TO: AIChE 2019 Student Design Competition Organizers

FROM: Design Group 14

DATE: March 14, 2019

SUBJECT: AIChE 2019 Student Design Competition "Manufacturing Facility for a Biopharmaceutical: Monoclonal Antibody"

Please find the attached proposal and preliminary design for the Monoclonal Antibody Biopharmaceutical Manufacturing Facility. This proposal provides a detailed preliminary design of the seed train, production reactor, purification processes, storage, waste treatment, clean in place, steam in place, and water for injection production. The team was able to optimize the manufacturing process such that it produced 1500 kg of mAb per year at a titer of 2 g/L while still meeting the other requirements and specifications set out in the problem statement. Over the 25 year project life, the process has a NPV of $31.4 billion and a DCFROR of 6350%.

The team strongly recommends that AICHE proceeds with the investment and construction of Manufacturing Facility for a Biopharmaceutical: Monoclonal Antibody with the process design provided.

Regards,

Design Group 14

Manufacturing Facility for a Biopharmaceutical: Monoclonal Antibody

AIChE 2019 Student Design Competition

by:

Group 14

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ABSTRACT

The objective of this preliminary design was to determine the technical and economic feasibility of constructing a biopharmaceutical production facility to produce humanized monoclonal antibodies from Chinese Hamster Ovary cells. The mAb production facility will need to produce a minimum of 1,000 kg of product a year at current titers of 1-2 g/L of mAb as well as at future titers of 5-10 g/L.

The team performed the preliminary design of the production facility based on the mAb production block flow diagram provided by The Company's management as well as the physical specifications of the CHO cell line. The final optimized design includes a seed train process to promote controlled cell culture growth, two mAb production bioreactors, a protein harvesting and downstream purification process, frozen storage, and a waste inactivation process. One of the major considerations taken by the design team was the sterile nature of the process. In order to provide a sterile environment for each step in the process, a water for injection production process was designed, as well as a comprehensive steam in place and clean in place system. The process designed proves technical feasibility of the project in meeting physical, safety, and health specifications.

The facility is estimated to require 44 operating personnel working at any given time in order to ensure safe operation. As a batch process, raw material handling presents both a safety hazard and biohazard. In order to mitigate either of these concerns, viral inactivation and assays are performed throughout the process, and storage of caustic and acidic buffers is minimized.

The economic analysis performed for the process proves that the project is economically attractive. A summary of the major economic parameters over the 25-year project life is provided in Table 1 below.

Table 1: Major Economic Parameters for mAb Production Facility Preliminary Design

Economic Parameters	
Fixed Capital Investment	$17.6 Million
Annual Sales Revenue	$6.95 Million
Annual Operating Cost	$34.9 Million
DCFROR	6354%
NPV	$31.4 Billion

The economic parameters show that the project's economic results far exceed the requirements for the project to be economically successful. The team suggests that The Company move forward with this project, as it is both technically feasible and economically attractive.

INTRODUCTION

mAbs

Antibodies are Y-shaped proteins produced by animal and human immune systems when they are attacked by viruses, bacteria, and other harmful pathogens. These proteins attach to the antigens on the targeted cell, marking them for white blood cells to attack [1]. This process of antigen-antibody binding is shown in Figure 1.

Antibodies produced in a lab or pharmaceutical manufacturing facility and grown from a single cell line are known as monoclonal antibodies (mAbs) [1]. There are several different types of monoclonal antibodies. Naked mAbs latch onto the antigen without any drugs or materials attached to them. They are the most common type of mAb in cancer treatments. Conjugated mAbs are combined with radioactive particles that attach to the targeted antigen. Lastly, there are bispecific mAbs. These drugs are made of two different mAb proteins that target two different types of antigens [1].

