LETTER OF TRANSMITTAL

To: Project Engineers and Upper Level Management

From: Project Evaluation Team

Date: March 14, 2019

Subject: Large-Scale Biomanufacturing Facility Design

This letter is a response to the design proposal for a large-scale biomanufacturing facility for monoclonal antibody production. Enclosed is the final report for the project tasked. In the design brief, it is stated that the biomanufacturing facility should be able to produce product at current reported titers of 1 to 2 g/L as well as projected future titers of 5 to 10 g/L. The design team was charged with determining whether or not the project was technically feasible and economically attractive based on current and future titers. The seed train portion of the project was simulated in MatLab using kinetic information while the purification portion of the process was simulated in SuperPro Designer. Based on the simulation and additional market information provided, an economic analysis was also performed. Upon finishing these analyses, it was determined that in both the best-case and worst-case scenarios, the MAb production process is both technically feasible and economically attractive. The design team hereby releases this design report to both project engineers and upper level management for their review.

Large-Scale Biomanufacturing Facility Design

Date Submitted:

March 14, 2019

Group #__________

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Abstract

Enclosed in this report is the feasibility study of a large-scale biomanufacturing facility. The study addresses the technical feasibility and economic attractiveness of the production of Monoclonal Antibodies from Chinese Hamster Ovary Cells in varying titers ranging from 1g/L to 10 g/L of MAb.

The proposed design follows the manufacturing process explicitly described in the design brief. The initial part of the design process that includes the seed train and production bioreactors was simulated and optimized in MatLab using the process' kinetic information. It was determined that three simultaneous trains of increasing reactor size up to 30,000 L needed to be run in order to achieve the minimum amount of MAb needed per year. The second part of the design process that includes the purification train was simulated and optimized in SuperPro Designer. It was determined that when the titers increased over 5 g/L, two purification trains are required in order to meet recovery specifications. The results from both simulations proved the proposed design is technically feasible. The design requires the purchase of multiple types of disposable or non-disposable bioreactors, multiple holding and mixing vessels, several resin columns, and multiple storage vessels and waste tanks for an initial capital investment of roughly $172 million.

Construction of the facility will begin in 2019 with operation beginning mid-year 2020. The plant would operate at the titer 1 g/L starting in 2020 and increase up to the titer of 10 g/L as needed. The plant size is designed for up to 10 g/L, so the yearly utility costs are estimated around $2,000,000 per year, while the raw materials and consumables costs are around $134 million per year. The total project evaluation life is 25 years assuming a tax rate of 30%, a minimum rate of return of 15%, and an escalation rate of 2%. The production has an annual revenue of over $6 billon in 2019 dollars. Using these economic metrics, it was determined that the net present value of project is $32 billion and the DCFROR is 22.3%, with a payback period of 0.045 years. Based on these results, the project is economically attractive and should continue into construction.

The capital cost of the project has the biggest impact on the economic viability of the proposed process. If the capital cost increases by 25%, the discounted rate of return will be 17.9%. If the capital cost decreases by 25%, the discounted rate of return is 29.8%. However, even during best-case and worst-case analysis, the DCFROR was still greater than the initial rate of return proving the process to be economically attractive.

Introduction and Design Basis

Introduction

In today's society, there are many classes of drugs in development, with the two largest classes being small molecule compounds and biopharmaceuticals. Small molecule compounds are the typical synthetic drugs that come to mind. Biopharmaceuticals are larger compounds that have become a major focus in medical drug production due to their many advantages. They are considered safer than traditional medications due to the high selectivity of reacting molecules. They are also highly effective in treating a variety of diseases and illnesses such as rheumatoid arthritis, cancers, and transplant rejection. [1]

A particular pharmaceutical company has decided to design a large-scale manufacturing facility focusing on the production of biologics. They are pursuing biopharmaceuticals due to the lucrative return on investment as it is considered a multibillion-dollar industry. Although there is a wide range of biopharmaceuticals, the company has decided to solely focus on monoclonal antibody production at this time.

Humanized Monoclonal Antibodies, or more simply MAbs, are part of the biopharmaceutical side of drug development known as biologics. Biologics or biomanufacturing produces a product derived from discoveries in recombinant DNA technology to manufacture biotherapeutic processes. A monoclonal antibody, also known as a "a therapeutic protein," is one of the most common biologics on the market today. MAbs are derived from the manipulation of various cells and the subsequent products the engineered cell systems produce. Figure 1 shows a biomanufacturing diagram of an upstream process for MAb production. [1]

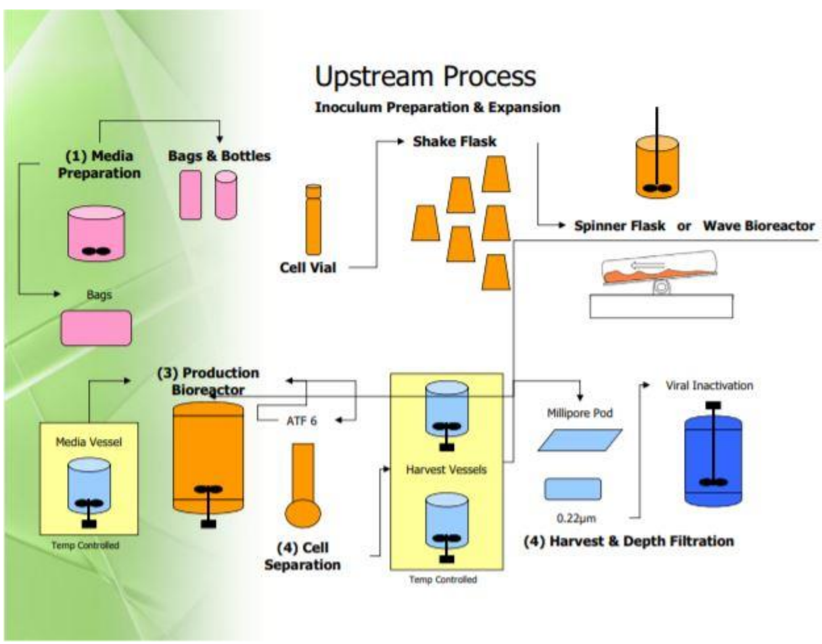


Figure 1: *Biomanufacturing Process Example* [1]

MAb production is up and coming in the field of biologics and biomanufacturing. Most biologic manufacturing processes are relatively similar in that a frozen vial of cells is mixed with some sort of chemically defined media allowing the cells to grow and multiply. Production of MAbs begins in the upstream process shown in Figure 1 with CHO cells, also known as Chinese Hamster Ovary Cells. Once desired amount of MAb has been synthesized, a rigorous purification takes place before being sold on the market.

Design Basis

The task given in the design brief was to design a manufacturing facility that would allow production of MAb at current reported titers of 1 to 2 g/L; however, the facility should be able to eventually handle production of up to titers of 5 to 10 g/L.
Listed below in Table 1 are specifications for the specific process outlined in the design brief.

Table 1: *Specific MAb Production Properties*

Specific MAb Production Properties	
Cell Doubling Time	36 hr
Minimum Glucose Concentration	2 g/L
MAb Production Rate	25 pg/cell*day
Yearly MAb Production	1,000 kg
Starting CHO Vial Size	1 mL
Starting CHO Cell Amount	1 x 10^6 cells

Table 2 below lists utility cost outlined in design brief as well as others found from other sources.

Table 2: *Utility Cost*

Utility Costs	
Electricity	$.05/kWhr
Sewer	$5.00/1,000 gal
Water	$.543/1,000 L
WFI	$1,000/1,000 L
Steam*	$12/MT
Compressed Air*	$2.38/1,000 kg
Labor*	$16.25/hr
Flare Waste*	$112.97/ton

Table 3 below gives the economic parameters given in the design brief for revenue purposes.

Table 3: *Economic Revenue*

Economic Revenue		
Product	2007 Revenue (US$ million)	Estimated Quantity (annual kg BDS)
Enbrel	$5,275	1,020
Remicade	$4,975	1,098
Rituxan/MabTherma	$4,600	1,175
Herceptin	$4,046	1,015
Avastin	$3,424	873
Humira	$3,000	121
Xolair	$613	246
Tysabri	$343	51
Vectibix	$170	28

Process Flow Diagram and Material Balances

Figure 2: *Process Flow Diagram*

Table 4: *Upstream Stream Table*

Table 5: *Downstream Stream Table*

Process Description

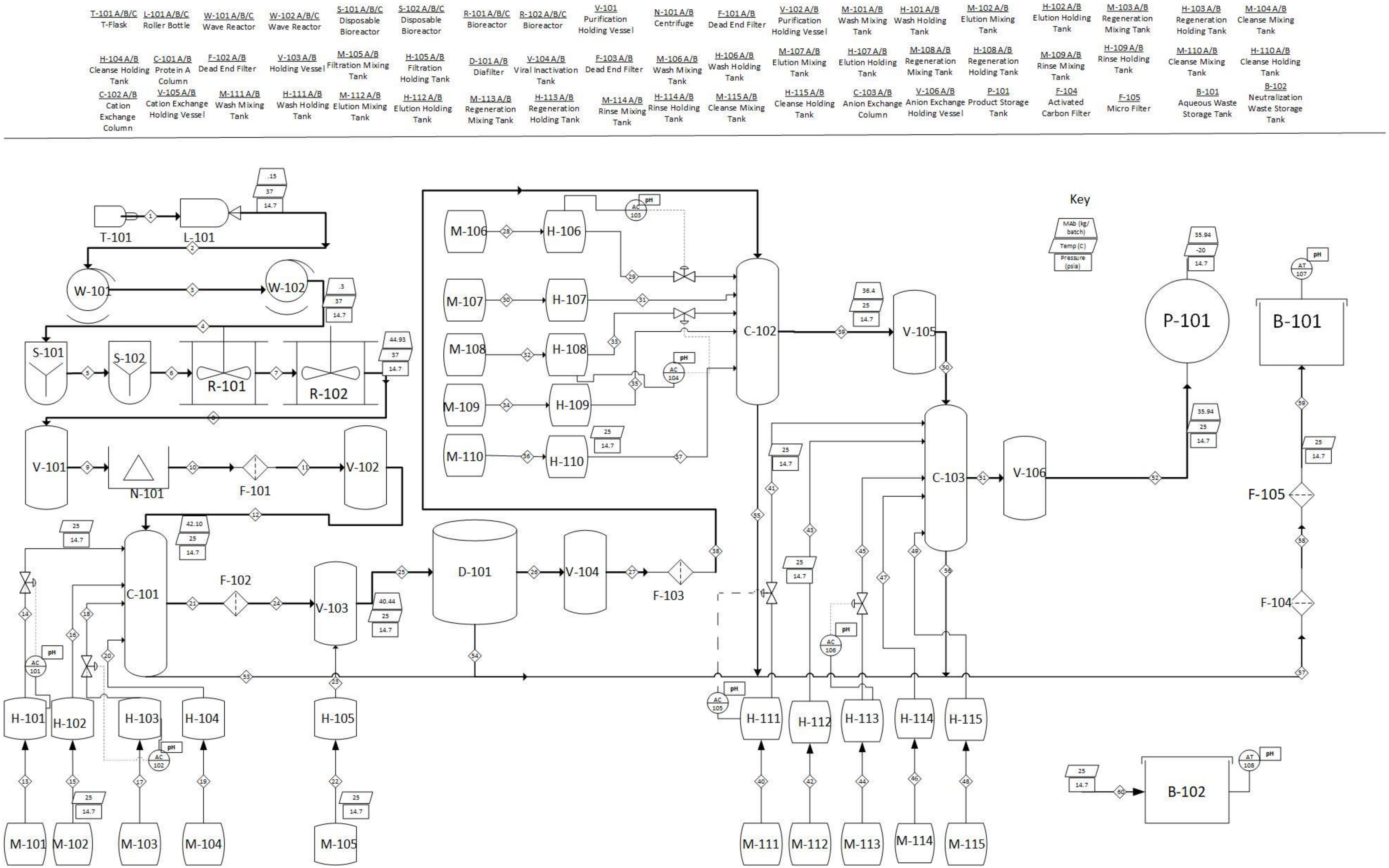
Media Prep

In designing this process, the first step in the production of MAbs is the preparation of the media that mixes with the biomass, which in this process is CHO cells. There are two types of media that can be mixed with the CHO cells, either serum-free powder which requires the addition of sterilized water, or liquid media bought directly from a manufacturer.

In terms of the process described above and researching both powder and liquid chemically defined media, it was determined that liquid media would be the best choice for the project. After gathering prices for both types of media, Lonza ProCHO AT serum-free media was chosen. Lonza ProCHO AT already contained the L-glutamine needed for the process. Lonza also proved to be more economical as the price for the liquid media was cheaper than both Lonza and Thermo Fisher powdered media with L-glutamine.

Seed Train & Production Reactors

Directly following the media prep portion of the process, the CHO cells and media transition to the seed train and production reactor portion of the process. The seed train consists of a 500mL T-flask, a 2.2 Roller Bottle, a 100 L Rocking Bioreactor, a 200 L Rocking Bioreactor, a 1200 L Disposable Bioreactor, and a 4000 Disposable Bioreactor. The production reactor portion of the process consists of a 10,000 L Bioreactor and a 30,000 L Bioreactor. The


T-101 A/B/C T-Flask
L-101 A/B/C Roller Bottle
W-101 A/B/C Wave Reactor
W-102 A/B/C Wave Reactor
S-101 A/B/C Disposable Bioreactor
S-102 A/B/C Disposable Bioreactor
R-101 A/B/C Bioreactor
R-102 A/B/C Bioreactor
V-101 Purification Holding Vessel
N-101 A/B Centrifuge
F-101 A/B Dead End Filter
V-102 A/B Purification Holding Vessel
M-101 A/B Wash Mixing Tank
H-101 A/B Wash Holding Tank
M-102 A/B Elution Mixing Tank
H-102 A/B Elution Holding Tank
M-103 A/B Regeneration Mixing Tank
H-103 A/B Regeneration Holding Tank
M-104 A/B Cleanse Mixing Tank
H-104 A/B Cleanse Holding Tank
C-101 A/B Protein A Column
F-102 A/B Dead End Filter
V-103 A/B Holding Vessel
M-105 A/B Filtration Mixing Tank
H-105 A/B Filtration Holding Tank
D-101 A/B Diafilter
V-104 A/B Viral Inactivation Tank
F-103 A/B Dead End Filter
M-106 A/B Wash Mixing Tank
H-106 A/B Wash Holding Tank
M-107 A/B Elution Mixing Tank
H-107 A/B Elution Holding Tank
M-108 A/B Regeneration Mixing Tank
H-108 A/B Regeneration Holding Tank
M-109 A/B Rinse Mixing Tank
H-109 A/B Rinse Holding Tank
M-110 A/B Cleanse Mixing Tank
H-110 A/B Cleanse Holding Tank
C-102 A/B Cation Exchange Column
V-105 A/B Cation Exchange Holding Vessel
M-111 A/B Wash Mixing Tank
H-111 A/B Wash Holding Tank
M-112 A/B Elution Mixing Tank
H-112 A/B Elution Holding Tank
M-113 A/B Regeneration Mixing Tank
H-113 A/B Regeneration Holding Tank
M-114 A/B Rinse Mixing Tank
H-114 A/B Rinse Holding Tank
M-115 A/B Cleanse Mixing Tank
H-115 A/B Cleanse Holding Tank
C-103 A/B Anion Exchange Column
V-106 A/B Anion Exchange Holding Vessel
P-101 Product Storage Tank
F-104 Activated Carbon Filter
F-105 Micro Filter
B-101 Aqueous Waste Storage Tank
B-102 Neutralization Waste Storage Tank
Key
MAb (kg/batch)
Temp (C)
Pressure (psia)

Stream	1	2	3	4	5	6	7	8
Media Added (L)	.225	.875	48.9	50	500	1400	3000	10000
Media Transferred (L)	0	.225	1.1	50	100	600	2000	5000
Total Media (L)	.225	1.1	50	100	600	2000	5000	15000
Number of Cells	1e6	1.02e6	1.93e6	2.86e6	1.22e7	3.83e7	9.42e7	2.81e8
Amount of Mab (g)	.2497	1.1035	49.9938	100.0416	601.1362	2000	5000	15000
Operating Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7
Operating Temperature (C)	37	37	37	37	37	37	37	37
Air (kg)	-	-	1117.3	45131.69	33351.93	36105.3	16675.97	50027.9
Time (hrs)	.241	..8158	33.13	20.46	75.28	59.38	46.78	56.7

Stream	8	9	10	11	12	13	14	15	16	17	18
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7
Temperature (C)	25	25	25	25	25	25	25	25	25	25	25
Acetic acid (kg)	-	-	-	-	-	-	-	-	-	172.54	22.39
Sodium Citrate (kg)	-	-	-	-	-	-	-	31.08	2.69	-	-
Polysorbate-80	-	-	-	-	-	-	-	-	-	-	-
EDTA (kg)	-	-	-	-	-	-	-	-	-	-	-
Ethyl Alcohol (kg)	-	-	-	-	-	700.12	145.34	-	-	-	-
NaCl (kg)	-	-	-	-	-	-	-	-	-	-	-
TRIS Base (kg)	-	-	-	-	-	-	-	-	-	-	-
TRIS HCl	-	-	-	-	-	-	-	-	-	-	-
KCl (kg)	-	-	-	-	-	-	-	-	-	-	-
KH2PO4 (kg)	-	-	-	-	-	-	-	-	-	-	-
NaH2PO4 (kg)	-	-	-	-	-	-	-	-	-	-	-
N-MDEA (kg)	-	-	-	-	-	-	-	-	-	-	-
Mab (kg)	44.93	44.93	-	44.93	44.93	-	-	-	-	-	-
Media (kg)	45248.59	45248.59	0.1	45248.58	45248.58	-	-	-	-	-	-
NaOH (kg)	-	-	-	-	-	-	-	-	-	-	-
H3PO4 (kg)	-	-	-	-	-	-	-	-	-	-	-
Water (kg)	-	-	-		-	-	-	-	-	-	-
WFI (kg)	-	-	-	-	-	6301.1	1308.09	17232.82	1490.62	28584.43	3708.77

Stream	19	20	21	22	23	24	25	26	27	28
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7
Temperature (C)	25	25	25	25	25	25	25	25	25	25
Acetic acid (kg)	-	-	18.75	-	-	18.75	18.76	6.9	6.9	-
Sodium Citrate (kg)	-	-	-	-	-	-	-	-	-	-
Polysorbate-80	-	-	-	-	-	-	-	-	.32	-
EDTA (kg)	141.39	21.82	-	-	-	-	-	-	-	-
Ethyl Alcohol (kg)	-	-	-	-	-	-	-	-	-	-
NaCl (kg)	70.69	10.9	-	-	-	-	-	-	-	80.97
TRIS Base (kg)	70.69	10.9	-	-	-	-	-	-	-	-
TRIS HCl	212.08	32.71	-	-	-	-	-	-	-	-
KCl (kg)	-	-	-	-	-	-	-	-	-	.03
KH2PO4 (kg)	-	-	-	-	-	-	-	-	-	.03
NaH2PO4 (kg)	-	-	-	-	-	-	-	-	-	9.90
N-MDEA (kg)	-	-	-	-	-	-	-	-	-	-
Mab (kg)	-	-	40.44	-	-	40.44	40.44	40.44	40.44	-
Media (kg)	-	-	-	-	-	-	-	-	-	-
NaOH (kg)	-	-	-	-	-	-	-	-	-	-
H3PO4 (kg)	-	-	-	-	-	-	-	-	-	-
Water (kg)	-	-	-	-	-	-	-	-	-	-
WFI (kg)	70198.74	10830.42	3107.05	3165.4	3165.4	3107.05	3166.25	3118	3118.69	8905.86

Stream	29	30	31	32	33	34	35	36	37	38
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7
Temperature (C)	25	25	25	25	25	25	25	25	25	25
Acetic acid (kg)	-	-	-	-	-	-	-	-	-	6.9
Sodium Citrate (kg)	-	-	-	-	-	-	-	-	-	-
Polysorbate-80 (kg)	-	-	-	-	-	-	-	-	-	.32
EDTA (kg)	-	-	-	-	-	-	-	-	-	-
Ethyl Alcohol (kg)	-	-	-	-	-	-	-	290.69	290.69	-
NaCl (kg)	80.97	-	-	173.99	173.99	15.17	15.17	-	-	-
TRIS Base (kg)	-	-	-	-	-	-	-	-	-	-
TRIS HCl	-	-	-	-	-	-	-	-	-	-
KCl (kg)	.03	-	-	-	-	-	-	-	-	-
KH2PO4 (kg)	.03	-	-	-	-	-	-	-	-	-
NaH2PO4 (kg)	9.90	-	-	-	-	2.88	2.88	-	-	-
N-MDEA (kg)	-	-	-	-	-	-	-	-	-	-
Mab (kg)	-	-	-	-	-	-	-	-	-	40.44
Media (kg)	-	-	-	-	-	-	-	-	-	-
NaOH (kg)	-	59.04	59.04	-	-	-	-	-	-	-
H3PO4 (kg)	-	-	-	-	-	-	-	-	-	-
Water (kg)	-	-	-	-	-	-	-	-	-	-
WFI (kg)	8905.86	2953.42	2953.42	2894.67	2894.67	275.6	257.6	2616.19	2616.19	3118.69

Stream	39	40	41	42	43	44	45	46	47	48	49
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7
Temperature (C)	25	25	25	25	25	25	25	25	25	25	25
Acetic acid (kg)	-	-	-	-	-	-	-	-	-	-	-
Sodium Citrate (kg)	-	-	-	-	-	-	-	-	-	-	-
Polysorbate-80 (kg)	-	-	-	-	-	-	-	-	-	-	-
EDTA (kg)	-	-	-	-	-	-	-	-	-	-	-
Ethyl Alcohol (kg)	-	-	-	-	-	-	-	-	-	436.03	436.03
NaCl (kg)	6.07	121.46	121.47	-	-	-	-	-	-	-	-
TRIS Base (kg)	-	-	-	-	-	-	-	88.67	88.67	-	-
TRIS HCl	-	-	-	-	-	-	-	-	-	-	-
KCl (kg)	-	.03	.03	13.65	13.65	261.23	261.23	-	-	-	-
KH2PO4 (kg)	-	03	.03	-	-	-	-	-	-	-	-
NaH2PO4 (kg)	6.07	14.84	14.85	-	-	-	-	-	-	-	-
N-MDEA (kg)	-	-	-	2.59	2.59	-	-	-	-	-	-
Mab (kg)	36.40	-	-	-	-	-	-	-	-	-	-
Media (kg)	-	-	-	-	-	-	-	-	-	-	-
NaOH (kg)	-	-	-	-	-	-	-	-	-	-	-
H3PO4 (kg)	-	-	-	-	-	-	-	-	-	-	-
Water (kg)	-	-	-	-	-	-	-	-	-	-	-
WFI (kg)	2007.64	13358.81	13500	248.04	248.04	4346.04	4346.04	4435.41	4435.41	3924.28	3924.28

Stream	50	51	52	53	54	55	56	57	58	59	60
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7
Temperature (C)	25	25	25	25	25	25	25	25	25	25	25
Acetic acid (kg)	-	-	-	3.63	11.86	6.9	-	22.39	-	-	-
Sodium Citrate (kg)	-	-	-	2.69	-	-	-	2.69	2.69	2.69	-
Polysorbate-80 (kg)	-	-	-	-	-	.32	-	.32	.32	.32	-
EDTA (kg)	-	-	-	21.81	-	-	-	21.81	-	-	-
Ethyl Alcohol (kg)	-	-	-	145.34	-	290.69	436.03	872.06	872.06	-	-
NaCl (kg)	6.07	-	-	10.9	-	264.06	127.53	402.49	402.49	-	-
TRIS Base (kg)	-	-	-	10.9	-	-	88.67	99.57	-	-	-
TRIS HCl	-	-	-	32.72	-	-	-	32.72	-	-	-
KCl (kg)	-	5.46	-	-	-	.02	269.45	274.93	274.93	-	-
KH2PO4 (kg)	-	-	-	-	-	.02	.03	.05	-	-	-
NaH2PO4 (kg)	1.15	-	-	-	-	11.62	16	27.62	-	-	-
N-MDEA (kg)	-	1.04	-	-	-	-	1.55	2.59	-	-	-
Mab (kg)	36.4	32.76	32.76	4.49	-	4.04	3.64	12.17	12.17	-	-
Media (kg)	-	-	-	45248.58	-	-	-	45248.59	45248.59	45248.59	-
NaOH (kg)	-	-	-	-	-	59.04	-	59.04	-	-	245.89
H3PO4 (kg)	-	-	-	-	-	-	-	-	-	-	880.89
Water (kg)	-	-	-	-	-	-	-	-	-	-	60373.51
WFI (kg)	2007.64	1806.4	1806.4	14230.84	3154.08	23500.3	30781.8	71667.02	71667.02	71667.02	29736.23

seed train is shown below in the Figure 3. The production reactors portion of the process is also shown below in Figure 4.

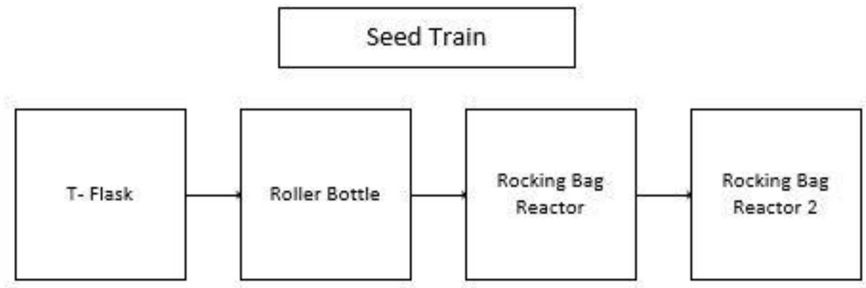


Figure 3: *Seed Train BFD*

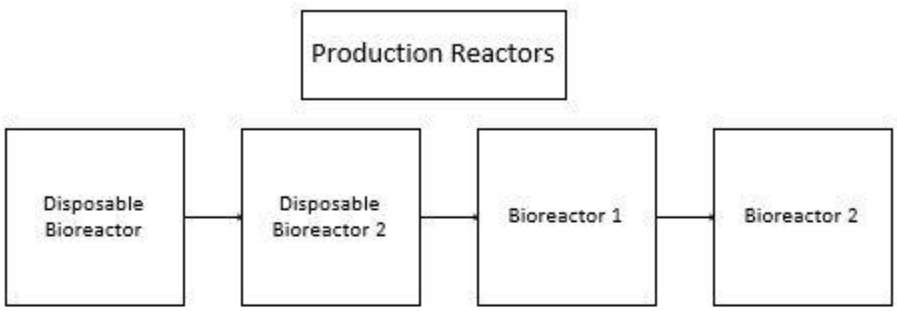


Figure 4: *Production Reactors BFD*

During the seed train and production reactor process, several assumptions are made. It is assumed during the seed train that the production of CHO cells is always in exponential growth. The assumption is made based upon the fact that the stationary phase is determined by the amount of glucose present. The glucose should not fall below 2 g/L, so it is assumed that the stationary phase is never reached. [2] Also, since the CHO cells are transferred into the same media, no lag time occurs after the first vial. Since lag time only occurs in the first vial, the assumption is made to allow one day for lag time within the process.

After assumptions were made about the growth of the CHO cells, reactor sizes were chosen. After a large literacy search, it showed that reactor volumes are picked arbitrarily or based on industry standards. Based on the MAb example in SuperPro Designer and optimization methods in MatlLab, it was decided the best sizes for the seed train reactors were the ones listed above. It was also assumed the reactors were halfway filled. Disposable reactors in the seed train process were chosen as they were cheaper, they prevented contamination, and lowered the turnaround time. The removal of the SIP and CIP steps due to the disposable reactor bags helped the most with cutting costs and lowering the turnaround time. The assumption was made to allow for extra volume to be added to the reactors or for the differing processes that are expected based on the project brief.

Once all basic assumptions were made, the seed train calculations were done based on kinetic models in MatLab software. Kinetics is used so cell density, glucose density, and MAb density can be tracked. Chapter 9 in *Essentials of Chemical Reaction Engineering* and Chapter 3 in *Environmental Biology* were used as references in determining kinetic models. The value of glucose consumption rate was also found to be 0.422 pg/cell day. [3] The equations used from both references are listed below:

$$2 = e^{\mu t}$$

$$t = doubling\ time$$

$$\mu = specific\ growth\ rate = 0.01925 \frac{1}{hrs}$$

$$r_g = \mu C_c$$

$$C_c = cell\ concentration$$

$$C_{co} = initial\ cell\ concentration = \frac{cells}{initial\ volume\ of\ media} = \frac{1 * 10^6\ cells}{0.25\ L}$$

$$\frac{dC_c}{dt} = r_g - r_d$$

$$r_d = cell\ death\ rate$$

$$\frac{dC_c}{dt} = \mu C_c$$

$$y_{G/c} = \frac{mass\ of\ glucose\ consumed}{new\ cells\ produced} = \frac{0.422 \frac{pg}{cell * day}}{0.01925 * 10^{-6} \frac{cell}{cell * hour}} = 9.134 * 10^{-7} \frac{g}{cell}$$

$$\frac{dC_G}{dt} = -y_{G/c} \mu C_c$$

$$G_o = 6.145 \frac{g}{L}$$

$$y_{P/c} = \frac{mass\ of\ product\ formed}{new\ cells\ formed}$$

$$\frac{dC_p}{dt} = y_{P/c} \mu C_c$$

The differential equations listed above were coded into MatLab in order to obtain the concentrations of glucose, CHO cells, and MAb over time. The Ode45 Solver was used to solve for the concentrations with respect to time. Based on the time needed per batch, it was decided that in order to reach the production goal of 1,000 kg/yr, three simultaneous batches need to be run. This assumption was made based on assuming the seed train cannot be started while one is already in progress.

Based on the results produced from MatLab, several optimization processes were run to find the lowest present worth cost of the process. The size of the last reactor in the process was varied to determine the cheapest, most efficient production option for the process. Ending reactor sizes of 10,000 L, 20,000 L, and 30,000 L were chosen to test. The following results are found below:

1. If the seed train is stopped at the 10,000 L container, a batch will take 238 hours including one day for lag time and one day for purification. Seven simultaneous batches would have to run 36 times a year to initially produce 1260 kg of MAb. However, after a 20% loss only 1008 kg of MAb would be produced. [4]
2. If the seed train is stopped at the 20,000 L container, a batch will take 274 hours including 1 day for lag time and 1 day for purification. Four simultaneous batches would have to run 32 times a year to initially produce 1280 kg of MAb. However, after a 20% loss only 1024 kg of MAb would be produced.
3. If the seed train is stopped at the 30,000 L container a batch will take 295 hours including 1 day for lag time and 1 day for purification. Three simultaneous batches would have to run 29 times a year to initially produce 1305 kg of MAb. However, after a 20% loss only 1044 kg of MAb would be produced.

