

Quantification of 3M™ Emphaze™ AEX Hybrid Purifier value in mAb manufacturing process

Alexei Voloshin, Himanshu Nivsarkar, 3M Separation and Purification Sciences Division, 3M Center, St. Paul, MN

Introduction

Ability to cure and manage life threatening and life-changing conditions such as cancer, diabetes, and arthritis forms the primary frontier of the early 21st century medicines, medical technology, and biopharmaceutical science. Significant efforts and successes have been made in managing such conditions using biotherapeutics including Rituxan®, Herceptin®, Humira®, and other current and emerging therapies.

Beyond the technical and medical ability needed to create these therapies lies the challenge of ensuring the availability and affordability of such treatments for the world population at large. This frontier is dictated, by a significant margin, by the ability to create robust and inexpensive manufacturing processes of such biopharmaceuticals at scales ranging from 100 kg to 10+ tons per year, depending on dosage and population size. Thus, winning the race to democratization of biotherapeutics hinges on being able to produce more product from more and more compact and high performance manufacturing processes, while ensuring the high degree of safety and efficacy of the biopharmaceuticals.

3M continues to be at the forefront of the biopharmaceutical manufacturing with innovative products such as the 3M™ Zeta Plus™ depth filtration platform, 3M™ LifeASSURE™ membrane filtration, and 3M™ Emphaze™ chromatography platform. This paper focuses on the 3M™ Emphaze™ AEX Hybrid Purifier and its potential effects on the cost of the manufacturing of the biopharmaceutical products. The 3M Emphaze AEX Hybrid Purifier product defines a new class of biopharmaceutical separation technologies that is able to address chromatographic separations of particles significantly larger than proteins.¹ Integrating the 3M Emphaze AEX Hybrid Purifier in the clarification stage may simplify customers' processes by reducing multiple types of impurities in a single process step, leading to a better process economics.

Modeling the 3M™ Emphaze™ AEX Hybrid Purifier in the Biopharmaceutical Process

The 3M Emphaze AEX Hybrid Purifier is an implementation of chromatography using quaternary ammonium (Q) functional anion exchange nonwoven material. The ability to reduce DNA, HCP, endotoxin, and cell debris early in the process helps achieve precise control of purification before capture chromatography by delivering consistent, high purity clarified process fluid through a combination of chromatographic and size exclusion mechanisms. This streamlines the process early on and allows for simplification of the downstream process at large scale.^{1,2} In this application note we explore the potential impact of such optimizations on the cost of monoclonal antibody therapeutic manufacturing. This work describes hypothetical scenarios. Depending upon product and process conditions, the effects covered in this app note may not be realized or may not be realized to the degree shown in the scenarios.

Modeling the Process

We modeled a typical single use large scale manufacturing facility using Biosolve software from Biopharm Services. The facility and process have the following attributes:

1. Reactor setup: 1800 L working volume
X 6 single use bioreactors
2. mAb titer = 5 g/L
3. 1 reactor is harvested at a time.
4. Downstream utilizes single use systems as much as possible

These attributes are similar to a single use manufacturing plant strategy used, for example, by Amgen in Singapore.³

Biosolve is an expansive model utilizing an enormous dataset from the industry in terms of operational strategy and cost. It is not possible to account for every scenario and detail. This investigation covers the key potential advantages of deploying the 3M™ Emphaze™ AEX Hybrid Purifier in the biopharmaceutical manufacturing process.

The 3M Emphaze AEX Hybrid Purifier is modeled as a single use clarifier at 4.5X cost of the standard depth filter in the model.

The basic performance metrics of the process are summarized below. More detailed information on process sequence and cost breakdowns for the base process and each scenario are included in the Appendix.

The downstream process efficiency of the base process is 50%. Each table includes Cost of Goods Sold (COGS).

COGS Table - Base Process

USD	Batch	Dose
Capital	\$72,705.64	\$4.89
Materials	\$31,494.05	\$2.12
Consumables	\$126,238.75	\$8.49
Labour	\$83,882.26	\$5.64
Other	\$19,744.37	\$1.33
Total	\$334,065.08	\$22.48

Key Metrics	
Total Installed Capital	\$48,758,682 USD
DSP Yield	50%
Doses per Year	2.0E+06
Batch Size	4.5 kg
Throughput	601.9 kg/yr
mAb Single Use Base Process	\$74.9 USD/g

Scenario 1: High Throughput, Product Recovery, and Sterilizing Filter Protection

The 3M Emphaze AEX Hybrid Purifier is a synthetic product composed of a Q-functional nonwoven and a 0.2 µm polyamide membrane. Due to its high charge capacity and size exclusion membrane, the 3M Emphaze AEX Hybrid Purifier may offer higher throughput than a 3M depth filter based on equivalent effluent quality (turbidity, DNA concentration, HCP concentration) and enable downsizing of the sterilizing grade membranes. In addition, mAb recovery > 95% in the

3M Emphaze AEX Hybrid Purifier unit operation may be achieved. This model shows the effect of deploying the 3M Emphaze AEX Hybrid Purifier in the process by doubling the throughput of the polishing stage of clarification and tripling the throughput of the final membrane stage. Additionally, we increased the product recovery of the secondary stage from 90% to 97%. In this hypothetical scenario, the purification yield increases to 53%, driving the cost of manufacturing down.

COGS Table - Scenario 1

USD	Batch	Dose
Capital	\$72,690.68	\$4.54
Materials	\$31,393.32	\$1.96
Consumables	\$124,222.10	\$7.76
Labour	\$83,882.26	\$5.24
Other	\$19,624.23	\$1.23
Total	\$331,812.59	\$20.72

Key Metrics	
Total Installed Capital	\$48,748,651 USD
DSP Yield	53%
Doses per Year	2.2E+06
Batch Size	4.8 kg
Throughput	648.7 kg/yr
mAb SU Base Modification 1	\$69.1 USD/g

Scenario 2: Increase in Protein A Product Capture Column Capacity

Protein A capture chromatography is the cornerstone of the mAb purification platform. The performance and robustness of this step across the candidate pipeline defines the platformability, speed to clinic, and efficiency of the commercial manufacturing. It has previously been shown that chromatin, comprised of genomic CHO DNA and histones, interferes with Protein A chromatography by lowering its capacity and separation fidelity.⁴ The 3M Emphaze AEX Hybrid Purifier is capable of protecting the Protein A column from such deficiencies by reducing the DNA/histone complex at clarification.⁵ The degree of DNA/histone reduction on mAb binding capacity of the protein A column depends upon the feed. Here we model the impact of a 15% increase in Protein A mAb binding capacity on the total manufacturing cost of the mAb biopharmaceutical. In this scenario, the capacity utilization is not limited by the mAb target loading and did not result in added process efficiency.

COGS Table - Scenario 2

USD	Batch	Dose
Capital	\$72,690.68	\$4.54
Materials	\$31,393.32	\$1.96
Consumables	\$124,222.10	\$7.76
Labour	\$83,882.26	\$5.24
Other	\$19,624.23	\$1.23
Total	\$331,812.59	\$20.72

Key Metrics

Total Installed Capital	\$48,748,651 USD
DSP Yield	53%
Doses per Year	2.2E+06
Batch Size	4.8 kg
Throughput	648.7 kg/yr
mAb SU Base Modification 2	\$69.1 USD/g

Scenario 3: Increase in Protein A Cycle Lifetime

A reduction in DNA coming onto the Protein A column and the reduction of post-elution residual process related DNA and HCP,¹ may enable less aggressive column stripping and washing, which could potentially increase the lifetime of the Protein A column. In this scenario, we explore the effect of doubling of the maximum Protein A chromatography resin cycles from 100 to 200 cycles.

COGS Table - Scenario 3

USD	Batch	Dose
Capital	\$72,690.68	\$4.54
Materials	\$31,393.32	\$1.96
Consumables	\$105,166.72	\$6.57
Labour	\$83,882.26	\$5.24
Other	\$19,623.91	\$1.23
Total	\$312,756.90	\$19.53

Key Metrics

Total Installed Capital	\$48,748,651 USD
DSP Yield	53%
Doses per Year	2.2E+06
Batch Size	4.8 kg
Throughput	648.7 kg/yr
mAb SU Base Modification 3	\$65.1 USD/g

Scenario 4: Elimination of Post Viral Inactivation Neutralization Pool Clarification

Turbidity post viral inactivation neutralization (VIN) step in mAb purification is a regular occurrence in a bioprocess. This phenomenon is likely the result of CHO genomic DNA precipitating HCP as the pH is raised from the viral inactivation condition of 2.8 – 3.5 to neutralized condition of pH 5.0–8.0. This is logical as the neutralization passes through the isoelectric point of the majority of HCP population, causing the reversal of charges and possible aggregation with long polymers of negatively charged genomic DNA.