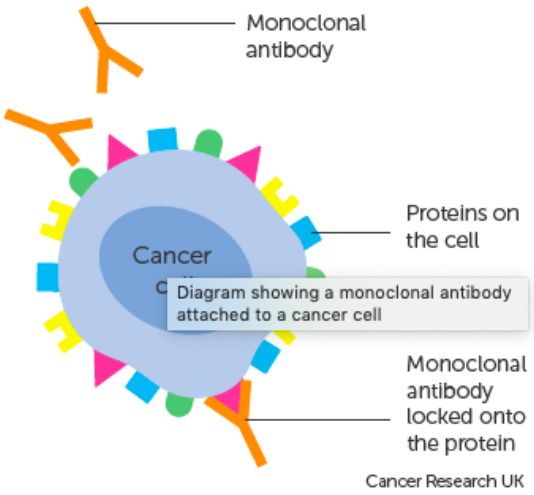


Figure 1 : *MAb antibody attaching to the cancer protein [2]*

MAb cells have three main applications: diagnostics, therapeutic, and protein purification [3]. Examples of how these applications are applied are shown in Table 2. For example, when used to battle cancer, mAbs are a type of immunotherapy [2]. MAbs like, vascular endothelial growth factor (VEGF), are used to attack types of cancers of vascular endothelial cells.

Table 2 : Applications of mAb [3]

Application of mAbs	Examples
Diagnostics	(a) Biochemical Analysis for pregnancy, cancer, hormonal disorders, infectious diseases, (b) Diagnostic Imaging for cardiovascular diseases, cancer, bacterial infections
Therapeutic	(a) Direct Agents for cancer, organ transplants, AIDS (b) Targeting Agents for immunotoxins, drug delivery, dissolution of blood clots, radio immunotherapy
Protein Purification	(a) Made with Immunoaffinity Chromatography
Miscellaneous	(a) Catalytic MAbs (ABZYMES) (b) Autoantibody Fingerprinting

CHO Cells

In biopharmaceutical production, host cells are needed to use the recombinant DNA to create new genetic combinations and therapeutic proteins [4]. The most commonly chosen host is Chinese hamster ovary cells (CHO) as they are the current mammalian platform. CHO cells are also desirable because they have more benefits than not which are down in Table 3. CHO cells make up more than half of the therapeutic protein market. The market is worth over $140 billion per year [4].

Table 3: Pros and Cons of CHO cells [5]

Pros	Cons
High viability, rapid growth, easy to culture, high expression levels, low cost	Variability in cell lines, genome stability

Market

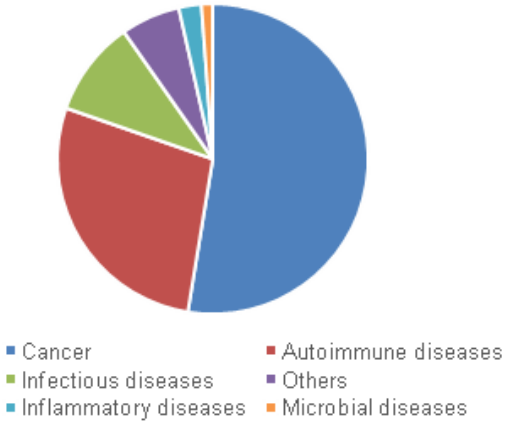


Figure 2: Breakdown of Mab cancer applications in 2016 [4]

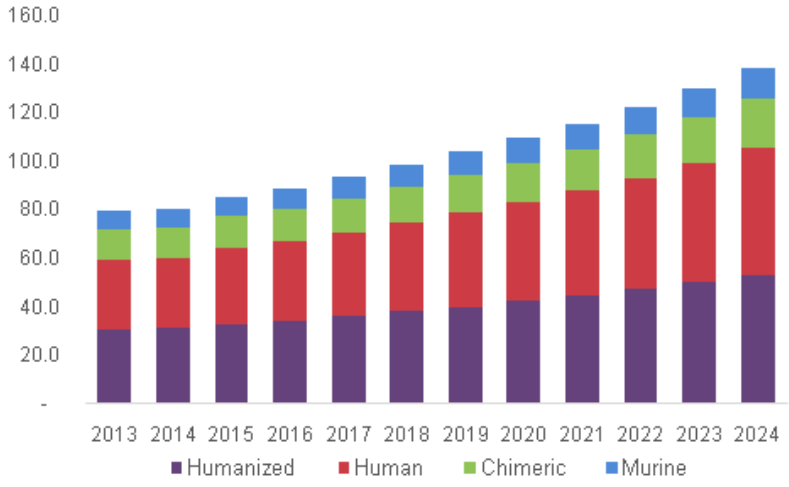


Figure 3: Mab Market (USD Billion) in 2016 [4]

Monoclonal antibodies are primarily used in hospitals and research facilities as they are also widely accepted by biologics [4]. Over 35% of the hospital mAb end-use is for cancer treatments [6]. MAbs are used to fight a variety of cancers as shown in Figure 2. A key contributor to predicted mAb market growth is an increase in use for treatment of chronic conditions, healthcare coverage, and public awareness of mAb treatments.