Primary Recovery

After the seed train process of MAb production, the newly produced CHO cells, MAb, and media transition to the primary recovery step of the manufacturing process. The primary recovery portion of the manufacturing process is to ensure that we are generating as many MAb cells as possible while discarding of the unwanted CHO cells and media. The primary recovery portion of the process is shown below in Figure 5.

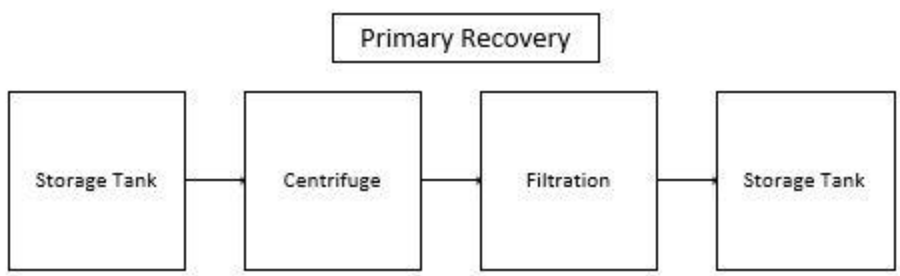


Figure 5: *Primary Recovery BFD*

After the 30,000 L bioreactor, the MAb, media, and CHO Cells are held in a 55,000 L storage tank prior to going through the centrifuge. This step ensures that all production will pool in one place before sending the newly formed MAb cells through the purification process. If production is running at titers below 5 g/L, only one of the purification train will be active. If production is making titers above 5 g/L, both purification trains will need to be active to achieve the desired product. [4] Once everything is in the storage tank, purification begins by sending everything through a centrifuge. The centrifuge separates the different layers of material by weight; therefore, the heavier layers are pulled down to the bottom to exit in the waste stream. This allows for the heavier media and CHO cells to exit in the waste stream while the MAb cells are transported to the filtering step of the primary recovery process. This removes about 80% of the CHO cells from the mixture in one step. The contents from the centrifuge are then passed through a filter, so any remaining CHO cells are left behind. Once filtering takes place, the remaining MAb and media, about 50,000 L total, are pooled in a storage tank before being passed through Protein A Chromatography.

It is important to note that beginning with the primary recovery process, Steaming-In-Place (SIP) and Cleaning-In-Place (CIP) take place in both storage tanks and the centrifuge. SIP and CIP were not needed before this step as the previous bioreactors were disposable. Both SIP and CIP processes are set up by using a flow rate to ensure proper cleanliness for each batch. The CIP process is five steps that are set up as follows: water rinse, base rinse, water rinse, acid rinse, followed by a final water rinse. [5] It is also important to note that all equipment in the primary recovery process is cleaned at the end of each batch before the next batch comes into the primary recovery area. Steam in place procedures were based on delivering steam at a flowrate of 1gpm from a 2” diameter pipe, based on industry standards. [6] This results in about 10 minutes of steaming for most pieces of equipment. CIP follows the standard practice of a 5-step cleaning procedure for most pieces of equipment. This process was a water rinse, a base cleanse with 0.5 M sodium hydroxide, another water rinse, an acid wash with 10 w% phosphoric acid, and a final rinse with WFI. These washes used the same flowrate as that of the SIP, with the aid and base step using less wash time but recirculating the flow to ensure equal residence time to clean while minimizing chemical usage. The total runtime for most CIP processes runs between 50-90 minutes based on the volume of the equipment, as the caustic and acid washes have residence times that need to be met to ensure proper sterilization of the equipment.

Protein A Chromatography

After primary recovery, the process is then purified by use of a Protein A Chromatography column. Protein A Chromatography is performed in a glass column with Protein A resin panels made of a variety of staphylococcus bacteria. The process catches the product stream while also allowing any previous solvent and impurities to flow past unhindered. [7] [8] The Protein A Chromatography process is shown below in Figure 6.

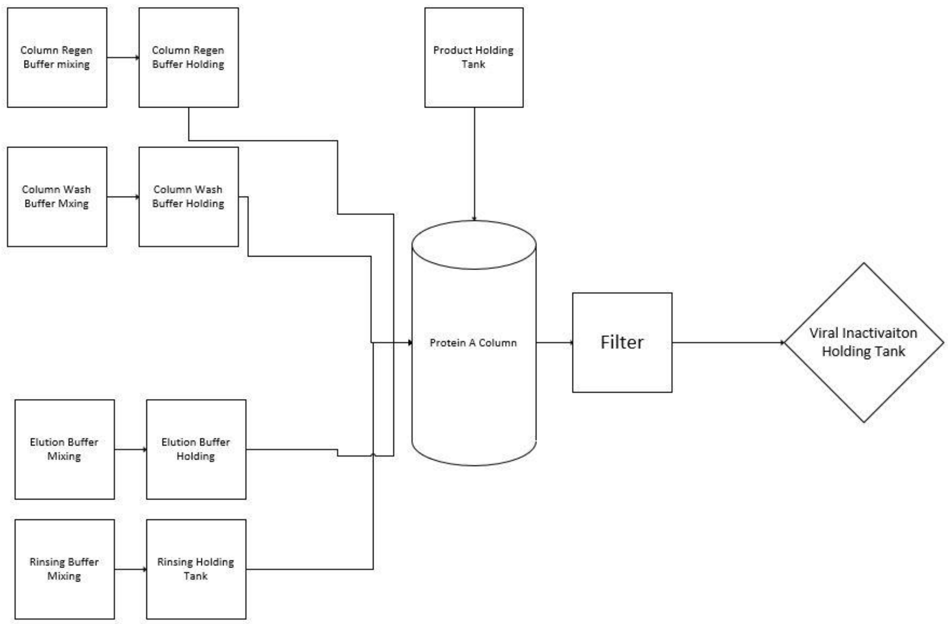


Figure 6: *Protein A Chromatography BFD*

Protein A Chromatography contains several elution steps that are intended to remove all remaining impurities from the primary recovery step, before flushing the product off the column. The column is initially rinsed with a mix of solvents; EDTA disodium, Sodium Chloride, TRIS Base, and TRIS HCl. This buffer is mixed and held in the Rinsing Buffer tanks. The column is then equilibrated with the same mixture. After that the column is washed with the solvent mixture, the production mixture is run over the column, followed by a wash of a sodium citrate solution to remove any further impurities from the column. This is mixed and stored in the Elution buffer tanks. Finally, an acetic acid wash is run through the column to fully remove all the product adhered to the column. This buffer was mixed and held in the column wash buffer tanks.   Once all solvents and brine mixtures are run through the column, the column follows a different CIP procedure; a caustic wash of .1M NaOH to cleanse the column, followed by a WFI wash. The column is also cleaned with a 10% ethyl alcohol mix before being the next batch of product. This solution is stored in the regeneration buffer tanks. This process uses 17,500 L of the mixed chemical solution, 31 kg of sodium citrate, 172 kg of acetic acid, and 700 kg of ethyl alcohol. All of these chemicals have been diluted with WFI.

By the end of Protein A Chromatography, all media has been removed from the product stream. The product stream contains a mixture of MAb, WFI, and acetic acid, which has been filtered through a microfiltration device to ensure any new contaminants that might have been introduced are now removed. Following the filtration step, the product stream is sent to a holding tank in preparation for viral inactivation.

Viral Inactivation

After Protein A Chromatography, the process goes through the virus inactivation stage. In the virus inactivation stage, the virus inside of the MAb cells is inactivated. Inactivation is completed by pulling WFI to a diafiltration device from the flushing tank to flush it and then running the production mixture though it into a holding tank. After the production mixture has been moved, it is then transferred back to the original holding tank to then be moved to the virus inactivation tank. Within the virus inactivation tank, Polysorbate-80, a detergent, is added to the mixture to inactivate any virus within the cells. This ensures the only remaining components inside the cells are the desired MAbs. Once virus inactivation is finished, the product stream is pulled through a polishing filter to remove any impurities which might have been transferred in with the WFI stream or the Polysorbate-80. The product is then transferred to the Cation Exchange Chromatography section of the process. This process requires about 0.32 kg of Polysorbate-80 per batch. The Viral Inactivation step of the process is shown below in Figure 7.

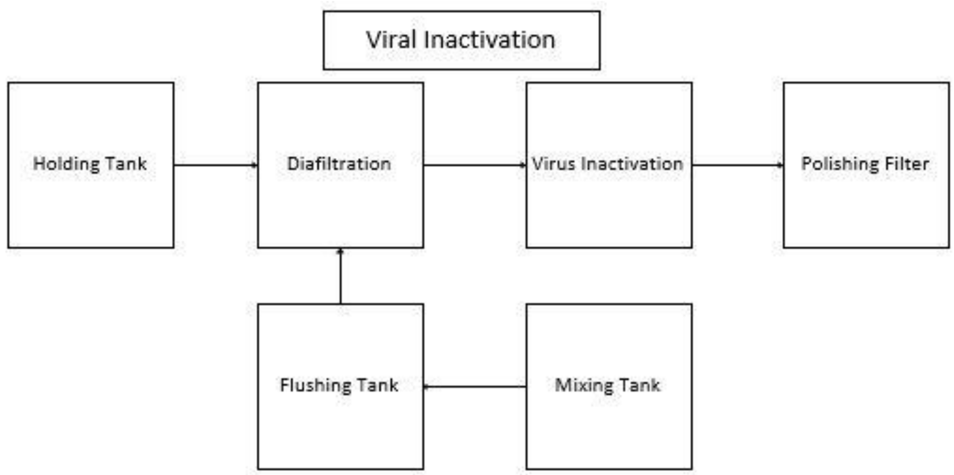


Figure 7: *Viral Inactivation BFD*

Cation Exchange Chromatography

Once Virus Inactivation is finished, the product stream is then transferred to the Cation Exchange Chromatography portion of the process. The column in the Cation Exchange Chromatography consists of a resin adhered to the glass column and is designed to specifically remove host protein cells, additional leached protein A, and aggregates of the antibodies which are no longer useful from the product stream. The resin has negatively charged substrates on the resin surface to adhere positively charged impurities while allowing the product to flow past. [9] The Cation Exchange Chromatography step of the process is shown below in Figure 8.

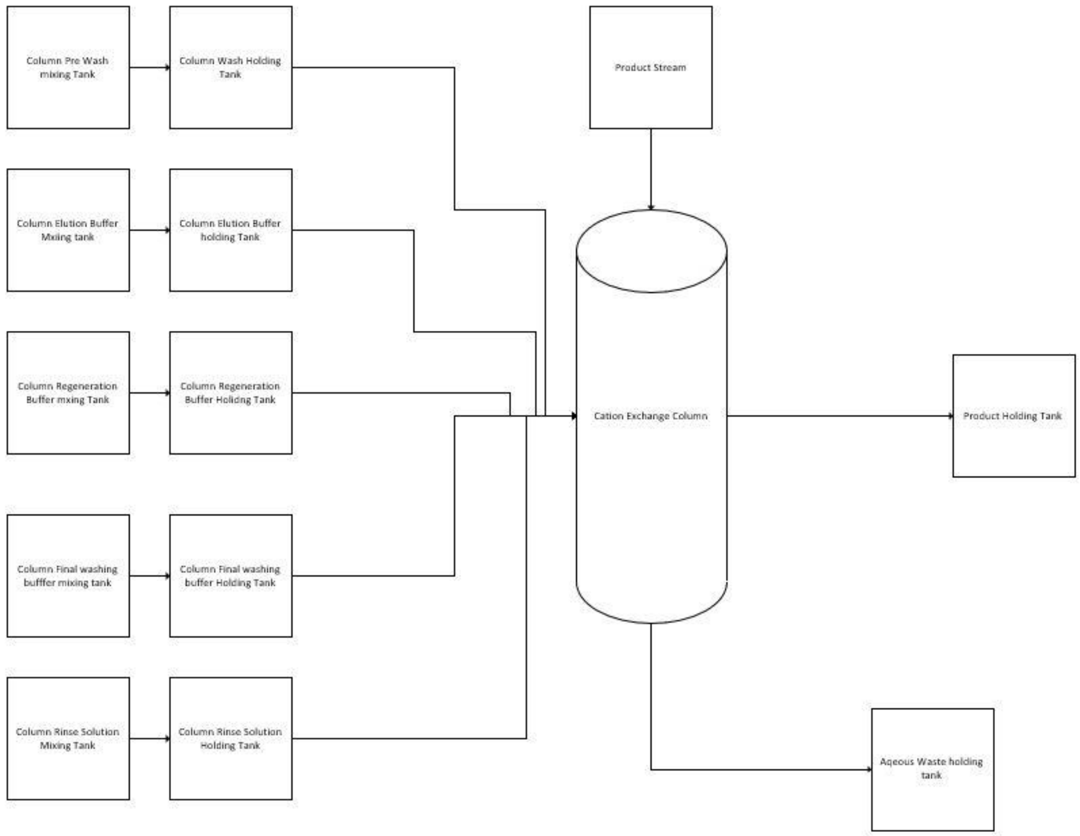


Figure 8: *Cation Exchange Chromatography BFD*

Cation Exchange Chromatography contains several elution steps that are intended to remove all remaining impurities before flushing the product off the column. The column is first washed with a mix of the following solvents: potassium chloride, sodium dihydrogen phosphate, potassium dihydrogen phosphate, and sodium chloride. After washing, the column is then equilibrated with the same mixture. This buffer solution is held in the wash tanks. After equilibration, it is held for a time before the product stream washes over, adhering the impurities. The column is then washed with a sodium hydroxide solution from the Elution buffer tank to remove some of the impurities followed by a sodium chloride wash from the regeneration tank to elute the column. The column is then washed with a sodium chloride and sodium dihydrogen phosphate solution from the final washing buffer tank to cleanse the column of any residual binding elements. This process uses about 10,000L of the chemical wash mixture, 59 kg of sodium hydroxide in the rinse stream, 174 kg of sodium chloride in the elution stream, and 15 kg of sodium chloride and 2.8 kg of sodium dihydrogen phosphate in the rinse stream.

Once all solvents are run through the column, the column follows the same CIP as the Protein A column; that is a caustic wash with 0.1 M NaOH and a WFI rinse, and then washed with a 10% weight ethyl alcohol solution from the rinse tank before moving to a storage tank. For the column size, this takes about 291 kg of ethyl alcohol per batch. The final product of the Cation Exchange Chromatography is held in the storage tank until it is transferred to the Anion Exchange Chromatography step of the production process.

Anion Exchange Chromatography

After Cation Exchange Chromatography, the product stream is run through the final purification methods, Anion Exchange Chromatography. Anion Exchange Chromatography is specifically designed to remove DNA, endotoxins, and leached Protein A from the stream. The column consists of a resin adhered to a glass column, with the resin having positively charged substrates on the surface to adhere to negatively charged impurities while also allowing the product to flow past. [10] The Anion Exchange Chromatography step of the process is shown below in Figure 9.

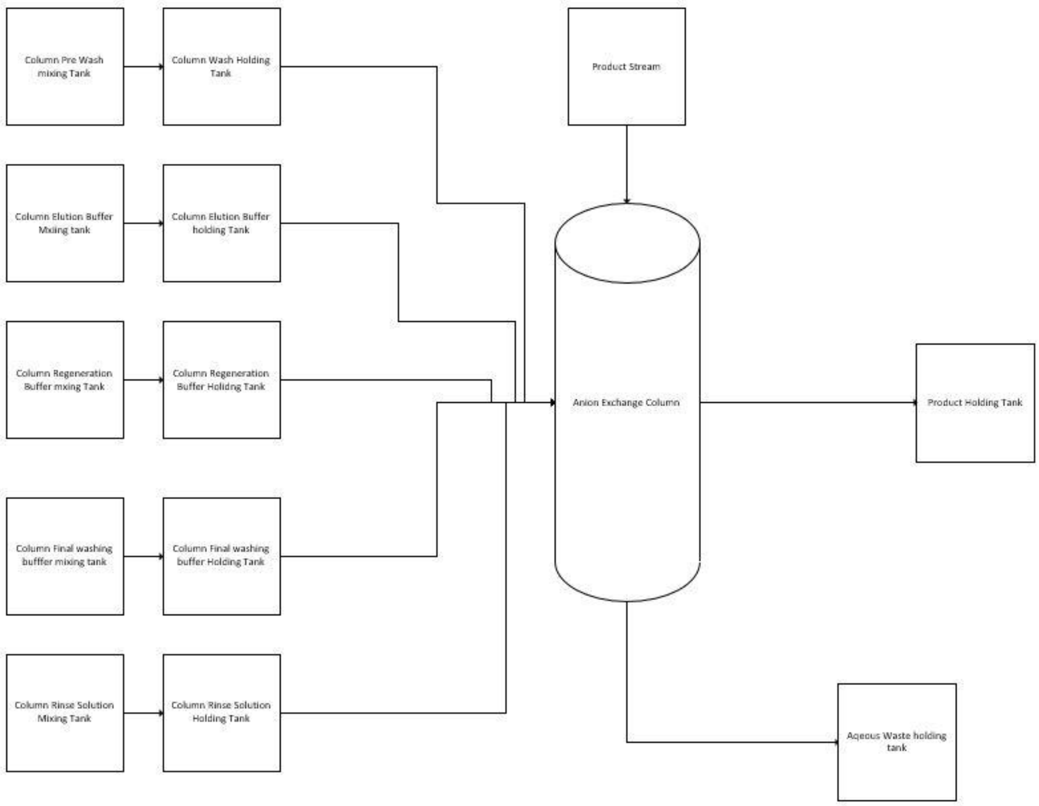


Figure 9: *Anion Exchange Chromatography BFD*

Anion Exchange Chromatography contains several elution steps that are intended to remove all remaining impurities before flushing the product off the column. The column is eluted with several solvents to remove the impurities. The column is first washed with a mixture of sodium chloride, potassium chloride, potassium dihydrogen phosphate, and sodium dihydrogen phosphate before being equilibrated with the same mixture from the wash tank. After equilibration, it is held for a time before the product stream washes over. Similarly to the Cation exchange column, this process involves the product washing over the column unimpaired while any impurities adhere to the column. The column is then washed with a mixture of potassium dihydrogen phosphate and N-Methyldiethanolamine (MDEA) from the elution buffer tank to remove some of the impurities followed by a potassium chloride wash from the regeneration buffer tank to further elute the column. Afterwards a TRIS Base solution from the final wash buffer tank is washed over the column to fully rinse any remaining adhering components off the column. Once all solvents are run through the column, the column follows the same CIP as the previous two columns; a 0.1 M NaOH wash followed by a WFI rinse, and then washed with a 10% weight ethyl alcohol solution from the rinse solution tank before moving to a storage tank. This process uses about 15,000 L of the chemical mixture, 13.5 kg potassium chloride and 2.5 kg of MDEA in the wash stream, 260 kg of potassium chloride in the elution stream, 88 kg of TRIS Base in the rinse stream, and 436 kg of ethyl alcohol per batch of the process. [10]

Storage

At this point the product has been purified, filtered, and "polished". It is now ready to store, so it is sent to large tanks and refrigerated to ensure its viability for the required year. This cold room is maintained at the –20 degrees Celsius by a glycerol cooling system. Roughly 20% of the product has been lost over the duration of the purification train. This value is pulled from literary expectations. [11]

Waste Disposal and Treatment

The waste from all steps, including the column solvents, are gathered into a single large tank, and then pH tested. The solution is neutralized as needed; however, this is unlikely due to the large amount of WFI which is present within the tank. This large volume should dilute the solvents to such a large extent that the pH is relatively near neutral. This tank is filtered twice, first with an activated carbon filter, and second with a sand microfiltration unit. These are designed to remove a majority of the chemicals from the process stream, as these chemicals cannot be emptied into the sewer. [12] The only exceptions to this are potassium citrate and Polysorbate-80. This chemical waste is sent to a disposal service, and the cost of disposal is noted. The only exceptions to this compiling tank are the NaOH solutions used in CIP, the NaOH washes from the Protein A, Cation Exchange, and Anion exchange operations and the phosphoric acid solution used for CIP. These are sent to a separate tank and used to neutralize each other. After they are added, the pH is tested and neutralized as needed. After this, the waste is then sent to the city drain.

Energy Balance and Utility Requirements

Table 6 and Table 7 below show both the annual utility usage for the proposed design as well as the annual utility cost for the facility respectively. SuperPro Designer gave values for the amount of steam usage in MT per year and electricity in kW-hr per year. SuperPro Designer also provided the amount of both water and WFI the process uses at each step in the process. Sewer values as well as waste sent to the flare per year were given in SuperPro Designer as well. The amount of air used per year was calculated based on values given by SuperPro Designer, and the number of operators needed was based on the labor calculation given in the book *Analysis, Synthesis, and Design*. Lastly, biohazard waste was calculated assuming each bag in the disposable reactors were one pound for a total of 348 lb of waste. [13]

Table 6: *Yearly Utility Usage*

Yearly Utility Usage								
	Upstream	Primary Recovery	Protein A	Viral Inactivation	CEX	AEX	Storage	Total Process
Steam (MT)	53	54	3,434	862	1,694	7,026	-	13,123
Electricity (kWhr)	50,333	9	3,581	22,937	6,145	1,897	64,344	149,246
Water (L)	85,813	58,695	3,795,551	1,353,500	5,305,937	20,641,516	-	31,241,012
WFI (L)	42,907	29,347	58,459,522	5,898,167	18,750,847	82,894,661	-	166,075,451
Sewer (gal)	-	-	-	-	-	-	-	52,128,450
Air(kg)	1,263,724	-	-	-	-	-	-	1,263,74
Labor (operators)	-	-	-	-	-	-	-	21
To Flare (ton)	-	-	-	-	-	-	-	1.89
Biohazard Waste (lb)	348	-	-	-	-	-	-	348

Table 7: *Yearly Utility Cost*

Yearly Utility Cost								
	Upstream	Primary Recovery	Protein A	Viral Inactivation	CEX	AEX	Storage	Total Process
Steam	$630	$648	$41,208	$10,344	$20,328	$84,312	-	$157,470
Electricity	$2,517	$0.43	$179	$1,147	$307	$95	$3,217	$7,462
Water	$70	$48	$33,805	$3,938	$13,063	$56,220	-	$107,144
WFI	$113	$78	$154,450	$15,583	$49,540	$219,008	-	$438,772
Sewer	-	-	-	-	-	-	-	$260,642
Air	$3,008	-	-	-	-	-	-	$3,008
Labor	-	-	-	-	-	-	-	$1,023,750
To Flare	-	-	-	-	-	-	-	$214
Biohazard Waste	$171							
Total	$6,512	$774	$229,642	$31,012	$83,238	$359,635	$3,217	$1,998,636

Pricing for electricity, WFI, water, and sewer waste were given in the design brief while the pricing value of steam at $12/MT was taken from the SuperPro Designer software. Pricing for labor was determined by assuming $16.25 per hour, as that was the average salary of a pharmaceutical operator per hour. [14] Compressed air was priced at $2.38 per 1000 kg and flare waste was calculated as $112.97 per ton. [15]

The only steam requirements for the plant are for SIP processes, which do not involve a transfer of heat to product streams or intermediate streams, but are instead a way to prepare the equipment and vessels for the incoming product, removing any detritus or impurities that may have accumulated since the previous CIP step. This steam has no effect on process or intermediate streams directly, merely cleaning the equipment. Because of this, the steam is purchased at the desired pressure and temperature, used to clean the equipment, and sent back into the city. This steam has already been optimized, as it was elected to use higher temperature steam and larger diameter pipes to minimize the steam flowrate into the equipment while maximizing the cleaning capacity of the steam. This is based upon a study done on the heat and cleaning capacity relationship of steam for SIP processes [6]. Additionally, this SIP was minimized, both through the steam flowrate and the amount of time needed to steam the process equipment.

For the CIP process, the amount of chemicals as well as the volume of water utilized were both minimized. This was done after determining that the residence time of the chemicals was more necessary to the cleaning process compared to the volume or concentration of chemicals. For this reason, 0.5 M sodium hydroxide was selected as the caustic wash for all equipment aside from the columns, which used 0.1 M sodium hydroxide due to the more sensitive nature of the column resins. [5] Additionally, 10% by weight phosphoric acid was selected for the acid wash due to its strong cleaning capacity without reactivity issues such as would be included with the use of hydrochloric or sulfuric acid. Due to these considerations, the residence time was increased for all the equipment by adding a recirculation step to the cleaning of all items. This increased the duration of the CIP step; however, this is not a concern due to the large time gap between batches due to the seed train incubation time. This increase in residence time led to a full minimization of acid and base requirements, which allowed the time for injection to be significantly reduced as well as the flowrate of the chemicals. Additionally, with the reduction of acid and base, the flowrate of water rinses and WFI rinse were also able to be reduced. It was elected to use water for the initial and intermediate rinses to simply save money due to the expense of WFI and use WFI for the final rinse after the acid wash due to the need for purity within the equipment.

This minimization of water, WFI, and chemical usage was economically as well as environmentally motivated. It was also decided to minimize waste further by utilizing the acid stream and the base stream from the CIP processes to neutralize each other. The waste from the CIP of all apparatuses in the process are pooled, which allows an almost total neutralization due to the massive volume of WFI and water, as well as the true chemical neutralization reaction, which only produces a water soluble salt which is not hazardous to wildlife or the environment, and thus can be flushed down the drain. This eliminates any special expense for the disposal of this waste.

Equipment List /Unit Descriptions/Spec Sheet

Table 8: *Equipment List*

Equipment List						
Unit Number	Unit Type	MOC	Size	Quantity	Operating Temperature	Operatin g Pressure
T-101 A/B/C/D	T-Flask	Plastic	500 mL	3	37	14.7
L-101 A/B/C/D	Roller Bottle	Plastic	2.2 L	3	37	14.7
W-101 A/B/C/D	Wave Reactor	SS316*	100 L	3	37	14.7
W-102 A/B/C/D	Wave Reactor	SS316*	200 L	3	37	14.7
S-101 A/B/C/D	Disposable Bioreactor	SS316*	1,200 L	3	37	14.7
S-102 A/B/C/D	Disposable Bioreactor	SS316*	4,000 L	3	37	14.7
R-101 A/B/C/D	Bioreactor	SS316*	10,000 L	3	37	14.7
R-102 A/B/C/D	Bioreactor	SS316*	30,000 L	3	37	14.7
V-101 A/B	Purification Holding Tank	SS316	55,000 L	1	25	14.7
N-101 A/B	Centrifuge	SS316	50,000 L/h	2	25	14.7
F-101 A/B	Dead End Filter	SS316*	190 m^2	2	25	14.7
V-102 A/B	Purification Holding Tank	SS316	55,000 L	2	25	14.7
M-101 A/B	Wash Mixing Tank	SS316	20,000 L	2	25	14.7
H-101 A/B	Wash Holding Tank	SS316	20,000 L	2	25	14.7
M-102 A/B	Elution Mixing Tank	SS316	35,000 L	2	25	14.7
H-102 A/B	Elution Holding Tank	SS316	35,000 L	2	25	14.7
M-103 A/B	Regeneration Mixing Tank	SS316	80,000 L	2	25	14.7

H-103 A/B	Regeneration Holding Tank	SS316	80,000 L	2	25	14.7
M-104 A/B	Cleanse Mixing Tank	SS316	10,000L	2	25	14.7
H-104 A/B	Cleanse Holding Tank	SS316	10,000L	2	25	14.7
C-101 A/B	Protein A Column	Glass	1,570 L	2	25	14.7
F-102 A/B	Dead End Filter	SS316*	30 m^2	2	25	14.7
M-105 A/B	Filtration Mixing Tank	SS316	4,000 L	2	25	14.7
H-105 A/B	Filtration Holding Tank	SS316	4,000 L	2	25	14.7
V-103 A/B	Holding Tank	SS316	4,000 L	2	25	14.7
D-101 A/B	Diafiltration	SS316	40 m^2	2	25	14.7
V-104 A/B	Viral Inactivation Tank	SS316	4,000 L	2	25	14.7
F-103 A/B	Dead End Filter	SS316*	20 m^2	2	25	14.7
M-106 A/B	Wash Mixing Tank	SS316	4,000 L	2	25	14.7
H-106 A/B	Wash Holding Tank	SS316	4,000 L	2	25	14.7
M-107 A/B	Elution Mixing Tank	SS316	4,000 L	2	25	14.7
H-107 A/B	Elution Holding Tank	SS316	4,000 L	2	25	14.7
M-108 A/B	Regeneration Mixing Tank	SS316	500 L	2	25	14.7
H-108 A/B	Regeneration Holding Tank	SS316	500 L	2	25	14.7
M-109 A/B	Rinse Mixing Tank	SS316	10,000 L	2	25	14.7
H-109 A/B	Rinse Holding Tank	SS316	10,000 L	2	25	14.7
M-110 A/B	Cleanse Mixing Tank	SS316	4,000 L	2	25	14.7
H-110 A/B	Cleanse Holding Tank	SS316	4,000 L	2	25	14.7
C-102 A/B	Cation Exchange Column	Glass	500 L	2	25	14.7
V-105 A/B	Exchange Holding Tank	SS316	2,500 L	2	25	14.7
M-111 A/B	Wash Mixing Tank	SS316	5,000 L	2	25	14.7
H-111	Wash Holding Tank	SS316	5,000 L	2	25	14.7

A/B						
M-112 A/B	Elution Mixing Tank	SS316	5,000 L	2	25	14.7
H-112 A/B	Elution Holding Tank	SS316	5,000 L	2	25	14.7
M-113 A/B	Regeneration Mixing Tank	SS316	500 L	2	25	14.7
H-113 A/B	Regeneration Holding Tank	SS316	500 L	2	25	14.7
M-114 A/B	Rinse Mixing Tank	SS316	15,000 L	2	25	14.7
H-114 A/B	Rinse Holding Tank	SS316	15,000 L	2	25	14.7
M-115 A/B	Cleanse Mixing Tank	SS316	5,000 L	2	25	14.7
H-115 A/B	Cleanse Holding Tank	SS316	5,000 L	2	25	14.7
C-103 A/B	Anion Exchange Column	Glass	1,500 L	2	25	14.7
V-106 A/B	Final Holding Tank	SS316	2,500 L	2	25	14.7
P-101	Storage Tank	SS316	4,000 L	29	-20	14.7
F-104	Activated Carbon Filter	SS316	290 m^2	1	25	14.7
F-105	Microfilter	SS316	280 m^2	1	25	14.7
B-101	Aqueous Waste Tank	SS316	15,000 L	1	25	14.7
B-102	Neutralization Waste Tank	SS316	200,000,000 L	1	25	14.7