In a conventional process, this precipitation is cleared by the combination of depth and membrane filtration in a stand-alone unit operation.⁶ It may be possible to avoid precipitates in the VIN pool by using the 3M™ Emphaze™ AEX Hybrid Purifier at clarification upstream of the Protein A column. This may eliminate the need for a downstream depth filtration unit operation, and in this scenario, we model the effect of its removal. We leave the membrane stage intact as a protection of the following chromatography column.

COGS Table - Scenario 4

USD	Batch	Dose
Capital	\$73,795.55	\$4.15
Materials	\$31,995.36	\$1.80
Consumables	\$105,800.02	\$5.94
Labour	\$83,882.26	\$4.71
Other	\$19,932.37	\$1.12
Total	\$315,405.55	\$17.72

Key Metrics

Total Installed Capital	\$49,489,611 USD
DSP Yield	59%
Doses per Year	2.4E+06
Batch Size	5.3 kg
Throughput	720.8 kg/yr
mAb SU Base Modification 4	\$59.1 USD/g

Scenario 5: Reducing the Polishing Anion Exchange Column Size

We have previously shown that reduction of DNA by the 3M™ Emphaze™ AEX Hybrid Purifier results in >10 X reduction of HCP and >1000 X reduction of DNA in the Protein A eluate pool.^{1,2} This suggests that a much smaller polishing AEX column may help address remaining process related HCP and DNA contaminants. We model this scenario as a process with 4X smaller AEX polishing column. The scaling on the AEX is dictated by the required viral clearance for this process step.

COGS Table - Scenario 5

USD	Batch	Dose
Capital	\$71,663.62	\$3.94
Materials	\$31,128.08	\$1.71
Consumables	\$101,345.97	\$5.58
Labour	\$82,146.36	\$4.52
Other	\$19,270.28	\$1.06
Total	\$305,554.31	\$16.81

Key Metrics

Total Installed Capital	\$48,059,873 USD
DSP Yield	61%
Doses per Year	2.5E+06
Batch Size	5.5 kg
Throughput	736.0 kg/yr
mAb SU Base Modification 5	\$56.0 USD/g

Scenario 6: Primary Clarification Centrifuge Replacement with Depth Filter Stage

Centrifuge technology has been a workhorse for solids removal applications in many industries. While being very successful in bacterial biopharmaceutical manufacturing, cell culture fluid harvesting in mammalian applications has proved difficult for the centrifuge technology as the CHO cells are prone to shear and do not behave like hard spheres during harvests.⁷ Thus, the industry wants to migrate away from the centrifuge to more controlled, low shear, and well understood methods, such as depth filtration. Here we model the replacement of the centrifuge as the primary clarification step with depth filtration at 100 L/m² throughput. The primary advantage of such a system is that unit operation yield typically rises from 85% to 90%+. We conservatively modeled depth filter unit operation product yield at 90% in this scenario.

COGS Table - Scenario 6

USD	Batch	Dose
Capital	\$74,966.59	\$3.69
Materials	\$31,547.36	\$1.55
Consumables	\$120,804.83	\$5.95
Labour	\$86,175.38	\$4.24
Other	\$20,381.12	\$1.00
Total	\$333,875.27	\$16.44

Key Metrics

Total Installed Capital	\$45,433,655 USD
DSP Yield	68%
Doses per Year	2.5E+06
Batch Size	6.1 kg
Throughput	743.3 kg/yr
mAb SU Base Modification 6	\$54.8 USD/g

Conclusion

The 3M Emphaze AEX Hybrid Purifier affects the presence of biological impurities of the process fluid early in the process, and thus the entire process. Reduction of DNA from the mAb Clarified Cell-Culture Fluid (CCCF) enables one to consider process simplifications that decrease the size and number of process steps and, thus, improve the productivity of the process. In effect, the process becomes more productive, and thus the cost of the mAb manufacturing decreases, as shown in the hypothetical process modeling scenarios discussed in this paper.

References

1. "Anion-Exchange Chromatographic Clarification: Bringing Simplification, Robustness, and Savings to mAb Purification", Angelines A. Castro Forero, Zona Jokondo, Alexei Voloshin, Jonathan F. Hester, BioProcess International, June 2015
2. "Enabling Higher Post Protein A Product Purity Using Novel Chromatographic Clarification Approach", Alexei Voloshin, Dmitri Smirnov, William Wessel, Ian Collins, Steven Hager, La Vague, #49, 2016.
3. "Applying New Biologic Manufacturing Technologies", Anthony Mire-Sluis, presented at CMC Forum Europe, 2014.
4. "The Secret Life of Protein A", Pete Gagnon, Rui Nian, Bioprocess International, October 2015.
5. Identification and tracking of problematic host cell proteins removed by a synthetic, highly functionalized nonwoven media in downstream bioprocessing of monoclonal antibodies. S.Gilgunna, H.El-Sabbahy, S.Albrecht, M.Gaikwada, K.Corrigan, L.Deakin, G.Jellum, J.Bonesad, In Press, <https://doi.org/10.1016/j.chroma.2019.02.056>
6. "Characterization of Postcapture Impurity Removal Across an Adsorptive Depth Filter", John Schreffler, Matthew Bailey, Tom Klimek, Peter Agneta, W. Erick Wiltsie, Michael Felo, Pam Maisey, Xun Zuo and Eric Routhier, Bioprocess International, March 2015.
7. Shear stress analysis of mammalian cell suspensions for prediction of industrial centrifugation and its verification. Biotechnol Bioeng. Hutchinson N1, Bingham N, Murrell N, Farid S, Hoare M. 2006 Oct 20;95(3):483-91.

Appendix - Process Sequence and Cost Breakdown Charts

Process Sequence: mAb SU Base

No	Process Stage	Unit Op Name	Conc (g/L)	Yield (%)	Duration (hr)	Adjusted Duration (hr)	Mass In (g)	Mass Out (g)	Vol In (g)	Vol Out (g)	Particles In	Particles Out	Target Out	Target capacity (kg/year)	Actual capacity (kg/year)
Feed			0.0			1.8									
1	Upstream	N-2 Seed	0.0	0%	52.5	8.8	0.0	0.0	1.8	18.0	0.0	0.0	0.0	0.0	0.0
2	Upstream	N-1 Seed	0.0	0%	52.5	8.8	0.0	0.0	18.0	180.0	0.0	0.0	0.0	0.0	0.0
3	Upstream	Production	5.0	100%	278.5	46.4	0.0	9000.0	180.0	1800.0	0.0	0.0	9.0	1215.0	1350.0
4	Recovery	Centrifugation	5.0	85%	8.0	8.0	9000.0	7650.0	1800.0	1530.0	0.0	0.0	7.7	1215.0	1620.0
5	Recovery	Secondary Depth Filtration	4.4	90%	5.2	5.2	7650.0	6885.0	1530.0	1579.5	0.0	0.0	6.9	1032.8	670.6
6	Purification	Filtration (0.2um)	4.2	98%	4.1	4.1	6885.0	6747.3	1579.5	1603.5	0.0	0.0	6.7	929.5	726.2
7	Purification	Protein A	6.1	90%	18.5	34.5	6747.3	6072.6	1603.5	997.6	0.0	0.0	6.1	910.9	959.2
8	Purification	Virus Inactivation	5.8	98%	5.5	5.5	6072.6	5951.1	997.6	1017.6	0.0	0.0	6.0	819.8	1208.5
9	Recovery	Depth Filtration	5.2	90%	5.1	5.1	5951.1	5356.0	1017.6	1034.1	0.0	0.0	5.4	803.4	1545.0
10	Purification	Filtration (0.2um)	5.0	98%	4.2	4.2	5356.0	5248.9	1034.1	1046.1	0.0	0.0	5.2	723.1	1721.6
11	Purification	AIEX Flow Through	4.8	95%	7.7	7.7	5248.9	4986.4	1046.1	1046.1	0.0	0.0	5.0	708.6	772.3
12	Purification	IEX Bind & Elute	9.5	95%	11.3	27.3	4986.4	4737.1	1046.1	498.8	0.0	0.0	4.7	673.2	752.7
13	Purification	Viral Filtration	9.1	98%	6.1	6.1	4737.1	4642.4	498.8	508.8	0.0	0.0	4.6	639.5	639.5
14	Purification	UF/DF	50.0	98%	11.0	11.0	4642.4	4549.5	508.8	91.0	0.0	0.0	4.5	626.7	2161.1
15	Purification	Filtration (0.2um)	47.4	98%	4.0	4.0	4549.5	4458.5	91.0	94.0	0.0	0.0	4.5	614.2	1535.5