Chimeric mAbs are derived from murine sources and their genetic sequence is only 70% human. The cell lines that generate human mAbs produce low titers and can be unstable. Humanized mAbs, like the antibodies produced from CHO cells have 95% of the human sequence. They are ideal because the non-human portion is where the antigen binding regions are. For this reason, the market for humanized mAbs is growing more rapidly than the other types as shown in Figure 3.

Project Overview

Much like many pharmaceutical manufacturers, The Company is trying to break into the mAb market. The Company has already received approval for at least one mAb product and has others that are currently in development. Due to momentum surrounding mAbs and associated biopharmaceuticals both within The Company and the larger medical community, the manufacturing branch of the company has been charged with designing a large-scale mAb manufacturing facility that can produce enough product to handle a full-scale commercial launch. The potential facility will be located next to the current 'Research and Development' building to capitalize on preexisting infrastructure. There is potential for the site to become a contract manufacturing facility in the future if the initial launch goes well. Therefore, the design needs to be flexible to allow for the production of a variety of mAbs at a variety of purities and for a variety of purposes. The site should be able to produce a minimum of 1000 kg of purified mAbs per year at titers ranging from 1-2 g/L to 5-10 g/L. The production facility should encompass the seed train, upstream (production), downstream (purification), packaging, and storage processes. From this facility, mAb products will be sent to another facility for final formulation and distribution. Since this is a completely new facility, every part of the process will need to be designed from the ground up—everything that is needed in the process must be accounted for in the design. Although the process should be able to accommodate a variety of mAb products, for the sake of this design, it is assumed that the production will be a VEGF antibody similar to Avastin ™. This report contains Global Manufacturing's mAb biopharmaceutical manufacturing facility design, economic analysis, and recommendations that the management of The Company has requested.

