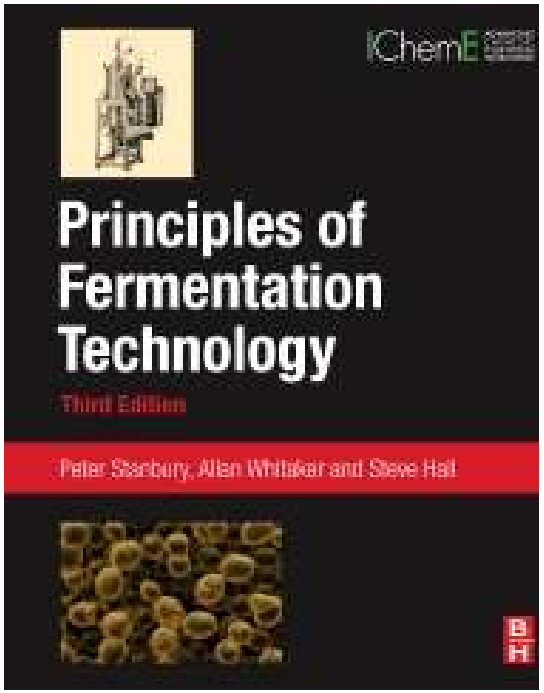
- DO hire a great PM – comms, drive and complexity
- DO a good business case and plan
- DO kill early
- DO fix the design brief first
- DO fit-for-purpose for fast time-to-invoice
- DON‘T over-engineer (ask why) or re-invent (KISS)

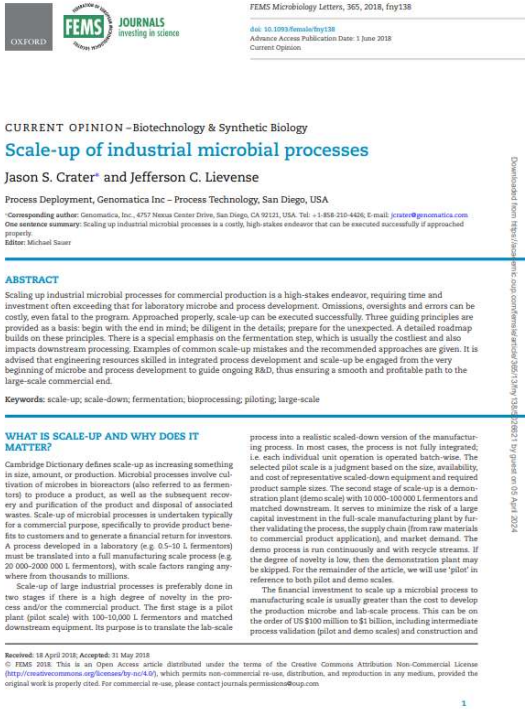


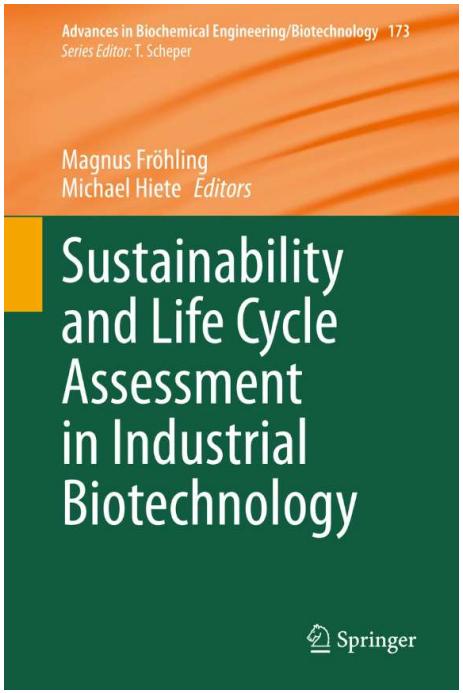
Overall Take Homes . .