Cost of Goods Breakdown for mAb SU Base (USD per batch)

	N-2 Seed 1	N-1 Seed 2	Production 3	Centrifugation 4	Secondary Depth Filtration 5	Filtration (0.2um) 6	Protein A 7	Virus Inactivation 8	Depth Filtration 9	Filtration (0.2um) 10	AIEX Flow Through 11	IEX Bind & Elute 12	Viral Filtration 13	UF/DF 14	Filtration (0.2um) 15
Equipment (Total)	376,459	1,199,727	4,582,471	816,685	139,557	127,345	968,784	178,041	126,395	125,825	794,958	831,759	92,409	561,898	64,387
Capital	2,491	7,939	30,325	5,404	924	843	6,411	1,178	836	833	5,261	5,504	612	3,718	426
Materials	921	2,096	13,273	823	857	958	4,686	958	849	955	1,219	1,339	804	948	808
Consumables	1,760	4,065	16,312	0	5,900	5,247	42,168	554	2,929	3,592	6,369	10,416	21,708	3,853	1,365
Labour	1,988	2,815	17,987	3,707	4,597	2,283	13,258	2,431	2,705	2,322	6,731	10,277	3,121	7,447	2,215
Other	626	1,998	7,689	1,393	308	406	1,938	493	277	402	1,391	1,514	170	1,012	127
	2%	6%	26%	3%	4%	3%	20%	2%	2%	2%	6%	9%	8%	5%	1%
Perfusion Factor	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Capital Charge	2,491	7,939	30,325	5,404	924	843	6,411	1,178	836	833	5,261	5,504	612	3,718	426
Materials	921	2,096	13,273	823	857	958	4,686	958	849	955	1,219	1,339	804	948	808
Media	130	1,305	12,482	0	0	0	0	0	0	0	0	0	0	0	0
Buffer	0	0	0	0	13	6	3,896	1	4	3	428	548	3	134	1
Direct RM	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bought WFI & PW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CIP	0	0	0	32	54	161	0	167	54	161	0	0	11	22	16
QC tests	791	791	791	791	791	791	791	791	791	791	791	791	791	791	791
Consumables	1,760	4,065	16,312	0	5,900	5,247	42,168	554	2,929	3,592	6,369	10,416	21,708	3,853	1,365
Resins/MA	0	0	0	0	0	0	38,111	0	0	0	1,608	7,115	0	0	0
Bags	1,760	4,065	16,312	0	2,924	1,937	3,116	554	1,937	1,937	4,760	3,301	1,418	951	951
Filters	0	0	0	0	2,976	3,310	941	0	992	1,655	0	0	20,290	2,902	414
Packages	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labour	1,988	2,815	17,987	3,707	4,597	2,283	13,258	2,431	2,705	2,322	6,731	10,277	3,121	7,447	2,215
Process	830	1,176	7,516	1,549	1,921	954	5,540	1,016	1,130	970	2,812	4,294	1,304	3,112	925
Quality	841	1,192	7,615	1,569	1,946	966	5,613	1,029	1,145	983	2,850	4,351	1,321	3,153	938
Indirect	316	447	2,856	589	730	362	2,105	386	430	369	1,069	1,632	495	1,182	352
Other	626	1,998	7,689	1,393	308	406	1,938	493	277	402	1,391	1,514	170	1,012	127
Insurance/other	129	410	1,564	279	48	43	331	61	43	43	271	284	32	192	22
Waste mgmt	1.12	0.42	5.51	0.50	6.17	4.16	6.49	2.06	2.27	3.01	8.38	6.02	2.61	0.90	0.66
Maintenance	125	397	1,516	270	46	42	321	59	42	42	263	275	31	186	21
Utilities	372	1,192	4,603	843	208	317	1,281	371	190	314	848	949	105	633	83
TOTAL (USD)	7,786	18,913	85,586	11,327	12,586	9,737	68,462	5,614	7,597	8,104	20,970	29,050	26,415	16,978	4,940
Total (USD/Gram normalized for the output)	1.7	4.2	19.2	2.5	2.8	2.2	15.4	1.3	1.7	1.8	4.7	6.5	5.9	3.8	1.1

Process Sequence: mAb SU Base Modification 1

No	Process Stage	Unit Op Name	Conc (g/L)	Yield (%)	Duration (hr)	Adjusted Duration (hr)	Mass In (g)	Mass Out (g)	Vol In (g)	Vol Out (g)	Particles In	Particles Out	Target Out	Target capacity (kg/year)	Actual capacity (kg/year)
<i>Feed</i>			<i>0.0</i>			<i>1.8</i>									
1	Upstream	N-2 Seed	0.0	0%	52.5	8.8	0.0	0.0	1.8	18.0	0.0	0.0	0.0	0.0	0.0
2	Upstream	N-1 Seed	0.0	0%	52.5	8.8	0.0	0.0	18.0	180.0	0.0	0.0	0.0	0.0	0.0
3	Upstream	Production	5.0	100%	278.5	46.4	0.0	9000.0	180.0	1800.0	0.0	0.0	9.0	1215.0	1350.0
4	Recovery	Centrifugation	5.0	85%	8.0	8.0	9000.0	7650.0	1800.0	1530.0	0.0	0.0	7.7	1215.0	1620.0
5	Recovery	Secondary Depth Filtration	4.7	97%	5.2	5.2	7650.0	7420.5	1530.0	1579.5	0.0	0.0	7.4	1032.8	670.6
6	Purification	Filtration (0.2um)	4.6	98%	5.0	5.0	7420.5	7272.1	1579.5	1588.5	0.0	0.0	7.3	1001.8	1252.2
7	Purification	Protein A	6.6	90%	18.5	34.5	7272.1	6544.9	1588.5	997.6	0.0	0.0	6.5	981.7	1075.5
8	Purification	Virus Inactivation	6.3	98%	5.5	5.5	6544.9	6414.0	997.6	1017.6	0.0	0.0	6.4	883.6	1302.5
9	Recovery	Depth Filtration	5.6	90%	5.1	5.1	6414.0	5772.6	1017.6	1034.1	0.0	0.0	5.8	865.9	1665.2
10	Purification	Filtration (0.2um)	5.4	98%	4.2	4.2	5772.6	5657.1	1034.1	1046.1	0.0	0.0	5.7	779.3	1855.5
11	Purification	AIEX Flow Through	5.1	95%	7.7	7.7	5657.1	5374.3	1046.1	1046.1	0.0	0.0	5.4	763.7	801.7
12	Purification	IEX Bind & Elute	10.2	95%	11.3	27.3	5374.3	5105.6	1046.1	498.8	0.0	0.0	5.1	725.5	781.4
13	Purification	Viral Filtration	9.8	98%	6.1	6.1	5105.6	5003.5	498.8	508.8	0.0	0.0	5.0	689.3	689.3
14	Purification	UF/DF	50.0	98%	11.0	11.0	5003.5	4903.4	508.8	98.1	0.0	0.0	4.9	675.5	2329.2
15	Purification	Filtration (0.2um)	47.5	98%	4.1	4.1	4903.4	4805.3	98.1	101.1	0.0	0.0	4.8	662.0	1654.9

Cost of Goods Breakdown for mAb SU Base Modification 1 (USD per batch)