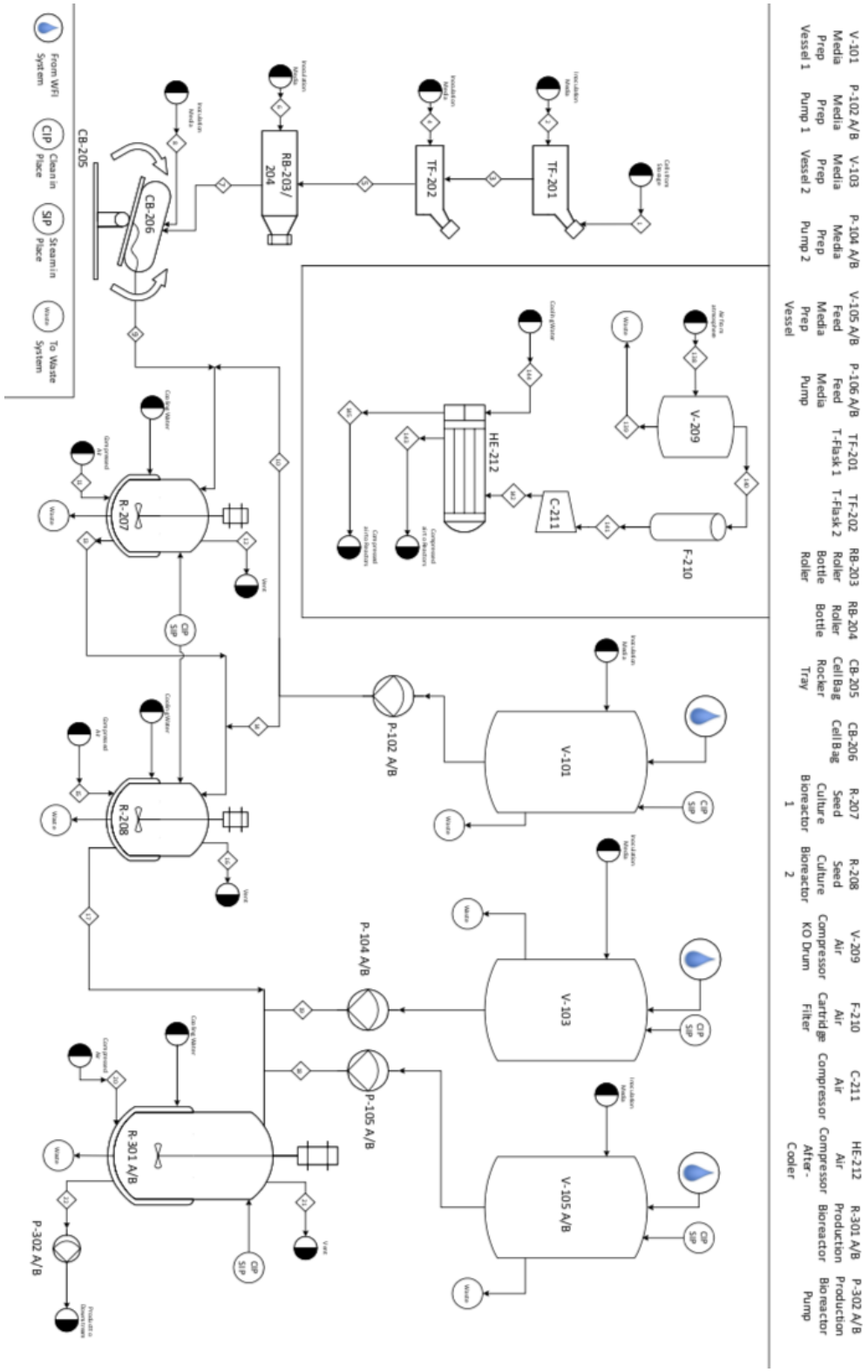
PROCESS FLOW DIAGRAM

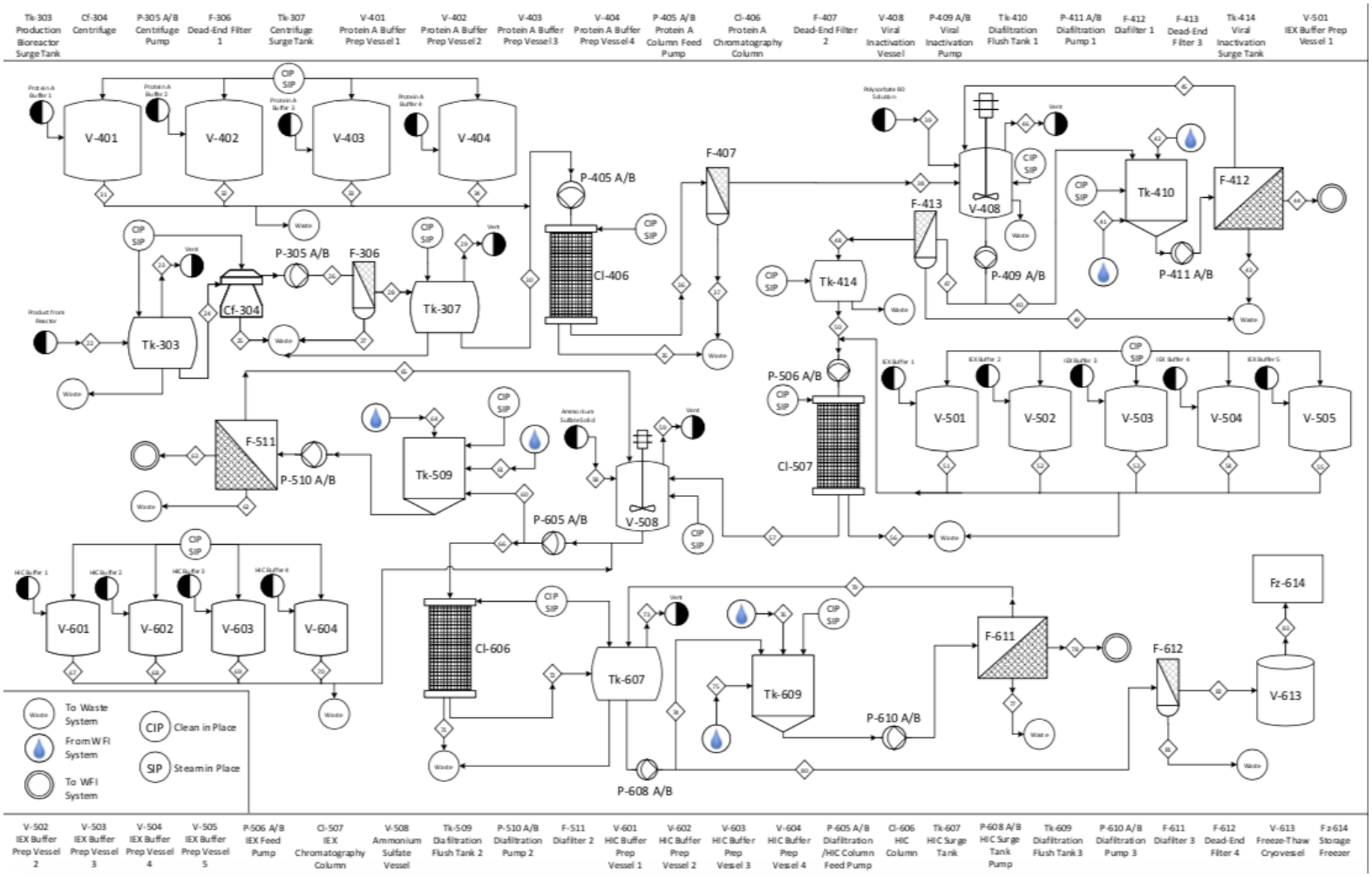
Table 4: Equipment Identification Key

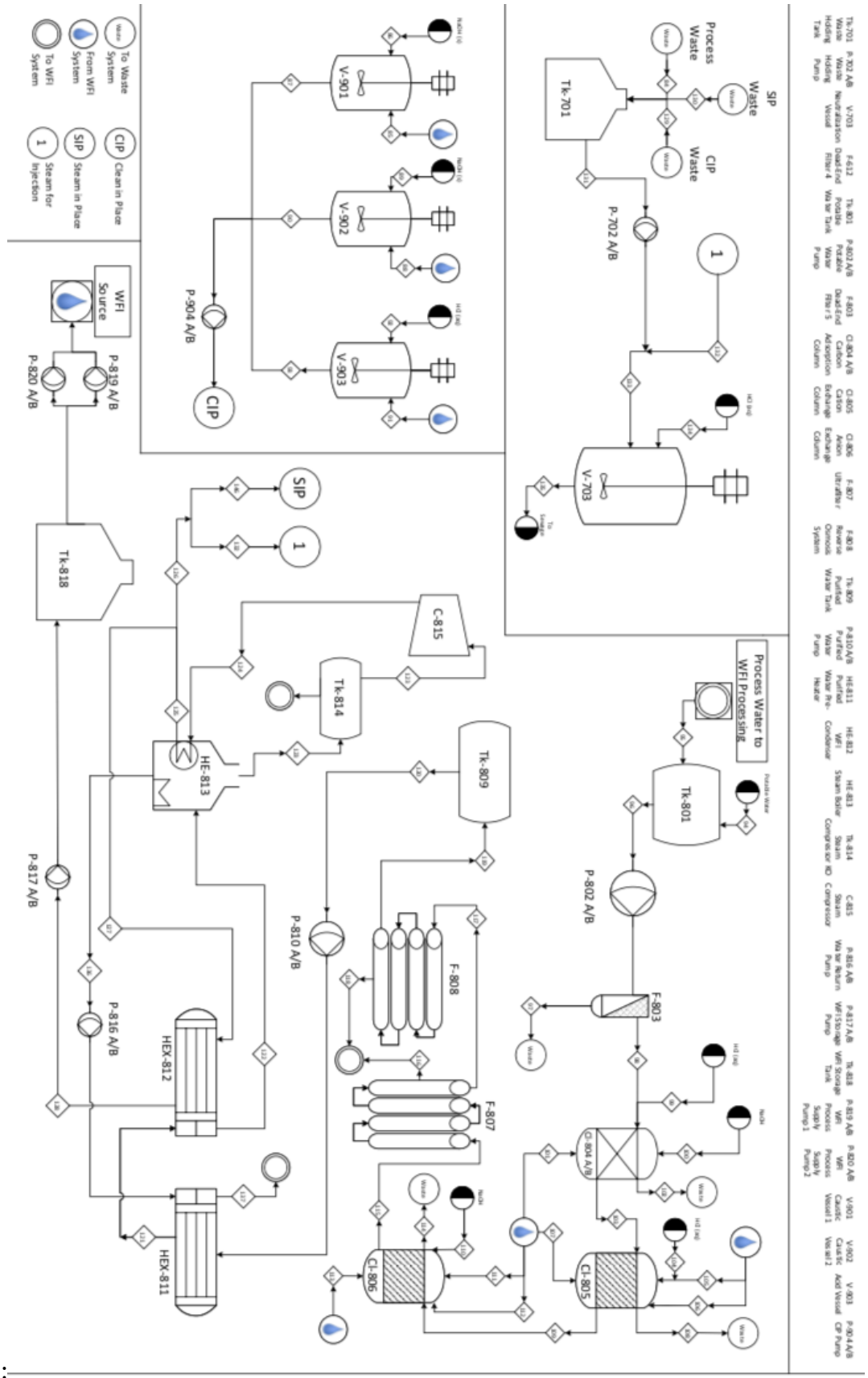
Equipment ID	Equipment
C-XXX	Compressor
CB-XXX	Cell Bag
Cf-XXX	Centrifuge
Cl-XXX	Column
F-XXX	Filter
Fz-XXX	Freezer
HE-XXX	Heat Exchanger
P-XXX	Pump
R-XXX	Reactor
RB-XXX	Roller Bottle
Tk-XXX	Tank (no mixer)
V-XXX	Vessel (mixer)