Table 9: *Equipment Function*

Equipment Function		
Unit Number	Unit Type	Function
T-101 A/B/C/D	T-Flask	Promotes growth of CHO Cells and Production of MAb
R-101 A/B/C/D	Roller Bottle	Promotes growth of CHO Cells and Production of MAb
W-101 A/B/C/D	Wave Reactor	Promotes growth of CHO Cells and Production of MAb
W-102 A/B/C/D	Wave Reactor	Promotes growth of CHO Cells and Production of MAb
S-101 A/B/C/D	Disposable Bioreactor	Promotes growth of CHO Cells and Production of MAb
S-102 A/B/C/D	Disposable Bioreactor	Promotes growth of CHO Cells and Production of MAb
R-101 A/B/C/D	Bioreactor	Promotes growth of CHO Cells and Production of MAb
R-102 A/B/C/D	Bioreactor	Promotes growth of CHO Cells and Production of MAb
V-101 A/B	Purification Holding Tank	Gathering of all of MAb, Media, and CHO Cells from all production lines and pool together.
N-101 A/B	Centrifuge	Separate the Media and CHO Cells from the MAb
F-101 A/B	Dead End Filter	Filter out all of the CHO cells from the process
V-102 A/B	Purification Holding Tank	Gathers the product from the primary recovery step of the process and holds it until it moves on to Protein A Chromatography
M-101 A/B	Wash Mixing Tank	Mixes buffer for the wash step in the Protein A Column
H-101 A/B	Wash Holding Tank	Holds buffer until the wash step in the Protein A Column
M-102 A/B	Elution Mixing Tank	Mixes buffer for the elution step in the Protein A Column
H-102 A/B	Elution Holding Tank	Holds buffer until the elution step in the Protein A Column
M-103 A/B	Regen Mixing Tank	Mixes buffer for the regeneration step in the Protein A Column
H-103 A/B	Regen Holding Tank	Holds buffer until the regeneration step in the Protein A Column
M-104 A/B	Cleanse Mixing Tank	Mixes buffer for the cleanse step in the Protein A Column
H-104 A/B	Cleanse Holding Tank	Holds buffer until the cleanse step in the Protein A Column
C-101 A/B	Protein A Column	Remove majority of impurities form product stream
F-102 A/B	Dead End Filter	Filter out chemicals and possible sediments which might contaminate stream

M-105 A/B	Filtration Mixing Tank	Mix water needed for filtration flushing
H-105 A/B	Filtration Wash Holding	Hold water used in each filtration flush step
V-103 A/B	Holding Tank	Gather post column product to store before next step
D-101 A/B	Diafiltration	Filter out majority of acetic acid in product stream, along with any remaining sediments
V-104 A/B	Viral Inactivation Tank	Deactivate the virus with Polysorbate-80 to ensure all remining biological material is only viable Mab
F-103 A/B	Dead End Filter	Filter out any sediments or impurities which entered with the Polysorbate-80 stream
M-106 A/B	Wash Mixing Tank	Mixes buffer for the wash step in the CEX Column
H-106 A/B	Wash Holding Tank	Holds buffer until the wash step in the CEX Column
M-107 A/B	Elution Mixing Tank	Mixes buffer for the elution step in the CEX Column
H-107 A/B	Elution Holding Tank	Holds buffer until the elution step in the CEX Column
M-108 A/B	Regen Mixing Tank	Mixes buffer for the regeneration step in the CEX Column
H-108 A/B	Regen Holding Tank	Holds buffer until the regeneration step in the CEX Column
M-109 A/B	Rinse Mixing Tank	Mixes buffer for the rinse step in the CEX Column
H-109 A/B	Rinse Holding Tank	Holds buffer until the rinse step in the CEX Column
M-110 A/B	Cleanse Mixing Tank	Mixes buffer for the cleanse step in the CEX Column
H-110 A/B	Cleanse Holding Tank	Holds buffer until the cleanse step in the CEX Column
C-102 A/B	Cation Exchange Column	Remove remaining impurities from the product stream, specifically host cell protein and aggregates
V-105 A/B	Exchange Holding Tank	Hold the post column product stream fractions prior to following step
M-111 A/B	Wash Mixing Tank	Mixes buffer for the wash step in the AEX Column
H-111 A/B	Wash Holding Tank	Holds buffer until the wash step in the AEX Column
M-112 A/B	Elution Mixing Tank	Mixes buffer for the elution step in the AEX Column
H-112 A/B	Elution Holding Tank	Holds buffer until the elution step in the AEX Column
M-113 A/B	Regen Mixing Tank	Mixes buffer for the regeneration step in the AEX Column
H-113 A/B	Regen Holding Tank	Holds buffer until the regeneration step in the AEX Column
M-114	Rinse Mixing Tank	Mixes buffer for the rinse step in the AEX Column

A/B		
H-114 A/B	Rinse Holding Tank	Holds buffer until the rinse step in the AEX Column
M-115 A/B	Cleanse Mixing Tank	Mixes buffer for the cleanse step in the AEX Column
H-115 A/B	Cleanse Holding Tank	Holds buffer until the cleanse step in the AEX Column
C-103 A/B	Anion Exchange Column	Remove any remaining impurities from the product stream, specifically any leached protein A, endotoxins, or DNA.
V-106 A/B	Final Holding Tank	Gather and hold product stream from column prior to sending to storage
P-101	Storage Tank	Stores final product of MAb for up to a year
F-104	Activated Carbon Filter	Remove particulate chemicals which cannot be disposed in sewer from waste stream
F-105	Microfilter	Remove all aqueous chemicals which cannot be disposed of in the sewer from waste stream
B-101	Aqueous Waste Tank	Store aqueous waste prior to disposal in the sewer
B-102	Neutralization Waste Tank	Store all neutralization waste from CIP steps across entire process prior to neutralization and disposal

Table 10: *Equipment Spec Sheet*

Reactors	**T-101 (A/B/C/D)**	**R-101 (A/B/C/D)**	**V-101 (A/B/C/D)**	**V-102 (A/B/C/D)**	**S-101 (A/B/C/D)**	**S-102 (A/B/C/D)**	**R-101 (A/B/C/D)**	**R-102 (A/B/C/D)**	-	-	-	-	-	-	-
Type	T-flask	Roller Bottle	Wave Reactor	Wave Reactor	Disposable Bioreactor	Disposable Reactor	Bioreactor	Bioreactor	-	-	-	-	-	-	-
Volume (L)	1	2	100	200	1,200	4,000	10,000	30,000	-	-	-	-	-	-	-
Temperature (°C)	37	37	37	37	37	37	37	37	-	-	-	-	-	-	-
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	-	-	-	-	-	-	-
MOC	Plastic	Plastic	SS316	SS316	SS316	SS316	SS316	SS316	-	-	-	-	-	-	-
Vessels	**V-101 (A/B)**	**V-102 (A/B)**	**V-103 (A/B)**	**V-104 (A/B)**	**V-105 (A/B)**	**V-106 (A/B)**	-	-	-	-	-	-	-	-	-
Type	Purification Holding Tank	Purification Holding Tank	Holding Tank	Viral Inactivation Tank	Exchange Holding Tank	Final Holding Tank	-	-	-	-	-	-	-	-	-
Volume (L)	55,000	55,000	4,000	4,000	2,500	2,500	-	-	-	-	-	-		-	-
Temperature (°C)	25	25	25	25	25	25	-	-	-	-	-	-	-	-	-
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	-	-	-	-	-	-	-	-	-
MOC	SS316	SS316	SS316	SS316	SS316	SS316	-	-	-	-	-	-	-	-	-
Columns	**C-101 (A/B)**	**C-102 (A/B)**	**C-103 (A/B)**	-	-	-	-	-	-	-	-	-	-	-	-
Type	Protein A Column	Cation Exchange Column	Anion Exchange Column	-	-	-	-	-	-	-	-	-	-	-	-
Volume (L)	1,570	500	1,500	-	-	-	-	-	-	-	-	-	-	-	-
Temperature (°C)	25	25	25	-	-	-	-	-	-	-	-	-	-	-	-
Pressure (psia)	14.7	14.7	14.7	-	-	-	-	-	-	-	-	-	-	-	-
MOC	Glass	Glass	Glass	-	-	-	-	-	-	-	-	-	-	-	-
Mixing Tanks	**M-101 (A/B)**	**M-102 (A/B)**	**M-103 (A/B)**	**M-104 (A/B)**	**M-105 (A/B)**	**M-106 (A/B)**	**M-107 (A/B)**	**M-108 (A/B)**	**M-109 (A/B)**	**M-110 (A/B)**	**M-111 (A/B)**	**M-112 (A/B)**	**M-113 (A/B)**	**M-114 (A/B)**	**M-115 (A/B)**
Type	Wash Mixing Tank	Elution Mixing Tank	Regeneration Mixing Tank	Cleanse Mixing Tank	Filtration Mixing Tank	Wash Mixing Tank	Elution Mixing Tank	Regeneration Mixing Tank	Rinse Mixing Tank	Cleanse Mixing Tank	Wash Mixing Tank	Elution Mixing Tank	Regeneration Mixing Tank	Rinse Mixing Tank	Cleanse Mixing Tank
Volume (L)	20,000	35,000	80,000	10,000	4,000	4,000	4,000	500	10,000	4,000	5,000	5,000	500	15,000	5,000
Temperature (°C)	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7
MOC	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316
Holding Tanks	**H-101 (A/B)**	**H-102 (A/B)**	**H-103 (A/B)**	**H-104 (A/B)**	**H-105 (A/B)**	**H-106 (A/B)**	**H-107 (A/B)**	**H-108 (A/B)**	**H-109 (A/B)**	**H-110 (A/B)**	**H-111 (A/B)**	**H-112 (A/B)**	**H-113 (A/B)**	**H-114 (A/B)**	**H-115 (A/B)**
Type	Wash Holding Tank	Elution Holding Tank	Regeneration Holding Tank	Cleanse Holding Tank	Filtration Holding Tank	Wash Holding Tank	Elution Holding Tank	Regeneration Holding Tank	Rinse Holding Tank	Cleanse Holding Tank	Wash Holding Tank	Elution Holding Tank	Regeneration Holding Tank	Rinse Holding Tank	Cleanse Holding Tank
Volume (L)	20,000	35,000	80,000	10,000	4,000	4,000	4,000	500	10,000	4,000	5,000	5,000	500	15,000	5,000
Temperature (°C)	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7	14.7
MOC	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316	SS316
Filters	**F-101 (A/B)**	**F-102 (A/B)**	**F-103 (A/B)**	**F-104 (A/B)**	**F-105 (A/B)**	**D-101 (A/B)**	-	-	-	-	-	-	-	-	-
Type	Dead End Filter	Dead End Filter	Dead End Filter	Activated Carbon Filter	Microfilter	Diafilter	-	-	-	-	-	-	-	-	-
Volume (m2)	190	30	20	290	280	40	-	-	-	-	-	-	-	-	-
Temperature (°C)	25	25	25	25	25	5	-	-	-	-	-	-	-	-	-
Pressure (psia)	14.7	14.7	14.7	14.7	14.7	14.7	-	-	-	-	-	-	-	-	-
MOC	SS316	SS316	SS316	SS316	SS316	SS316	-	-	-	-	-	-	-	-	-
Storage Tanks and Centrifuge	**P-101**	**B-101**	**B-102**	**N-101**	-	-	-	-	-	-	-	-	-	-	-
Type	Product Storage	Aqueous Waste Tank	Neutralization Waste Storage	Centrifuge	-	-	-	-	-	-	-	-	-	-	-
Volume (L or L/hr (centrifuge))	4,000	15,000	200,000,000	50,000	-	-	-	-	-	-	-	-		-	-
Temperature (°C)	-20	25	25	25	-	-	-	-	-	-	-	-	-	-	-
Pressure (psia)	14.7	14.7	14.7	14.7	-	-	-	-	-	-	-	-	-	-	-
MOC	SS316	SS316	SS316	SS316	-	-	-	-	-	-	-	-	-	-	-

Equipment Cost Summary

Table 11: *Equipment Cost Summary*

Equipment Cost Summary						
Quantity	Name	Description	Unit Cost	Purchase Cost	Installed Cost Multiplier	Total Installed Cost
3	W-101	Wave Reactor Skid Volume: 100 L	$255,000	$765,000	1.5	$1,147,500
3	W-102	Wave Reactor Skid Volume: 200 L	$255,000	$765,000	1.5	$1,147,500
3	S-101	Disposable Bioreactor Skid Volume: 200 L	$269,316	$807,948	1.5	$1,211,922
3	S-102	Disposable Bioreactor Skid Volume: 4,000 L	$897,839	$2,693,517	1.5	$4,040,276
3	R-101	Bioreactor Volume: 10,000 L	$1,738,000	$5,214,000	1.3	$6,778,200
3	R-102	Bioreactor Volume: 30,000 L	$2,568,000	$7,704,000	1.3	$10,015,200
1	V-101	Purification Holding Tank Volume: 55,000 L	$430,000	$430,000	1.3	$559,000
2	N-101	Centrifuge Capacity: 50,000 L/h	$122,000	$244,000	1.5	$366,000
2	F-101	Dead End Filter: Area: 190 m^2	$671,000	$1,342,000	1.5	$2,013,000
2	V-102	Purification Holding Tank Volume: 55,000 L	$430,000	$860,000	1.3	$1,118,000
2	M-101	Wash Mixing Tank Volume: 20,000 L	$319,000	$638,000	1.3	$829,400
2	H-101	Washing Holding Tank Volume: 20,000 L	$319,000	$638,000	1.3	$829,400
2	M-102	Elution Mixing Tank Volume: 35,000 L	$364,000	$728,000	1.3	$946,400
2	H-102	Elution Holding Tank Volume: 35,000 L	$364,000	$728,000	1.3	$946,400
2	M-103	Regen Mixing Tank Volume: 80,000 L	$487,000	$974,000	1.3	$1,266,200
2	H-103	Regen Holding Tank Volume: 80,000 L	$487,000	$974,000	1.3	$1,266,200
2	M-104	Cleanse Mixing Tank Volume: 10,000 L	$287,000	$574,000	1.3	$746,200
2	H-104	Cleanse Holding Tank Volume: 10,000 L	$287,000	$571,000	1.3	$746,200
2	C-101	Protein A Column Volume: 1,570 L	$558,000	$1,116,000	1.05	$1,171,800
2	F-102	Dead End Filter	$115,000	$230,000	1.5	$345,000

		Area: 30 m^2				
2	M-105	Filtration Mixing Tank Volume: 4,000 L	$258,000	$516,000	1.3	$670,800
2	H-105	Filtration Wash Holding Volume: 4,000 L	$258,000	$516,000	1.3	$670,800
2	V-103	Holding Tank Volume: 4,000 L	$258,000	$516,000	1.3	$670,800
2	D-101	Diafiltration Area: 40 m^2	$108,000	$216,000	1.5	$324,000
2	V-104	Viral Inactivation Tank Volume: 4,000 L	$258,000	$516,000	1.3	$670,800
2	F-103	Dead End Filter Area: 20 m^2	$80,000	$160,000	1.5	$240,000
2	M-106	Wash Mixing Tank Volume: 4,000 L	$258,000	$516,000	1.3	$670,800
2	H-106	Wash Holding Tank Volume: 4,000	$258,000	$516,000	1.3	$670,800
2	M-107	Elution Mixing Tank Volume: 4,000 L	$258,000	$516,000	1.3	$670,800
2	H-107	Elution Holding Tank Volume: 4,000 L	$258,000	$516,000	1.3	$670,800
2	M-108	Regen Mixing Tank Volume: 500 L	$193,000	$386,000	1.3	$501,800
2	H-108	Regen Holding Tank Volume: 500 L	$193,000	$386,000	1.3	$501,800
2	M-109	Rinse Mixing Tank Volume: 10,000 L	$278,000	$556,000	1.3	$722,800
2	H-109	Rinse Holding Tank Volume: 10,000 L	$278,000	$556,000	1.3	$722,800
2	M-110	Cleanse Mixing Tank Volume: 4,000 L	$258,000	$516,000	1.3	$670,800
2	H-110	Cleanse Holding Tank Volume: 4,000 L	$258,000	$516,000	1.3	$670,800
2	C-102	Cation Exchange Column Volume: 500 L	$557,000	$1,114,000	1.05	$1,169,700
2	V-105	Exchange Holding Tank Volume: 2,500 L	$242,000	$484,000	1.3	$629,200
2	M-111	Wash Mixing Tank Volume: 5,000 L	$266,000	$532,000	1.3	$691,600
2	H-111	Wash Holding Tank Volume: 5,000 L	$266,000	$532,000	1.3	$691,600
2	M-112	Elution Mixing Tank Volume: 5,000 L	$266,000	$532,000	1.3	$691,600
2	H-112	Elution Holding Tank Volume: 5,000 L	$266,000	$532,000	1.3	$691,600
2	M-113	Regen Mixing Tank	$193,000	$386,000	1.3	$501,800

		Volume: 500 L				
2	H-113	Regen Holding Tank Volume: 500 L	$193,000	$386,000	1.3	$501,800
2	M-114	Rinse Mixing Tank Volume: 15,000 L	$301,000	$602,000	1.3	$782,600
2	H-114	Rinse Holding Tank Volume: 15,000 L	$301,000	$602,000	1.3	$782,600
2	M-115	Cleanse Mixing Tank Volume: 5,000 L	$266,000	$532,000	1.3	$691,600
2	H-115	Cleanse Holding Tank Volume: 5000 L	$266,000	$532,000	1.3	$691,600
2	C-103	Anion Exchange Column Volume: 1,500 L	$561,000	$1,122,000	1.05	$1,1178,100
2	V-106	Final Holding Tank Volume: 2,500 L	$242,000	$484,000	1.3	$629,200
29	P-101	Storage Tank Volume: 4,000 L	$6,025	$174,725	1	$174,725
1	F-104	Activated Carbon Filter Area: 290 m^2	$323,000	$323,000	1	$323,000
1	F-105	Microfilter Area: 280 m^2	$316,000	$316,000	1	$316,000
1	B-101	Aqueous Waste Tank Volume: 15,000 L	$447,967	$447,967	1	$447,967
1	B-102	Neutralization Waste Tank Volume: 200,000,000 L	$77,038,49 3	$77,038,49 3	1	$77,038,493
1	*	CIP Water System	$225,000	$225,000	1	$225,000
1	*	CIP Acid System	$225,000	$225,000	1	$225,000
1	*	CIP Base System	$225,000	$225,000	1	$225,000
1	*	Vapor Compression Distillation System	$1,040,000	$1,040,000	1	$1,040,000
1	*	Cold Room for Mab Storage	$42,200	$42,200	1	$42,200
1	*	Building	$9,218,375	$9,218,375	1	$9,218,375
Total Capital Cost						$171,604,603

Fixed Capital Investment Summary

The final fixed-capital investment of the proposed design is listed in Table 11 above. Table 11 above also contains the name of the equipment as it is shown in the PFD, the description of each piece of equipment, the quantity of each piece of equipment, and the unit cost, purchase cost, and installed cost.

In order to achieve the minimum production of MAb per year given in the project brief, it is necessary to run three simultaneous upstream processes, so three of each piece of equipment upstream is needed. In addition to the three simultaneous upstream processes needed, two purification trains are needed if the process increases to the projected titers of 5 g/L or 10 g/L.

Purchase costs for everything but the disposable bioreactors, the vapor compression skid, the CIP skid, the 4,000 L product storage tanks, the waste tanks, and the cold room for storage were pulled directly from the SuperPro Designer software. The disposable bioreactor skids were priced using both the SuperPro Designer software and a quote from GE health. A double ratio of price and size was used to more accurately price both the 1,200 L and 4,000 L disposable bioreactors. In terms of the vapor compression skid, the price was given by a quote from AWS Biofarma. The CIP skid's price was given by Sani Matic and the 4,000 L storage tanks were priced as $6,035 per tank. [16] The prices of the waste tanks were calculated using the costing method in *Analysis, Synthesis, and Design of Chemical Processes*, and the cost of the cold room was determined to be $42,200. [18] Lastly, the cost of a 200,000 square foot building was estimated to house our equipment from a brochure from SMET Construction Services.

Figure 10 below shows a breakdown of the installed equipment costs in terms of sections of the process. The sections of the process include upstream, primary recovery, protein A chromatography, viral inactivation, CEX, AEX, storage, and other. The other category includes CIP, WFI treatment, and waste treatment. This figure shows that storage for the process comprises the largest percentage of the installed equipment cost. This is followed by the upstream process, protein A chromatography, AEX, and CEX. Primary recovery, viral inactivation and the other parts of the process make up only 8% of the total installed equipment cost.

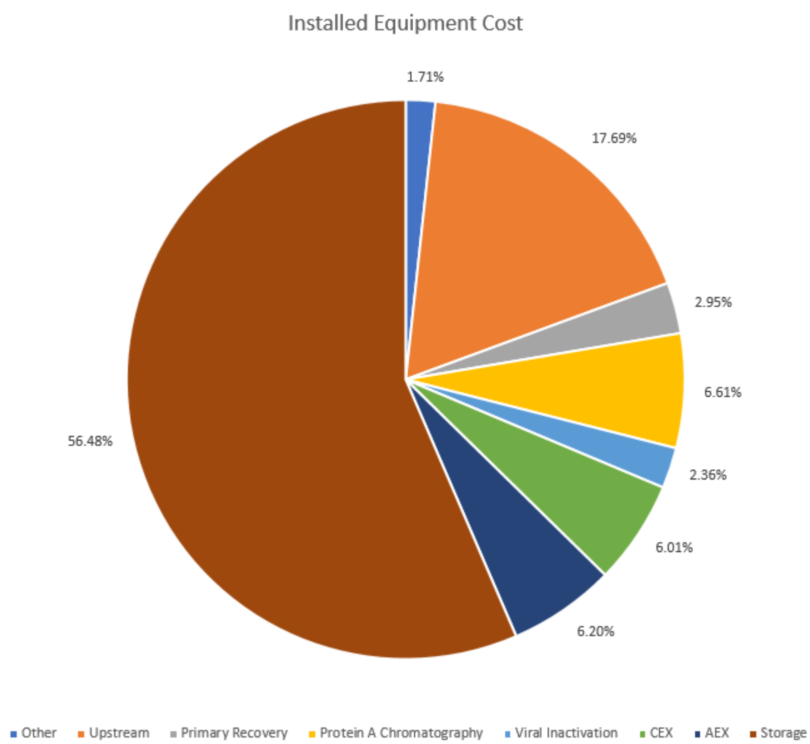


Figure 10: *Installed Equipment Cost*

The quotes given while determining the installation cost for all equipment included both purchase and installation cost; however, for equipment pricing taken from SuperPro Designer, the installation factors listed above in Table 11 were also taken from the SuperPro Designer software. The factor was multiplied by the purchase cost to find the final installation cost. All dollars are in 2019 dollars and a contingency and fees rate of 18% was also added for all fixed capital to cover the cost of the control system and any other fees associated with the project.

Health, Safety, and Environmental Considerations

Health and Safety

1. Safeguards Incorporated in Design
    - There are separated waste disposal tanks to ensure no incompatible chemical mixing occurs. [19]
    - All waste is neutralized prior to disposal to ensure environmental compliance. [20]
    - The use of mostly mild chemicals is in place to minimize exposure hazards.
    - All streams are diluted for use in columns with WFI to minimize concentration of chemicals.
    - The disposable reactor bags are treated as biohazard and disposed of properly. [21]

2. Additional Safeguard Evaluations and Requirements

    Table 12 below shows the safeguard techniques used involving sodium hydroxide, eco-toxic chemicals, and non-neutralized chemicals throughout the process. The evaluation for each hazard is listed followed by the safeguard requirement in place to eliminate the hazard.

Table 12: *Additional Safeguard Evaluations and Requirements*

Additional Safeguard Evaluations and Requirements		
Hazard	Evaluation	Requirement
Chemical Incompatibility	Sodium hydroxide is incompatible with most everything else	Store sodium hydroxide waste separate from the rest of the waste
Potentially eco-toxic chemicals	Some chemicals are toxic to wildlife	Filter out eco-toxic chemicals and dispose of them separately
Non-Neutral chemicals in aqueous waste tank	Need to neutralize chemicals before disposal	Mix sodium hydroxide and phosphoric acid to neutralize for disposal

3. Safety Assessment Summary

After thorough safety considerations, it was determined that there are no dire safety concerns or the potential for project termination to occur. The only major concerns regarding the process are the hazards associated with the chemicals and the mixing of the chemicals. However, extensive safeguards have been discussed to ensure that hazard identification and proper procedures are in place for using any of the chemicals within the process.

Although there are no critical safety concerns that could cause termination, there are a few PSM related concerns with the process. The biohazard waste in the upstream portion of the process is a critical PSM related concern. During the upstream portion of the process, the virus used to produce MAb is not yet inactivated. Due to the health and safety concern associated with the inactivated virus, the disposable reactor bags are discarded in biohazard waste containers and removed from the facility. Neutralization of the waste is also a special PSM related concern of the project. All waste needs to be under certain pH values before going down the drain.

Other than biohazard waste and neutralization of waste, dilution of the chemicals entering the process is both a PSM and an RMP concern. Some of the chemicals themselves have toxic or corrosive qualities that could cause harm to the operators handling them. However, the chemicals are also a potential risk factor to the process because if the chemicals are not the correct pH, the entire production of MAb could be ruined. Overall, the process design mentioned above is relatively safe and should not be denied start up due to any safety concerns.

4. Inherently Safer Design Application Summary

Table 13 below includes a brief description of the inherently safer design applications involved in the process. Hazards are identified, followed by the inherent safety concept associated with each hazard. Lastly, the incorporation of the inherently safer design for each hazard into the preliminary design is listed.

Table 13: *Inherently Safer Design Application Summary*

Inherently Safer Design Application Summary		
Hazard	Inherent Safety Concept	How Incorporated in Preliminary Design
Flammability of ethyl alcohol stored on site	Minimization	Sealed in an air tight container, storage is minimized
Acetic acid flammability	Minimization	Sealed in an air tight container, storage is minimized
Compressed air explosive pressure release	Minimization	Storage of compressed air is minimized
Sodium hydroxide corrosivity	Minimization	Storage of sodium hydroxide is minimized

Chemical reactivity	Moderation	Dilution of all chemicals with WFI
Use of sulfuric acid in process	Substitution	Replaced with phosphoric acid due to sulfuric acid heat of mixing with water
Use of ethylene glycol in process	Substitution	Replaced with glycerol due to toxicity of ethylene glycol
Use of compressed oxygen and nitrogen	Simplification	Replace both gas streams with a single compressed air line

Environmental

The chemicals in this process are specifically designed to be used in biological systems, so they have very little environmental impact. Some of these chemicals are toxic to wildlife in high concentrations. These chemicals include sodium chloride, acetic acid, tris-base, potassium chloride, potassium dihydrogen phosphate, sodium dihydrogen phosphate, sodium hydroxide, phosphoric acid, N-methyldiethanolamine. All of these eco-toxic chemicals are sent to be flared for disposal.

Process Safety Considerations

Inherently Safer Design

The goal of any manufacturing facility, whether biomanufacturing or any other type of manufacturing field, is to be inherently safe as well as having an inherently safer design. Within the new monoclonal antibody production facility designed in this project, there are ways in which it is designed in an inherently safer manner. This section discusses passive, active, and procedural methods of the inherently safer design.

In any biomanufacturing facility design, there are several strategies in which to ensure ISD. In the case of this design, there are several passive strategies that are put into place to guarantee the facility is inherently safer. One of the first steps to ensure ISD is to secure the lines from the tanks and columns in the biomanufacturing process. This simple task protects the facility or workers from leaks or spills of any potentially hazardous materials. Along with securing the lines between tanks and columns, allowing ventilation to occur within areas is another way to minimize exposure of any toxic chemicals in the event of spills. Closed areas as well as closed containers in transportation are other passive methods of ISD design that are accounted for in designing an inherently safer facility. [22]

Although passive strategies might be the best and easiest way to ensure ISD, there are also a few active strategies of ISD that can be used in the proposed design. Having a control system for solvent flow is an example of an active strategy of ISD. In the case of an overflow of solvent material or in the rare case of a reaction happening due to the leakage of solvent material, a control system is in place to help divert solvent or to stop the flow of solvent completely. Another example of an active strategy of inherently safer design in the process is the use of alarms on material or equipment. The purpose of the alarms is to alert the lab technician or other workers of a dangerous situation happening within the equipment in the facility; therefore, creating a sense of inherent safety in the workplace.

Besides the passive and active strategies of ISD, the design of the biomanufacturing facility also contains a few procedural strategies of inherently safer design. One of the biggest procedural strategies of ISD that can be put into place is training. Making sure all technicians and employees are trained on the process and equipment is a big portion of ISD. Along with training, emergency cleaning methods and venting of certain areas are classified as procedural strategies of inherently safer design. While the above safety measures seem daunting, the addition of them in the design stage limits the need for later additions which could lead to higher operational or capital costs.

Hazards Identification and Risk Analysis

Table 14 below indicates the source and hazard involved with each of the hazardous chemicals in the process.

Table 14: *Hazard Identification*

Hazard Identification	
Source	Hazard
N-Methyldiethanolamine Corrosivity	N-Methyldiethanolamine causes skin, eye, and respiratory irritation.
Potassium Chloride Corrosivity	Potassium Chloride causes acute skin and eye irritation.
TRIS Hydrochloride Corrosivity	TRIS Hydrochloride causes mild skin, eye, and respiratory irritation.
TRIS Base Reactivity	TRIS Base causes mild skin, eye, and respiratory irritation.
Ethyl Alcohol Flammability	Ethyl Alcohol has a lower explosive limit of 3.3% in air.
Acetic Acid Flammability	Acetic Acid has a lower explosive limit of 4% in air.
Acetic Acid Corrosivity	Acetic Acid causes severe skin, eye, and respiratory irritation.
Sodium Chloride Toxicity	Sodium Chloride is very dangerous and toxic if large quantities are ingested.
Sodium Citrate Corrosivity	Sodium Citrate causes mild skin, eye, and respiratory irritation.
Ethylenediaminetetraacetic acid Corrosivity	Ethylenediaminetetraacetic acid causes mild skin, eye, and respiratory irritation.
Sodium Hydroxide Toxicity	Sodium Hydroxide causes burning of respiratory tract if ingested or inhaled.
Sodium Hydroxide Corrosivity	Sodium Hydroxide causes severe burning and instant irritation with contact to skin and eyes.

Phosphoric Acid Toxicity	Phosphoric Acid causes a risk of burns and permanent tissue damage to digestive tract if ingested.
Phosphoric Acid Corrosivity	Phosphoric Acid causes severe burns, ulcers, and irreversible eye injury
Compressed Air Explosive Pressure Release	A release of compressed air causes severe physical and personnel damage due to the explosion.