	N-2 Seed 1	N-1 Seed 2	Production 3	Centrifugation 4	Secondary Depth Filtration 5	Filtration (0.2um) 6	Protein A 7	Virus Inactivation 8	Depth Filtration 9	Filtration (0.2um) 10	AIEX Flow Through 11	IEX Bind & Elute 12	Viral Filtration 13	UF/DF 14	Filtration (0.2um) 15
Equipment (Total)	376,475	1,199,777	4,582,665	816,719	139,718	120,693	968,825	178,048	126,452	125,867	794,992	831,794	92,444	563,510	67,237
Capital	2,491	7,939	30,324	5,404	925	799	6,411	1,178	837	833	5,261	5,504	612	3,729	445
Materials	921	2,096	13,273	823	857	858	4,686	958	849	955	1,219	1,339	804	948	808
Consumables	1,760	4,065	16,312	0	5,900	3,179	42,168	554	2,929	3,592	6,369	10,416	21,708	3,853	1,417
Labour	1,979	2,802	17,907	3,690	4,580	2,616	13,185	2,420	2,694	2,312	6,701	10,231	3,107	7,437	2,222
Other	626	1,998	7,689	1,393	308	279	1,938	493	277	402	1,391	1,514	170	1,014	131
	2%	6%	26%	3%	4%	2%	21%	2%	2%	2%	6%	9%	8%	5%	2%
Perfusion Factor	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Capital Charge	2,491	7,939	30,324	5,404	925	799	6,411	1,178	837	833	5,261	5,504	612	3,729	445
Materials	921	2,096	13,273	823	857	858	4,686	958	849	955	1,219	1,339	804	948	808
Media	130	1,305	12,482	0	0	0	0	0	0	0	0	0	0	0	0
Buffer	0	0	0	0	13	2	3,896	1	4	3	428	548	3	134	1
Direct RM	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bought WFI & PW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CIP	0	0	0	32	54	65	0	167	54	161	0	0	11	22	16
QC tests	791	791	791	791	791	791	791	791	791	791	791	791	791	791	791
Consumables	1,760	4,065	16,312	0	5,900	3,179	42,168	554	2,929	3,592	6,369	10,416	21,708	3,853	1,417
Resins/MA	0	0	0	0	0	0	38,111	0	0	0	1,608	7,115	0	0	0
Bags	1,760	4,065	16,312	0	2,924	1,937	3,116	554	1,937	1,937	4,760	3,301	1,418	951	1,003
Filters	0	0	0	0	2,976	1,241	941	0	992	1,655	0	0	20,290	2,902	414
Packages	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labour	1,979	2,802	17,907	3,690	4,580	2,616	13,185	2,420	2,694	2,312	6,701	10,231	3,107	7,437	2,222
Process	827	1,171	7,482	1,542	1,914	1,093	5,509	1,011	1,126	966	2,800	4,275	1,298	3,107	928
Quality	838	1,186	7,581	1,562	1,939	1,108	5,582	1,124	1,141	979	2,837	4,331	1,316	3,149	941
Indirect	314	445	2,843	586	727	415	2,094	384	428	367	1,064	1,624	493	1,181	353
Other	626	1,998	7,689	1,393	308	279	1,938	493	277	402	1,391	1,514	170	1,014	131
Insurance/other	129	410	1,564	279	48	41	331	61	43	43	271	284	32	192	23
Waste mgmt	1.12	0.42	5.51	0.50	6.17	2.25	6.48	2.06	2.27	3.01	8.38	6.02	2.61	0.89	0.79
Maintenance	125	397	1,516	270	46	40	321	59	42	42	263	275	31	186	22
Utilities	372	1,192	4,603	843	208	195	1,281	371	190	314	848	949	105	635	85
TOTAL (USD)	7,777	18,900	85,504	11,310	12,570	7,730	68,389	5,603	7,587	8,094	20,940	29,004	26,401	16,980	5,022
Total (USD/Gram normalized for the output)	1.6	3.9	17.8	2.4	2.6	1.6	14.2	1.2	1.6	1.7	4.4	6.0	5.5	3.5	1.0

Process Sequence: mAb SU Base Modification 2

No	Process Stage	Unit Op Name	Conc (g/L)	Yield (%)	Duration (hr)	Adjusted Duration (hr)	Mass In (g)	Mass Out (g)	Vol In (g)	Vol Out (g)	Particles In	Particles Out	Target Out	Target capacity (kg/year)	Actual capacity (kg/year)
Feed			0.0						1.8						
1	Upstream	N-2 Seed	0.0	0%	52.5	8.8	0.0	0.0	1.8	18.0	0.0	0.0	0.0	0.0	0.0
2	Upstream	N-1 Seed	0.0	0%	52.5	8.8	0.0	0.0	18.0	180.0	0.0	0.0	0.0	0.0	0.0
3	Upstream	Production	5.0	100%	278.5	46.4	0.0	9000.0	180.0	1800.0	0.0	0.0	9.0	1215.0	1350.0
4	Recovery	Centrifugation	5.0	85%	8.0	8.0	9000.0	7650.0	1800.0	1530.0	0.0	0.0	7.7	1215.0	1620.0
5	Recovery	Secondary Depth Filtration	4.7	97%	5.2	5.2	7650.0	7420.5	1530.0	1579.5	0.0	0.0	7.4	1032.8	670.6
6	Purification	Filtration (0.2um)	4.6	98%	5.0	5.0	7420.5	7272.1	1579.5	1588.5	0.0	0.0	7.3	1001.8	1252.2
7	Purification	Protein A	6.6	90%	18.5	34.5	7272.1	6544.9	1588.5	997.6	0.0	0.0	6.5	981.7	1075.5
8	Purification	Virus Inactivation	6.3	98%	5.5	5.5	6544.9	6414.0	997.6	1017.6	0.0	0.0	6.4	883.6	1302.5
9	Recovery	Depth Filtration	5.6	90%	5.1	5.1	6414.0	5772.6	1017.6	1034.1	0.0	0.0	5.8	865.9	1665.2
10	Purification	Filtration (0.2um)	5.4	98%	4.2	4.2	5772.6	5657.1	1034.1	1046.1	0.0	0.0	5.7	779.3	1855.5
11	Purification	AIEX Flow Through	5.1	95%	7.7	7.7	5657.1	5374.3	1046.1	1046.1	0.0	0.0	5.4	763.7	801.7
12	Purification	IEX Bind & Elute	10.2	95%	11.3	27.3	5374.3	5105.6	1046.1	498.8	0.0	0.0	5.1	725.5	781.4
13	Purification	Viral Filtration	9.8	98%	6.1	6.1	5105.6	5003.5	498.8	508.8	0.0	0.0	5.0	689.3	689.3
14	Purification	UF/DF	50.0	98%	11.0	11.0	5003.5	4903.4	508.8	98.1	0.0	0.0	4.9	675.5	2329.2
15	Purification	Filtration (0.2um)	47.5	98%	4.1	4.1	4903.4	4805.3	98.1	101.1	0.0	0.0	4.8	662.0	1654.9

Cost of Goods Breakdown for mAb SU Base Modification 2 (USD per batch)