First, think last
Solid business case and plan
Spend time on the design brief - iterate
Don‘t over-engineer, steal with pride
Actively manage the stakeholders, comms is key
Get a good project manager

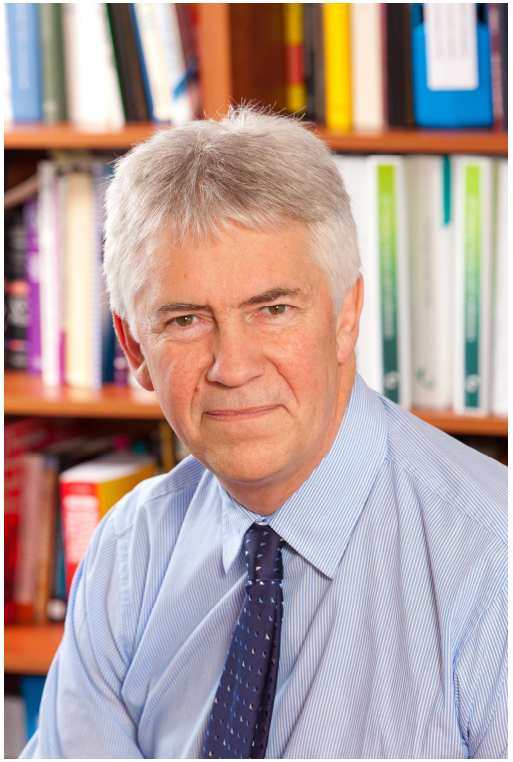
Information sources:







