Application of BioSolve computer simulation tool for investigating the process economics of antibody production

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BioSolve
insight through analysis

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Abstract

Antibody therapies are some of the most expensive drugs on the market however there is a rapid increase in their demand for treating degenerative diseases. The company has developed a process to produce an IgG antibody therapy aimed at treating arthritis and is currently producing for phase II clinical trials. There are conflicting pressures on the company to scale up the process and achieve the scales required quickly, whilst optimising the process economics.

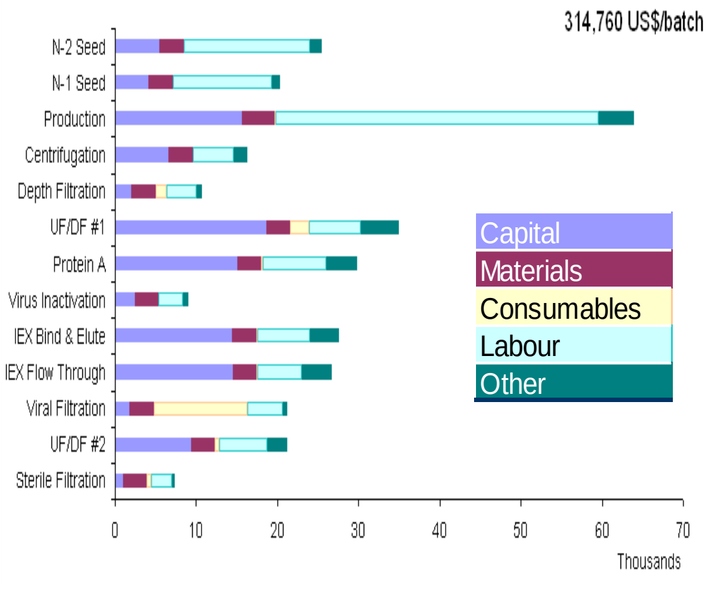
The following work shows how the team were able to model the process scale up, and identify bottlenecks ,using BioSolve computer simulation tools. This allowed a rapid analysis of various scenarios, focused on the area of greatest cost, with automated sensitivity analysis.

Phase II Clinical trial scale

A 100L bioreactor at pilot plant scale was used to produce 1.1kg/yr (titre 0.5g/L)

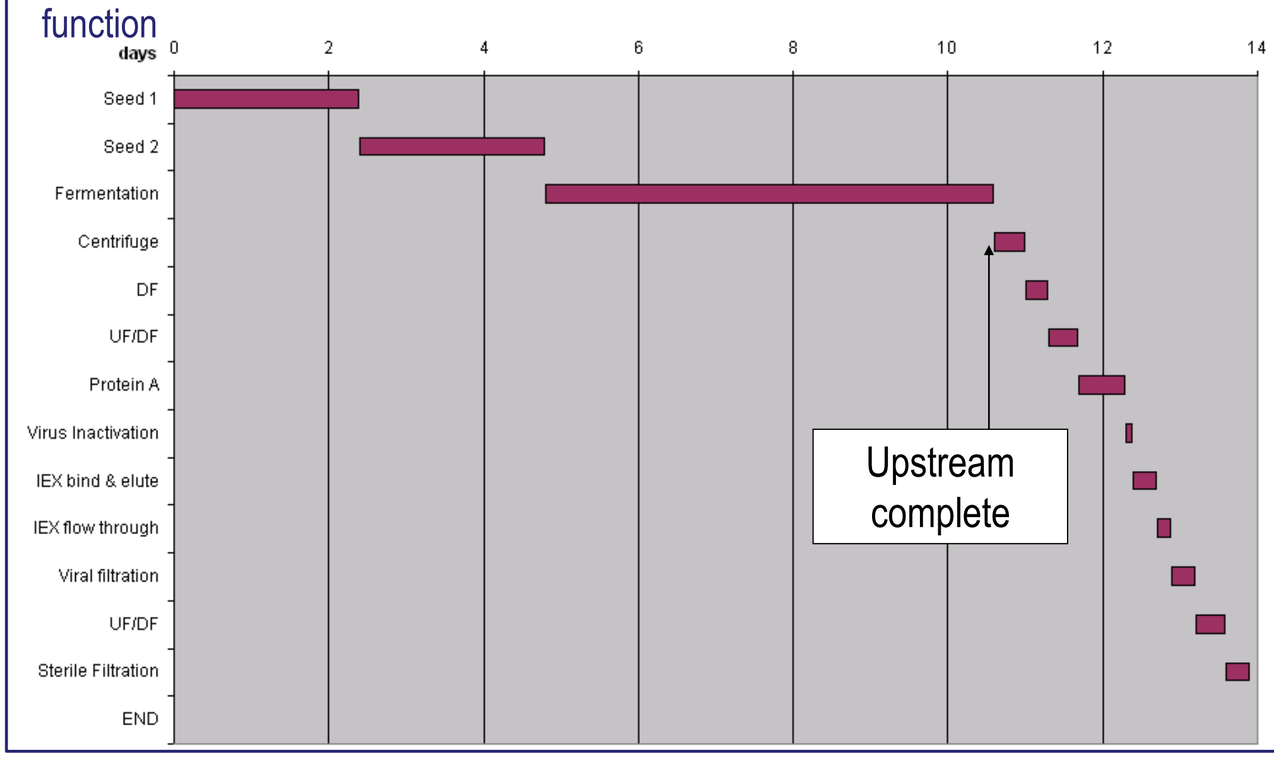
Process Sequence
Feed
1 N-2 Seed
2 N-1 Seed
3 Production
4 Centrifugation
5 Depth Filtration
6 UF/DF #1
7 Protein A
8 Virus Inactivation
9 IEX Bind & Elute
10 IEX Flow Through
11 Viral Filtration
12 UF/DF #2
13 Sterile Filtration