	N-2 Seed 1	N-1 Seed 2	Production 3	Centrifugation 4	Secondary Depth Filtration 5	Filtration (0.2um) 6	Protein A 7	Virus Inactivation 8	Depth Filtration 9	Filtration (0.2um) 10	AIEX Flow Through 11	IEX Bind & Elute 12	Viral Filtration 13	UF/DF 14	Filtration (0.2um) 15
Equipment (Total)	376,475	1,199,777	4,582,665	816,719	139,718	120,693	968,825	178,048	126,452	125,867	794,992	831,794	92,444	563,510	67,237
Capital	2,491	7,939	30,324	5,404	925	799	6,411	1,178	837	833	5,261	5,504	612	3,729	445
Materials	921	2,096	13,273	823	857	858	4,686	958	849	955	1,219	1,339	804	948	808
Consumables	1,760	4,065	16,312	0	5,900	3,179	42,168	554	2,929	3,592	6,369	10,416	21,708	3,853	1,417
Labour	1,979	2,802	17,907	3,690	4,580	2,616	13,185	2,420	2,694	2,312	6,701	10,231	3,107	7,437	2,222
Other	626	1,998	7,689	1,393	308	279	1,938	493	277	402	1,391	1,514	170	1,014	131
	2%	6%	26%	3%	4%	2%	21%	2%	2%	2%	6%	9%	8%	5%	2%
Perfusion Factor	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Capital Charge	2,491	7,939	30,324	5,404	925	799	6,411	1,178	837	833	5,261	5,504	612	3,729	445
Materials	921	2,096	13,273	823	857	858	4,686	958	849	955	1,219	1,339	804	948	808
Media	130	1,305	12,482	0	0	0	0	0	0	0	0	0	0	0	0
Buffer	0	0	0	0	13	2	3,896	1	4	3	428	548	3	134	1
Direct RM	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bought WFI & PW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CIP	0	0	0	32	54	65	0	167	54	161	0	0	11	22	16
QC tests	791	791	791	791	791	791	791	791	791	791	791	791	791	791	791
Consumables	1,760	4,065	16,312	0	5,900	3,179	42,168	554	2,929	3,592	6,369	10,416	21,708	3,853	1,417
Resins/MA	0	0	0	0	0	0	38,111	0	0	0	1,608	7,115	0	0	0
Bags	1,760	4,065	16,312	0	2,924	1,937	3,116	554	1,937	1,937	4,760	3,301	1,418	951	1,003
Filters	0	0	0	0	2,976	1,241	941	0	992	1,655	0	0	20,290	2,902	414
Packages	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labour	1,979	2,802	17,907	3,690	4,580	2,616	13,185	2,420	2,694	2,312	6,701	10,231	3,107	7,437	2,222
Process	827	1,171	7,482	1,542	1,914	1,093	5,509	1,011	1,126	966	2,800	4,275	1,298	3,107	928
Quality	838	1,186	7,581	1,562	1,939	1,108	5,582	1,024	1,141	979	2,837	4,331	1,316	3,149	941
Indirect	314	445	2,843	586	727	415	2,094	384	428	367	1,064	1,624	493	1,181	353
Other	626	1,998	7,689	1,393	308	279	1,938	493	277	402	1,391	1,514	170	1,014	131
Insurance/other	129	410	1,564	279	48	41	331	61	43	43	271	284	32	192	23
Waste mgmt	1.12	0.42	5.51	0.50	6.17	2.25	6.48	2.06	2.27	3.01	8.38	6.02	2.61	0.89	0.79
Maintenance	125	397	1,516	270	46	40	321	59	42	42	263	275	31	186	22
Utilities	372	1,192	4,603	843	208	195	1,281	371	190	314	848	949	105	635	85
TOTAL (USD)	7,777	18,900	85,504	11,310	12,570	7,730	68,389	5,603	7,587	8,094	20,940	29,004	26,401	16,980	5,022
Total (USD/Gram normalized for the output)	1.6	3.9	17.8	2.4	2.6	1.6	14.2	1.2	1.6	1.7	4.4	6.0	5.5	3.5	1.0

Process Sequence: mAb SU Base Modification 3

No	Process Stage	Unit Op Name	Conc (g/L)	Yield (%)	Duration (hr)	Adjusted Duration (hr)	Mass In (g)	Mass Out (g)	Vol In (g)	Vol Out (g)	Particles In	Particles Out	Target Out	Target capacity (kg/year)	Actual capacity (kg/year)
<i>Feed</i>			<i>0.0</i>			<i>1.8</i>									
1	Upstream	N-2 Seed	0.0	0%	52.5	8.8	0.0	0.0	1.8	18.0	0.0	0.0	0.0	0.0	0.0
2	Upstream	N-1 Seed	0.0	0%	52.5	8.8	0.0	0.0	18.0	180.0	0.0	0.0	0.0	0.0	0.0
3	Upstream	Production	5.0	100%	278.5	46.4	0.0	9000.0	180.0	1800.0	0.0	0.0	9.0	1215.0	1350.0
4	Recovery	Centrifugation	5.0	85%	8.0	8.0	9000.0	7650.0	1800.0	1530.0	0.0	0.0	7.7	1215.0	1620.0
5	Recovery	Secondary Depth Filtration	4.7	97%	5.2	5.2	7650.0	7420.5	1530.0	1579.5	0.0	0.0	7.4	1032.8	670.6
6	Purification	Filtration (0.2um)	4.6	98%	5.0	5.0	7420.5	7272.1	1579.5	1588.5	0.0	0.0	7.3	1001.8	1252.2
7	Purification	Protein A	6.6	90%	18.5	34.5	7272.1	6544.9	1588.5	997.6	0.0	0.0	6.5	981.7	1075.5
8	Purification	Virus Inactivation	6.3	98%	5.5	5.5	6544.9	6414.0	997.6	1017.6	0.0	0.0	6.4	883.6	1302.5
9	Recovery	Depth Filtration	5.6	90%	5.1	5.1	6414.0	5772.6	1017.6	1034.1	0.0	0.0	5.8	865.9	1665.2
10	Purification	Filtration (0.2um)	5.4	98%	4.2	4.2	5772.6	5657.1	1034.1	1046.1	0.0	0.0	5.7	779.3	1855.5
11	Purification	AIEX Flow Through	5.1	95%	7.7	7.7	5657.1	5374.3	1046.1	1046.1	0.0	0.0	5.4	763.7	801.7
12	Purification	IEX Bind & Elute	10.2	95%	11.3	27.3	5374.3	5105.6	1046.1	498.8	0.0	0.0	5.1	725.5	781.4
13	Purification	Viral Filtration	9.8	98%	6.1	6.1	5105.6	5003.5	498.8	508.8	0.0	0.0	5.0	689.3	689.3
14	Purification	UF/DF	50.0	98%	11.0	11.0	5003.5	4903.4	508.8	98.1	0.0	0.0	4.9	675.5	2329.2
15	Purification	Filtration (0.2um)	47.5	98%	4.1	4.1	4903.4	4805.3	98.1	101.1	0.0	0.0	4.8	662.0	1654.9

Cost of Goods Breakdown for mAb SU Base Modification 3 (USD per batch)

	N-2 Seed 1	N-1 Seed 2	Production 3	Centrifugation 4	Secondary Depth Filtration 5	Filtration (0.2um) 6	Protein A 7	Virus Inactivation 8	Depth Filtration 9	Filtration (0.2um) 10	AIEX Flow Through 11	IEX Bind & Elute 12	Viral Filtration 13	UF/DF 14	Filtration (0.2um) 15
Equipment (Total)	376,475	1,199,777	4,582,665	816,719	139,718	120,693	968,825	178,048	126,452	125,867	794,992	831,794	92,444	563,510	67,237
Capital	2,491	7,939	30,324	5,404	925	799	6,411	1,178	837	833	5,261	5,504	612	3,729	445
Materials	921	2,096	13,273	823	857	858	4,686	958	849	955	1,219	1,339	804	948	808
Consumables	1,760	4,065	16,312	0	5,900	3,179	23,113	554	2,929	3,592	6,369	10,416	21,708	3,853	1,417
Labour	1,979	2,802	17,907	3,690	4,580	2,616	13,185	2,420	2,694	2,312	6,701	10,231	3,107	7,437	2,222
Other	626	1,998	7,689	1,393	308	279	1,938	493	277	402	1,391	1,514	170	1,014	131
	2%	6%	27%	4%	4%	2%	16%	2%	2%	3%	7%	9%	8%	5%	2%
Perfusion Factor	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Capital Charge	2,491	7,939	30,324	5,404	925	799	6,411	1,178	837	833	5,261	5,504	612	3,729	445
Materials	921	2,096	13,273	823	857	858	4,686	958	849	955	1,219	1,339	804	948	808
Media	130	1,305	12,482	0	0	0	0	0	0	0	0	0	0	0	0
Buffer	0	0	0	0	13	2	3,896	1	4	3	428	548	3	134	1
Direct RM	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bought WFI & PW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CIP	0	0	0	32	54	65	0	167	54	161	0	0	11	22	16
QC tests	791	791	791	791	791	791	791	791	791	791	791	791	791	791	791
Consumables	1,760	4,065	16,312	0	5,900	3,179	23,113	554	2,929	3,592	6,369	10,416	21,708	3,853	1,417
Resins/MA	0	0	0	0	0	0	19,055	0	0	0	1,608	7,115	0	0	0
Bags	1,760	4,065	16,312	0	2,924	1,937	3,116	554	1,937	1,937	4,760	3,301	1,418	951	1,003
Filters	0	0	0	0	2,976	1,241	941	0	992	1,655	0	0	20,290	2,902	414
Packages	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labour	1,979	2,802	17,907	3,690	4,580	2,616	13,185	2,420	2,694	2,312	6,701	10,231	3,107	7,437	2,222
Process	827	1,171	7,482	1,542	1,914	1,093	5,509	1,011	1,126	966	2,800	4,275	1,298	3,107	928
Quality	838	1,186	7,581	1,562	1,939	1,108	5,582	1,186	1,141	979	2,837	4,331	1,316	3,149	941
Indirect	314	445	2,843	586	727	415	2,094	384	428	367	1,064	1,624	493	1,181	353
Other	626	1,998	7,689	1,393	308	279	1,938	493	277	402	1,391	1,514	170	1,014	131
Insurance/other	129	410	1,564	279	48	41	331	61	43	43	271	284	32	192	23
Waste mgmt	1.12	0.42	5.51	0.50	6.17	2.25	6.16	2.06	2.27	3.01	8.38	6.02	2.61	0.89	0.79
Maintenance	125	397	1,516	270	46	40	321	59	42	42	263	275	31	186	22
Utilities	372	1,192	4,603	843	208	195	1,281	371	190	314	848	949	105	635	85
TOTAL (USD)	7,777	18,900	85,504	11,310	12,570	7,730	49,333	5,603	7,587	8,094	20,940	29,004	26,401	16,980	5,022
Total (USD/Gram normalized for the output)	1.6	3.9	17.8	2.4	2.6	1.6	10.3	1.2	1.6	1.7	4.4	6.0	5.5	3.5	1.0