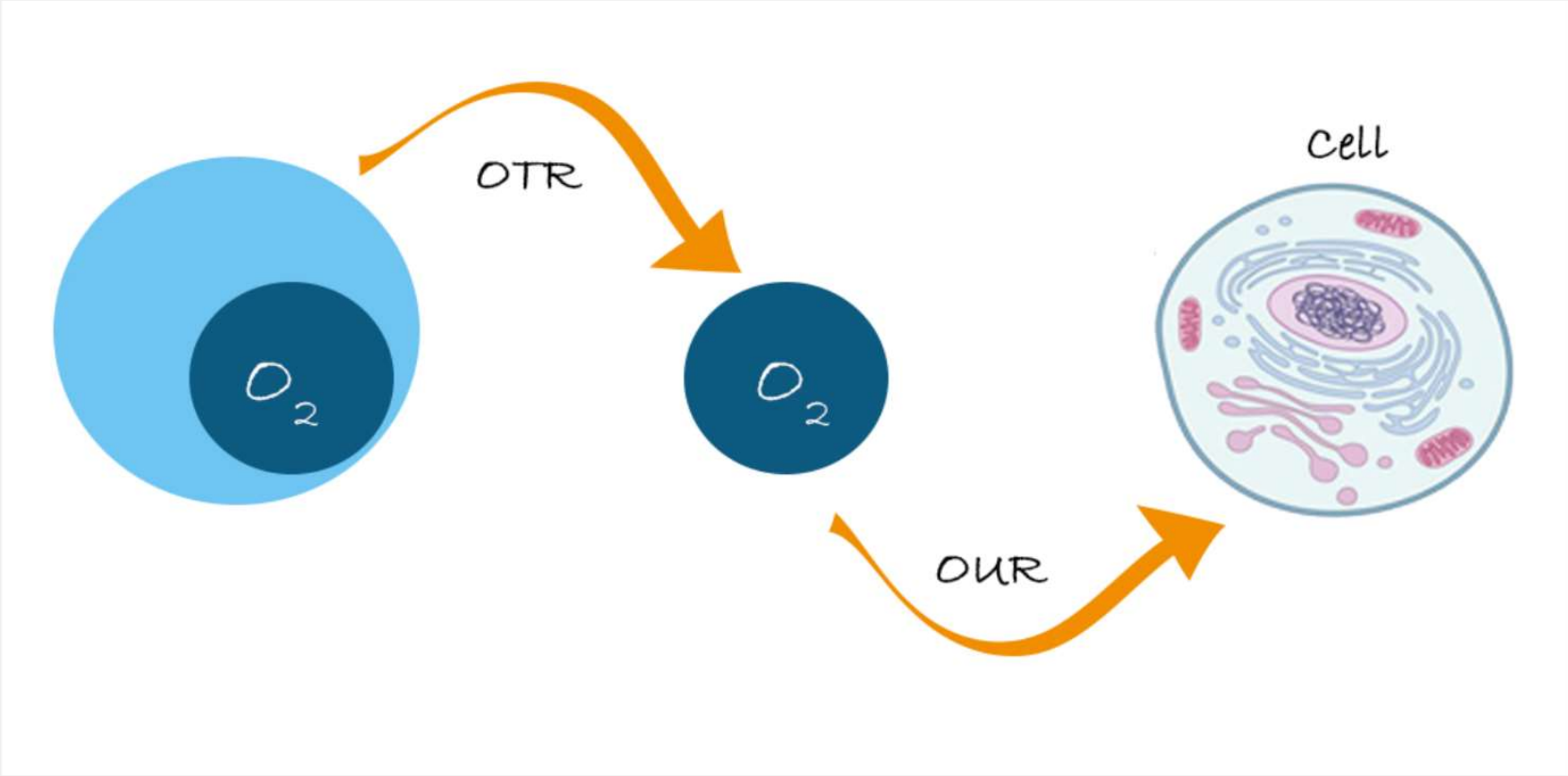
andrew.ellis@biocatalysts.com



Stuart West: 1953-2024

1. k_La, OTR, OUR – What Is The Difference?

The k_La (Volumetric Mass Transfer Coefficient) and the OTR (Oxygen Transfer Rate) detail how efficient oxygen is transferred from the gas bubbles into the bioreactor medium, i.e. how much oxygen is available for the cultivated biomass. The rate at which the biomass absorbs the available oxygen is described using the so-called OUR (Oxygen Uptake Rate).



From Lab to Large Scale: Real Time Insights and Strategies in Bioprocess Scaling

3rd BBNet Annual Conference, Sheffield
10-12th April 2024

Yvonne Armitage, CPI

Pharmaceuticals

Engineering Biology

Energy / Hydrogen

Fuels & Chemicals

Agrifood

Recycling and circularity

Decarbonisation

Research & Invention

Developing the fundamental science of the process

Innovation

Translating science into profitable and environmentally responsible processes, and demonstrating them at industrially relevant scale