Costs



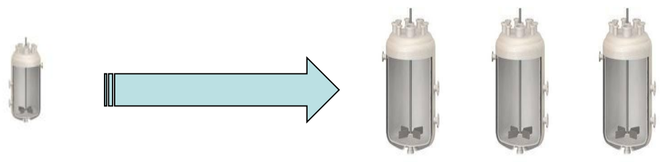
Original Gantt Chart

This chart shows the sequencing of the process base case before and after scale-up – this cannot show the fermentation scheduling as BioSolve does not have this function



Process Scale- Up (Fermentation scheduling)

Pilot Scale



Production Scale

The same process was kept when scaling up but a new titre of 2.5g/L

Staggered fermentations (3 x 3,000L fermenters)

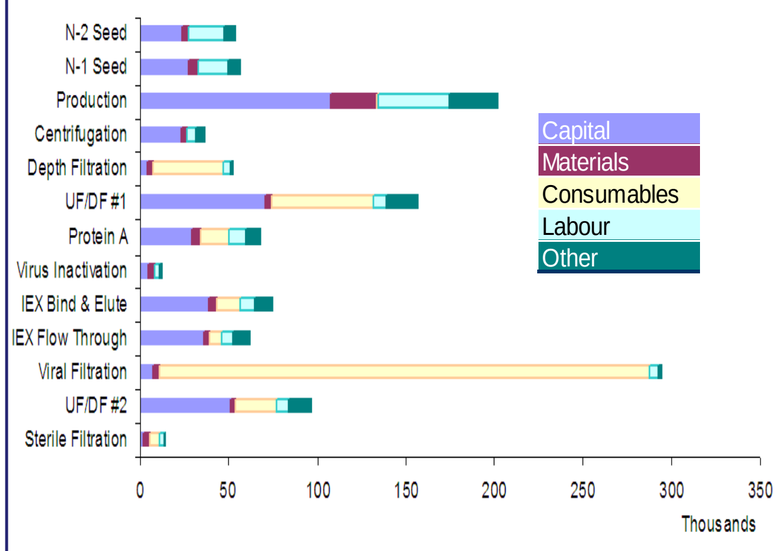
1 DSP suite services all three fermenters