Table 4 relates equipment type in the Process Flow Diagram (Figure 4) to its equipment ID abbreviation.

Figure 4: PFD


V-101 Media Prep Vessel 1
P-102 A/B Media Prep Pump 1
V-103 Media Prep Vessel 2
P-104 A/B Media Prep Pump 2
V-105 A/B Feed Media Prep Vessel
P-106 A/B Feed Media Pump
TF-201 T-Flask 1
TF-202 T-Flask 2
RB-203 Roller Bottle Roller
RB-204 Roller Bottle
CB-205 Cell Bag Rocker Tray
CB-206 Cell Bag
R-207 Seed Culture Bioreactor 1
R-208 Seed Culture Bioreactor 2
V-209 Air Compressor KO Drum
F-210 Air Cartridge Filter
C-211 Air Compressor
HE-212 Air Compressor After-Cooler
R-301 A/B Production Bioreactor
P-302 A/B Production Bioreactor Pump
From WFI System
CIP Clean in Place
SIP Steam in Place
To Waste System
CB-205
CB-206
RB-203/ 204
TF-201
TF-202
V-209
HE-212
C-211
F-210
R-207
R-208
V-101
V-103
V-105 A/B
R-301 A/B
P-102 A/B
P-104 A/B
P-105 A/B
P-302 A/B
CIP SIP
Water
Vent


Tk-303 Production Bioreactor Surge Tank
Cf-304 Centrifuge
P-305 A/B Centrifuge Pump
F-306 Dead-End Filter 1
Tk-307 Centrifuge Surge Tank
V-401 Protein A Buffer Prep Vessel 1
V-402 Protein A Buffer Prep Vessel 2
V-403 Protein A Buffer Prep Vessel 3
V-404 Protein A Buffer Prep Vessel 4
P-405 A/B Protein A Column Feed Pump
Cl-406 Protein A Chromatography Column
F-407 Dead-End Filter 2
V-408 Viral Inactivation Vessel
P-409 A/B Viral Inactivation Pump
Tk-410 Diafiltration Flush Tank 1
P-411 A/B Diafiltration Pump 1
F-412 Diafilter 1
F-413 Dead-End Filter 3
Tk-414 Viral Inactivation Surge Tank
V-501 IEX Buffer Prep Vessel 1
V-502 IEX Buffer Prep Vessel 2
V-503 IEX Buffer Prep Vessel 3
V-504 IEX Buffer Prep Vessel 4
V-505 IEX Buffer Prep Vessel 5
P-506 A/B IEX Feed Pump
Cl-507 IEX Chromatography Column
V-508 Ammonium Sulfate Vessel
Tk-509 Diafiltration Flush Tank 2
P-510 A/B Diafiltration Pump 2
F-511 Diafilter 2
V-601 HIC Buffer Prep Vessel 1
V-602 HIC Buffer Prep Vessel 2
V-603 HIC Buffer Prep Vessel 3
V-604 HIC Buffer Prep Vessel 4
P-605 A/B Diafiltration /HIC Column Feed Pump
Cl-606 HIC Column
Tk-607 HIC Surge Tank
P-608 A/B HIC Surge Tank Pump
Tk-609 Diafiltration Flush Tank 3
P-610 A/B Diafiltration Pump 3
F-611 Diafilter 3
F-612 Dead-End Filter 4
V-613 Freeze-Thaw Cryovessel
Fz-614 Storage Freezer
CIP Clean in Place
SIP Steam in Place
To Waste System
From WFI System
To WFI System