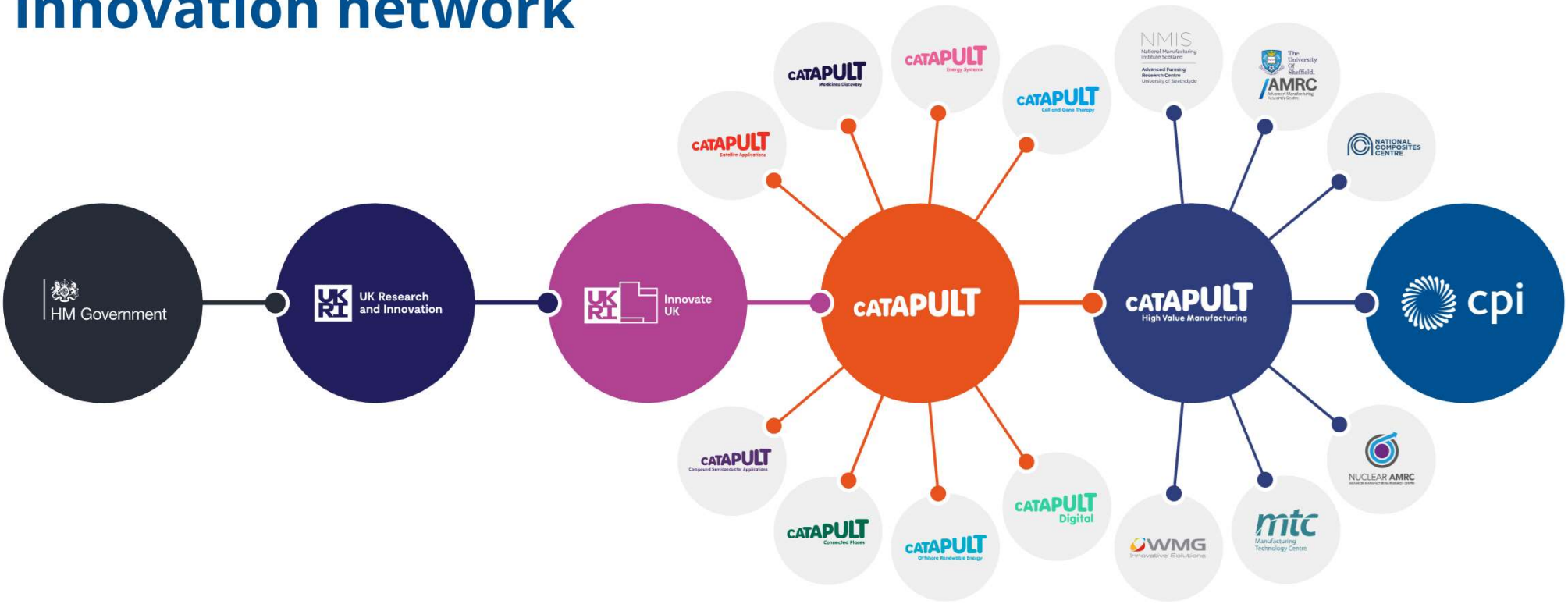
Commercial Market

Delivering the commercial end product to the market

cpi

www.uk-cpi.com

Supported by an extensive innovation network



The Scale-Up Journey

CPI @ Wilton Centre

Process design

Laboratory Development

Developing the fundamental science of the process

Concept & Feasibility

Translating the science into credible process concepts at pilot or production scale

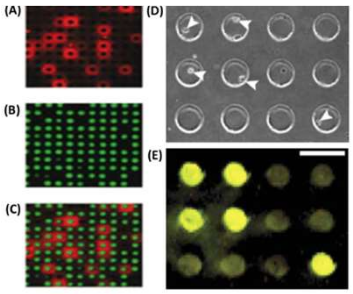
FEED & Detailed Engineering Design

Delivering the detailed engineering design and build for the process at scale

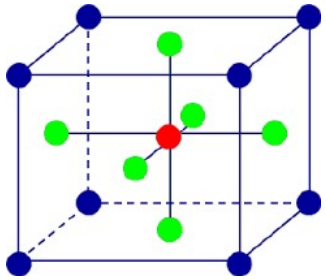
Reduce scale-up risk by integrating solutions early in process development

Integrative approach circa 1-3 years

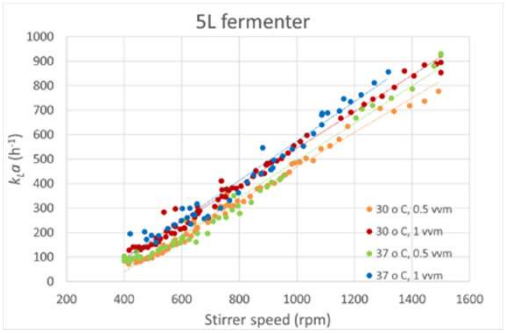
Rational proof-of-concept → Process-integrated rational strain development → Lower risk demo → Market