Table 15 below shows the consequences of the various chemicals in the process including the consequences on equipment damage, environmental compliance, loss of life, disruptions of other business units, legal and PR, and community impact.

Table 15: *Potential Consequence Summary*

Potential Consequence Summary						
Hazard	Equipment Damage	Environmental Compliance	Loss of Life	Disruption of Other Business Units	Legal/PR	Community Impact
N-Methyldiethanol amine Corrosivity	low	low	low	-	low	-
Potassium Chloride Corrosivity	low	low	low	-	low	-
TRIS Hydrochloride Corrosivity	-	low	-	-	low	-
TRIS Base Reactivity	-	low	-	-	low	-
Ethyl Alcohol Flammability	high	moderate	moderate	high	high	low
Acetic Acid Flammability	moderate	moderate	moderate	moderate	high	low
Acetic Acid Corrosivity	moderate	moderate	low	low	low	-
Sodium Chloride Toxicity	low	low	low	-	low	-
Sodium Citrate Corrosivity	-	low	-	-	low	-
Ethylenediaminetetraacetic acid Corrosivity	-	moderate	-	-	low	-
Sodium Hydroxide Toxicity	low	moderate	moderate	-	moderate	low
Sodium Hydroxide Corrosivity	moderate	moderate	low	low	moderate	low
Phosphoric Acid Toxicity	low	moderate	moderate	-	moderate	low

Phosphoric Acid Corrosivity	moderate	moderate	moderate	low	moderate	low
Compressed Air Explosive Pressure Release	high	-	high	high	high	low

Siting and Layout of Processes and Equipment

The layout of the process is divided among several sections. All of the sections are kept separate due to the necessity of maintaining quarantine conditions. [23] Cross contamination between sections must be strictly avoided due to the risk of contamination of purified product. Clean rooms are necessary for both the final product storage and the seed train. The complete layout for the process is shown below in Figure 11.

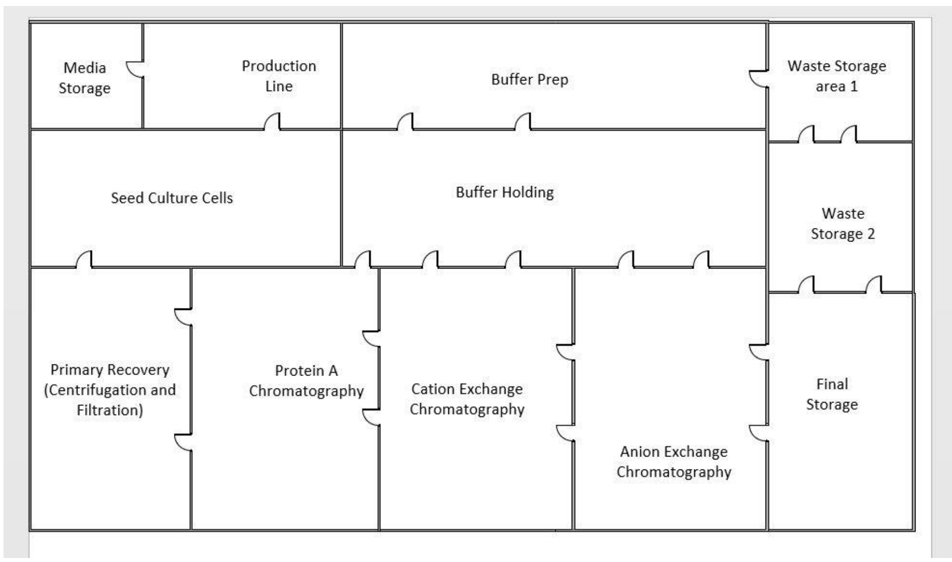


Figure 11: *Site Layout*

From Figure11 above, all buffers are prepared and stored in separate locations. Media storage is also available before it enters the seed train. Figure 11 also shows that the layout of the processing plant follows the same layout of the process itself. Lastly, there are three separate storage areas; one for product storage and two for waste storage. [23]

Other Important Considerations

In addition to the previously stated safety concerns and considerations, a final consideration is the need to control the pH of several streams for use within column washing or elution, as well as the pH of the waste storage tanks. The pH of the waste disposal tanks is important due to the potential for environmental damage should a non-neutral solution be dumped into the water source. The pH of the streams entering the columns needs to be monitored and controlled as our product is a biological product, thus it must be ensured that pH remains close to biological ranges to prevent damage to the product. Therefore, pH monitors and control valves were attached to all the streams to the columns which might result in a very basic or very acidic pH. This way, if the monitor reads a pH too far from the acceptable range of solvents coming into contact with the product, which is about 5-9, then the valve will close, preventing this stream form contacting the product, and an operator will be dispatched to adjust the chemical composition of the stream to return the pH to the acceptable range. Some streams will have a pH outside of the safe range, but this is due to the fact that these streams are only used to elute impurities from the ion exchange columns, and do not contact the product stream. Thus, the pH of any stream contacting the product stream is controlled and monitored.

Operation Costs

Listed below in Table 16 are the yearly consumable costs for the process. Quantity values were chosen based on number of batches per a year, as well as volumes of various pieces of equipment. The media and the biohazard waste container unit costs were pulled from Lonza's website and Zoro's websites respectively. The CHO cell vial unit cost was found on Thermo Fisher Scientific's manufacturing website. The rest of the unit cost values were pulled from SuperPro Designer.

Table 16: *Consumable Cost Summary*

Consumable Cost Summary				
Consumable	Quantity	Unit Cost ($)	Annual Cost ($)	% of Consumable Cost
500 mL T-flask	87	$5.54	$482	~0%
2.2 L Roller Bottle	87	$6.00	$522	~0%
Sartorius CultiBag RM 100	87	$840	$73,080	0.06%
Sartorius CultiBag RM 200	87	$990	$86,130	0.07%
Sartorius CultiBag RM 1200	87	$6,109	$531,483	0.42%
Sartorius CultiBag RM 4000	87	$20,363	$1,771,581	1.39%
Lonza Media	45,000 L	$74 / L	$96,570,000	75.61%
Dead End Filter Cartridge	174	$1,000	$174,000	0.15%
Protein A Resin	3,142 L	$7,358	$23,116,992	18.10%
Viral Inactivation Filter	2 (40 m^2)	$400/ m^2	$31,776	0.02%
Resin for CEX	1,800 L	$1,500 / L	$2,700,000	2.11%
Resin for AEX	1,620 L	$1,500 / L	$2,430,060	1.90%
Carbon Activated Filter	1	$116,000	$116,000	0.09%
Microfilter	1	$112,000	$112,000	0.09%
Biohazard Waste Container	2	$260/roll	$520	~0%
CHO Cell Vial	87	$954	$82,998	0.06%
Total Consumable Cost			$127,797,624	100%

The raw materials used throughout the process are listed below in the table 17. Density and unit cost values for acetic acid, ethyl alcohol, sodium chloride, and sodium citrate were given in the SuperPro Designer software. The density and unit costs for the rest of the raw materials were pulled from both Sigma Aldrich as well as Lab Depot Inc. Quantities were calculated from values given in the SuperPro Designer software.

Table 17: *Raw Material Cost Summary*

Raw Materials Cost Summary					
Raw Material	Quantity	Density (kg/L)	Unit Cost ($)	Annual Cost ($)	% of Consumable Cost
10 wt% Phosphoric Acid	255,461 kg	1.88	$4.66/L	$633,209	10.00%
.1 M Sodium Hydroxide	90,741 kg	1	$4.99/L	$452,798	7.15%
.5 M Sodium Hydroxide	203,000 kg	1.02	$5.18/L	$1,031,193	16.28%
Acetic Acid	5,539 kg	-	$0.73/kg	$4,398	.07%
EDTA, Sodium	4,089 kg	-	$171.56/kg	$703,449	11.11%
Ethyl Alcohol	41,383 kg	-	$0.75/kg	$33,698	0.53%
Sodium Chloride	13,601 kg	-	$4.00/kg	$58,991	0.93%
Sodium Citrate	899 kg	-	$10.00/kg	$9,787	0.15%
TRIS Base	4,640 kg	-	$20.000/kg	$92,429	1.46%
TRIS Hydrochloride	6,148 kg	--	$50.00/kg	$307,516	4.86%
Potassium Chloride	7,975 kg	-	$24.00/kg	$191,351	3.02%
Potassium Dihydrogen Phosphate	46,980 L	-	$126.00/L	$183	~0%
Sodium Dihydrogen Phosphate	835 kg	-	$16.88/kg	$14,084	0.22%
Polysorbate 80	9 kg	1.09	$45.12/kg	$384	0.01%
N-Methyldiethanolamine	75 kg	1.04	$23.61/kg	$4,705	0.03%
Glycerol	29,000 L	-	$96.50/L	$2,798,500	44.18%
Total Raw Material Cost				$6,333,850	100%

The total annual costs for consumables and raw materials are more than $127 million and $6.3 million respectively. The consumables make up 94% of the annual operating cost, and the raw materials makes up 5% of the annual operating cost. The last 1% is utility costs.

Economic Analysis

a. Economic Basis

Construction for this biomanufacturing process and facility will begin in 2019, with startup in midyear 2020, so all economic evaluations are completed in terms of 2019 dollars. According to a large literature survey a project evaluation life of 25 was chosen, with year 0 in 2019 and year 25 in 2044. The process revenue, raw material costs, and utility costs were all escalated over the 25-year evaluation period to take into account the change in value of the process. An escalation rate of 2% was deemed acceptable according to a referenced source. [24] A hurdle rate of 15% was applied while evaluating this process. [25] Taxes were considered to be 30% based on the current tax rate. [26]

The equipment capital cost and the building cost were both acceptable values considered for depreciation. Therefore, MACRS depreciation was calculated for both capital investments.

The equipment was depreciated over a 7-year MACRS depreciation schedule, while the building was depreciated over a 39-year schedule, with write-off of the remaining depreciation value occurring in the final year of project evaluation. MACRS depreciation schedule was pulled from the IRS Publication 946.

The revenue for this process was calculated using the comparable current marketed drug Enbrel. According to the AIChE design brief, Enbrel was chosen because the dose requirements, treatment cost, and production process are very similar to monoclonal antibodies. The market price of Enbrel is $5.17 million per 1 kg of Enbrel sold in 2007 dollars. This value was scaled up using CEPCI values and then multiplied by the production rate of this process in kg per year to find our yearly revenue in 2019 dollars.

In order to determine the optimal operating capacities for this process, the size of the last reactor in the seed train section of the process was varied at 20,000 L and 30,000 L. Each process then had unique aspects including required batches per year to meet demand as well as sizing and costing for the remainder of the downstream process. Full simulations and economics evaluations were done on each of the two processes to determine which scenario was optimal.

b. Optimization

Each of the optimization scenarios had its own set of costs associated with the process. The cost variations are detailed below in table 18. All economic evaluations including depreciation, NPV, and DCFROR were calculated using the appropriate values for each process.

Table 18: *Yearly Cost per Optimization Process*

Yearly Cost per Optimization Process		
	20,000 L Process	30,000 L Process
Fixed Equipment Capital	$174,388,110	$162,386,228
Consumables Cost	$127,042,961	$127,714,106
Raw Material Cost	$5,825,691	$6,333,850
Utility Cost	$1,952,657	$1,998,460
Building Cost	$9,218,375	$9,218,375

Attached below is the cash flow table for the 20,000 L optimization process.

Table 19: *20,000 L Cash Flow Table*

Attached below is the cash flow table for the 30,000 L optimization process.

Table 20: *30,000 Cash Flow Table*

Escalation Rate	0.02												
Tax Rate	0.30												
Given i*	0.15												
End of Year	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Project Year	0	1	2	3	4	5	6	7	8	9	10	11	12
Escalation Factor (F/Pn)	1.00	1.02	1.04	1.06	1.08	1.10	1.13	1.15	1.17	1.20	1.22	1.24	1.27
Sales Revenue	-	6,333,440,000	6,460,108,800	6,589,310,976	6,721,097,196	6,855,519,139	6,992,629,522	7,132,482,113	7,275,131,755	7,420,634,390	7,569,047,078	7,720,428,019	7,874,836,580
Net Revenue	-	6,333,440,000	6,460,108,800	6,589,310,976	6,721,097,196	6,855,519,139	6,992,629,522	7,132,482,113	7,275,131,755	7,420,634,390	7,569,047,078	7,720,428,019	7,874,836,580
- Raw Material Costs	-	(135,650,579)	(138,363,591)	(141,130,863)	(143,953,480)	(146,832,550)	(149,769,201)	(152,764,585)	(155,819,876)	(158,936,274)	(162,114,999)	(165,357,299)	(168,664,445)
- Utilities	-	(1,991,710)	(2,031,544)	(2,072,175)	(2,113,618)	(2,155,891)	(2,199,009)	(2,242,989)	(2,287,848)	(2,333,605)	(2,380,278)	(2,427,883)	(2,476,441)
- Depreciation of Equipment	-	(24,920,061)	(42,707,648)	(30,500,480)	(21,781,075)	(15,572,858)	(15,555,419)	(15,572,858)	(7,777,710)	-	-	-	-
- Depreciation of Building	-	(128,228)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)
- Writeoff	-	-	-	-	-	-	-	-	-	-	-	-	-
Taxable Income	-	6,170,749,422	6,276,769,658	6,415,371,099	6,553,012,663	6,690,721,482	6,824,869,535	6,961,665,322	7,109,009,961	7,259,128,152	7,404,315,442	7,552,406,478	7,703,459,335
- Tax @ 40%	-	(1,851,224,827)	(1,883,030,897)	(1,924,611,330)	(1,965,903,799)	(2,007,216,445)	(2,047,460,860)	(2,088,499,597)	(2,132,702,988)	(2,177,738,446)	(2,221,294,633)	(2,265,721,943)	(2,311,037,800)
Net Income	-	4,319,524,596	4,393,738,761	4,490,759,769	4,587,108,864	4,683,505,037	4,777,408,674	4,873,165,725	4,976,306,973	5,081,389,706	5,183,020,809	5,286,684,535	5,392,421,534
+ Depreciation	-	25,048,288	42,944,007	30,736,840	22,017,434	15,809,217	15,791,779	15,809,217	8,014,069	236,359	236,359	236,359	236,359
+ Write off	-	-	-	-	-	-	-	-	-	-	-	-	-
- Fixed Equipment Capital	(174,388,110)	-	-	-	-	-	-	-	-	-	-	-	-
- Fixed Building Captial	(9,218,375)	-	-	-	-	-	-	-	-	-	-	-	-
Cash Flow	(183,606,485)	4,344,572,884	4,436,682,768	4,521,496,609	4,609,126,298	4,699,314,255	4,793,200,453	4,888,974,943	4,984,321,042	5,081,626,065	5,183,257,168	5,286,920,894	5,392,657,893
Discount Factor (P/Fi*n)	1.00	0.87	0.76	0.66	0.57	0.50	0.43	0.38	0.33	0.28	0.25	0.21	0.19
Discounted Cash Flow	(183,606,485)	3,777,889,465	3,354,769,579	2,972,957,415	2,635,282,920	2,336,389,719	2,072,232,828	1,837,946,768	1,629,383,390	1,444,515,282	1,281,221,900	1,136,387,815	1,007,926,319
NPV @ i*	31,548,957,175												
DCFROR	20.46												

Escalation Rate	0.02												
Tax Rate	0.30												
Given i*	0.15												
End of Year	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044
Project Year	13	14	15	16	17	18	19	20	21	22	23	24	25
Escalation Factor (F/Pn)	1.29	1.32	1.35	1.37	1.40	1.43	1.46	1.49	1.52	1.55	1.58	1.61	1.64
Sales Revenue	8,032,333,311	8,192,979,978	8,356,839,577	8,523,976,369	8,694,455,896	8,868,345,014	9,045,711,914	9,226,626,153	9,411,158,676	9,599,381,849	9,791,369,486	9,987,196,876	10,186,940,813
Net Revenue	8,032,333,311	8,192,979,978	8,356,839,577	8,523,976,369	8,694,455,896	8,868,345,014	9,045,711,914	9,226,626,153	9,411,158,676	9,599,381,849	9,791,369,486	9,987,196,876	10,186,940,813
- Raw Material Costs	(172,037,734)	(175,478,489)	(178,988,059)	(182,567,820)	(186,219,176)	(189,943,560)	(193,742,431)	(197,617,279)	(201,569,625)	(205,601,018)	(209,713,038)	(213,907,299)	(218,185,445)
- Utilities	(2,525,970)	(2,576,489)	(2,628,019)	(2,680,579)	(2,734,191)	(2,788,875)	(2,844,652)	(2,901,545)	(2,959,576)	(3,018,768)	(3,079,143)	(3,140,726)	(3,203,540)
- Depreciation of Equipment	-	-	-	-	-	-	-	-	-	-	-	-	-
- Depreciation of Building	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)
- Writeoff	-	-	-	-	-	-	-	-	-	-	-	-	(3,417,528)
Taxable Income	7,857,533,249	8,014,688,641	8,174,987,141	8,338,491,611	8,505,266,170	8,675,376,221	8,848,888,472	9,025,870,969	9,206,393,115	9,390,525,705	9,578,340,946	9,769,912,492	9,961,897,941
- Tax @ 40%	(2,357,259,975)	(2,404,406,592)	(2,452,496,142)	(2,501,547,483)	(2,551,579,851)	(2,602,612,866)	(2,654,666,542)	(2,707,761,291)	(2,761,917,935)	(2,817,157,711)	(2,873,502,284)	(2,930,973,748)	(2,988,569,382)
Net Income	5,500,273,274	5,610,282,049	5,722,490,999	5,836,944,128	5,953,686,319	6,072,763,354	6,194,221,931	6,318,109,678	6,444,475,181	6,573,367,993	6,704,838,662	6,838,938,745	6,973,328,559
+ Depreciation	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359
+ Write off	-	-	-	-	-	-	-	-	-	-	-	-	3,417,528
- Fixed Equipment Capital	-	-	-	-	-	-	-	-	-	-	-	-	-
- Fixed Building Captial	-	-	-	-	-	-	-	-	-	-	-	-	-
Cash Flow	5,500,509,633	5,610,518,408	5,722,727,358	5,837,180,487	5,953,922,678	6,072,999,714	6,194,458,290	6,318,346,037	6,444,711,540	6,573,604,353	6,705,075,022	6,839,175,104	6,976,982,446
Discount Factor (P/Fi*n)	0.16	0.14	0.12	0.11	0.09	0.08	0.07	0.06	0.05	0.05	0.04	0.03	0.03
Discounted Cash Flow	893,986,591	792,927,037	703,291,633	623,788,949	553,273,544	490,729,464	435,255,599	386,052,705	342,411,889	303,704,393	269,372,535	238,921,677	211,944,242
NPV @ i*	31,548,957,175												
DCFROR	20.46												

Escalation Rate	0.02												
Tax Rate	0.30												
Given i*	0.15												
End of Year	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Project Year	0	1	2	3	4	5	6	7	8	9	10	11	12
Escalation Factor (F/Pn)	1.00	1.02	1.04	1.06	1.08	1.10	1.13	1.15	1.17	1.20	1.22	1.24	1.27
Sales Revenue	-	6,457,140,000	6,586,282,800	6,718,008,456	6,852,368,625	6,989,415,998	7,129,204,318	7,271,788,404	7,417,224,172	7,565,568,656	7,716,880,029	7,871,217,629	8,028,641,982
Net Revenue	-	6,457,140,000	6,586,282,800	6,718,008,456	6,852,368,625	6,989,415,998	7,129,204,318	7,271,788,404	7,417,224,172	7,565,568,656	7,716,880,029	7,871,217,629	8,028,641,982
- Raw Material Costs	-	(136,813,573)	(139,549,845)	(142,340,841)	(145,187,658)	(148,091,411)	(151,053,240)	(154,074,304)	(157,155,791)	(160,298,906)	(163,504,884)	(166,774,982)	(170,110,482)
- Utilities	-	(2,038,429)	(2,079,198)	(2,120,782)	(2,163,197)	(2,206,461)	(2,250,590)	(2,295,602)	(2,341,514)	(2,388,345)	(2,436,111)	(2,484,834)	(2,534,530)
- Depreciation of Equipment	-	(23,204,992)	(39,768,387)	(28,401,351)	(20,282,040)	(14,501,090)	(14,484,852)	(14,501,090)	(7,242,426)	-	-	-	-
- Depreciation of Building	-	(128,228)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)
- Writeoff	-	-	-	-	-	-	-	-	-	-	-	-	-
Taxable Income	-	6,294,954,779	6,404,649,012	6,544,909,123	6,684,499,371	6,824,380,676	6,961,179,277	7,100,681,048	7,250,248,083	7,402,645,046	7,550,702,674	7,701,721,454	7,855,760,611
- Tax @ 40%	-	(1,888,486,434)	(1,921,394,704)	(1,963,472,737)	(2,005,349,811)	(2,047,314,203)	(2,088,353,783)	(2,130,204,314)	(2,175,074,425)	(2,220,793,514)	(2,265,210,802)	(2,310,516,436)	(2,356,728,183)
Net Income	-	4,406,468,345	4,483,254,308	4,581,436,386	4,679,149,560	4,777,066,473	4,872,825,494	4,970,476,734	5,075,173,658	5,181,851,532	5,285,491,872	5,391,205,018	5,499,032,427
+ Depreciation	-	23,333,220	40,004,746	28,637,710	20,518,399	14,737,449	14,721,211	14,737,449	7,478,785	236,359	236,359	236,359	236,359
+ Write off	-	-	-	-	-	-	-	-	-	-	-	-	-
- Fixed Equipment Capital	(162,386,228)	-	-	-	-	-	-	-	-	-	-	-	-
- Fixed Building Captial	(9,218,375)	-	-	-	-	-	-	-	-	-	-	-	-
Cash Flow	(171,604,603)	4,429,801,565	4,523,259,055	4,610,074,096	4,699,667,959	4,791,803,922	4,887,546,705	4,985,214,183	5,082,652,443	5,182,087,891	5,285,728,231	5,391,441,377	5,499,268,787
Discount Factor (P/Fi*n)	1.00	0.87	0.76	0.66	0.57	0.50	0.43	0.38	0.33	0.28	0.25	0.21	0.19
Discounted Cash Flow	(171,604,603)	3,852,001,360	3,420,233,690	3,031,198,551	2,687,050,409	2,382,373,430	2,113,021,317	1,874,126,663	1,661,528,099	1,473,072,803	1,306,551,179	1,158,853,785	1,027,852,657
NPV @ i*	32,185,393,585												
DCFROR	22.3348												

Escalation Rate	0.02												
Tax Rate	0.30												
Given i*	0.15												
End of Year	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044
Project Year	13	14	15	16	17	18	19	20	21	22	23	24	25
Escalation Factor (F/Pn)	1.29	1.32	1.35	1.37	1.40	1.43	1.46	1.49	1.52	1.55	1.58	1.61	1.64
Sales Revenue	8,189,214,822	8,352,999,118	8,520,059,100	8,690,460,282	8,864,269,488	9,041,554,878	9,222,385,975	9,406,833,695	9,594,970,369	9,786,869,776	9,982,607,172	10,182,259,315	10,385,904,501
Net Revenue	8,189,214,822	8,352,999,118	8,520,059,100	8,690,460,282	8,864,269,488	9,041,554,878	9,222,385,975	9,406,833,695	9,594,970,369	9,786,869,776	9,982,607,172	10,182,259,315	10,385,904,501
- Raw Material Costs	(173,512,691)	(176,982,945)	(180,522,604)	(184,133,056)	(187,815,717)	(191,572,032)	(195,403,472)	(199,311,542)	(203,297,773)	(207,363,728)	(211,511,003)	(215,741,223)	(220,056,047)
- Utilities	(2,585,221)	(2,636,925)	(2,689,664)	(2,743,457)	(2,798,326)	(2,854,293)	(2,911,379)	(2,969,606)	(3,028,998)	(3,089,578)	(3,151,370)	(3,214,397)	(3,278,685)
- Depreciation of Equipment	-	-	-	-	-	-	-	-	-	-	-	-	-
- Depreciation of Building	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)	(236,359)
- Writeoff	-	-	-	-	-	-	-	-	-	-	-	-	(3,417,528)
Taxable Income	8,012,880,550	8,173,142,888	8,336,610,473	8,503,347,410	8,673,419,085	8,846,892,194	9,023,834,765	9,204,316,188	9,388,407,239	9,576,180,111	9,767,708,440	9,963,067,336	10,158,915,882
- Tax @ 40%	(2,403,864,165)	(2,451,942,866)	(2,500,983,142)	(2,551,004,223)	(2,602,025,726)	(2,654,067,658)	(2,707,150,430)	(2,761,294,856)	(2,816,522,172)	(2,872,854,033)	(2,930,312,532)	(2,988,920,201)	(3,047,674,765)
Net Income	5,609,016,385	5,721,200,022	5,835,627,331	5,952,343,187	6,071,393,360	6,192,824,536	6,316,684,336	6,443,021,331	6,571,885,067	6,703,326,077	6,837,395,908	6,974,147,135	7,111,241,117
+ Depreciation	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359	236,359
+ Write off	-	-	-	-	-	-	-	-	-	-	-	-	3,417,528
- Fixed Equipment Capital	-	-	-	-	-	-	-	-	-	-	-	-	-
- Fixed Building Captial	-	-	-	-	-	-	-	-	-	-	-	-	-
Cash Flow	5,609,252,744	5,721,436,381	5,835,863,690	5,952,579,546	6,071,629,719	6,193,060,895	6,316,920,695	6,443,257,691	6,572,121,426	6,703,562,437	6,837,632,267	6,974,383,494	7,114,895,004
Discount Factor (P/Fi*n)	0.16	0.14	0.12	0.11	0.09	0.08	0.07	0.06	0.05	0.05	0.04	0.03	0.03
Discounted Cash Flow	911,660,387	808,602,925	717,195,464	636,121,043	564,211,576	500,431,022	443,860,459	393,684,842	349,181,263	309,708,533	274,697,946	243,645,085	216,133,699
NPV @ i*	32,185,393,585												
DCFROR	22.3346												

As seen in the cash flow tables, both options are individually economically attractive. Both processes have a net present value greater than 0, and a discounted cash flow rate of return greater than the hurtle rate value of 15%. The calculated values are listed below in Table 21.

Table 21: *NPV and DCFROR per Optimization Process*

NPV and DCFROR per Optimization Process		
	20,000 L Process	30,000 L Process
NPV	\$31.55 billion	\$32.19 billion
DCFROR	20.5%	22.3%

Since both options are individually economically attractive, the optimal operating process was determined to be evaluated and presented. NPV analysis was used to compare the options. As seen in the table above, the 30,000 L process has an NPV greater than that of the 20,000 L process. The NPV of the 30,000 L process is \$635 million greater than the NPV of the 20,000 L process. Therefore, it was determined that the 30,000 L process was the optimal operating condition and process to maximize NPV over the 25-year project life evaluation period.

The payback period was also calculated for the optimal operating process, to determine how long after startup it would take to make back the capital investments. As seen below in the calculation, the payback period was determined to be 0.0445 years, or 2.3 weeks.

$$Payback\ Period = 0 + \frac{171{,}604{,}603}{3{,}852{,}019{,}440} \approx 0.0445\ years \approx 2.3\ weeks$$

Since this is a batch process, and the batches take longer than 2.3 weeks, this payback period is an approximation. The payback period would be 2.3 weeks if the process was being run under continuous conditions and the product was being sold continuously as well. More realistically, the payback period would be within the first year.

c. Sensitivity Analysis-Tornado Chart

Four variables were chosen to evaluate the sensitivity of the project to determine its viability with fluctuations in the economy as well as uncertainties when choosing the evaluation period. The four variables chosen for this process were project life, capital cost, raw material cost, and revenue. The project life was varied by ±5 years due to a wide survey of literature that stated that biomanufacturing facilities usually run for 20 to 30 years before a renovation was required. The capital cost and raw material cost were varied by ±25% because this report falls somewhere between a study and a preliminary exploration as described in *Analysis, Synthesis, and Design of Chemical Processes.* Lastly, the revenue was varied by ±10% due to the difference in the average of the revenue per kg in Table 3 and the selling price of Enbrel. The NPV and DCFROR values for each case are listed below in Table 22.

Table 22: *Sensitivity Analysis NPV and DCFROR*

Sensitivity Analysis NPV and DCFROR		
	NPV	DCFROR
Project Life +5 years	$32.95 billion	22.3%
Project Life –5 years	$30.79 billion	22.3%
Capital Cost +25%	$32.15 billion	17.9%
Capital Cost –25%	$32.22 billion	29.8%
Raw Material Cost +25%	$32.01 billion	22.2%
Raw Material Cost –25%	$32.36 billion	22.5%
Revenue +10%	$35.49 billion	24.6%
Revenue –10%	$28.88 billion	20.0%

Since all of the NPV values are greater than 0, and every DCFROR value is greater than the hurtle rate of 15%, the project is viable even when individual aspects of the economic value of the process vary. A tornado chart was made by comparing the adjusted DCFROR values to the original case, to weigh the effect each variable has on the discounted cash flow rate of return.

The tornado chart below, Figure 12, shows that varying the capital cost by ±25% has the greatest effect on the DCFROR, followed by varying the revenue by ±10% for the process. Varying both the raw materials by ±10% and the project life by ±5 years resulted in miniscule variances in the DCFROR.