Process Sequence: mAb SU Base Modification 4

No	Process Stage	Unit Op Name	Conc (g/L)	Yield (%)	Duration (hr)	Adjusted Duration (hr)	Mass In (g)	Mass Out (g)	Vol In (g)	Vol Out (g)	Particles In	Particles Out	Target Out	Target capacity (kg/year)	Actual capacity (kg/year)
Feed			0.0			1.8									
1	Upstream	N-2 Seed	0.0	0%	52.5	8.8	0.0	0.0	1.8	18.0	0.0	0.0	0.0	0.0	0.0
2	Upstream	N-1 Seed	0.0	0%	52.5	8.8	0.0	0.0	18.0	180.0	0.0	0.0	0.0	0.0	0.0
3	Upstream	Production	5.0	100%	278.5	46.4	0.0	9000.0	180.0	1800.0	0.0	0.0	9.0	1215.0	1350.0
4	Recovery	Centrifugation	5.0	85%	8.0	8.0	9000.0	7650.0	1800.0	1530.0	0.0	0.0	7.7	1215.0	1620.0
5	Recovery	Secondary Depth Filtration	4.7	97%	5.2	5.2	7650.0	7420.5	1530.0	1579.5	0.0	0.0	7.4	1032.8	670.6
6	Purification	Filtration (0.2um)	4.6	98%	5.0	5.0	7420.5	7272.1	1579.5	1588.5	0.0	0.0	7.3	1001.8	1252.2
7	Purification	Protein A	6.6	90%	18.5	34.5	7272.1	6544.9	1588.5	997.6	0.0	0.0	6.5	981.7	1075.5
8	Purification	Virus Inactivation	6.3	98%	5.5	5.5	6544.9	6414.0	997.6	1017.6	0.0	0.0	6.4	883.6	1302.5
9	Purification	Filtration (0.2um)	6.1	98%	4.2	4.2	6414.0	6285.7	1017.6	1029.6	0.0	0.0	6.3	865.9	2061.6
10	Purification	AIEX Flow Through	5.8	95%	6.3	6.3	6285.7	5971.4	1029.6	1029.6	0.0	0.0	6.0	848.6	1080.4
11	Purification	IEX Bind & Elute	11.4	95%	11.3	27.3	5971.4	5672.8	1029.6	498.8	0.0	0.0	5.7	806.1	823.7
12	Purification	Viral Filtration	10.9	98%	6.1	6.1	5672.8	5559.4	498.8	508.8	0.0	0.0	5.6	765.8	765.8
13	Purification	UF/DF	50.0	98%	11.1	11.1	5559.4	5448.2	508.8	109.0	0.0	0.0	5.4	750.5	2501.7
14	Purification	Filtration (0.2um)	47.7	98%	4.1	4.1	5448.2	5339.2	109.0	112.0	0.0	0.0	5.3	735.5	1471.0

Cost of Goods Breakdown for mAb SU Base Modification 4 (USD per batch)

	N-2 Seed 1	N-1 Seed 2	Production 3	Centri- fugation 4	Secondary Depth Filtration 5	Filtration (0.2um) 6	Protein A 7	Virus Inactivation 8	Filtration (0.2um) 9	AIEX Flow Through 10	IEX Bind & Elute 11	Viral Filtration 12	UF/DF 13	Filtration (0.2um) 14
Equipment (Total)	375,428	1,196,443	4,569,929	814,449	136,842	119,905	991,005	177,553	124,915	1,185,855	762,338	91,685	542,062	66,900
Capital	2,484	7,915	30,231	5,388	905	793	6,556	1,175	826	7,845	5,043	607	3,586	443
Materials	978	2,152	13,329	879	914	914	4,743	1,015	1,012	1,926	1,395	861	1,013	864
Consumables	1,760	4,065	16,312	0	5,900	3,179	23,113	554	3,592	9,879	10,416	21,708	3,905	1,417
Labour	1,998	2,830	18,085	3,727	4,621	2,641	13,317	2,444	2,329	8,835	10,044	3,137	7,603	2,269
Other	624	1,992	7,665	1,388	304	277	1,974	492	400	2,138	1,398	169	980	131
	2%	6%	27%	4%	4%	2%	16%	2%	3%	10%	9%	8%	5%	2%
Perfusion Factor	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Capital Charge	2,484	7,915	30,231	5,388	905	793	6,556	1,175	826	7,845	5,043	607	3,586	443
Materials	978	2,152	13,329	879	914	914	4,743	1,015	1,012	1,926	1,395	861	1,013	864
Media	130	1,305	12,482	0	0	0	0	0	0	0	0	0	0	0
Buffer	0	0	0	0	13	2	3,896	1	3	1,079	548	3	144	1
Direct RM	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bought WFI & PW	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CIP	0	0	0	32	54	65	0	167	161	0	0	11	22	16
QC tests	847	847	847	847	847	847	847	847	847	847	847	847	847	847
Consumables	1,760	4,065	16,312	0	5,900	3,179	23,113	554	3,592	9,879	10,416	21,708	3,905	1,417
Resins/MA	0	0	0	0	0	0	19,055	0	0	4,052	7,115	0	0	0
Bags	1,760	4,065	16,312	0	2,924	1,937	3,116	554	1,937	5,827	3,301	1,418	1,003	1,003
Filters	0	0	0	0	2,976	1,241	941	0	1,655	0	0	20,290	2,902	414
Packages	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labour	1,998	2,830	18,085	3,727	4,621	2,641	13,317	2,444	2,329	8,835	10,044	3,137	7,603	2,269
Process	835	1,182	7,557	1,557	1,931	1,104	5,564	1,021	973	3,692	4,197	1,311	3,177	948
Quality	846	1,198	7,657	1,578	1,956	1,118	5,638	1,035	986	3,741	4,253	1,328	3,219	961
Indirect	317	449	2,872	592	734	419	2,114	388	370	1,403	1,595	498	1,207	360
Other	624	1,992	7,665	1,388	304	277	1,974	492	400	2,138	1,398	169	980	131
Insurance/other	128	408	1,559	278	47	41	338	61	43	404	260	31	185	23
Waste mgmt	112	0.42	5.51	0.50	6.17	2.25	6.16	2.06	3.01	10.45	6.02	2.61	1.03	0.79
Maintenance	124	396	1,512	269	45	40	328	59	41	392	252	30	179	22
Utilities	371	1,188	4,589	841	205	195	1,302	371	313	1,331	880	105	615	85
TOTAL (USD)	7,844	18,954	85,623	11,383	12,644	7,805	49,702	5,679	8,160	30,624	28,297	26,482	17,087	5,124
Total (USD/Gram normalized for the output)	1.5	3.5	16.0	2.1	2.4	1.5	9.3	1.1	1.5	5.7	5.3	5.0	3.2	1.0