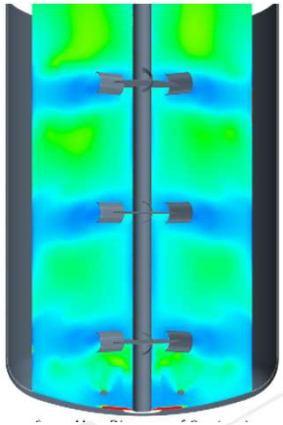
Host strain screening



Design of experiments

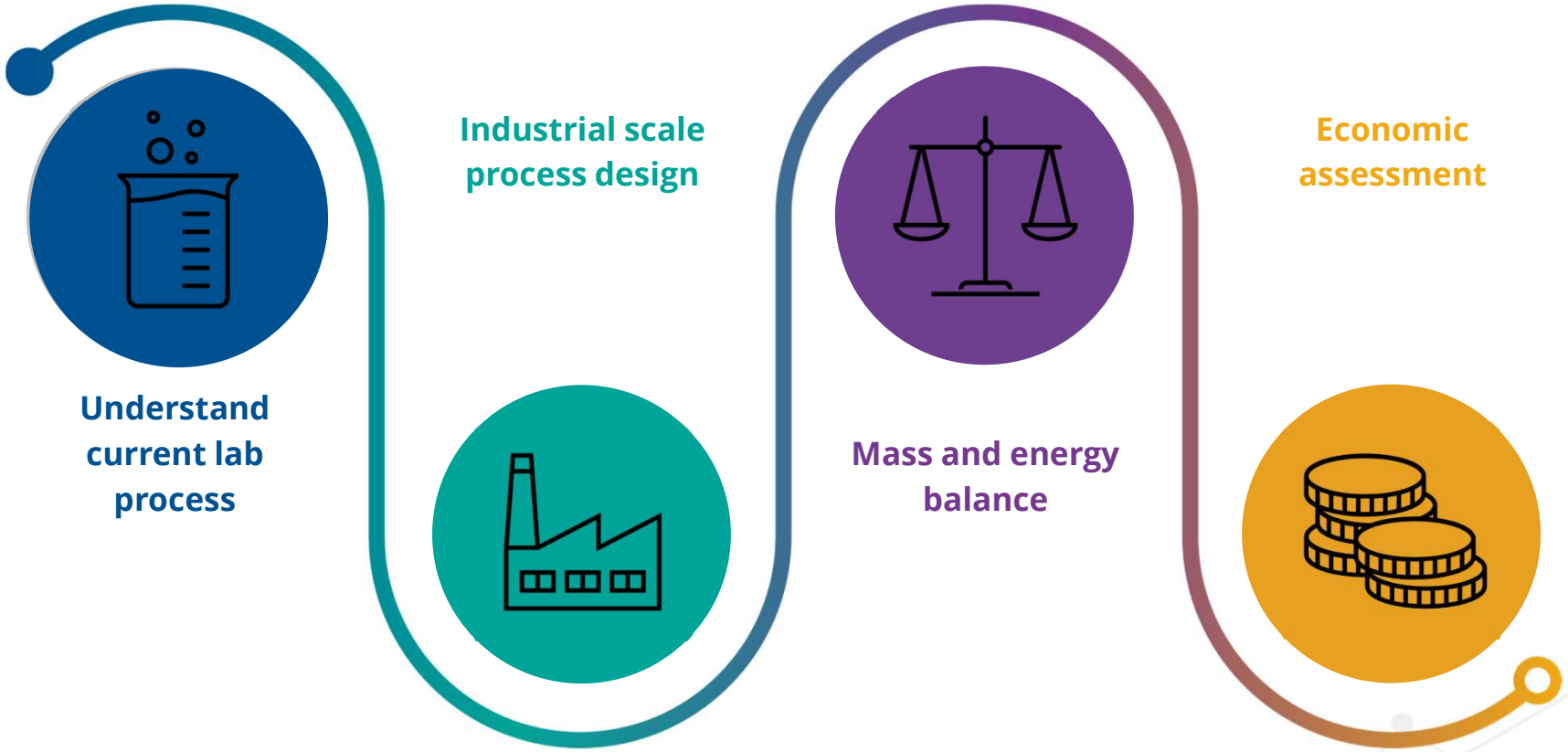


Rational scale down

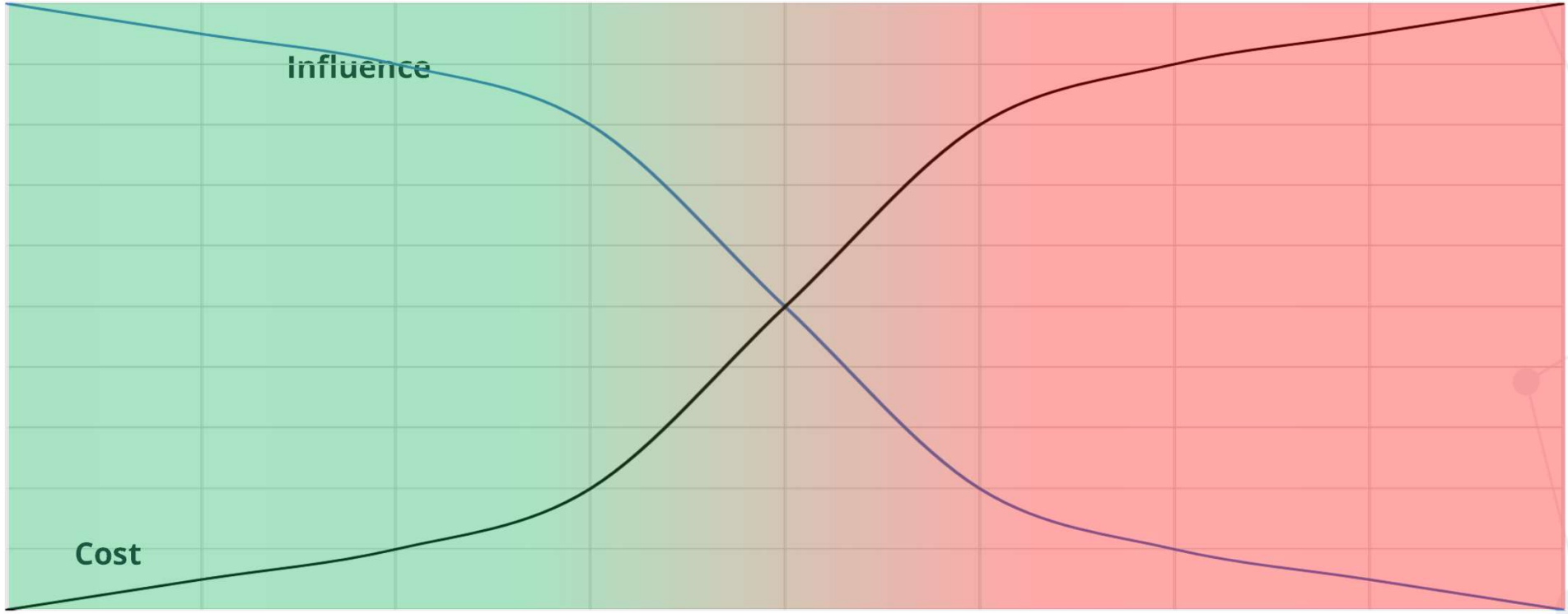


Computational fluid dynamics

Feasibility and scale up assessment

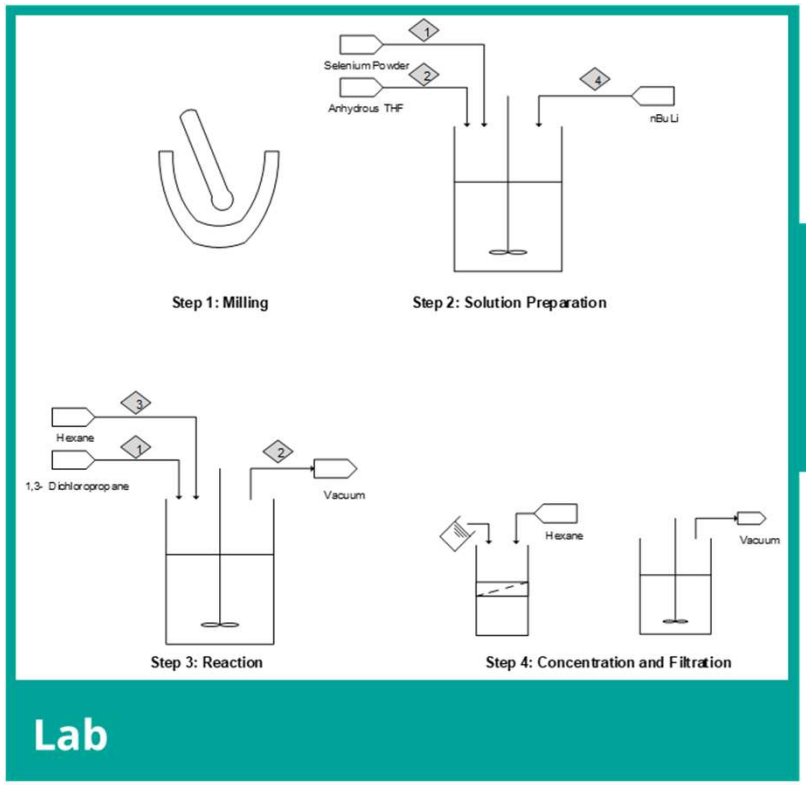


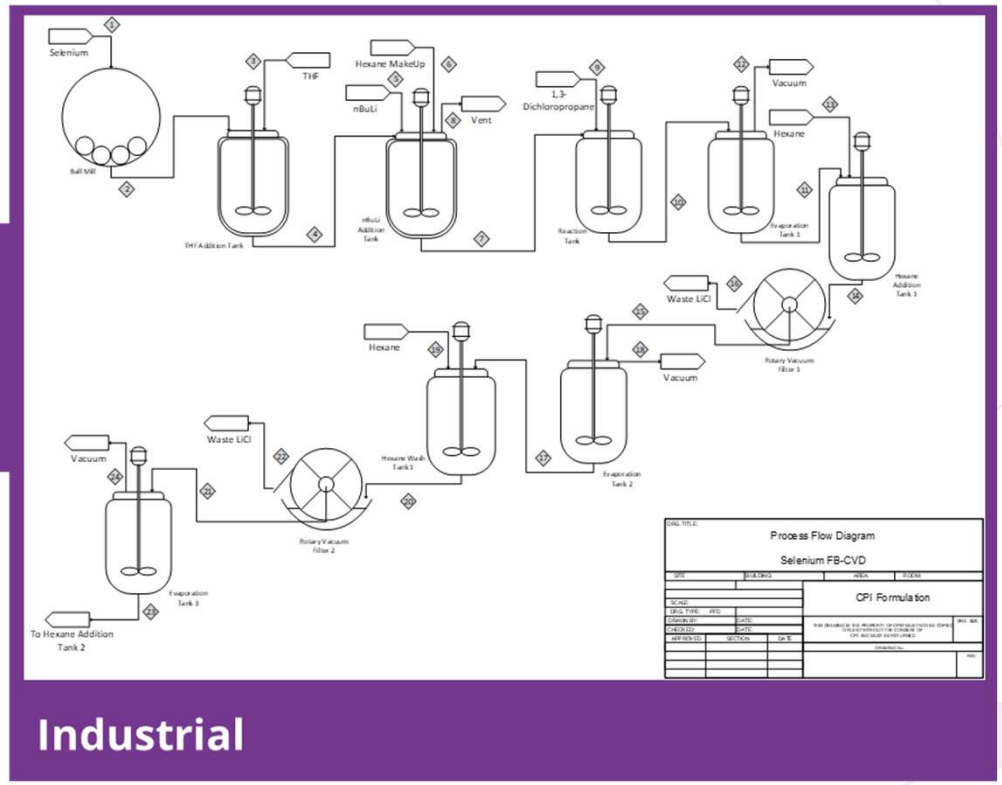
Influence vs cost



R&D | Concept Generation | Pre-FEED | FEED | Detailed Design | Construct | Commission | Operate

Scaling the process





Bioprocess scale-up at CPI

Feedstock → Strain and cell lines → Process → Downstream processing → Product

Bench and small-scale

1ml – 1000ml