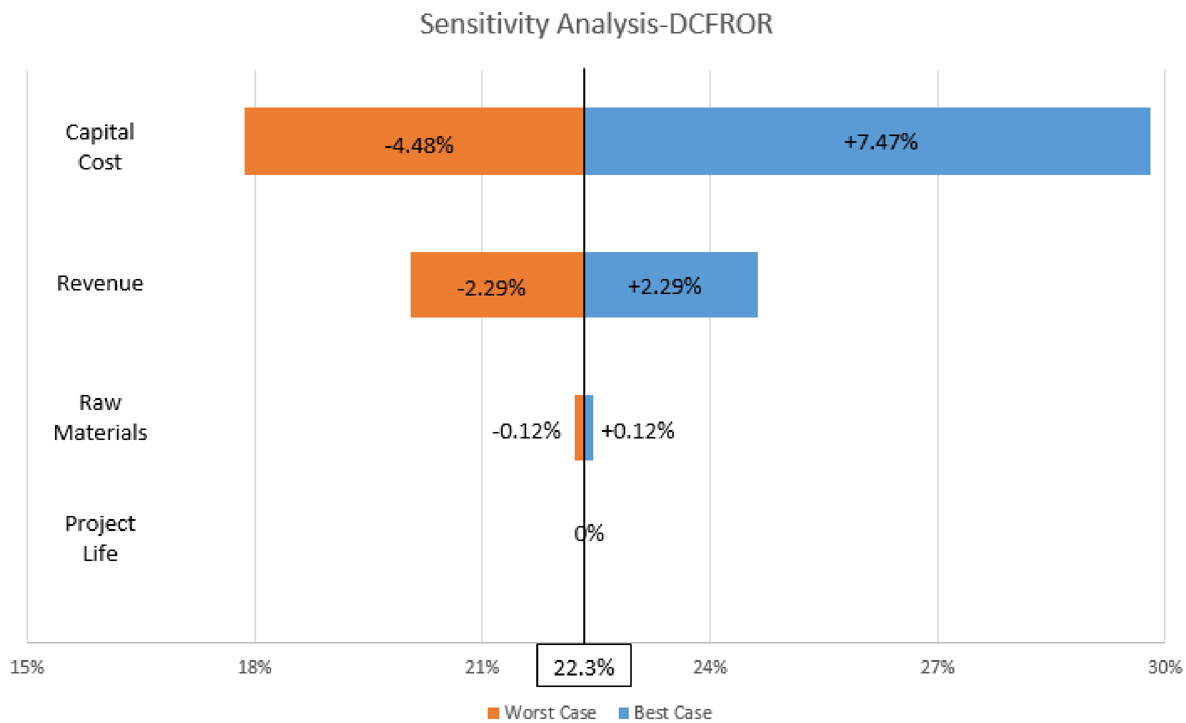


Figure 12: *Sensitivity Tornado Chart*

d. Best and Worst Cases

Best-case and worst-case scenarios were also evaluated to ensure that in the event where multiple variances occurred, the process would still be economically attractive. Best-case scenario was determined by maximizing revenue, minimizing costs, and expanding the project life. The worst-case scenario was determined by minimizing revenue, maximizing costs, and compressing the project life. As seen below in Table 23, the best and worst-case scenarios are described, and the NPV and DCFROR values are presented.

Table 23: *Sensitivity Analysis Variance*

Sensitivity Analysis Variance		
	Best Case	Worst Case
Project Life	+5 years	-5 years
Capital Cost	-25%	+25%
Raw Material Cost	-25%	+25%
Revenue	+10%	-10%
NPV	$36.55 billion	$27.43 billion
DCFROR	33.0%	15.9%

This table shows that the project is more economically attractive in the best-case scenario as expected, but it also shows that even in the worst-case scenario, the NPV is greater than 0 and the DCFROR value is greater than the hurtle rate. This shows that in both the best-case and the worst-case scenarios that the project is economically attractive.

Conclusions and Recommendations

Conclusions

1. MAb is produced at a significantly higher rate than glucose; therefore, each step reached 1 g/L of MAb before moving to the next reactor.
2. Since glucose is consumed at such a slow rate, the starting concentration is always assumed to be 6.145 g/L. This assumption is made even though in reality it is changing slightly because of the addition of broth to new media.
3. By economic analysis, the upstream process that ends with a reactor size of 30,000 L gives the highest NPV and the greatest DCFROR.
4. Even with the target concentration of 1 g/L, the process still produces the desired product rate of 1,000 kg/yr.
5. Most of the capital costs incurred during the project will be a one-time purchase and will last for the entire project life.
6. The majority of the cost associated with the project design are incurred in the purification train portion of the project design.

7. Sartorius CultiBags for disposable reactors and cartridges for filters are replaced after every batch of production.
8. The composition of solutions within the process are mostly Water for Injection (WFI); therefore, low amounts of chemicals are used in the process.
9. Neutralize waste in both tanks, disposing of filtered chemicals at an outside incinerator facility.

Recommendations

1. Due to massive amounts of WFI, it is recommended to investigate regenerating the WFI, if possible, from the aqueous waste tank.
2. Industry seems to have gone to a 1 mL vial of CHO cells with at least 1 x 10^7 cells instead of the 1 x 10^6 cells vials mentioned in the project brief. Look at starting with more cells in the seed train.
3. Recycle steam into water either for use in WFI or the mixing of buffers.

Acknowledgements

We would like to acknowledge sales representatives from GE Health and Santi Matic who provided us with quotes for some of the equipment needed in the process.

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Appendix

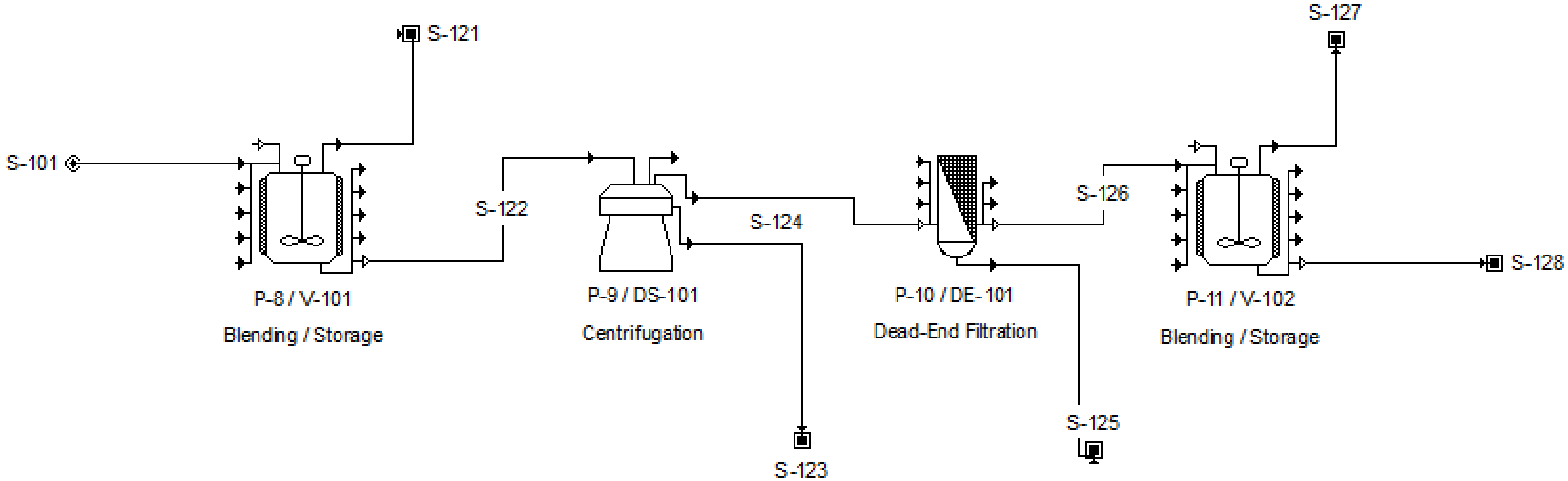
APPENDIX A: MatLab Code

```
%% Design Project
%% ode45
function example_ode45_Projectv2
%% Imputs for Simulation
clear; % clears any variables
t0=0; tf=.241; % Limits of integration in hours
Volume = .25; %Volume of container in L
Cells0= 1e6;%cells
Mab0=0; %grams from previous containter
graph = 1;
%% Initial Conditions from Imputs
C0=Cells0/Volume; %cells/volume
G0=6.145; %g/L
M0= Mab0/Volume; %g/L
y0=[C0,G0,M0];
%% Call ode45
soln=ode45(@f,[t0,tf],y0);
%% Model Solution
t=linspace(t0,tf,1000);
y1=deval(soln,t,1);
y2=deval(soln,t,2);
y3=deval(soln,t,3);
```

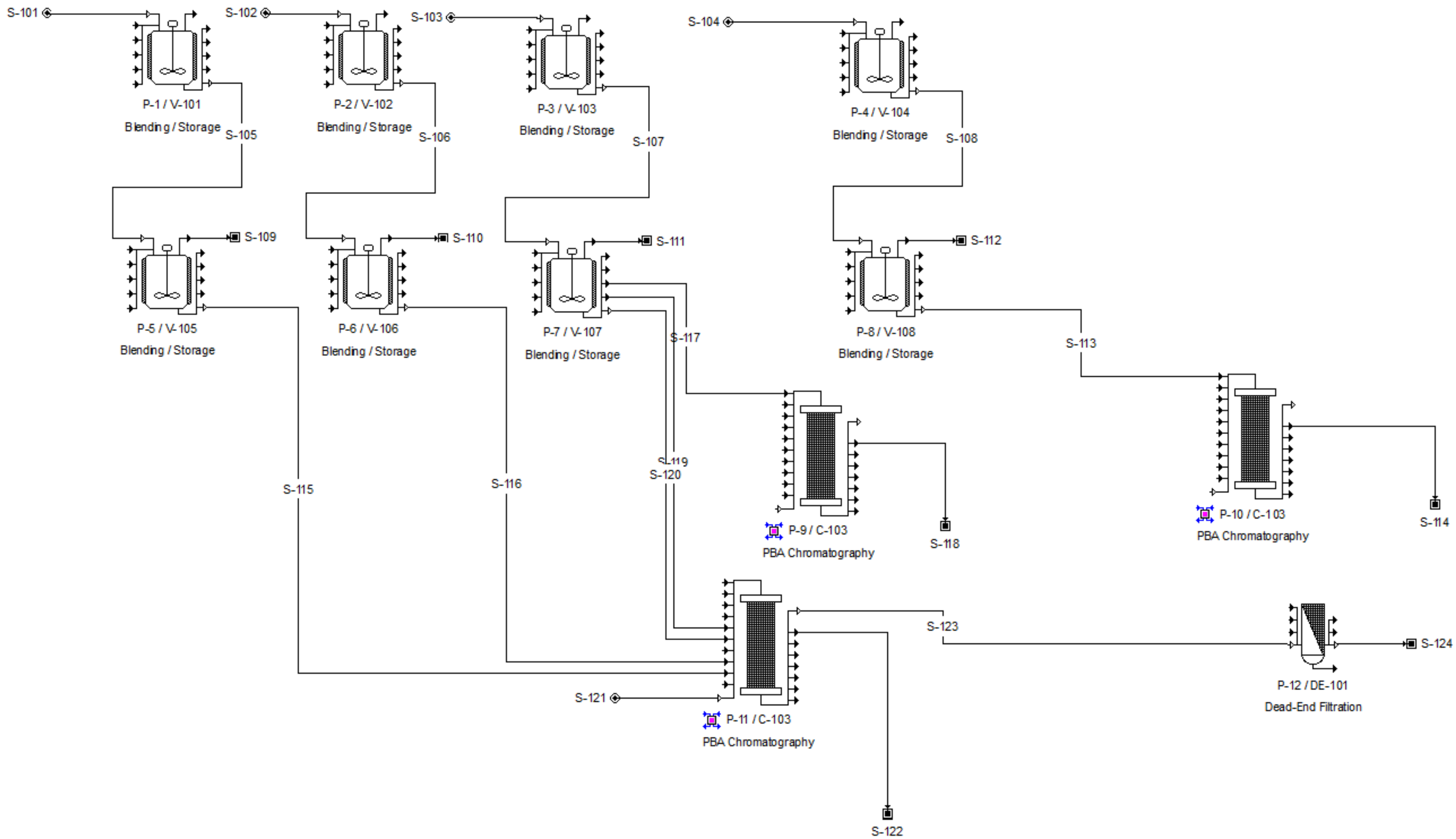
```
%% Plot
if graph == 1
figure(1) %Plotting Glucose in g
plot(t,y1)
xlabel('time (hr)'); ylabel('Cell Concentration (Cells/L)');
title('Cell Concentration vs Time')
figure(2)%Plotting Mab in g
plot(t,y2)
xlabel('time (hr)'); ylabel('Glucose (g/L)');
title('Glucose Concentration vs Time')
figure(3)
plot(t,y3)
xlabel('time (hr)'); ylabel('Mab Concentration (g/L)');
title('Mab Concentration vs Time')
end
    %% Function
    function dydt=f(t,y)
    C = y(1);
    G = y(2);
    M = y(3);
    mu = 0.01925; %1/h
    Ysc = 9.134e-7 %9.063e-10; %g/cell
    Ypc = 5.369e-5; %g/cell
    Cf=C*Volume
    Mf=M*Volume
    %Equations
    dydt(1)= mu*C;
    dydt(2)= -Ysc*mu*C;
    dydt(3)= Ypc*mu*C;
    dydt=dydt';
    end
end
```

APPENDIX B: SuperPro Designer Simulation Screenshots

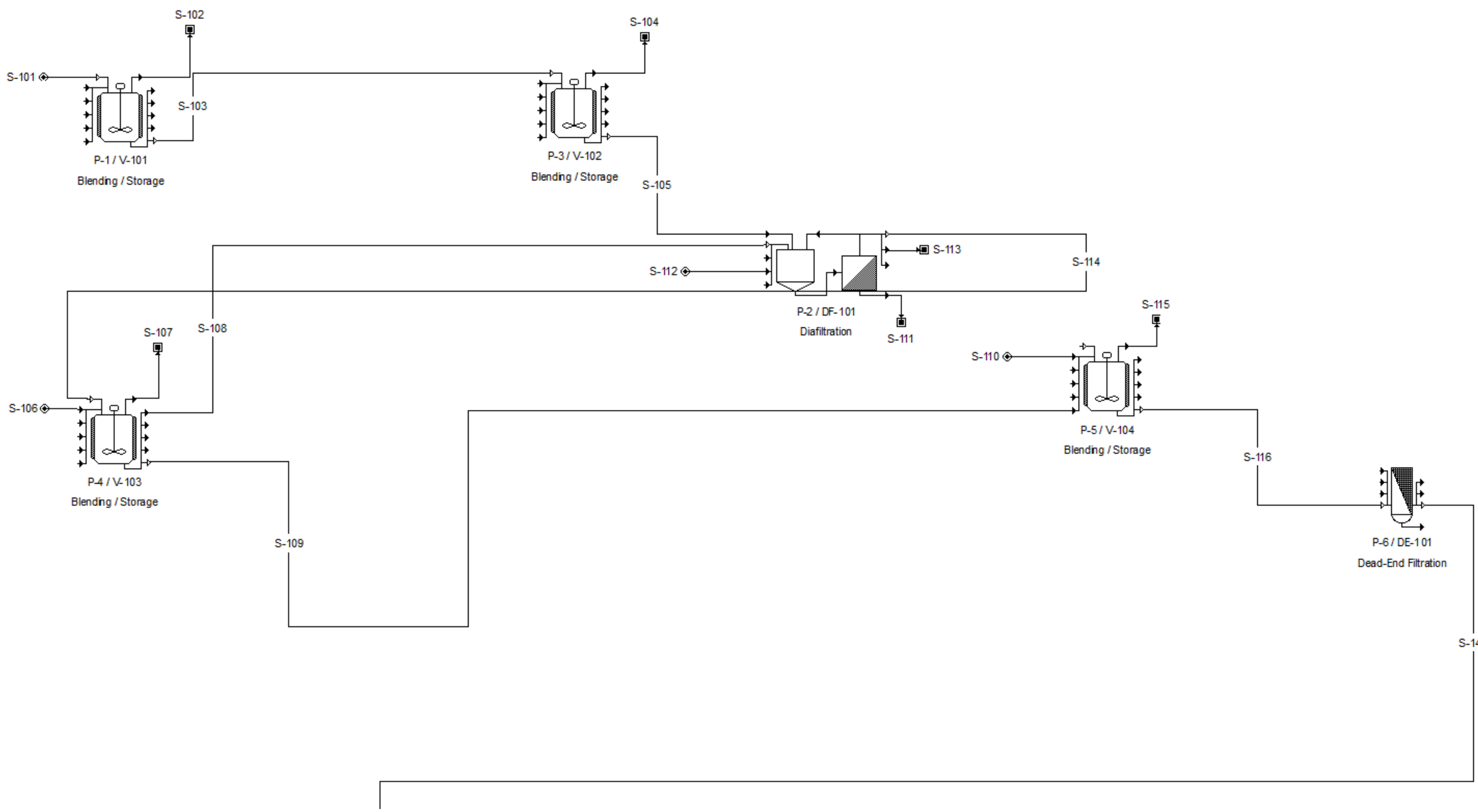
20,000 Flow-Primary Recovery



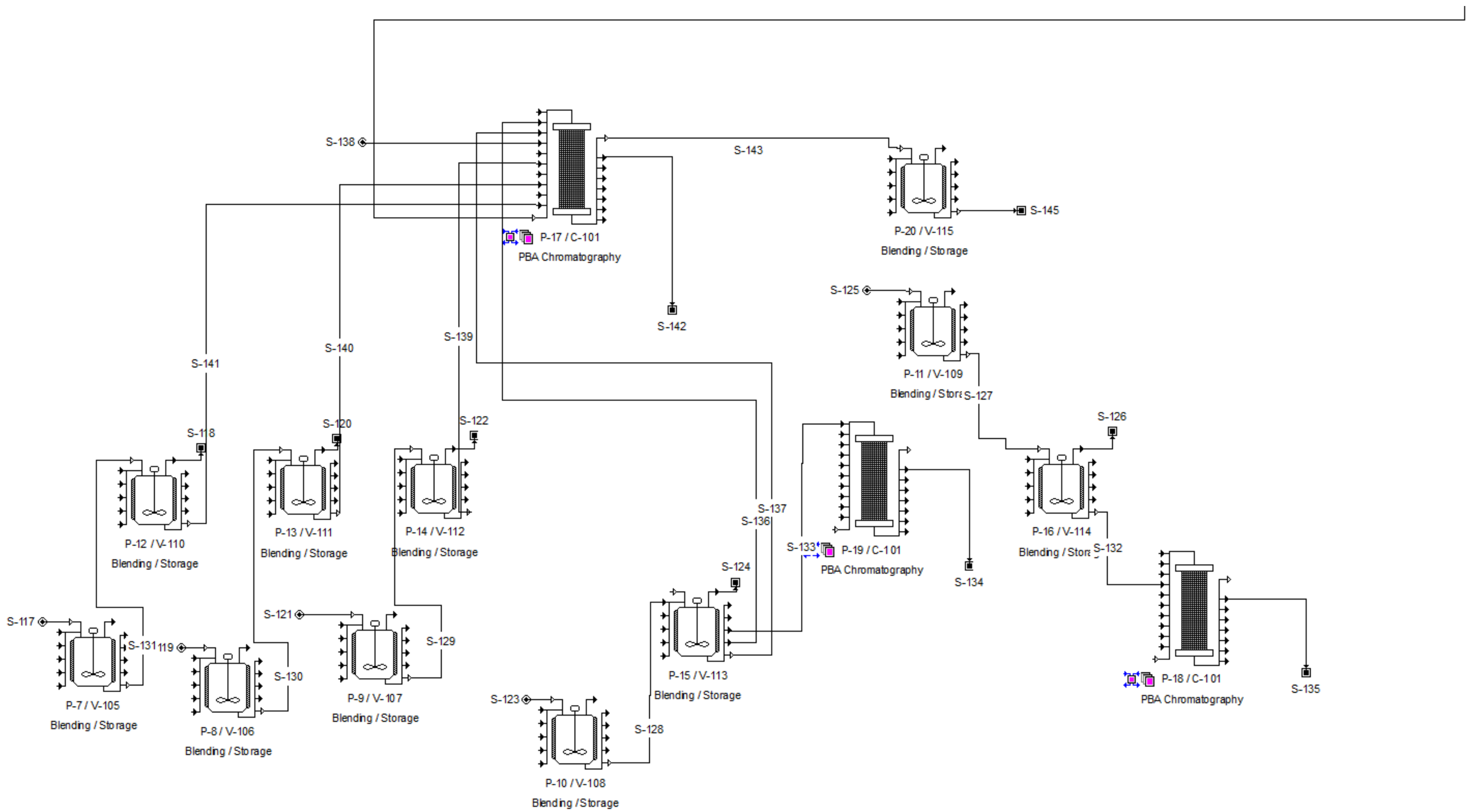
20,000 Flow- Protein A Chromatography



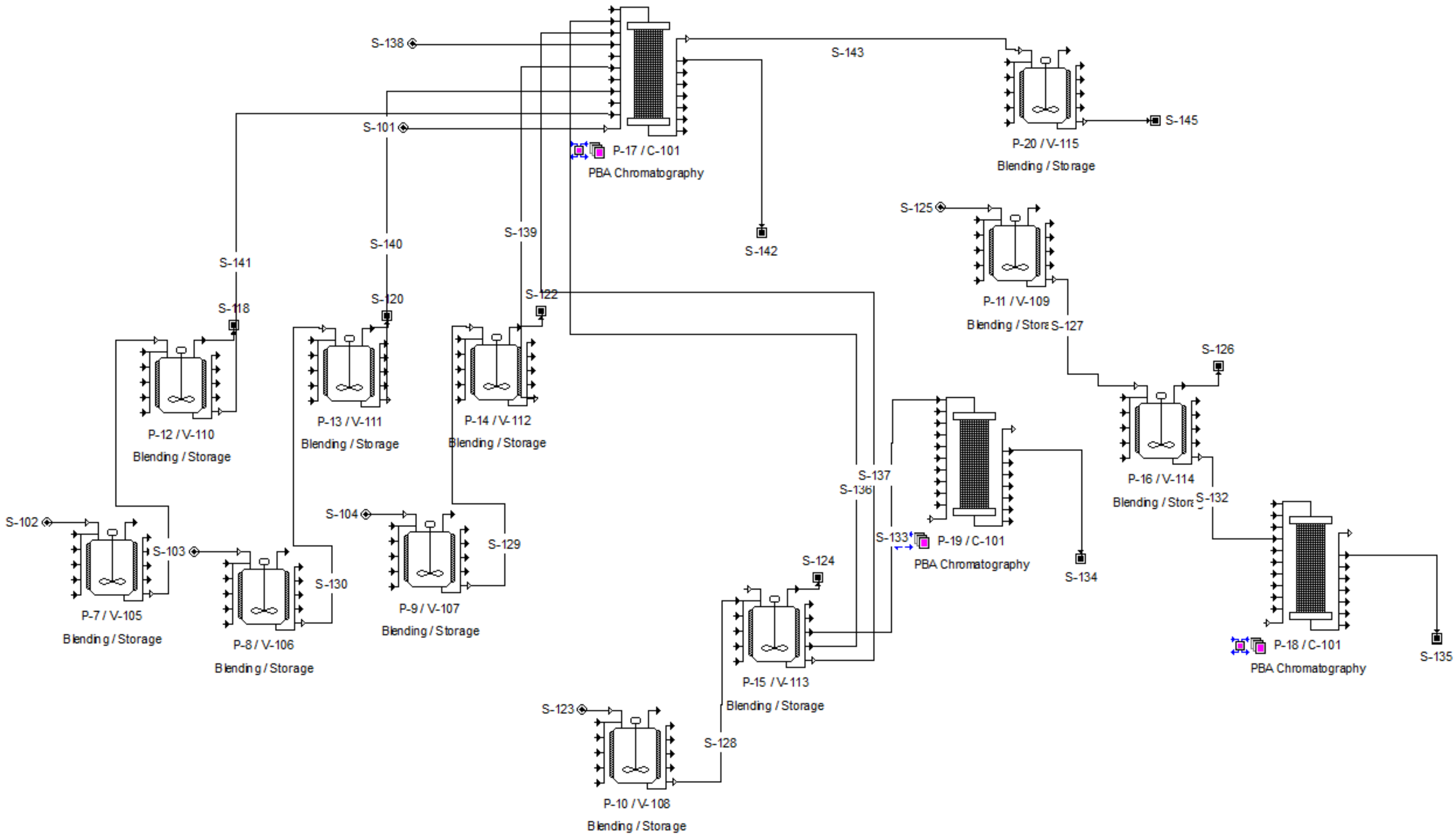
20,000 Flow-Viral Inactivation and CEX Part 1



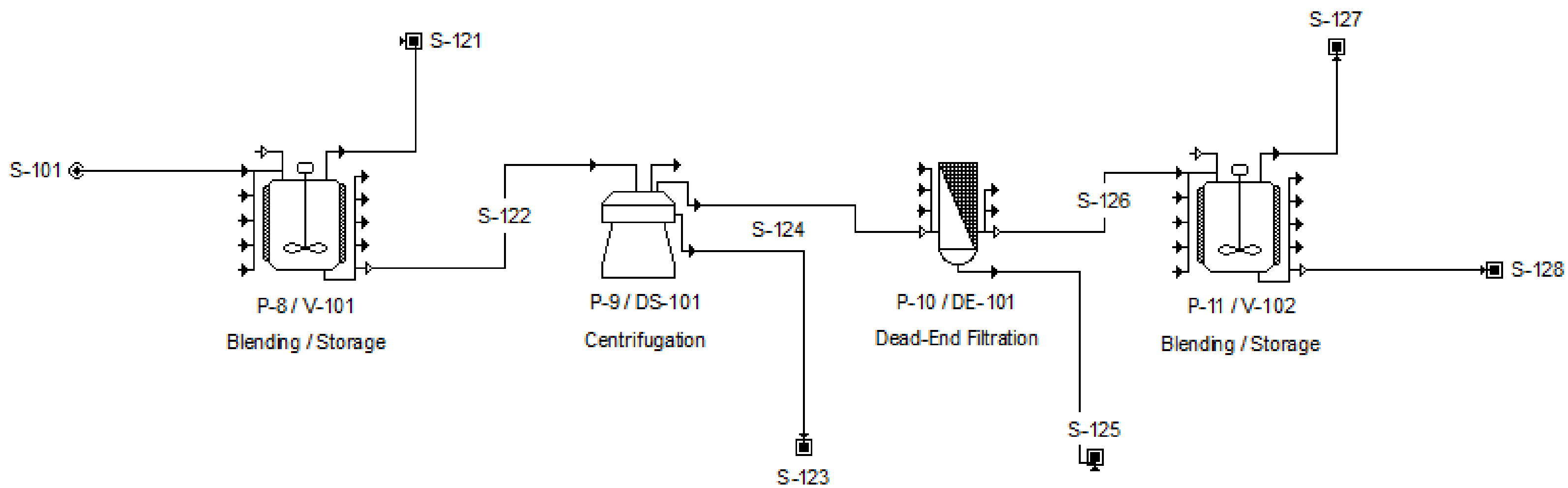
20,000 Flow-Viral Inactivation and CEX Part 2