Tk-703 Waste Holding Tank
P-702 A/B Waste Holding Pump
V-703 Neutralization Vessel
F-812 Dead End Filter 4
Tk-801 Potable Water Tank
P-802 A/B Potable Water Pump
F-803 Dead End Filter 5
CI-804 A/B Carbon Adsorption Column
CI-805 Carbon Exchange Column
CI-806 Anion Exchange Column
F-807 Ultrafilter
F-808 Reverse Osmosis System
Tk-809 Purified Water Tank
P-810 A/B Purified Water Pump
HE-811 Purified Water Pre-Heater
HE-812 WFI Condenser
HE-813 Steam Boiler
Tk-814 Steam Compressor KO
C-815 Steam Compressor
P-816 A/B Water Return Pump
P-817 A/B WFI Storage Pump
Tk-818 WFI Storage Tank
P-819 A/B Process WFI Supply Pump 1
P-820 A/B Process WFI Supply Pump 2
V-901 Caustic Vessel 1
V-902 Caustic Vessel 2
V-903 Acid Vessel
P-904 A/B CIP Pump
SIP Waste
Process Waste
CIP Waste
Tk-701
P-702 A/B
V-901
V-902
V-903
P-904 A/B
CIP
WFI Source
P-819 A/B
P-820 A/B
Process Water to WFI Processing
Tk-801
P-802 A/B
F-803
CI-804 A/B
CI-805
CI-806
F-807
F-808
Tk-809
P-810 A/B
C-815
Tk-814
HE-813
Tk-818
P-817 A/B
P-816 A/B
HEX-812
HEX-811
SIP
1
To Waste System
From WFI System
To WFI System
Steam for Injection
Clean in Place
Steam in Place

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MATERIAL AND ENERGY BALANCES

One of the most important aspects of a preliminary design is its technical feasibility. On the most basic level, mass and energy must balance throughout the entire process for the technical validity of the process to be verified. Table 5 below summarizes the pressure, temperature, mass flow, and enthalpy for each stream in the mAb production process, allowing for verification of material and energy balances throughout the process.