Laboratory scale

5L – 50L vessels

Pilot scale

20L – 750L vessels

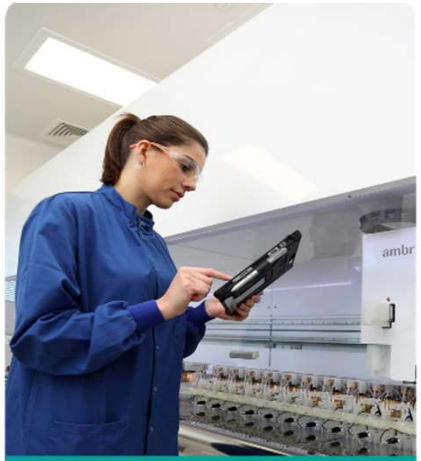
Demonstration scale

10,000L vessel

Engineering *(Chemical engineering - concept design, computational fluid dynamics, techno-economics, hazard studies, process control, equipment sizing and specification)*

Downstream processing is key for success

Production host characteristics



Product and process development

Prototype, demonstration and scale-up

Production at final scale

Start here

Upstream development

Downstream development

Upstream and downstream development work in parallel

Every key step in development is geared towards answering where the process needs to be:

- Product profile: purity, activity & concentration
- Commercialisation: amount, scale & economics

Some scale-up considerations

Safety & environment

Materials in

Waste/co-products out
Licence to operate

Economics

Capital cost
Operating costs
Profit
Payback time

Process performance

Technology vs process

Heat transfer/Mixing

Sterility

Downstream processing

CAPEX

Bespoke or off the shelf

Scale up or scale out
Practical scale limitations

Materials availability

Sold in bulk at required grade?
Sold near target location?
Transport issues?