Process Sequence: mAb SU Base Modification 5

No	Process Stage	Unit Op Name	Conc (g/L)	Yield (%)	Duration (hr)	Adjusted Duration (hr)	Mass In (g)	Mass Out (g)	Vol In (g)	Vol Out (g)	Particles In	Particles Out	Target Out	Target capacity (kg/year)	Actual capacity (kg/year)
Feed			0.0						1.8						
1	Upstream	N-2 Seed	0.0	0%	52.5	8.8	0.0	0.0	1.8	18.0	0.0	0.0	0.0	0.0	0.0
2	Upstream	N-1 Seed	0.0	0%	52.5	8.8	0.0	0.0	18.0	180.0	0.0	0.0	0.0	0.0	0.0
3	Upstream	Production	5.0	100%	278.5	46.4	0.0	9000.0	180.0	1800.0	0.0	0.0	9.0	1215.0	1350.0
4	Recovery	Centrifugation	5.0	85%	8.0	8.0	9000.0	7650.0	1800.0	1530.0	0.0	0.0	7.7	1215.0	1620.0
5	Recovery	Secondary Depth Filtration	4.7	97%	5.2	5.2	7650.0	7420.5	1530.0	1579.5	0.0	0.0	7.4	1032.8	670.6
6	Purification	Filtration (0.2um)	4.6	98%	5.0	5.0	7420.5	7272.1	1579.5	1588.5	0.0	0.0	7.3	1001.8	1252.2
7	Purification	Protein A	6.6	90%	18.5	34.5	7272.1	6544.9	1588.5	997.6	0.0	0.0	6.5	981.7	1075.5
8	Purification	Virus Inactivation	6.3	98%	5.5	5.5	6544.9	6414.0	997.6	1017.6	0.0	0.0	6.4	883.6	1302.5
9	Purification	Filtration (0.2um)	6.1	98%	4.2	4.2	6414.0	6285.7	1017.6	1029.6	0.0	0.0	6.3	865.9	2061.6
10	Purification	AIEX Flow Through	5.9	97%	9.9	9.9	6285.7	6097.1	1029.6	1029.6	0.0	0.0	6.1	848.6	1180.5
11	Purification	IEX Bind & Elute	11.6	95%	11.3	27.3	6097.1	5792.3	1029.6	498.8	0.0	0.0	5.8	823.1	832.3
12	Purification	Viral Filtration	11.2	98%	6.1	6.1	5792.3	5676.4	498.8	508.8	0.0	0.0	5.7	782.0	782.0
13	Purification	UF/DF	50.0	98%	11.1	11.1	5676.4	5562.9	508.8	111.3	0.0	0.0	5.6	766.3	2554.4
14	Purification	Filtration (0.2um)	47.7	98%	4.2	4.2	5562.9	5451.6	111.3	114.3	0.0	0.0	5.5	751.0	1502.0

Cost of Goods Breakdown for mAb SU Base Modification 5 (USD per batch)

	N-2 Seed 1	N-1 Seed 2	Production 3	Centri- fugation 4	Secondary Depth Filtration 5	Filtration (0.2um) 6	Protein A 7	Virus Inactivation 8	Filtration (0.2um) 9	AIEX Flow Through 10	IEX Bind & Elute 11	Viral Filtration 12	UF/DF 13	Filtration (0.2um) 14
Equipment (Total)	377,355	1,202,584	4,593,384	818,630	139,733	120,919	1,017,563	170,904	126,086	702,417	848,754	92,597	535,785	67,376
Capital	2,501	7,969	30,440	5,425	926	801	6,743	1,133	836	4,655	5,625	614	3,551	446
Materials	978	2,152	13,329	879	914	914	4,743	1,015	1,012	1,056	1,395	861	1,016	864
Consumables	1,760	4,065	16,312	0	5,900	3,179	23,113	554	3,592	5,425	10,416	21,708	3,905	1,417
Labour	1,978	2,801	17,902	3,689	4,572	2,614	13,182	2,419	2,305	7,160	10,623	3,105	7,544	2,251
Other	629	2,006	7,719	1,398	309	279	2,022	481	402	1,206	1,544	171	972	132
	3%	6%	28%	4%	4%	3%	16%	2%	3%	6%	10%	9%	6%	2%
Perfusion Factor	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Capital Charge	2,501	7,969	30,440	5,425	926	801	6,743	1,133	836	4,655	5,625	614	3,551	446
Materials	978	2,152	13,329	879	914	914	4,743	1,015	1,012	1,056	1,395	861	1,016	864
Media	130	1,305	12,482	0	0	0	0	0	0	0	0	0	0	0
Buffer	0	0	0	0	13	2	3,896	1	3	209	548	3	147	1
Direct RM	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bought WFI & PW	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CIP	0	0	0	32	54	65	0	167	161	0	0	11	22	16
QC tests	847	847	847	847	847	847	847	847	847	847	847	847	847	847
Consumables	1,760	4,065	16,312	0	5,900	3,179	23,113	554	3,592	5,425	10,416	21,708	3,905	1,417
Resins/MA	0	0	0	0	0	0	19,055	0	0	785	7,115	0	0	0
Bags	1,760	4,065	16,312	0	2,924	1,937	3,116	554	1,937	4,640	3,301	1,418	1,003	1,003
Filters	0	0	0	0	2,976	1,241	941	0	1,655	0	0	20,290	2,902	414
Packages	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labour	1,978	2,801	17,902	3,689	4,572	2,614	13,182	2,419	2,305	7,160	10,623	3,105	7,544	2,251
Process	829	1,173	7,499	1,546	1,915	1,095	5,522	1,013	966	2,999	4,450	1,301	3,160	943
Quality	835	1,182	7,553	1,557	1,929	1,103	5,561	1,021	973	3,021	4,482	1,310	3,183	950
Indirect	315	446	2,850	587	728	416	2,098	385	367	1,140	1,691	494	1,201	358
Other	629	2,006	7,719	1,398	309	279	2,022	481	402	1,206	1,544	171	972	132
Insurance/other	129	411	1,571	280	48	41	348	58	43	240	290	32	183	23
Waste mgmt	112	0.42	5.51	0.50	6.17	2.25	6.16	2.06	3.01	8.03	6.02	2.61	1.03	0.79
Maintenance	125	398	1,522	271	46	40	337	57	42	233	281	31	178	22
Utilities	374	1,196	4,620	846	209	196	1,330	364	314	725	967	106	610	86
TOTAL (USD)	7,845	18,994	85,702	11,392	12,620	7,788	49,802	5,602	8,147	19,502	29,604	26,458	16,988	5,111
Total (USD/Gram normalized for the output)	1.4	3.5	15.7	2.1	2.3	1.4	9.1	1.0	1.5	3.6	5.4	4.9	3.1	0.9