DSP <1/3 of the time of Fermentation

BioSolve lacks this functionality

Throughput: 512kg/yr

Yield: 48%



Cost reduction and other options

1.10,000L fermenter instead of 3x3,000L

	1 x 10,000L	3 x 3,000L
Capital	16,880,493	20,070,412
Materials	6,481,484	3,263,739
Consumables	67,079,904	20,695,769
Labour	6,982,958	6,376,237
Other	4,732,305	5,176,186
TOTAL	102,157,144	55,582,343

This solution is clearly not preferable

2.Unit operation scheduling based on original scale up to further reduce costs **$55.6**

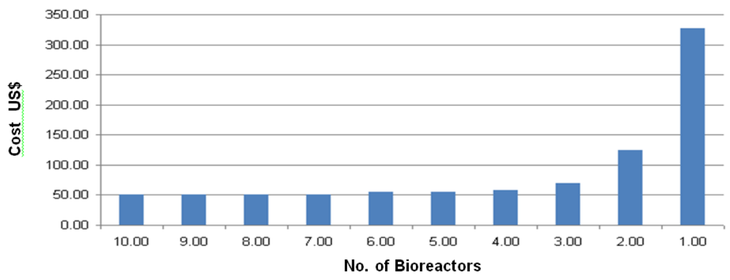
- 9.8	
•Increased Viral filtration length 4x	**$45.8**
Cost reduced by 18% to $45.8m	- 3.2
•Increased UF/DF #1 length 3x	**$42.6**
Cost reduced by 6.9% to $42.6m	- 1.2
•Increased Depth filtration length 3x	**$41.3**
Cost reduced by 2.9% to $41.3m	- 1.4
•Increased UF/DF #1 length 2x	**$39.8**
Cost reduced by 3.5% to $39.8m	

3.Combination of scheduling methods and introduction of disposables

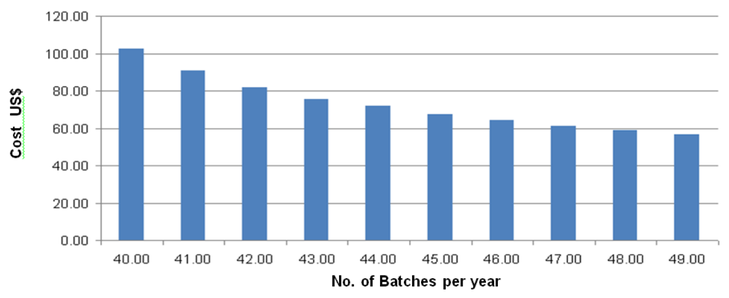
Comparison	Traditional	Single-Use	% Change
Annual CoG (US$)	39,875,743	32,671,518	-18%
Capital	18,119,906	11,631,519	-36%
Materials	3,249,975	3,093,311	-5%
Consumables	7,382,549	10,924,215	48%
Labour	6,448,586	4,130,273	-36%
Other	4,674,727	2,892,200	-38%
Other metrics			
Water usage (m3 per batch)	125.53	29.57	-76%
Plastics waste (kg per batch)	153.02	454.55	197%
Total Installed Capital (US$M)	86.72	55.67	-36%

Sensitivity Analysis

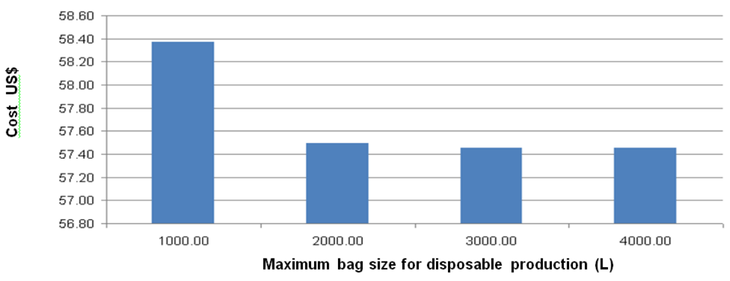
1.No. of fermenters



2.No. of batches per year



3.Size of disposable bags



Conclusion

- Multiple Smaller fermenters were 50% cheaper
- Use of disposables reduces cost
- Changes to the length of certain unit operations allowed further decreases in cost
- Overall cost of using multiple smaller staggered disposable reactors with changes to DSP as opposed to 1 large reactor and the standard process was $33m vs. $102m

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