Operability

Utilities

Maintenance
Manual operations
Material handling
Complexity

Key reflections to enable success

Safety & regulatory – Regulatory approval: GRAS-FDA, QPS-EFSA; History of safe use; GM Status / antibiotic resistance; consumer acceptance; different globally

Robust and resource efficient processes – energy use, raw materials, waste, by-products and repeatability; final product form

Feedstock – Consistency of feedstock; downstream effects

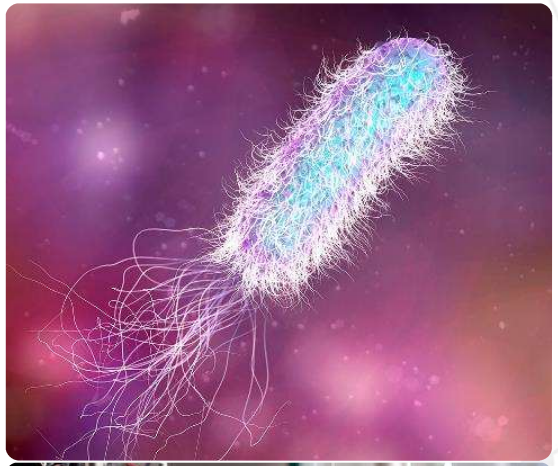
Genetic amenability – Established tools or non-model organism; Strain stability; Antibiotic use; Glycosylation; Proteolysis

Target product – Ingredient or final product; Market size; Protein; Lipid; Carbohydrate; Other metabolite

Downstream processing – Level of purity required; Intracellular or secreted product

Scalability – History of use at scale; process parameters, design of plant

Consumer Acceptance – Responsible research and innovation and effective communications



Sustainable feed ingredients

CALYSTA®
PROTEIN WITHOUT LIMITS

- Demonstration of a gas fermentation process
- Design and build of Calysta's novel-size loop reactor in only 18 months
- Production of multi tonnes of FeedKind protein ingredient in pilot plant
- Production plant in China (20,000 te/a)

Nitrogen-fixing bacterium

- Support moving from spin out development company to product company
- TRL progression from 4 to 8
- Enhanced process robustness and productivity
- Supply of product for field trials and commercialisation
- Supporting roll out to global markets with reproducible batches
- Enabled Azotic to secure funding for continued commercial roll out

Advancing RNA vaccine production

Department for Business, Energy & Industrial Strategy

Imperial College London

UK Vaccine Taskforce

Development, manufacture and supply of a saRNA COVID-19 Vaccine

Vaccine Taskforce funded programme to support manufacture and supply of Imperial College's saRNA COVID-19 Vaccine

Tech transfer, re-development, optimisation and scale up of a saRNA synthesis, purification and LNP encapsulation process

Establishment of a GMP facility and supply chain

Establishment of RNA Centre of Excellence

Novel biopesticide

Grant no 773554

- Traditional pesticides can cause harm to people, pollinators, other wildlife and the environment
- Production of naturally occurring (spider venom) toxins as alternative pesticides
- Target a crop's pests without killing other species
- Development of a fusion protein system
- Production of naturally occurring proteins to act as carriers for natural toxins through fermentation and downstream processing at pilot scale via yeast expression system

Newcastle University

Let's innovate together
www.uk-cpi.com
cpi

Summary & final thoughts

Multi-disciplinary teams needed with knowledge of **production requirements**

Knowledge from existing technologies applied to the production of new products and processes

Accelerated scale-up by reducing the risk at development stage

Engineering Biology provides new routes to existing and next generation products

Public acceptability and supportive regulations are key for commercial success

Sustainable development that can be translated into commercial products and processes

Thank you

For more information visit **www.uk-cpi.com**

Dr Yvonne Armitage
Principal Strategic Programme Manager

Yvonne.Armitage@uk-cpi.com
+44(0)7850 602680

twitter.com/**ukCPI**
facebook.com/**ukCPI**
linkedin.com/company/**uk-CPI**
youtube.com/**ukCPI**

Let's innovate together
www.uk-cpi.com

cpi