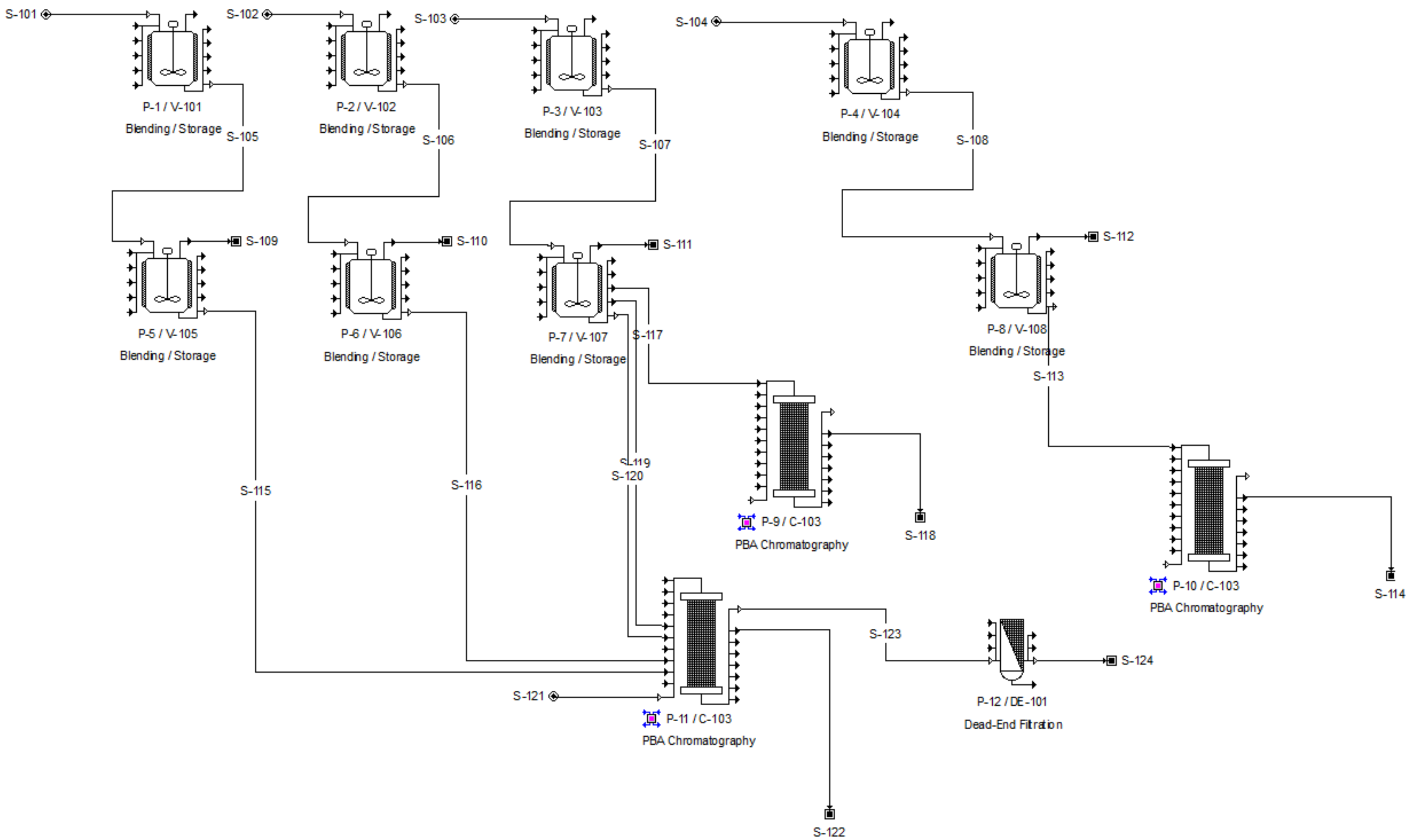
20,000 Flow- AEX



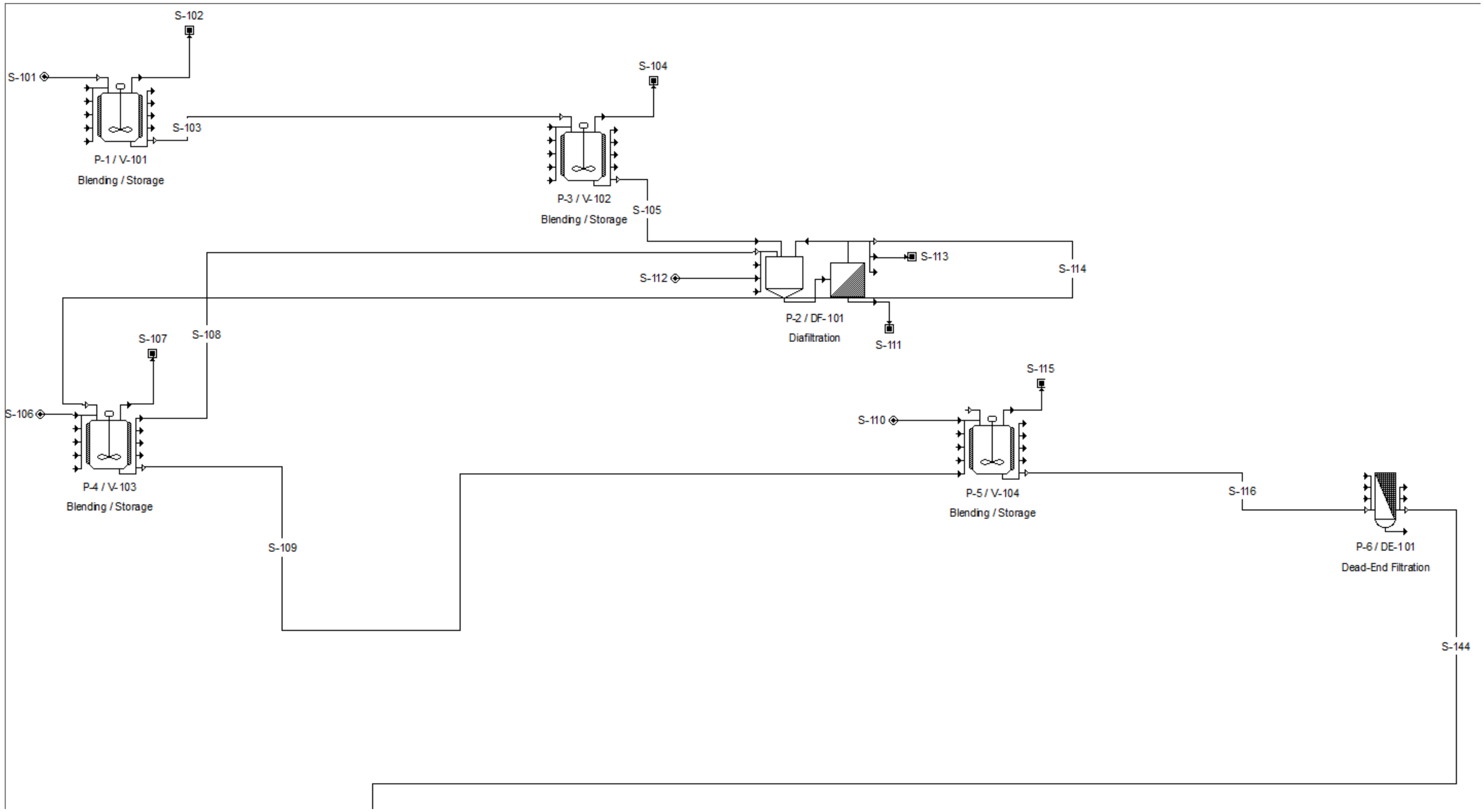
30,000 Flow-Primary Recovery



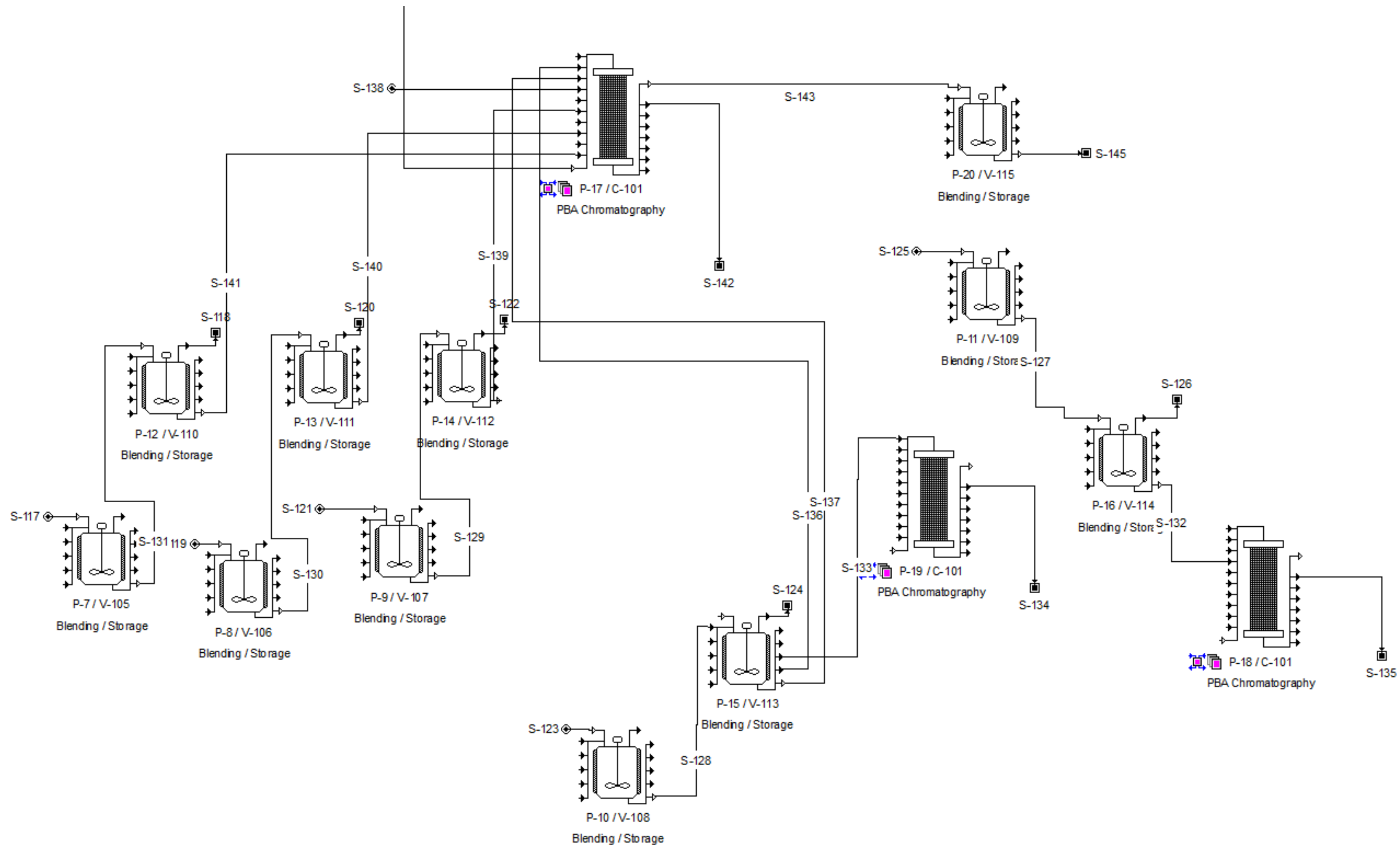
30,000 Flow-Protein A Chromatography



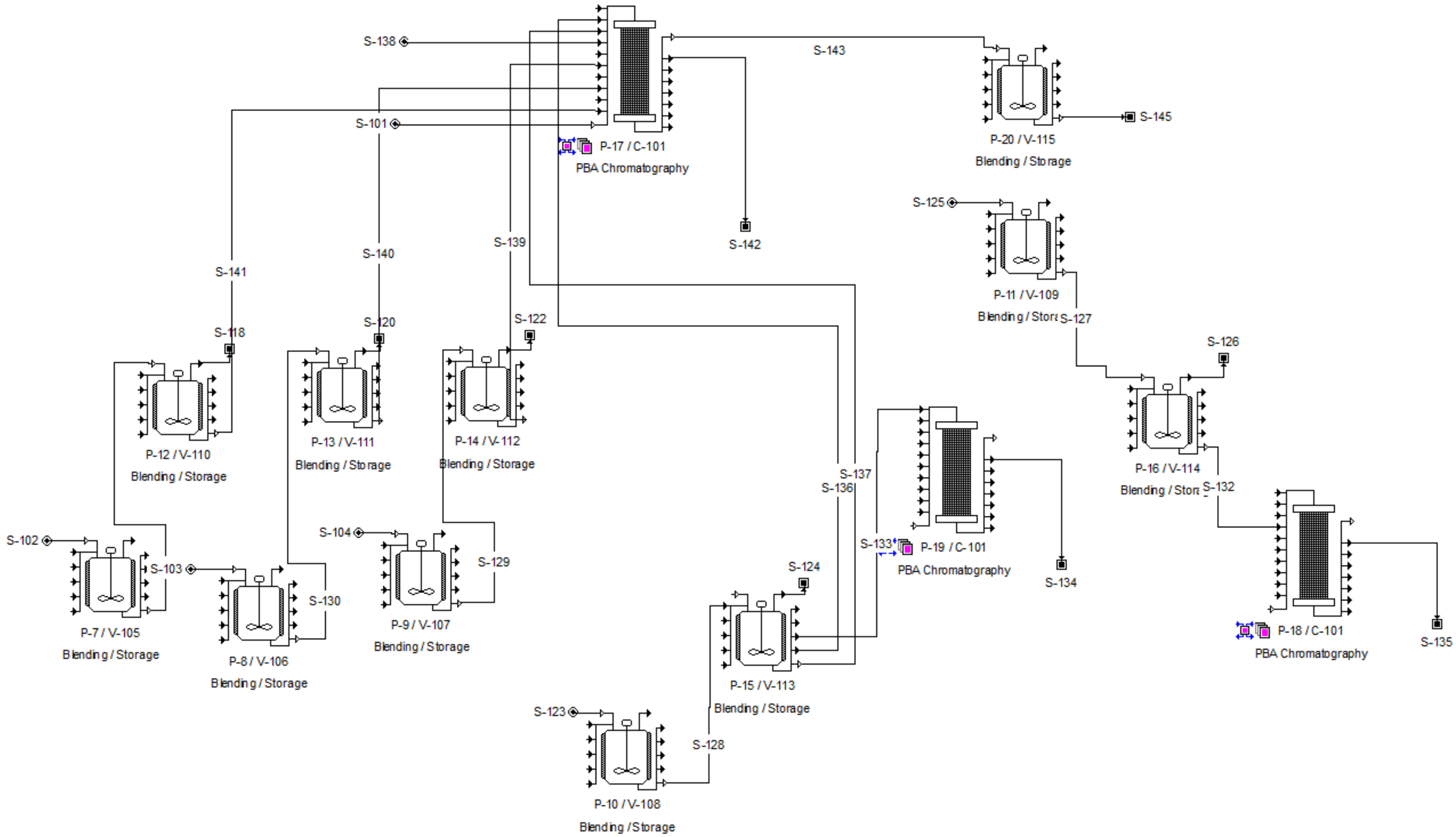
30,000 Flow-Viral Inactivation Part 1



30,000 Flow-Viral Inactivation Part 2



30,000 Flow-AEX



APPENDIX B: SuperPro Designer Material Streams

20K: Primary Recovery

2.1 STARTING MATERIAL REQUIREMENTS (per Section)

Section	Starting Material	Active Product	Amount Needed (kg Sin/kg MP)	Molar Yield (%)	Mass Yield (%)	Gross Mass Yield (%)
Main Section	(none)	(none)	Unknown	Unknown	Unknown	Unknown

Sin = Section Starting Material, Aout = Section Active Product

2.2 BULK MATERIALS (Entire Process)

Material	kg/yr	kg/batch	kg/kg MP
CHO Cells	0	0.00	
H3PO4 10w%	31,732	556.70	
MAb	2,280	40.00	
Media	2,295,960	40,280.00	
NaOH (0.5 M)	29,099	510.50	
Water	77,960	1,367.72	
TOTAL	2,437,030	42,754.92	

2.4 BULK MATERIALS (per Material)

CHO Cells				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	100.00	0	0.00	
TOTAL	100.00	0	0.00	

H3PO4 10w%				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	40.00	12,693	222.68	

2.5 BULK MATERIALS: SECTION TOTALS (kg/batch)

Raw Material	Main Section
CHO Cells	0.00
H3PO4 10w%	556.70
MAb	40.00
Media	40,280.00
NaOH (0.5 M)	510.50
Water	1,367.72
TOTAL	42,754.92

2.6 BULK MATERIALS: SECTION TOTALS (kg/yr)

Raw Material	Main Section
CHO Cells	0
H3PO4 10w%	31,732
MAb	2,280
Media	2,295,960
NaOH (0.5 M)	29,099
Water	77,960
TOTAL	2,437,030

P-11	28.18	21,971	385.45	
TOTAL	100.00	77,960	1,367.72	

3. STREAM DETAILS

Stream Name	S-101	S-122	S-124	S-123
Source	INPUT	P-8	P-9	P-9
Destination	P-8	P-9	P-10	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	5.35	5.35	1.01
Density (g/L)	994.70	994.70	994.70	994.70
Total Enthalpy (kW-h)	1,176.62	1,176.62	1,176.62	0.00
Specific Enthalpy (kcal/kg)	25.11	25.11	25.11	25.11
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
CHO Cells	0.00	0.00	0.00	0.00
MAb	40.00	40.00	40.00	0.00
Media	40,280.00	40,280.00	40,279.99	0.01
TOTAL (kg/batch)	40,320.00	40,320.00	40,319.99	0.01
TOTAL (L/batch)	40,534.66	40,534.66	40,534.65	0.01

Stream Name	S-126	S-125	S-128
Source	P-10	P-10	P-11
Destination	P-11	OUTPUT	OUTPUT
Stream Properties			
Activity (U/ml)	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00
Pressure (bar)	5.35	5.35	5.35
Density (g/L)	994.70	994.70	994.70
Total Enthalpy (kW-h)	1,176.62	0.00	1,176.62
Specific Enthalpy (kcal/kg)	25.11	25.11	25.11
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00
Component Flowrates (kg/batch)			
CHO Cells	0.00	0.00	0.00
MAb	40.00	0.00	40.00
Media	40,279.99	0.00	40,279.99
TOTAL (kg/batch)	40,319.99	0.00	40,319.99
TOTAL (L/batch)	40,534.65	0.00	40,534.65

20k: Protein A Chromatography

2.1 STARTING MATERIAL REQUIREMENTS (per Section)

Section	Starting Material	Active Product	Amount Needed (kg Sin/kg MP)	Molar Yield (%)	Mass Yield (%)	Gross Mass Yield (%)
Main Section	(none)	(none)	Unknown	Unknown	Unknown	Unknown

Sin = Section Starting Material, Aout = Section Active Product

2.2 BULK MATERIALS (Entire Process)

Material	kg/yr	kg/batch	kg/kg MP
Acetic Acid	77,989	172.54	
EDTA, Sodium	9,860	21.81	
Ethyl Alcohol	65,695	145.34	
H3PO4 10 w%	603,908	1,336.08	
MAb	18,080	40.00	
Media	18,206,556	40,279.99	
NaOH (0.5 M)	553,790	1,225.20	
NaOH .1M	235,718	521.50	
Sodium Chloride	4,930	10.91	
Sodium Citrate	14,046	31.08	
TRIS Base	4,930	10.91	
TRIS HCl	14,790	32.72	
Water	5,844,658	12,930.66	
WFI	26,370,227	58,341.21	
TOTAL	52,025,177	115,099.95	

2.3 BULK MATERIALS (per Section)

SECTIONS IN: Main Branch			
Main Section			
Material	**kg/yr**	**kg/batch**	**kg/kg MP**
Acetic-Acid	77,989	172.54	
EDTA, Sodium	9,860	21.81	
Ethyl Alcohol	65,695	145.34	
H3PO4 10 w%	603,908	1,336.08	
MAb	18,080	40.00	
Media	18,206,556	40,279.99	
NaOH (0.5 M)	553,790	1,225.20	
NaOH .1M	235,718	521.50	
Sodium Chloride	4,930	10.91	
Sodium Citrate	14,046	31.08	
TRIS Base	4,930	10.91	
TRIS HCl	14,790	32.72	
Water	5,844,658	12,930.66	
WFI	26,370,227	58,341.21	
TOTAL	52,025,177	115,099.95	

2.4 BULK MATERIALS (per Material)

Acetic-Acid				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-2	100.00	77,989	172.54	
TOTAL	100.00	77,989	172.54	

EDTA, Sodium				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-3	100.00	9,860	21.81	
TOTAL	100.00	9,860	21.81	

Ethyl Alcohol				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-4	100.00	65,695	145.34	
TOTAL	100.00	65,695	145.34	

H3PO4 10 w%				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-1	16.67	100,651	222.68	
P-2	16.67	100,651	222.68	
P-3	16.67	100,651	222.68	
P-4	16.67	100,651	222.68	
P-5	16.67	100,651	222.68	
P-6	16.67	100,651	222.68	
TOTAL	100.00	603,908	1,336.08	

MAb				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-11	100.00	18,080	40.00	
TOTAL	100.00	18,080	40.00	

Media				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-11	100.00	18,206,556	40,279.99	
TOTAL	100.00	18,206,556	40,279.99	

NaOH (0.5 M)				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-1	16.67	92,298	204.20	
P-2	16.67	92,298	204.20	
P-3	16.67	92,298	204.20	
P-4	16.67	92,298	204.20	
P-5	16.67	92,298	204.20	
P-6	16.67	92,298	204.20	
TOTAL	100.00	553,790	1,225.20	

NaOH .1M				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-10	100.00	235,718	521.50	
TOTAL	100.00	235,718	521.50	

Sodium Chloride				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-3	100.00	4,930	10.91	
TOTAL	100.00	4,930	10.91	

Sodium Citrate				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	100.00	14,046	31.08	
TOTAL	100.00	14,046	31.08	

TRIS Base				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-3	100.00	4,930	10.91	
TOTAL	100.00	4,930	10.91	

TRIS HCl				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-3	100.00	14,790	32.72	
TOTAL	100.00	14,790	32.72	

Water				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-2	2.98	174,222	385.45	
P-3	2.98	174,222	385.45	
P-4	2.98	174,222	385.45	
P-5	2.98	174,222	385.45	
P-6	2.98	174,222	385.45	
P-7	5.00	292,244	646.56	
P-8	5.00	292,244	646.56	
P-10	75.10	4,389,057	9,710.30	
TOTAL	100.00	5,844,658	12,930.66	

WFI				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	30.20	7,963,459	17,618.27	
P-2	49.00	12,920,162	28,584.43	
P-3	18.56	4,895,347	10,830.41	
P-4	2.24	591,259	1,308.09	
TOTAL	100.00	26,370,227	58,341.21	

2.5 BULK MATERIALS: SECTION TOTALS (kg/batch)

Raw Material	Main Section
Acetic-Acid	172.54
EDTA, Sodium	21.81
Ethyl Alcohol	145.34
H3PO4 10 w%	1,336.08
MAb	40.00
Media	40,279.99
NaOH (0.5 M)	1,225.20
NaOH .1M	521.50
Sodium Chloride	10.91
Sodium Citrate	31.08
TRIS Base	10.91
TRIS HCl	32.72
Water	12,930.66
WFI	58,341.21
TOTAL	115,099.95

2.6 BULK MATERIALS: SECTION TOTALS (kg/yr)

Raw Material	Main Section
Acetic-Acid	77,989
EDTA, Sodium	9,860
Ethyl Alcohol	65,695
H3PO4 10 w%	603,908
MAb	18,080
Media	18,206,556
NaOH (0.5 M)	553,790
NaOH .1M	235,718
Sodium Chloride	4,930
Sodium Citrate	14,046
TRIS Base	4,930
TRIS HCl	14,790
Water	5,844,658
WFI	26,370,227
TOTAL	52,025,177

3. STREAM DETAILS

Stream Name	S-101	S-105	S-115	S-102
Source	INPUT	P-1	P-5	INPUT
Destination	P-1	P-5	P-11	P-2
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	7.62	7.62	1.01
Density (g/L)	995.54	995.54	995.54	994.98
Total Enthalpy (kW-h)	502.95	502.95	43.50	836.61
Specific Enthalpy (kcal/kg)	25.07	25.07	25.07	25.03
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
Acetic-Acid	0.00	0.00	0.00	172.54
Sodium Citrate	31.08	31.08	2.69	0.00
WFI	17,232.82	17,232.82	1,490.62	28,584.43
TOTAL (kg/batch)	17,263.90	17,263.90	1,493.30	28,756.97
TOTAL (L/batch)	17,341.30	17,341.30	1,500.00	28,902.19

Stream Name	S-106	S-116	S-103	S-107
Source	P-2	P-6	INPUT	P-3
Destination	P-6	P-11	P-3	P-7
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	5.82	5.82	1.01	1.17
Density (g/L)	994.98	994.98	998.35	998.35
Total Enthalpy (kW-h)	836.61	108.55	316.43	316.43
Specific Enthalpy (kcal/kg)	25.03	25.03	24.96	24.96
Heat Capacity (kcal/kg-°C)	1.00	1.00	0.99	0.99
Component Flowrates (kg/batch)				
Acetic-Acid	172.54	22.39	0.00	0.00
EDTA, Sodium	0.00	0.00	21.81	21.81
Sodium Chloride	0.00	0.00	10.91	10.91
TRIS Base	0.00	0.00	10.91	10.91
TRIS HCl	0.00	0.00	32.72	32.72
WFI	28,584.43	3,708.77	10,830.41	10,830.41
TOTAL (kg/batch)	28,756.97	3,731.16	10,906.76	10,906.76
TOTAL (L/batch)	28,902.19	3,750.00	10,924.78	10,924.78

Stream Name	S-117	S-119	S-120	S-118
Source	P-7	P-7	P-7	P-9
Destination	P-9	P-11	P-11	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	10.13	1.16	2.08	10.13
Density (g/L)	998.35	998.35	998.35	998.35
Total Enthalpy (kW-h)	136.49	43.45	136.49	136.49
Specific Enthalpy (kcal/kg)	24.96	24.96	24.96	24.96
Heat Capacity (kcal/kg-°C)	0.99	0.99	0.99	0.99
Component Flowrates (kg/batch)				
EDTA, Sodium	9.41	3.00	9.41	9.41
Sodium Chloride	4.70	1.50	4.70	4.70
TRIS Base	4.70	1.50	4.70	4.70
TRIS HCl	14.11	4.49	14.11	14.11
WFI	4,671.69	1,487.04	4,671.69	4,671.69
TOTAL (kg/batch)	4,704.62	1,497.53	4,704.62	4,704.62
TOTAL (L/batch)	4,712.39	1,500.00	4,712.39	4,712.39

Stream Name	S-123	S-124	S-104	S-108
Source	P-11	P-12	INPUT	P-4
Destination	P-12	OUTPUT	P-4	P-8
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	1.01	1.01	1.22
Density (g/L)	994.97	994.97	968.96	968.96
Total Enthalpy (kW-h)	91.99	91.99	40.65	40.65
Specific Enthalpy (kcal/kg)	25.03	25.03	24.06	24.06
Heat Capacity (kcal/kg-°C)	1.00	1.00	0.96	0.96
Component Flowrates (kg/batch)				
Acetic Acid	18.75	18.75	0.00	0.00
Ethyl Alcohol	0.00	0.00	145.34	145.34
MAb	36.00	36.00	0.00	0.00
WFI	3,107.05	3,107.05	1,308.09	1,308.09
TOTAL (kg/batch)	3,161.81	3,161.81	1,453.44	1,453.44
TOTAL (L/batch)	3,177.78	3,177.78	1,500.00	1,500.00

Stream Name	S-113	S-121	S-122	S-114
Source	P-8	INPUT	P-11	P-10
Destination	P-10	P-11	OUTPUT	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.22	1.01	1.01	1.22
Density (g/L)	968.96	994.70	995.20	968.96
Total Enthalpy (kW-h)	40.65	1,176.62	1,416.63	40.65
Specific Enthalpy (kcal/kg)	24.06	25.11	25.09	24.06
Heat Capacity (kcal/kg-°C)	0.96	1.00	1.00	0.96
Component Flowrates (kg/batch)				
Acetic-Acid	0.00	0.00	3.63	0.00
EDTA, Sodium	0.00	0.00	12.40	0.00
Ethyl Alcohol	145.34	0.00	0.00	145.34
MAb	0.00	40.00	4.00	0.00
Media	0.00	40,279.99	40,279.99	0.00
Sodium Chloride	0.00	0.00	6.20	0.00
Sodium Citrate	0.00	0.00	2.69	0.00
TRIS Base	0.00	0.00	6.20	0.00
TRIS HCl	0.00	0.00	18.61	0.00
WFI	1,308.09	0.00	8,251.06	1,308.09
TOTAL (kg/batch)	1,453.44	40,319.99	48,584.79	1,453.44
TOTAL (L/batch)	1,500.00	40,534.65	48,819.25	1,500.00

Viral Inactivation and CEX 20k

2.2 BULK MATERIALS (Entire Process)

Material	kg/yr	kg/batch	kg/kg MP
.1 M NaOH	731,143	1,043.00	
Acetic-Acid	13,150	18.76	
Ethyl Alcohol	203,772	290.69	
H3PO4 10 w%	2,341,480	3,340.20	
KCl	13	0.02	
KH2PO4	13	0.02	
MAb	25,236	36.00	
NaH2PO4	8,733	12.46	
NaOH (0.5 M)	2,147,163	3,063.00	
Polysorbate 80	222	0.32	
Sodium Chloride	188,194	268.46	
Sodium Hydroxid	41,390	59.04	
Water	18,346,686	26,172.16	
WFI	20,395,074	29,094.26	
TOTAL	44,442,268	63,398.38	

2.3 BULK MATERIALS (per Section)

SECTIONS IN: Main Branch

Main Section

Material	kg/yr	kg/batch	kg/kg MP
.1 M NaOH	731,143	1,043.00	
Acetic-Acid	13,150	18.76	
Ethyl Alcohol	203,772	290.69	
H3PO4 10 w%	2,341,480	3,340.20	
KCl	13	0.02	
KH2PO4	13	0.02	
MAb	25,236	36.00	
NaH2PO4	8,733	12.46	
NaOH (0.5 M)	2,147,163	3,063.00	
Polysorbate 80	222	0.32	
Sodium Chloride	188,194	268.46	
Sodium Hydroxid	41,390	59.04	
Water	18,346,686	26,172.16	
WFI	20,395,074	29,094.26	
TOTAL	44,442,268	63,398.38	

2.4 BULK MATERIALS (per Material)

.1 M NaOH

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-18	100.00	731,143	1,043.00	
TOTAL	100.00	731,143	1,043.00	

Acetic-Acid

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-4	100.00	13,150	18.76	
TOTAL	100.00	13,150	18.76	

Ethyl Alcohol

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-11	100.00	203,772	290.69	
TOTAL	100.00	203,772	290.69	

H3PO4 10 w%

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	6.67	156,099	222.68	
P-3	6.67	156,099	222.68	
P-4	6.67	156,099	222.68	
P-5	6.67	156,099	222.68	
P-7	6.67	156,099	222.68	
P-8	6.67	156,099	222.68	
P-9	6.67	156,099	222.68	
P-10	6.67	156,099	222.68	
P-11	6.67	156,099	222.68	
P-12	6.67	156,099	222.68	
P-13	6.67	156,099	222.68	
P-14	6.67	156,099	222.68	
P-15	6.67	156,099	222.68	
P-16	6.67	156,099	222.68	
P-20	6.67	156,099	222.68	
TOTAL	100.00	2,341,480	3,340.20	

KCl

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	100.00	13	0.02	
TOTAL	100.00	13	0.02	

KH2PO4

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	100.00	13	0.02	
TOTAL	100.00	13	0.02	

MAb

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-4	100.00	25,236	36.00	
TOTAL	100.00	25,236	36.00	

NaH2PO4

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-9	20.56	1,796	2.56	
P-10	79.44	6,937	9.90	
TOTAL	100.00	8,733	12.46	

NaOH (0.5 M)

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	6.67	143,144	204.20	
P-3	6.67	143,144	204.20	
P-4	6.67	143,144	204.20	
P-5	6.67	143,144	204.20	
P-7	6.67	143,144	204.20	
P-8	6.67	143,144	204.20	
P-9	6.67	143,144	204.20	
P-10	6.67	143,144	204.20	
P-11	6.67	143,144	204.20	
P-12	6.67	143,144	204.20	
P-13	6.67	143,144	204.20	
P-14	6.67	143,144	204.20	
P-15	6.67	143,144	204.20	
P-16	6.67	143,144	204.20	
P-20	6.67	143,144	204.20	
TOTAL	100.00	2,147,163	3,063.00	

Polysorbate 80

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-5	100.00	222	0.32	
TOTAL	100.00	222	0.32	

Sodium Chloride

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	64.81	121,969	173.99	
P-9	5.03	9,463	13.50	
P-10	30.16	56,761	80.97	
TOTAL	100.00	188,194	268.46	

Sodium Hydroxid

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-7	100.00	41,390	59.04	
TOTAL	100.00	41,390	59.04	

Water

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	1.47	270,199	385.45	
P-2	3.71	679,856	969.84	
P-3	1.47	270,199	385.45	
P-4	1.47	270,199	385.45	
P-5	1.47	270,199	385.45	
P-7	1.47	270,199	385.45	

P-8	1.47	270,199	385.45	
P-9	1.47	270,199	385.45	
P-10	1.47	270,199	385.45	
P-11	1.47	270,199	385.45	
P-12	1.47	270,199	385.45	
P-13	1.47	270,199	385.45	
P-14	1.47	270,199	385.45	
P-15	1.47	270,199	385.45	
P-16	1.47	270,199	385.45	
P-18	74.20	13,613,846	19,420.61	
P-20	1.47	270,199	385.45	
TOTAL	100.00	18,346,686	26,172.16	

WFI

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	10.86	2,215,832	3,160.96	
P-2	3.40	692,448	987.80	
P-4	10.68	2,178,044	3,107.05	
P-5	0.00	222	0.32	
P-7	10.15	2,070,345	2,953.42	
P-8	9.95	2,029,166	2,894.67	
P-9	0.84	171,982	245.34	
P-10	30.61	6,243,016	8,905.87	
P-11	8.99	1,833,948	2,616.19	
P-17	14.51	2,960,072	4,222.64	
TOTAL	100.00	20,395,074	29,094.26	

2.5 BULK MATERIALS: SECTION TOTALS (kg/batch)

Raw Material	Main Section
.1 M NaOH	1,043.00
Acetic-Acid	18.76
Ethyl Alcohol	290.69
H3PO4 10 w%	3,340.20
KCl	0.02
KH2PO4	0.02
MAb	36.00
NaH2PO4	12.46
NaOH (0.5 M)	3,063.00
Polysorbate 80	0.32
Sodium Chloride	268.46
Sodium Hydroxid	59.04
Water	26,172.16
WFI	29,094.26
TOTAL	63,398.38

2.6 BULK MATERIALS: SECTION TOTALS (kg/yr)

Raw Material	Main Section
.1 M NaOH	731,143
Acetic-Acid	13,150
Ethyl Alcohol	203,772
H3PO4 10 w%	2,341,480
KCl	13
KH2PO4	13
MAb	25,236
NaH2PO4	8,733
NaOH (0.5 M)	2,147,163
Polysorbate 80	222
Sodium Chloride	188,194
Sodium Hydroxid	41,390
Water	18,346,686
WFI	20,395,074
TOTAL	44,442,268