Process Sequence: mAb SU Base Modification 6

No	Process Stage	Unit Op Name	Conc (g/L)	Yield (%)	Duration (hr)	Adjusted Duration (hr)	Mass In (g)	Mass Out (g)	Vol In (g)	Vol Out (g)	Particles In	Particles Out	Target Out	Target capacity (kg/year)	Actual capacity (kg/year)
Feed			0.0			1.8									
1	Upstream	N-2 Seed	0.0	0%	52.5	8.8	0.0	0.0	1.8	18.0	0.0	0.0	0.0	0.0	0.0
2	Upstream	N-1 Seed	0.0	0%	52.5	8.8	0.0	0.0	18.0	180.0	0.0	0.0	0.0	0.0	0.0
3	Upstream	Production	5.0	100%	278.5	46.4	0.0	9000.0	180.0	1800.0	0.0	0.0	9.0	1098.0	1220.0
4	Recovery	Primary Depth Filtration	4.5	95%	4.6	4.6	9000.0	8550.0	1800.0	1899.0	0.0	0.0	8.6	1098.0	305.0
5	Recovery	Secondary Depth Filtration	4.3	97%	4.5	4.5	8550.0	8293.5	1899.0	1948.5	0.0	0.0	8.3	1043.1	549.0
6	Purification	Filtration (0.2um)	4.1	98%	4.9	4.9	8293.5	8127.6	1948.5	1960.5	0.0	0.0	8.1	1011.8	1011.8
7	Purification	Protein A	7.3	90%	19.3	51.3	8127.6	7314.9	1960.5	997.6	0.0	0.0	7.3	991.6	1027.6
8	Purification	Virus Inactivation	7.0	98%	5.5	5.5	7314.9	7168.6	997.6	1017.6	0.0	0.0	7.2	892.4	1315.5
9	Purification	Filtration (0.2um)	6.8	98%	4.2	4.2	7168.6	7025.2	1017.6	1029.6	0.0	0.0	7.0	874.6	2082.3
10	Purification	AIEX Flow Through	6.6	97%	9.9	9.9	7025.2	6814.4	1029.6	1029.6	0.0	0.0	6.8	857.1	1127.8
11	Purification	IEX Bind & Elute	10.3	95%	7.0	7.0	6814.4	6473.7	1029.6	628.3	0.0	0.0	6.5	831.4	1058.5
12	Purification	Viral Filtration	9.9	98%	5.7	5.7	6473.7	6344.2	628.3	643.3	0.0	0.0	6.3	789.8	1518.8
13	Purification	UF/DF	50.0	98%	11.3	11.3	6344.2	6217.4	643.3	124.3	0.0	0.0	6.2	774.0	2120.5
14	Purification	Filtration (0.2um)	47.8	98%	4.2	4.2	6217.4	6093.0	124.3	127.3	0.0	0.0	6.1	758.5	1517.0

Cost of Goods Breakdown for mAb SU Base Modification 6 (USD per batch)

	N-2 Seed 1	N-1 Seed 2	Production 3	Centrifugation 4	Secondary Depth Filtration 5	Filtration (0.2um) 6	Protein A 7	Virus Inactivation 8	Filtration (0.2um) 9	AIEX Flow Through 10	IEX Bind & Elute 11	Viral Filtration 12	UF/DF 13	Filtration (0.2um) 14
Equipment (Total)	373,227	1,189,429	4,543,138	42,637	135,651	119,344	1,006,432	168,092	124,088	702,949	1,158,575	96,167	508,341	66,484
Capital	2,734	8,712	33,278	312	994	874	7,372	1,231	909	5,149	8,486	704	3,724	487
Materials	978	2,152	13,329	980	968	915	4,743	1,015	1,012	1,056	1,619	878	1,039	864
Consumables	1,760	4,065	16,312	6,938	4,913	3,592	23,113	554	3,592	5,652	12,654	31,853	4,388	1,417
Labour	2,013	2,850	18,214	8,034	4,339	2,614	13,751	2,441	2,338	6,920	9,754	2,993	7,595	2,320
Other	687	2,193	8,434	228	387	298	2,180	506	421	1,331	2,337	214	1,023	142
	2%	6%	27%	5%	3%	2%	15%	2%	2%	6%	10%	11%	5%	2%
Perfusion Factor	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Capital Charge	2,734	8,712	33,278	312	994	874	7,372	1,231	909	5,149	8,486	704	3,724	487
Materials	978	2,152	13,329	980	968	915	4,743	1,015	1,012	1,056	1,619	878	1,039	864
Media	130	1,305	12,482	0	0	0	0	0	0	0	0	0	0	0
Buffer	0	0	0	25	13	3	3,896	1	3	209	772	4	170	1
Direct RM	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bought WFI & PW	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CIP	0	0	0	108	108	65	0	167	161	0	0	27	22	16
QC tests	847	847	847	847	847	847	847	847	847	847	847	847	847	847
Consumables	1,760	4,065	16,312	6,938	4,913	3,592	23,113	554	3,592	5,652	12,654	31,853	4,388	1,417
Resins/MA	0	0	0	0	0	0	19,055	0	0	785	8,963	0	0	0
Bags	1,760	4,065	16,312	987	1,937	1,937	3,116	554	1,937	4,867	3,691	1,418	1,003	1,003
Filters	0	0	0	5,952	2,976	1,655	941	0	1,655	0	0	30,435	3,385	414
Packages	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labour	2,013	2,850	18,214	8,034	4,339	2,614	13,751	2,441	2,338	6,920	9,754	2,993	7,595	2,320
Process	840	1,189	7,601	3,353	1,811	1,091	5,739	1,019	976	2,888	4,070	1,249	3,170	968
Quality	854	1,209	7,725	3,407	1,840	1,108	5,832	1,035	992	2,935	4,136	1,269	3,221	984
Indirect	319	452	2,888	1,274	688	414	2,181	387	371	1,097	1,547	475	1,204	368
Other	687	2,193	8,434	228	387	298	2,180	506	421	1,331	2,337	214	1,023	142
Insurance/other	141	451	1,721	16	51	45	381	64	47	266	439	36	193	25
Waste mgmt	112	0.42	5.51	8.14	4.39	2.54	6.24	2.06	3.01	8.06	7.08	3.43	1.12	0.79
Maintenance	137	436	1,664	16	50	44	369	62	45	257	424	35	186	24
Utilities	408	1,307	5,043	188	281	207	1,424	379	325	799	1,467	139	643	92
TOTAL (USD)	8,171	19,973	89,567	16,492	11,600	8,293	51,159	5,747	8,272	20,108	34,851	36,642	17,769	5,230
Total (USD/Gram normalized for the output)	1.3	3.3	14.7	2.7	1.9	1.4	8.4	0.9	1.4	3.3	5.7	6.0	2.9	0.9

Intended Use: Single-use processing of aqueous based biological pharmaceuticals (drugs) and vaccines to remove biological contamination strictly following the product operating instructions and cGMP requirements, where applicable.

Prohibited Use: As a component in a medical device that is regulated by any agency, and/or globally exemplary agencies, including but not limited to: a) FDA, b) European Medical Device Directive (MDD), c) Japan Pharmaceuticals and Medical Devices Agency (PMDA); Applications involving permanent implantation into the body; Life-sustaining medical applications; Applications requiring FDA Food Contact compliance.

Technical Information: The technical information, guidance, and other statements contained in this document or otherwise provided by 3M are based upon records, tests, or experience that 3M believes to be reliable, but the accuracy, completeness, and representative nature of such information is not guaranteed. Such information is intended for people with knowledge and technical skills sufficient to assess and apply their own informed judgment to the information. No license under any 3M or third party intellectual property rights is granted or implied with this information.

Product Selection and Use: Many factors beyond 3M's control and uniquely within user's knowledge and control can affect the use and performance of a 3M product in a particular application. As a result, end-user is solely responsible for evaluating the product and determining whether it is appropriate and suitable for end-user's application, including completing a risk assessment that considers the product leachable characteristics and its impact on drug safety conducting a workplace hazard assessment and reviewing all applicable regulations and standards (e.g., OSHA, ANSI, etc.). Failure to properly evaluate, select, and use a 3M product and appropriate safety products, or to meet all applicable safety regulations, may result in injury, sickness, death, and/or harm to property.

Warranty, Limited Remedy, and Disclaimer: Unless a different warranty is specifically stated on the applicable 3M product packaging or product literature (in which case such warranty governs), 3M warrants that each 3M product meets the applicable 3M product specification at the time 3M ships the product. 3M MAKES NO OTHER WARRANTIES OR CONDITIONS, EXPRESS OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OR CONDITION OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR ARISING OUT OF A COURSE OF DEALING, CUSTOM, OR USAGE OF TRADE. If a 3M product does not conform to this warranty, then the sole and exclusive remedy is, at 3M's option, replacement of the 3M product or refund of the purchase price.

Limitation of Liability: Except for the limited remedy stated above, and except to the extent prohibited by law, 3M will not be liable for any loss or damage arising from or related to the 3M product, whether direct, indirect, special, incidental, or consequential (including, but not limited to, lost profits or business opportunity), regardless of the legal or equitable theory asserted, including, but not limited to, warranty, contract, negligence, or strict liability.



3M Purification Inc.
3M Separation and Purification Sciences Division
3M India Limited
48-51, Electronic City, Phase-1, Bangalore-560100

Phone 1800-425-3030
Web www.3mindia.in/3M/en_IN/bioprocessing-in/

3M, Emphaze, LifeASSURE and Zeta Plus are trademarks of 3M Company. All other trademarks are property of their respective owners. All rights reserved.