3. STREAM DETAILS

Stream Name	S-101	S-103	S-105	S-114
Source	INPUT	P-1	P-3	P-2
Destination	P-1	P-3	P-2	P-4
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.43
Pressure (bar)	1.01	4.93	4.93	4.93
Density (g/L)	994.70	994.70	994.70	994.64
Total Enthalpy (kW-h)	92.24	92.24	92.24	93.74
Specific Enthalpy (kcal/kg)	25.11	25.11	25.11	25.51
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
Acetic-Acid	0.00	0.00	0.00	6.90
MAb	0.00	0.00	0.00	36.00
WFI	3,160.96	3,160.96	3,160.96	3,118.37
TOTAL (kg/batch)	3,160.96	3,160.96	3,160.96	3,161.27
TOTAL (L/batch)	3,177.79	3,177.79	3,177.79	3,178.29

Stream Name	S-106	S-108	S-109	S-112
Source	INPUT	P-4	P-4	INPUT
Destination	P-4	P-2	P-5	P-2
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.43	25.00
Pressure (bar)	1.01	4.93	4.94	1.01
Density (g/L)	994.97	994.97	994.64	994.70
Total Enthalpy (kW-h)	91.99	91.99	93.74	28.83
Specific Enthalpy (kcal/kg)	25.03	25.03	25.51	25.11
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
Acetic-Acid	18.76	18.76	6.90	0.00
MAb	36.00	36.00	36.00	0.00
WFI	3,107.05	3,107.05	3,118.37	987.80
TOTAL (kg/batch)	3,161.81	3,161.81	3,161.27	987.80
TOTAL (L/batch)	3,177.79	3,177.79	3,178.29	993.06

Stream Name	S-113	S-111	S-110	S-116
Source	P-2	P-2	INPUT	P-5
Destination	OUTPUT	OUTPUT	P-5	P-6
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.43	25.00	25.43
Pressure (bar)	1.01	4.93	1.01	4.94
Density (g/L)	994.70	994.71	870.19	994.62
Total Enthalpy (kW-h)	28.83	93.67	0.01	93.76
Specific Enthalpy (kcal/kg)	25.11	25.49	13.77	25.51
Heat Capacity (kcal/kg-°C)	1.00	1.00	0.55	1.00
Component Flowrates (kg/batch)				
Acetic-Acid	0.00	11.86	0.00	6.90
MAb	0.00	0.00	0.00	36.00
Polysorbate 80	0.00	0.00	0.32	0.32
WFI	987.80	3,149.64	0.32	3,118.69
TOTAL (kg/batch)	987.80	3,161.50	0.63	3,161.90
TOTAL (L/batch)	993.06	3,178.30	0.73	3,179.02

Stream Name	S-144	S-117	S-131	S-141
Source	P-6	INPUT	P-7	P-12
Destination	P-17	P-7	P-12	P-17
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.43	25.00	25.00	25.00
Pressure (bar)	4.94	1.01	7.09	7.09
Density (g/L)	994.62	1,004.15	1,004.15	1,004.15
Total Enthalpy (kW-h)	93.76	87.08	87.08	87.08
Specific Enthalpy (kcal/kg)	25.51	24.87	24.87	24.87
Heat Capacity (kcal/kg-°C)	1.00	0.99	0.99	0.99
Component Flowrates (kg/batch)				
Acetic-Acid	6.90	0.00	0.00	0.00
MAb	36.00	0.00	0.00	0.00
Polysorbate 80	0.32	0.00	0.00	0.00
Sodium Hydroxid	0.00	59.04	59.04	59.04
WFI	3,118.69	2,953.42	2,953.42	2,953.42
TOTAL (kg/batch)	3,161.90	3,012.46	3,012.46	3,012.46
TOTAL (L/batch)	3,179.02	3,000.00	3,000.00	3,000.00

Stream Name	S-119	S-130	S-140	S-121
Source	INPUT	P-8	P-13	INPUT
Destination	P-8	P-13	P-17	P-9
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	7.09	7.09	1.01
Density (g/L)	1,022.89	1,022.89	1,022.89	1,025.59
Total Enthalpy (kW-h)	87.63	87.63	87.63	7.42
Specific Enthalpy (kcal/kg)	24.57	24.57	24.57	24.41
Heat Capacity (kcal/kg-°C)	0.98	0.98	0.98	0.97
Component Flowrates (kg/batch)				
NaH2PO4	0.00	0.00	0.00	2.56
Sodium Chloride	173.99	173.99	173.99	13.50
WFI	2,894.67	2,894.67	2,894.67	245.34
TOTAL (kg/batch)	3,068.67	3,068.67	3,068.67	261.40
TOTAL (L/batch)	3,000.00	3,000.00	3,000.00	254.88

Stream Name	S-129	S-139	S-123	S-128
Source	P-9	P-14	INPUT	P-10
Destination	P-14	P-17	P-10	P-15
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	6.74	6.74	1.01	10.13
Density (g/L)	1,025.59	1,025.59	999.64	999.64
Total Enthalpy (kW-h)	7.42	7.42	261.41	261.41
Specific Enthalpy (kcal/kg)	24.41	24.41	25.00	25.00
Heat Capacity (kcal/kg-°C)	0.97	0.97	1.00	1.00
Component Flowrates (kg/batch)				
KCl	0.00	0.00	0.02	0.02
KH2PO4	0.00	0.00	0.02	0.02
NaH2PO4	2.56	2.56	9.90	9.90
Sodium Chloride	13.50	13.50	80.97	80.97
WFI	245.34	245.34	8,905.87	8,905.87
TOTAL (kg/batch)	261.40	261.40	8,996.77	8,996.77
TOTAL (L/batch)	254.88	254.88	9,000.00	9,000.00

Stream Name	S-133	S-136	S-137	S-143
Source	P-15	P-15	P-15	P-17
Destination	P-19	P-17	P-17	P-20
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.01
Pressure (bar)	10.13	2.53	1.45	1.01
Density (g/L)	999.64	999.64	999.64	996.42
Total Enthalpy (kW-h)	87.14	87.14	87.14	53.22
Specific Enthalpy (kcal/kg)	25.00	25.00	25.00	25.08
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
KCl	0.01	0.01	0.01	0.00
KH2PO4	0.01	0.01	0.01	0.00
MAb	0.00	0.00	0.00	32.40
NaH2PO4	3.30	3.30	3.30	1.02
Sodium Chloride	26.99	26.99	26.99	5.40
WFI	2,968.62	2,968.62	2,968.62	1,787.19
TOTAL (kg/batch)	2,998.92	2,998.92	2,998.92	1,826.02
TOTAL (L/batch)	3,000.00	3,000.00	3,000.00	1,832.58

Stream Name	S-145	S-125	S-127	S-132
Source	P-20	INPUT	P-11	P-16
Destination	OUTPUT	P-11	P-16	P-18
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.01	25.00	25.00	25.00
Pressure (bar)	3.80	1.01	7.09	7.09
Density (g/L)	996.42	968.96	968.96	968.96
Total Enthalpy (kW-h)	53.22	81.30	81.30	81.30
Specific Enthalpy (kcal/kg)	25.08	24.06	24.06	24.06
Heat Capacity (kcal/kg-°C)	1.00	0.96	0.96	0.96
Component Flowrates (kg/batch)				
Ethyl Alcohol	0.00	290.69	290.69	290.69
MAb	32.40	0.00	0.00	0.00
NaH2PO4	1.02	0.00	0.00	0.00
Sodium Chloride	5.40	0.00	0.00	0.00
WFI	1,787.19	2,616.19	2,616.19	2,616.19
TOTAL (kg/batch)	1,826.02	2,906.88	2,906.88	2,906.88
TOTAL (L/batch)	1,832.58	3,000.00	3,000.00	3,000.00

Stream Name	S-134	S-138	S-142	S-135
Source	P-19	INPUT	P-17	P-18
Destination	OUTPUT	P-17	OUTPUT	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.08	25.00
Pressure (bar)	10.13	1.01	1.01	7.09
Density (g/L)	999.64	994.70	1,002.94	968.96
Total Enthalpy (kW-h)	87.14	123.23	520.16	81.30
Specific Enthalpy (kcal/kg)	25.00	25.11	25.00	24.06
Heat Capacity (kcal/kg-°C)	1.00	1.00	0.99	0.96
Component Flowrates (kg/batch)				
Acetic Acid	0.00	0.00	6.90	0.00
Ethyl Alcohol	0.00	0.00	0.00	290.69
KCl	0.01	0.00	0.01	0.00
KH2PO4	0.01	0.00	0.01	0.00
MAb	0.00	0.00	3.60	0.00
NaH2PO4	3.30	0.00	8.13	0.00
Polysorbate 80	0.00	0.00	0.32	0.00
Sodium Chloride	26.99	0.00	236.07	0.00
Sodium Hydroxid	0.00	0.00	59.04	0.00
WFI	2,968.62	4,222.64	17,584.81	2,616.19
TOTAL (kg/batch)	2,998.92	4,222.64	17,898.91	2,906.88
TOTAL (L/batch)	3,000.00	4,245.12	17,846.43	3,000.00

AEX- 20k

2.1 STARTING MATERIAL REQUIREMENTS (per Section)

Section	Starting Material	Active Product	Amount Needed (kg Sin/kg MP)	Molar Yield (%)	Mass Yield (%)	Gross Mass Yield (%)
Main Section	(none)	(none)	Unknown	Unknown	Unknown	Unknown

Sin = Section Starting Material, Aout = Section Active Product

2.2 BULK MATERIALS (Entire Process)

Material	kg/yr	kg/batch	kg/kg MP
.1M NaOH	2,802,020	1,564.50	
Ethyl Alcohol	780,932	436.03	
H3PO4 10w%	3,988,199	2,226.80	
KCl	489,677	273.41	
KH2PO4	48	0.03	
MAb	58,030	32.40	
N-Methyldiethan	4,129	2.31	
NaH2PO4	28,422	15.87	
NaOH (0.5 M)	3,291,500	1,837.80	
Sodium Chloride	227,199	126.86	
TRIS Base	158,812	88.67	
Water	61,192,561	34,166.70	
WFI	57,082,814	31,872.03	
TOTAL	130,104,342	72,643.41	

2.3 BULK MATERIALS (per Section)

SECTIONS IN: Main Branch

Main Section			
Material	**kg/yr**	**kg/batch**	**kg/kg MP**
.1M NaOH	2,802,020	1,564.50	
Ethyl Alcohol	780,932	436.03	
H3PO4 10w%	3,988,199	2,226.80	
KCl	489,677	273.41	
KH2PO4	48	0.03	
MAb	58,030	32.40	
N-Methyldiethan	4,129	2.31	
NaH2PO4	28,422	15.87	
NaOH (0.5 M)	3,291,500	1,837.80	
Sodium Chloride	227,199	126.86	
TRIS Base	158,812	88.67	
Water	61,192,561	34,166.70	
WFI	57,082,814	31,872.03	
TOTAL	130,104,342	72,643.41	

2.4 BULK MATERIALS (per Material)

.1M NaOH				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-18	100.00	2,802,020	1,564.50	
TOTAL	100.00	2,802,020	1,564.50	

Ethyl Alcohol				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-11	100.00	780,932	436.03	
TOTAL	100.00	780,932	436.03	

H3PO4 10w%				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-7	10.00	398,820	222.68	
P-8	10.00	398,820	222.68	
P-9	10.00	398,820	222.68	
P-10	10.00	398,820	222.68	
P-11	10.00	398,820	222.68	
P-12	10.00	398,820	222.68	
P-13	10.00	398,820	222.68	

P-14	10.00	398,820	222.68	
P-15	10.00	398,820	222.68	
P-16	10.00	398,820	222.68	
TOTAL	100.00	3,988,199	2,226.80	

KCl

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	95.55	467,867	261.23	
P-9	4.44	21,761	12.15	
P-10	0.01	48	0.03	
TOTAL	100.00	489,677	273.41	

KH2PO4

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	100.00	48	0.03	
TOTAL	100.00	48	0.03	

MAb

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-17	100.00	58,030	32.40	
TOTAL	100.00	58,030	32.40	

N-Methyldiethan

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-9	100.00	4,129	2.31	
TOTAL	100.00	4,129	2.31	

NaH2PO4

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	93.54	26,587	14.84	
P-17	6.46	1,835	1.02	
TOTAL	100.00	28,422	15.87	

NaOH (0.5 M)

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	11.11	365,722	204.20	
P-9	11.11	365,722	204.20	
P-10	11.11	365,722	204.20	
P-11	11.11	365,722	204.20	
P-12	11.11	365,722	204.20	
P-13	11.11	365,722	204.20	
P-14	11.11	365,722	204.20	
P-15	11.11	365,722	204.20	
P-16	11.11	365,722	204.20	

TOTAL	100.00	3,291,500	1,837.80	

Sodium Chloride

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	95.74	217,529	121.46	
P-17	4.26	9,671	5.40	
TOTAL	100.00	227,199	126.86	

TRIS Base

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-7	100.00	158,812	88.67	
TOTAL	100.00	158,812	88.67	

Water

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-7	1.71	1,046,640	584.39	
P-8	1.13	690,337	385.45	
P-9	1.13	690,337	385.45	
P-10	1.13	690,337	385.45	
P-11	1.13	690,337	385.45	
P-12	1.13	690,337	385.45	
P-13	1.13	690,337	385.45	
P-14	1.13	690,337	385.45	
P-15	1.13	690,337	385.45	
P-16	1.13	690,337	385.45	
P-18	85.30	52,195,908	29,143.44	
P-20	2.84	1,736,978	969.84	
TOTAL	100.00	61,192,561	34,166.70	

WFI

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-7	13.92	7,943,820	4,435.41	
P-8	13.64	7,783,763	4,346.04	
P-9	0.69	395,471	220.81	
P-10	41.91	23,925,623	13,358.81	
P-11	12.31	7,028,390	3,924.28	
P-17	17.53	10,005,747	5,586.68	
TOTAL	100.00	57,082,814	31,872.03	

2.5 BULK MATERIALS: SECTION TOTALS (kg/batch)

Raw Material	Main Section
.1M NaOH	1,564.50
Ethyl Alcohol	436.03
H3PO4 10w%	2,226.80
KCl	273.41
KH2PO4	0.03
MAb	32.40
N-Methyldiethan	2.31
NaH2PO4	15.87
NaOH (0.5 M)	1,837.80
Sodium Chloride	126.86
TRIS Base	88.67
Water	34,166.70
WFI	31,872.03
TOTAL	72,643.41

2.6 BULK MATERIALS: SECTION TOTALS (kg/yr)

Raw Material	Main Section
.1M NaOH	2,802,020
Ethyl Alcohol	780,932
H3PO4 10w%	3,988,199
KCl	489,677
KH2PO4	48
MAb	58,030
N-Methyldiethan	4,129
NaH2PO4	28,422
NaOH (0.5 M)	3,291,500
Sodium Chloride	227,199
TRIS Base	158,812
Water	61,192,561
WFI	57,082,814
TOTAL	130,104,342

3. STREAM DETAILS

Stream Name	S-102	S-131	S-141	S-103
Source	INPUT	P-7	P-12	INPUT
Destination	P-7	P-12	P-17	P-8
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	10.13	10.13	1.01
Density (g/L)	1,005.35	1,005.35	1,005.35	1,023.84
Total Enthalpy (kW-h)	129.73	129.73	129.73	128.61
Specific Enthalpy (kcal/kg)	24.67	24.67	24.67	24.02
Heat Capacity (kcal/kg-°C)	0.98	0.98	0.98	0.96
Component Flowrates (kg/batch)				
KCl	0.00	0.00	0.00	261.23
TRIS Base	88.67	88.67	88.67	0.00
WFI	4,435.41	4,435.41	4,435.41	4,346.04
TOTAL (kg/batch)	4,524.08	4,524.08	4,524.08	4,607.28
TOTAL (L/batch)	4,500.00	4,500.00	4,500.00	4,500.00

Stream Name	S-130	S-140	S-104	S-129
Source	P-8	P-13	INPUT	P-9
Destination	P-13	P-17	P-9	P-14
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	10.13	10.13	1.01	4.37
Density (g/L)	1,023.84	1,023.84	1,021.17	1,021.17
Total Enthalpy (kW-h)	128.61	128.61	6.54	6.54
Specific Enthalpy (kcal/kg)	24.02	24.02	23.91	23.91
Heat Capacity (kcal/kg-°C)	0.96	0.96	0.95	0.95
Component Flowrates (kg/batch)				
KCl	261.23	261.23	12.15	12.15
N-Methyldiethan	0.00	0.00	2.31	2.31
WFI	4,346.04	4,346.04	220.81	220.81
TOTAL (kg/batch)	4,607.28	4,607.28	235.27	235.27
TOTAL (L/batch)	4,500.00	4,500.00	230.39	230.39

Stream Name	S-139	S-123	S-128	S-133
Source	P-14	INPUT	P-10	P-15
Destination	P-17	P-10	P-15	P-19
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	4.37	1.01	10.13	10.13
Density (g/L)	1,021.17	999.64	999.64	999.64
Total Enthalpy (kW-h)	6.54	392.11	392.11	130.70
Specific Enthalpy (kcal/kg)	23.91	25.00	25.00	25.00
Heat Capacity (kcal/kg-°C)	0.95	1.00	1.00	1.00
Component Flowrates (kg/batch)				
KCl	12.15	0.03	0.03	0.01
KH2PO4	0.00	0.03	0.03	0.01
N-Methyldiethan	2.31	0.00	0.00	0.00
NaH2PO4	0.00	14.84	14.84	4.95
Sodium Chloride	0.00	121.46	121.46	40.49
WFI	220.81	13,358.81	13,358.81	4,452.94
TOTAL (kg/batch)	235.27	13,495.16	13,495.16	4,498.39
TOTAL (L/batch)	230.39	13,500.00	13,500.00	4,500.00

Stream Name	S-136	S-137	S-143	S-145
Source	P-15	P-15	P-17	P-20
Destination	P-17	P-17	P-20	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	2.53	1.45	1.01	5.78
Density (g/L)	999.64	999.64	996.18	996.18
Total Enthalpy (kW-h)	130.70	130.70	47.82	47.82
Specific Enthalpy (kcal/kg)	25.00	25.00	25.04	25.04
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
KCl	0.01	0.01	4.86	4.86
KH2PO4	0.01	0.01	0.00	0.00
MAb	0.00	0.00	29.16	29.16
N-Methyldiethan	0.00	0.00	0.92	0.92
NaH2PO4	4.95	4.95	0.00	0.00
Sodium Chloride	40.49	40.49	0.00	0.00
WFI	4,452.94	4,452.94	1,608.12	1,608.12
TOTAL (kg/batch)	4,498.39	4,498.39	1,643.06	1,643.06
TOTAL (L/batch)	4,500.00	4,500.00	1,649.36	1,649.36

Stream Name	S-125	S-127	S-132	S-134
Source	INPUT	P-11	P-16	P-19
Destination	P-11	P-16	P-18	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	10.13	10.13	10.13
Density (g/L)	968.96	968.96	968.96	999.64
Total Enthalpy (kW-h)	121.95	121.95	121.95	130.70
Specific Enthalpy (kcal/kg)	24.06	24.06	24.06	25.00
Heat Capacity (kcal/kg-°C)	0.96	0.96	0.96	1.00
Component Flowrates (kg/batch)				
Ethyl Alcohol	436.03	436.03	436.03	0.00
KCl	0.00	0.00	0.00	0.01
KH2PO4	0.00	0.00	0.00	0.01
NaH2PO4	0.00	0.00	0.00	4.95
Sodium Chloride	0.00	0.00	0.00	40.49
WFI	3,924.28	3,924.28	3,924.28	4,452.94
TOTAL (kg/batch)	4,360.31	4,360.31	4,360.31	4,498.39
TOTAL (L/batch)	4,500.00	4,500.00	4,500.00	4,500.00

Stream Name	S-138	S-101	S-142	S-135
Source	INPUT	INPUT	P-17	P-18
Destination	P-17	P-17	OUTPUT	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	1.01	1.01	10.13
Density (g/L)	994.70	996.42	1,005.06	968.96
Total Enthalpy (kW-h)	110.88	53.20	642.55	121.95
Specific Enthalpy (kcal/kg)	25.11	25.07	24.74	24.06
Heat Capacity (kcal/kg-°C)	1.00	1.00	0.99	0.96
Component Flowrates (kg/batch)				
Ethyl Alcohol	0.00	0.00	0.00	436.03
KCl	0.00	0.00	268.54	0.00
KH2PO4	0.00	0.00	0.02	0.00
MAb	0.00	32.40	3.24	0.00
N-Methyldiethan	0.00	0.00	1.38	0.00
NaH2PO4	0.00	1.02	10.92	0.00
Sodium Chloride	0.00	5.40	86.37	0.00
TRIS Base	0.00	0.00	88.67	0.00
WFI	3,799.49	1,787.19	21,886.70	3,924.28
TOTAL (kg/batch)	3,799.49	1,826.02	22,345.84	4,360.31
TOTAL (L/batch)	3,819.72	1,832.57	22,233.32	4,500.00

Primary Recovery 30K

2.1 STARTING MATERIAL REQUIREMENTS (per Section)

Section	Starting Material	Active Product	Amount Needed (kg Sin/kg MP)	Molar Yield (%)	Mass Yield (%)	Gross Mass Yield (%)
Main Section	(none)	(none)	Unknown	Unknown	Unknown	Unknown

Sin = Section Starting Material, Aout = Section Active Product

2.2 BULK MATERIALS (Entire Process)

Material	kg/yr	kg/batch	kg/kg MP
10 w% H3PO4	22,713	445.36	
CHO Cells	0	0.00	
MAb	2,292	44.93	
Media	2,307,678	45,248.59	
NaOH (0.5 M)	20,828	408.40	
Water	49,639	973.32	
WFI	19,201	376.50	
TOTAL	2,422,352	47,497.10	

2.3 BULK MATERIALS (per Section)

SECTIONS IN: Main Branch

Main Section

Material	kg/yr	kg/batch	kg/kg MP
10 w% H3PO4	22,713	445.36	
CHO Cells	0	0.00	
MAb	2,292	44.93	
Media	2,307,678	45,248.59	
NaOH (0.5 M)	20,828	408.40	
Water	49,639	973.32	
WFI	19,201	376.50	
TOTAL	2,422,352	47,497.10	

2.4 BULK MATERIALS (per Material)

10 w% H3PO4

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	50.00	11,357	222.68	
P-11	50.00	11,357	222.68	
TOTAL	100.00	22,713	445.36	

CHO Cells

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	100.00	0	0.00	
TOTAL	100.00	0	0.00	

MAb

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	100.00	2,292	44.93	
TOTAL	100.00	2,292	44.93	

Media

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	100.00	2,307,678	45,248.59	
TOTAL	100.00	2,307,678	45,248.59	

NaOH (0.5 M)

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	50.00	10,414	204.20	
P-11	50.00	10,414	204.20	
TOTAL	100.00	20,828	408.40	

Water

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-9	61.32	30,438	596.82	
P-11	38.68	19,201	376.50	
TOTAL	100.00	49,639	973.32	

WFI				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-8	100.00	19,201	376.50	
TOTAL	100.00	19,201	376.50	

2.5 BULK MATERIALS: SECTION TOTALS (kg/batch)

Raw Material	Main Section
10 w% H3PO4	445.36
CHO Cells	0.00
MAb	44.93
Media	45,248.59
NaOH (0.5 M)	408.40
Water	973.32
WFI	376.50
TOTAL	47,497.10

2.6 BULK MATERIALS: SECTION TOTALS (kg/yr)

Raw Material	Main Section
10 w% H3PO4	22,713
CHO Cells	0
MAb	2,292
Media	2,307,678
NaOH (0.5 M)	20,828
Water	49,639
WFI	19,201
TOTAL	2,422,352

3. STREAM DETAILS

Stream Name	S-101	S-122	S-124	S-123
Source	INPUT	P-8	P-9	P-9
Destination	P-8	P-9	P-10	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	5.89	5.89	1.01
Density (g/L)	994.70	994.70	994.70	994.70
Total Enthalpy (kW-h)	1,321.76	1,321.76	1,321.76	0.00
Specific Enthalpy (kcal/kg)	25.11	25.11	25.11	25.11
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
CHO Cells	0.00	0.00	0.00	0.00
MAb	44.93	44.93	44.93	0.00
Media	45,248.59	45,248.59	45,248.58	0.01
TOTAL (kg/batch)	45,293.52	45,293.52	45,293.51	0.01
TOTAL (L/batch)	45,534.66	45,534.66	45,534.65	0.01

Stream Name	S-126	S-125	S-128
Source	P-10	P-10	P-11
Destination	P-11	OUTPUT	OUTPUT
Stream Properties			
Activity (U/ml)	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00
Pressure (bar)	5.89	5.89	5.89
Density (g/L)	994.70	994.70	994.70
Total Enthalpy (kW-h)	1,321.76	0.00	1,321.76
Specific Enthalpy (kcal/kg)	25.11	25.11	25.11
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00
Component Flowrates (kg/batch)			
CHO Cells	0.00	0.00	0.00
MAb	44.93	0.00	44.93
Media	45,248.58	0.00	45,248.58
TOTAL (kg/batch)	45,293.51	0.00	45,293.51
TOTAL (L/batch)	45,534.65	0.00	45,534.65

Protein A Chromatography – 30 K

2.1 STARTING MATERIAL REQUIREMENTS (per Section)

Section	Starting Material	Active Product	Amount Needed (kg Sin/kg MP)	Molar Yield (%)	Mass Yield (%)	Gross Mass Yield (%)
Main Section	(none)	(none)	Unknown	Unknown	Unknown	Unknown

Sin = Section Starting Material, Aout = Section Active Product

2.2 BULK MATERIALS (Entire Process)

Material	kg/yr	kg/batch	kg/kg MP
.1M NaOH	235,718	521.50	
Acetic-Acid	77,989	172.54	
EDTA, Sodium	63,907	141.39	
Ethyl Alcohol	316,455	700.12	
H3PO4 10w%	805,211	1,781.44	
MAb	20,310	44.93	
Media	20,452,357	45,248.58	
NaOH (0.5 M)	738,387	1,633.60	
Sodium Chloride	31,954	70.69	
Sodium Citrate	14,046	31.08	
TRIS Base	31,954	70.69	
TRIS HCl	95,861	212.08	
Water	5,582,178	12,349.95	
WFI	55,457,503	122,693.59	
TOTAL	83,923,829	185,672.19	

2.3 BULK MATERIALS (per Section)

SECTIONS IN: Main Branch

Main Section

Material	kg/yr	kg/batch	kg/kg MP
.1M NaOH	235,718	521.50	
Acetic-Acid	77,989	172.54	
EDTA, Sodium	63,907	141.39	
Ethyl Alcohol	316,455	700.12	
H3PO4 10w%	805,211	1,781.44	
MAb	20,310	44.93	
Media	20,452,357	45,248.58	
NaOH (0.5 M)	738,387	1,633.60	
Sodium Chloride	31,954	70.69	
Sodium Citrate	14,046	31.08	
TRIS Base	31,954	70.69	
TRIS HCl	95,861	212.08	
Water	5,582,178	12,349.95	
WFI	55,457,503	122,693.59	
TOTAL	83,923,829	185,672.19	

2.4 BULK MATERIALS (per Material)

.1M NaOH

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	100.00	235,718	521.50	
TOTAL	100.00	235,718	521.50	

Acetic-Acid

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-2	100.00	77,989	172.54	
TOTAL	100.00	77,989	172.54	

EDTA, Sodium

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-3	100.00	63,907	141.39	
TOTAL	100.00	63,907	141.39	

Ethyl Alcohol				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-4	100.00	316,455	700.12	
TOTAL	100.00	316,455	700.12	

H3PO4 10w%				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	12.50	100,651	222.68	
P-2	12.50	100,651	222.68	
P-3	12.50	100,651	222.68	
P-4	12.50	100,651	222.68	
P-5	12.50	100,651	222.68	
P-6	12.50	100,651	222.68	
P-7	12.50	100,651	222.68	
P-8	12.50	100,651	222.68	
TOTAL	100.00	805,211	1,781.44	

MAb				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-11	100.00	20,310	44.93	
TOTAL	100.00	20,310	44.93	

Media				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-11	100.00	20,452,357	45,248.58	
TOTAL	100.00	20,452,357	45,248.58	

NaOH (0.5 M)				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	12.50	92,298	204.20	
P-2	12.50	92,298	204.20	
P-3	12.50	92,298	204.20	
P-4	12.50	92,298	204.20	
P-5	12.50	92,298	204.20	
P-6	12.50	92,298	204.20	
P-7	12.50	92,298	204.20	
P-8	12.50	92,298	204.20	
TOTAL	100.00	738,387	1,633.60	

Sodium Chloride				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-3	100.00	31,954	70.69	
TOTAL	100.00	31,954	70.69	

Sodium Citrate				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	100.00	14,046	31.08	
TOTAL	100.00	14,046	31.08	

TRIS Base				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-3	100.00	31,954	70.69	
TOTAL	100.00	31,954	70.69	

TRIS HCl				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-3	100.00	95,861	212.08	
TOTAL	100.00	95,861	212.08	

Water				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-2	3.05	170,176	376.50	
P-3	3.05	170,176	376.50	
P-4	3.05	170,176	376.50	
P-5	3.05	170,176	376.50	
P-6	3.05	170,176	376.50	
P-7	3.05	170,176	376.50	
P-8	3.05	170,176	376.50	
P-10	78.66	4,390,946	9,714.48	
TOTAL	100.00	5,582,178	12,349.95	

WFI				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	14.35	7,959,413	17,609.32	
P-2	23.30	12,920,162	28,584.43	
P-3	57.21	31,729,833	70,198.74	
P-4	5.14	2,848,096	6,301.10	
TOTAL	100.00	55,457,503	122,693.59	

2.5 BULK MATERIALS: SECTION TOTALS (kg/batch)

Raw Material	Main Section
.1M NaOH	521.50
Acetic-Acid	172.54
EDTA, Sodium	141.39
Ethyl Alcohol	700.12
H3PO4 10w%	1,781.44
MAb	44.93
Media	45,248.58
NaOH (0.5 M)	1,633.60
Sodium Chloride	70.69
Sodium Citrate	31.08
TRIS Base	70.69
TRIS HCl	212.08
Water	12,349.95
WFI	122,693.59
TOTAL	185,672.19

2.6 BULK MATERIALS: SECTION TOTALS (kg/yr)

Raw Material	Main Section
.1M NaOH	235,718
Acetic-Acid	77,989
EDTA, Sodium	63,907
Ethyl Alcohol	316,455
H3PO4 10w%	805,211
MAb	20,310
Media	20,452,357
NaOH (0.5 M)	738,387
Sodium Chloride	31,954
Sodium Citrate	14,046
TRIS Base	31,954
TRIS HCl	95,861
Water	5,582,178
WFI	55,457,503
TOTAL	83,923,829

3. STREAM DETAILS

Stream Name	S-101	S-105	S-115	S-102
Source	INPUT	P-1	P-5	INPUT
Destination	P-1	P-5	P-11	P-2
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	7.62	7.62	1.01
Density (g/L)	995.54	995.54	995.54	994.98
Total Enthalpy (kW-h)	502.95	502.95	43.50	836.61
Specific Enthalpy (kcal/kg)	25.07	25.07	25.07	25.03
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
Acetic-Acid	0.00	0.00	0.00	172.54
Sodium Citrate	31.08	31.08	2.69	0.00
WFI	17,232.82	17,232.82	1,490.62	28,584.43
TOTAL (kg/batch)	17,263.90	17,263.90	1,493.30	28,756.97
TOTAL (L/batch)	17,341.30	17,341.30	1,500.00	28,902.19

Stream Name	S-106	S-116	S-103	S-107
Source	P-2	P-6	INPUT	P-3
Destination	P-6	P-11	P-3	P-7
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	5.82	5.82	1.01	8.82
Density (g/L)	994.98	994.98	998.35	998.35
Total Enthalpy (kW-h)	836.61	108.55	2,050.99	2,050.99
Specific Enthalpy (kcal/kg)	25.03	25.03	24.96	24.96
Heat Capacity (kcal/kg-°C)	1.00	1.00	0.99	0.99
Component Flowrates (kg/batch)				
Acetic-Acid	172.54	22.39	0.00	0.00
EDTA, Sodium	0.00	0.00	141.39	141.39
Sodium Chloride	0.00	0.00	70.69	70.69
TRIS Base	0.00	0.00	70.69	70.69
TRIS HCl	0.00	0.00	212.08	212.08
WFI	28,584.43	3,708.77	70,198.74	70,198.74
TOTAL (kg/batch)	28,756.97	3,731.16	70,693.60	70,693.60
TOTAL (L/batch)	28,902.19	3,750.00	70,810.37	70,810.37

Stream Name	S-117	S-119	S-120	S-118
Source	P-7	P-7	P-7	P-9
Destination	P-9	P-11	P-11	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	8.82	4.35	5.83	8.82
Density (g/L)	998.35	998.35	998.35	998.35
Total Enthalpy (kW-h)	136.49	43.45	136.49	136.49
Specific Enthalpy (kcal/kg)	24.96	24.96	24.96	24.96
Heat Capacity (kcal/kg-°C)	0.99	0.99	0.99	0.99
Component Flowrates (kg/batch)				
EDTA, Sodium	9.41	3.00	9.41	9.41
Sodium Chloride	4.70	1.50	4.70	4.70
TRIS Base	4.70	1.50	4.70	4.70
TRIS HCl	14.11	4.49	14.11	14.11
WFI	4,671.69	1,487.04	4,671.69	4,671.69
TOTAL (kg/batch)	4,704.62	1,497.53	4,704.62	4,704.62
TOTAL (L/batch)	4,712.39	1,500.00	4,712.39	4,712.39

Stream Name	S-123	S-124	S-104	S-108
Source	P-11	P-12	INPUT	P-4
Destination	P-12	OUTPUT	P-4	P-8
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	1.01	1.01	3.65
Density (g/L)	994.97	994.97	968.96	968.96
Total Enthalpy (kW-h)	92.12	92.12	195.81	195.81
Specific Enthalpy (kcal/kg)	25.03	25.03	24.06	24.06
Heat Capacity (kcal/kg-°C)	1.00	1.00	0.96	0.96
Component Flowrates (kg/batch)				
Acetic-Acid	18.75	18.75	0.00	0.00
Ethyl Alcohol	0.00	0.00	700.12	700.12
MAb	40.44	40.44	0.00	0.00
WFI	3,107.05	3,107.05	6,301.10	6,301.10
TOTAL (kg/batch)	3,166.25	3,166.25	7,001.22	7,001.22
TOTAL (L/batch)	3,182.25	3,182.25	7,225.51	7,225.51

30k: Viral Inact

2.1 STARTING MATERIAL REQUIREMENTS (per Section)

Section	Starting Material	Active Product	Amount Needed (kg Sin/kg MP)	Molar Yield (%)	Mass Yield (%)	Gross Mass Yield (%)
Main Section	(none)	(none)	Unknown	Unknown	Unknown	Unknown

Sin = Section Starting Material, Aout = Section Active Product

2.2 BULK MATERIALS (Entire Process)

Material	kg/yr	kg/batch	kg/kg MP
.1M NaOH	733,229	1,043.00	
Acetic-Acid	13,187	18.76	
Ethyl Alcohol	204,353	290.69	
H3PO4 10w%	2,905,222	4,132.61	
KCl	13	0.02	
KH2PO4	13	0.02	
MAb	28,430	40.44	
NaH2PO4	8,980	12.77	
NaOH (0.5 M)	1,866,184	2,654.60	
Polysorbate 80	223	0.32	
Sodium Chloride	189,901	270.13	
Sodium Hydroxid	41,508	59.04	
Water	18,025,721	25,641.14	
WFI	20,844,806	29,651.22	
TOTAL	44,861,770	63,814.75	

2.3 BULK MATERIALS (per Section)

SECTIONS IN: Main Branch

Main Section

Material	kg/yr	kg/batch	kg/kg MP
.1M NaOH	733,229	1,043.00	
Acetic-Acid	13,187	18.76	
Ethyl Alcohol	204,353	290.69	
H3PO4 10w%	2,905,222	4,132.61	
KCl	13	0.02	
KH2PO4	13	0.02	
MAb	28,430	40.44	
NaH2PO4	8,980	12.77	
NaOH (0.5 M)	1,866,184	2,654.60	
Polysorbate 80	223	0.32	
Sodium Chloride	189,901	270.13	
Sodium Hydroxid	41,508	59.04	
Water	18,025,721	25,641.14	
WFI	20,844,806	29,651.22	
TOTAL	44,861,770	63,814.75	

2.4 BULK MATERIALS (per Material)

.1M NaOH

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-18	100.00	733,229	1,043.00	
TOTAL	100.00	733,229	1,043.00	

Acetic-Acid

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-4	100.00	13,187	18.76	
TOTAL	100.00	13,187	18.76	

Ethyl Alcohol

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-11	100.00	204,353	290.69	
TOTAL	100.00	204,353	290.69	

H3PO4 10w%				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-4	5.39	156,544	222.68	
P-5	5.39	156,544	222.68	
P-7	5.39	156,544	222.68	
P-8	5.39	156,544	222.68	
P-9	5.39	156,544	222.68	
P-10	5.39	156,544	222.68	
P-11	35.34	1,026,693	1,460.45	
P-12	5.39	156,544	222.68	
P-13	5.39	156,544	222.68	
P-14	5.39	156,544	222.68	
P-15	5.39	156,544	222.68	
P-16	5.39	156,544	222.68	
P-20	5.39	156,544	222.68	
TOTAL	100.00	2,905,222	4,132.61	

KCl				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	100.00	13	0.02	
TOTAL	100.00	13	0.02	

KH2PO4				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	100.00	13	0.02	
TOTAL	100.00	13	0.02	

MAb				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-4	100.00	28,430	40.44	
TOTAL	100.00	28,430	40.44	

NaH2PO4				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-9	22.53	2,023	2.88	
P-10	77.47	6,957	9.90	
TOTAL	100.00	8,980	12.77	

NaOH (0.5 M)				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-4	7.69	143,553	204.20	
P-5	7.69	143,553	204.20	
P-7	7.69	143,553	204.20	
P-8	7.69	143,553	204.20	
P-9	7.69	143,553	204.20	
P-10	7.69	143,553	204.20	
P-11	7.69	143,553	204.20	
P-12	7.69	143,553	204.20	
P-13	7.69	143,553	204.20	
P-14	7.69	143,553	204.20	
P-15	7.69	143,553	204.20	
P-16	7.69	143,553	204.20	
P-20	7.69	143,553	204.20	
TOTAL	100.00	1,866,184	2,654.60	

Polysorbate 80				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-5	100.00	223	0.32	
TOTAL	100.00	223	0.32	

Sodium Chloride				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	64.41	122,317	173.99	
P-9	5.61	10,661	15.17	
P-10	29.97	56,923	80.97	
TOTAL	100.00	189,901	270.13	

Sodium Hydroxid				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-7	100.00	41,508	59.04	
TOTAL	100.00	41,508	59.04	

Water				
Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	1.47	264,676	376.50	
P-2	2.20	397,015	564.74	
P-3	1.47	264,676	376.50	
P-4	1.47	264,676	376.50	
P-5	1.47	264,676	376.50	
P-7	1.47	264,676	376.50	
P-8	1.47	264,676	376.50	
P-9	1.47	264,676	376.50	

P-10	1.47	264,676	376.50	
P-11	1.47	264,676	376.50	
P-12	1.47	264,676	376.50	
P-13	1.47	264,676	376.50	
P-14	1.47	264,676	376.50	
P-15	1.47	264,676	376.50	
P-16	1.47	264,676	376.50	
P-18	75.77	13,658,561	19,428.96	
P-20	1.47	264,676	376.50	
TOTAL	100.00	18,025,721	25,641.14	

WFI

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-1	10.68	2,225,276	3,165.40	
P-2	3.34	695,399	989.19	
P-4	10.48	2,184,258	3,107.05	
P-5	0.00	223	0.32	
P-7	9.96	2,076,252	2,953.42	
P-8	9.76	2,034,965	2,894.67	
P-9	0.93	193,747	275.60	
P-10	30.04	6,260,827	8,905.87	
P-11	8.82	1,839,180	2,616.19	
P-17	16.00	3,334,688	4,743.51	
TOTAL	100.00	20,844,806	29,651.22	

2.5 BULK MATERIALS: SECTION TOTALS (kg/batch)

Raw Material	Main Section
.1M NaOH	1,043.00
Acetic-Acid	18.76
Ethyl Alcohol	290.69
H3PO4 10w%	4,132.61
KCl	0.02
KH2PO4	0.02
MAb	40.44
NaH2PO4	12.77
NaOH (0.5 M)	2,654.60
Polysorbate 80	0.32
Sodium Chloride	270.13
Sodium Hydroxid	59.04
Water	25,641.14
WFI	29,651.22
TOTAL	63,814.75

2.6 BULK MATERIALS: SECTION TOTALS (kg/yr)

Raw Material	Main Section
.1M NaOH	733,229
Acetic Acid	13,187
Ethyl Alcohol	204,353
H3PO4 10w%	2,905,222
KCl	13
KH2PO4	13
MAb	28,430
NaH2PO4	8,980
NaOH (0.5 M)	1,866,184
Polysorbate 80	223
Sodium Chloride	189,901
Sodium Hydroxid	41,508
Water	18,025,721
WFI	20,844,806
TOTAL	44,861,770

3. STREAM DETAILS

Stream Name	**S-101**	**S-103**	**S-105**	**S-114**
Source	**INPUT**	**P-1**	**P-3**	**P-2**
Destination	**P-1**	**P-3**	**P-2**	**P-4**
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.43
Pressure (bar)	1.01	4.96	4.96	4.96
Density (g/L)	994.70	994.70	994.70	994.64
Total Enthalpy (kW-h)	92.37	92.37	92.37	93.87
Specific Enthalpy (kcal/kg)	25.11	25.11	25.11	25.51
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
Acetic-Acid	0.00	0.00	0.00	6.90
MAb	0.00	0.00	0.00	40.44
WFI	3,165.40	3,165.40	3,165.40	3,118.37
TOTAL (kg/batch)	3,165.40	3,165.40	3,165.40	3,165.71
TOTAL (L/batch)	3,182.25	3,182.25	3,182.25	3,182.76

Stream Name	**S-106**	**S-108**	**S-109**	**S-112**
Source	**INPUT**	**P-4**	**P-4**	**INPUT**
Destination	**P-4**	**P-2**	**P-5**	**P-2**
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.43	25.00
Pressure (bar)	1.01	4.96	4.97	1.01
Density (g/L)	994.97	994.97	994.64	994.70
Total Enthalpy (kW-h)	92.12	92.12	93.87	28.87
Specific Enthalpy (kcal/kg)	25.03	25.03	25.51	25.11
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
Acetic-Acid	18.76	18.76	6.90	0.00
MAb	40.44	40.44	40.44	0.00
WFI	3,107.05	3,107.05	3,118.37	989.19
TOTAL (kg/batch)	3,166.25	3,166.25	3,165.71	989.19
TOTAL (L/batch)	3,182.25	3,182.25	3,182.76	994.45

Stream Name	S-119	S-130	S-140	S-121
Source	INPUT	P-8	P-13	INPUT
Destination	P-8	P-13	P-17	P-9
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	4.05	4.05	1.01
Density (g/L)	1,022.89	1,022.89	1,022.89	1,025.59
Total Enthalpy (kW-h)	87.63	87.63	87.63	8.33
Specific Enthalpy (kcal/kg)	24.57	24.57	24.57	24.41
Heat Capacity (kcal/kg-°C)	0.98	0.98	0.98	0.97
Component Flowrates (kg/batch)				
NaH2PO4	0.00	0.00	0.00	2.88
Sodium Chloride	173.99	173.99	173.99	15.17
WFI	2,894.67	2,894.67	2,894.67	275.60
TOTAL (kg/batch)	3,068.67	3,068.67	3,068.67	293.64
TOTAL (L/batch)	3,000.00	3,000.00	3,000.00	286.32

Stream Name	S-129	S-139	S-123	S-128
Source	P-9	P-14	INPUT	P-10
Destination	P-14	P-17	P-10	P-15
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	3.57	3.57	1.01	10.13
Density (g/L)	1,025.59	1,025.59	999.64	999.64
Total Enthalpy (kW-h)	8.33	8.33	261.41	261.41
Specific Enthalpy (kcal/kg)	24.41	24.41	25.00	25.00
Heat Capacity (kcal/kg-°C)	0.97	0.97	1.00	1.00
Component Flowrates (kg/batch)				
KCl	0.00	0.00	0.02	0.02
KH2PO4	0.00	0.00	0.02	0.02
NaH2PO4	2.88	2.88	9.90	9.90
Sodium Chloride	15.17	15.17	80.97	80.97
WFI	275.60	275.60	8,905.87	8,905.87
TOTAL (kg/batch)	293.64	293.64	8,996.77	8,996.77
TOTAL (L/batch)	286.32	286.32	9,000.00	9,000.00

Stream Name	S-133	S-136	S-137	S-143
Source	P-15	P-15	P-15	P-17
Destination	P-19	P-17	P-17	P-20
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.01
Pressure (bar)	10.13	2.53	1.45	1.01
Density (g/L)	999.64	999.64	999.64	996.42
Total Enthalpy (kW-h)	87.14	87.14	87.14	59.78
Specific Enthalpy (kcal/kg)	25.00	25.00	25.00	25.08
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
KCl	0.01	0.01	0.01	0.00
KH2PO4	0.01	0.01	0.01	0.00
MAb	0.00	0.00	0.00	36.40
NaH2PO4	3.30	3.30	3.30	1.15
Sodium Chloride	26.99	26.99	26.99	6.07
WFI	2,968.62	2,968.62	2,968.62	2,007.64
TOTAL (kg/batch)	2,998.92	2,998.92	2,998.92	2,051.26
TOTAL (L/batch)	3,000.00	3,000.00	3,000.00	2,058.63

Stream Name	S-145	S-125	S-127	S-132
Source	P-20	INPUT	P-11	P-16
Destination	OUTPUT	P-11	P-16	P-18
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.01	25.00	25.00	25.00
Pressure (bar)	10.13	1.01	4.05	4.05
Density (g/L)	996.42	968.96	968.96	968.96
Total Enthalpy (kW-h)	59.78	81.30	81.30	81.30
Specific Enthalpy (kcal/kg)	25.08	24.06	24.06	24.06
Heat Capacity (kcal/kg-°C)	1.00	0.96	0.96	0.96
Component Flowrates (kg/batch)				
Ethyl Alcohol	0.00	290.69	290.69	290.69
MAb	36.40	0.00	0.00	0.00
NaH2PO4	1.15	0.00	0.00	0.00
Sodium Chloride	6.07	0.00	0.00	0.00
WFI	2,007.64	2,616.19	2,616.19	2,616.19
TOTAL (kg/batch)	2,051.26	2,906.88	2,906.88	2,906.88
TOTAL (L/batch)	2,058.63	3,000.00	3,000.00	3,000.00

Stream Name	S-134	S-138	S-142	S-135
Source	P-19	INPUT	P-17	P-18
Destination	OUTPUT	P-17	OUTPUT	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.08	25.00
Pressure (bar)	10.13	1.01	1.01	4.05
Density (g/L)	999.64	994.70	1,002.82	968.96
Total Enthalpy (kW-h)	87.14	138.43	529.84	81.30
Specific Enthalpy (kcal/kg)	25.00	25.11	25.01	24.06
Heat Capacity (kcal/kg-°C)	1.00	1.00	0.99	0.96
Component Flowrates (kg/batch)				
Acetic-Acid	0.00	0.00	6.90	0.00
Ethyl Alcohol	0.00	0.00	0.00	290.69
KCl	0.01	0.00	0.01	0.00
KH2PO4	0.01	0.00	0.01	0.00
MAb	0.00	0.00	4.04	0.00
NaH2PO4	3.30	0.00	8.32	0.00
Polysorbate 80	0.00	0.00	0.32	0.00
Sodium Chloride	26.99	0.00	237.07	0.00
Sodium Hydroxid	0.00	0.00	59.04	0.00
WFI	2,968.62	4,743.51	17,915.49	2,616.19
TOTAL (kg/batch)	2,998.92	4,743.51	18,231.22	2,906.88
TOTAL (L/batch)	3,000.00	4,768.76	18,179.94	3,000.00

AEX – 30 k

2.1 STARTING MATERIAL REQUIREMENTS (per Section)

Section	Starting Material	Active Product	Amount Needed (kg Sin/kg MP)	Molar Yield (%)	Mass Yield (%)	Gross Mass Yield (%)
Main Section	(none)	(none)	Unknown	Unknown	Unknown	Unknown

Sin = Section Starting Material, Aout = Section Active Product

2.2 BULK MATERIALS (Entire Process)

Material	kg/yr	kg/batch	kg/kg MP
.1M NaOH	2,770,730	1,564.50	
Ethyl Alcohol	772,212	436.03	
H3PO4 10w%	4,338,029	2,449.48	
KCl	486,862	274.91	
KH2PO4	48	0.03	
MAb	64,457	36.40	
N-Methyldiethan	4,587	2.59	
NaH2PO4	28,328	16.00	
NaOH (0.5 M)	3,978,020	2,246.20	
Sodium Chloride	225,842	127.52	
TRIS Base	157,038	88.67	
Water	58,963,405	33,293.85	
WFI	57,713,687	32,588.19	
TOTAL	129,503,245	73,124.36	

2.3 BULK MATERIALS (per Section)

SECTIONS IN: Main Branch

Main Section			
Material	**kg/yr**	**kg/batch**	**kg/kg MP**
.1M NaOH	2,770,730	1,564.50	
Ethyl Alcohol	772,212	436.03	
H3PO4 10w%	4,338,029	2,449.48	
KCl	486,862	274.91	
KH2PO4	48	0.03	
MAb	64,457	36.40	
N-Methyldiethan	4,587	2.59	
NaH2PO4	28,328	16.00	
NaOH (0.5 M)	3,978,020	2,246.20	
Sodium Chloride	225,842	127.52	
TRIS Base	157,038	88.67	
Water	58,963,405	33,293.85	
WFI	57,713,687	32,588.19	
TOTAL	129,503,245	73,124.36	

2.4 BULK MATERIALS (per Material)

.1M NaOH				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-18	100.00	2,770,730	1,564.50	
TOTAL	100.00	2,770,730	1,564.50	

Ethyl Alcohol				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-11	100.00	772,212	436.03	
TOTAL	100.00	772,212	436.03	

H3PO4 10w%				
Procedure	**% Total**	**kg/yr**	**kg/batch**	**kg/kg MP**
Main Section (Main Branch)				
P-7	9.09	394,366	222.68	
P-8	9.09	394,366	222.68	
P-9	9.09	394,366	222.68	
P-10	9.09	394,366	222.68	
P-11	9.09	394,366	222.68	
P-12	9.09	394,366	222.68	
P-13	9.09	394,366	222.68	

P-14	9.09	394,366	222.68	
P-15	9.09	394,366	222.68	
P-16	9.09	394,366	222.68	
P-20	9.09	394,366	222.68	
TOTAL	100.00	4,338,029	2,449.48	

KCl

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-8	95.03	462,643	261.23	
P-9	4.96	24,171	13.65	
P-10	0.01	48	0.03	
TOTAL	100.00	486,862	274.91	

KH2PO4

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	100.00	48	0.03	
TOTAL	100.00	48	0.03	

MAb

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-17	100.00	64,457	36.40	
TOTAL	100.00	64,457	36.40	

N-Methyldiethan

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-9	100.00	4,587	2.59	
TOTAL	100.00	4,587	2.59	

NaH2PO4

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	92.80	26,290	14.84	
P-17	7.20	2,039	1.15	
TOTAL	100.00	28,328	16.00	

NaOH (0.5 M)

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-7	9.09	361,638	204.20	
P-8	9.09	361,638	204.20	
P-9	9.09	361,638	204.20	
P-10	9.09	361,638	204.20	
P-11	9.09	361,638	204.20	
P-12	9.09	361,638	204.20	
P-13	9.09	361,638	204.20	
P-14	9.09	361,638	204.20	

P-15	9.09	361,638	204.20	
P-16	9.09	361,638	204.20	
P-20	9.09	361,638	204.20	
TOTAL	100.00	3,978,020	2,246.20	

Sodium Chloride

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-10	95.24	215,099	121.46	
P-17	4.76	10,743	6.07	
TOTAL	100.00	225,842	127.52	

TRIS Base

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-7	100.00	157,038	88.67	
TOTAL	100.00	157,038	88.67	

Water

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-7	1.13	666,774	376.50	
P-8	1.13	666,774	376.50	
P-9	1.13	666,774	376.50	
P-10	1.13	666,774	376.50	
P-11	1.13	666,774	376.50	
P-12	1.13	666,774	376.50	
P-13	1.13	666,774	376.50	
P-14	1.13	666,774	376.50	
P-15	1.13	666,774	376.50	
P-16	1.13	666,774	376.50	
P-18	87.53	51,613,040	29,143.44	
P-20	1.16	682,628	385.45	
TOTAL	100.00	58,963,405	33,293.85	

WFI

Procedure	% Total	kg/yr	kg/batch	kg/kg MP
Main Section (Main Branch)				
P-7	13.61	7,855,112	4,435.41	
P-8	13.34	7,696,842	4,346.04	
P-9	0.76	439,271	248.04	
P-10	40.99	23,658,447	13,358.81	
P-11	12.04	6,949,904	3,924.28	
P-17	19.26	11,114,111	6,275.61	
TOTAL	100.00	57,713,687	32,588.19	

2.5 BULK MATERIALS: SECTION TOTALS (kg/batch)

Raw Material	Main Section
.1M NaOH	1,564.50
Ethyl Alcohol	436.03
H3PO4 10w%	2,449.48
KCl	274.91
KH2PO4	0.03
MAb	36.40
N-Methyldiethan	2.59
NaH2PO4	16.00
NaOH (0.5 M)	2,246.20
Sodium Chloride	127.52
TRIS Base	88.67
Water	33,293.85
WFI	32,588.19
TOTAL	73,124.36

2.6 BULK MATERIALS: SECTION TOTALS (kg/yr)

Raw Material	Main Section
.1M NaOH	2,770,730
Ethyl Alcohol	772,212
H3PO4 10w%	4,338,029
KCl	486,862
KH2PO4	48
MAb	64,457
N-Methyldiethan	4,587
NaH2PO4	28,328
NaOH (0.5 M)	3,978,020
Sodium Chloride	225,842
TRIS Base	157,038
Water	58,963,405
WFI	57,713,687
TOTAL	129,503,245

3. STREAM DETAILS

Stream Name	S-102	S-131	S-141	S-103
Source	INPUT	P-7	P-12	INPUT
Destination	P-7	P-12	P-17	P-8
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	10.13	10.13	1.01
Density (g/L)	1,005.35	1,005.35	1,005.35	1,023.84
Total Enthalpy (kW-h)	129.73	129.73	129.73	128.61
Specific Enthalpy (kcal/kg)	24.67	24.67	24.67	24.02
Heat Capacity (kcal/kg-°C)	0.98	0.98	0.98	0.96
Component Flowrates (kg/batch)				
KCl	0.00	0.00	0.00	261.23
TRIS Base	88.67	88.67	88.67	0.00
WFI	4,435.41	4,435.41	4,435.41	4,346.04
TOTAL (kg/batch)	4,524.08	4,524.08	4,524.08	4,607.28
TOTAL (L/batch)	4,500.00	4,500.00	4,500.00	4,500.00

Stream Name	S-130	S-140	S-104	S-129
Source	P-8	P-13	INPUT	P-9
Destination	P-13	P-17	P-9	P-14
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	10.13	10.13	1.01	7.38
Density (g/L)	1,023.84	1,023.84	1,021.17	1,021.17
Total Enthalpy (kW-h)	128.61	128.61	7.34	7.34
Specific Enthalpy (kcal/kg)	24.02	24.02	23.91	23.91
Heat Capacity (kcal/kg-°C)	0.96	0.96	0.95	0.95
Component Flowrates (kg/batch)				
KCl	261.23	261.23	13.65	13.65
N-Methyldiethan	0.00	0.00	2.59	2.59
WFI	4,346.04	4,346.04	248.04	248.04
TOTAL (kg/batch)	4,607.28	4,607.28	264.27	264.27
TOTAL (L/batch)	4,500.00	4,500.00	258.79	258.79

Stream Name	S-139	S-123	S-128	S-133
Source	P-14	INPUT	P-10	P-15
Destination	P-17	P-10	P-15	P-19
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	7.38	1.01	10.13	10.13
Density (g/L)	1,021.17	999.64	999.64	999.64
Total Enthalpy (kW-h)	7.34	392.11	392.11	130.70
Specific Enthalpy (kcal/kg)	23.91	25.00	25.00	25.00
Heat Capacity (kcal/kg-°C)	0.95	1.00	1.00	1.00
Component Flowrates (kg/batch)				
KCl	13.65	0.03	0.03	0.01
KH2PO4	0.00	0.03	0.03	0.01
N-Methyldiethan	2.59	0.00	0.00	0.00
NaH2PO4	0.00	14.84	14.84	4.95
Sodium Chloride	0.00	121.46	121.46	40.49
WFI	248.04	13,358.81	13,358.81	4,452.94
TOTAL (kg/batch)	264.27	13,495.16	13,495.16	4,498.39
TOTAL (L/batch)	258.79	13,500.00	13,500.00	4,500.00

Stream Name	S-136	S-137	S-143	S-145
Source	P-15	P-15	P-17	P-20
Destination	P-17	P-17	P-20	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	2.53	1.45	1.01	3.91
Density (g/L)	999.64	999.64	996.18	996.18
Total Enthalpy (kW-h)	130.70	130.70	53.71	53.71
Specific Enthalpy (kcal/kg)	25.00	25.00	25.04	25.04
Heat Capacity (kcal/kg-°C)	1.00	1.00	1.00	1.00
Component Flowrates (kg/batch)				
KCl	0.01	0.01	5.46	5.46
KH2PO4	0.01	0.01	0.00	0.00
MAb	0.00	0.00	32.76	32.76
N-Methyldiethan	0.00	0.00	1.04	1.04
NaH2PO4	4.95	4.95	0.00	0.00
Sodium Chloride	40.49	40.49	0.00	0.00
WFI	4,452.94	4,452.94	1,806.40	1,806.40
TOTAL (kg/batch)	4,498.39	4,498.39	1,845.65	1,845.65
TOTAL (L/batch)	4,500.00	4,500.00	1,852.72	1,852.72

Stream Name	S-125	S-127	S-132	S-134
Source	INPUT	P-11	P-16	P-19
Destination	P-11	P-16	P-18	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	10.13	10.13	10.13
Density (g/L)	968.96	968.96	968.96	999.64
Total Enthalpy (kW-h)	121.95	121.95	121.95	130.70
Specific Enthalpy (kcal/kg)	24.06	24.06	24.06	25.00
Heat Capacity (kcal/kg-°C)	0.96	0.96	0.96	1.00
Component Flowrates (kg/batch)				
Ethyl Alcohol	436.03	436.03	436.03	0.00
KCl	0.00	0.00	0.00	0.01
KH2PO4	0.00	0.00	0.00	0.01
NaH2PO4	0.00	0.00	0.00	4.95
Sodium Chloride	0.00	0.00	0.00	40.49
WFI	3,924.28	3,924.28	3,924.28	4,452.94
TOTAL (kg/batch)	4,360.31	4,360.31	4,360.31	4,498.39
TOTAL (L/batch)	4,500.00	4,500.00	4,500.00	4,500.00

Stream Name	S-138	S-101	S-142	S-135
Source	INPUT	INPUT	P-17	P-18
Destination	P-17	P-17	OUTPUT	OUTPUT
Stream Properties				
Activity (U/ml)	0.00	0.00	0.00	0.00
Temperature (°C)	25.00	25.00	25.00	25.00
Pressure (bar)	1.01	1.01	1.01	10.13
Density (g/L)	994.70	996.42	1,004.86	968.96
Total Enthalpy (kW-h)	124.55	59.76	657.69	121.95
Specific Enthalpy (kcal/kg)	25.11	25.07	24.75	24.06
Heat Capacity (kcal/kg-°C)	1.00	1.00	0.99	0.96
Component Flowrates (kg/batch)				
Ethyl Alcohol	0.00	0.00	0.00	436.03
KCl	0.00	0.00	269.44	0.00
KH2PO4	0.00	0.00	0.02	0.00
MAb	0.00	36.40	3.64	0.00
N-Methyldiethan	0.00	0.00	1.55	0.00
NaH2PO4	0.00	1.15	11.05	0.00
Sodium Chloride	0.00	6.07	87.04	0.00
TRIS Base	0.00	0.00	88.67	0.00
WFI	4,267.96	2,007.66	22,404.58	3,924.28
TOTAL (kg/batch)	4,267.96	2,051.27	22,865.98	4,360.31
TOTAL (L/batch)	4,290.68	2,058.63	22,755.39	4,500.00