STREAM FLOW SUMMARY

Table 5

Stream No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
Temperature [C]	37.0	25.0	37.0	25.0	37.0	25.0	37.0	25.0	37.0	25.0	25.0	37.0	37.0	25.0	25.0	37.0	37.0	25.0	25.0	25.0	37.0	37.0	37.0	37.0	44.1	44.1	44.1
Pressure [bara]	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01
Enthalpy [kW-hr/batch]	0.00	0.00	1.00E-03	1.40E-02	2.20E-02	0.43	2.20E-02	0.28	0.43	4.79	0.56	0.94	7.53	96.61	14.66	23.87	150.7	95.75	1159	478.8	1742	1004	1.20E-02	1004.09	44.22	1151	0.35
Total Mass Flow Rate [kg/batch]	1.00E-03	5.00E-03	6.00E-03	2.00E-02	2.60E-02	4.74E-02	0.50	9.47	9.96	164.6	80.16	79.92	175.0	3316	2084	2080	3500	3286	1.64E+04	1.65E+05	1.65E+05	2.33E+04	0.80	23326	863.0	2.25E+04	6.82
Molar Flow Rate [kmol/batch]																											
Biomass	1.00E-09	-	9.09E-07	-	1.00E-07	-	8.00E-05	-	1.42E-03	-	-	-	2.85E-02	-	-	-	0.57	-	-	-	-	7.13	-	7.13	6.99	0.14	0.14
Impurities	6.00E-05	-	-	-	1.00E-07	-	1.00E-05	-	5.00E-04	-	-	-	9.45E-02	-	-	-	0.18	-	-	-	-	2.28	-	2.28	6.79E-02	2.21	3.30E-04
BalanCD Media	-	6.51E-06	4.55E-07	2.32E-05	1.00E-07	6.04E-04	2.00E-05	1.22E-02	1.00E-05	2.12E-01	-	-	8.84E-02	4.27	-	-	1.89	-	21.13	-	-	-	-	-	-	-	-
Feed 4 Media	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4.23	-	-	-	12.83	-	12.83	0.38	12.45	1.83E-03
Mab	-	-	4.55E-07	-	1.00E-06	-	2.00E-05	-	2.70E-04	-	-	-	1.02E-02	-	-	-	0.21	-	-	-	-	2.60	-	2.59	7.76E-02	2.52	3.70E-04
Sodium Bicarbonate	-	1.26E-06	4.55E-07	4.51E-06	1.00E-06	1.17E-04	1.00E-05	2.37E-03	2.50E-04	4.11E-02	-	-	4.36E-03	0.83	-	-	8.73E-02	0.82	4.11	-	-	0.58	-	0.58	1.73E-02	0.56	8.00E-04
Water	-	2.73E-04	3.27E-04	9.76E-04	1.43E-03	2.54E-02	2.75E-02	5.13E-01	5.49E-01	8.90	-	-	9.54	179.4	-	-	190.8	177.8	889.0	-	-	1265	-	1265	37.27	1227	0.18
Oxygen	-	-	-	-	-	-	-	-	-	-	0.58	0.52	-	-	15.17	13.81	-	-	-	1200	9.79	-	5.90E-03	-	-	-	
Nitrogen	-	-	-	-	-	-	-	-	-	-	2.19	2.20	-	-	57.08	57.20	-	-	-	4515	4516	-	2.20E-02	-	-	-	
Carbon Dioxide	-	-	-	-	-	-	-	-	-	-	-	4.04E-02	-	-	-	0.81	-	-	-	-	1183	-	-	-	-	-	
Acetic-Acid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Hydrochloric acid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Ammonium Sulfate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
TRIS Base	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
TRIS HCl	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Sodium Hydroxide	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
EDTA Disodium	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Disodium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Monosodium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Sodium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Tributyl phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Sodium Chloride	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Guanidinium Chloride	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Potassium Chloride	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Monopotassium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Polysorbate 80	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Total	6.00E-05	2.80E-04	3.30E-04	1.00E-03	1.43E-03	2.60E-02	9.12	0.53	0.55	9.12	2.78	2.76	9.77	183.8	72.25	71.81	193.7	182.1	910.6	5715	5709	1290	2.79E-02	1290	44.80	1245	0.33

Stream No.	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54
Temperature [C]	44.1	44.1	44.1	25.0	25.0	25.0	25.0	35.7	25.5	25.0	25.5	25.0	25.5	25.0	25.0	26.1	25.0	26.1	25.0	26.0	25.0	25.0	26.0	25.0	25.0	25.0	25.0
Pressure [bara]	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01
Enthalpy [kW-hr/batch]	1151	2.20E-02	1151	72.32	119.6	239.1	124.6	1656	50.04	-	50.04	0.15	50.05	14.51	19.69	61.50	14.51	10.27	1.40E-02	10.39	29.41	-	10.39	40.65	67.82	136.6	68.15
Total Mass Flow Rate [kg/batch]	2.25E+04	1.79	2.25E+04	2508	4126	8220	5000	4.1E+04	1687	-	1687	9.24	1687	497.4	674.8	2025	497.4	337.4	2.42	346.6	346.6	-	346.6	1399	2342	4806	2387
Molar Flow Rate [kmol/batch]																											
Biomass	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Impurities	2.21	-	2.21	-	-	-	-	2.08	0.13	-	0.13	-	0.13	-	-	0.10	-	9.74E-02	-	9.74E-02	9.74E-02	-	9.74E-02	-	-	-	-
BalanCD Media	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Feed 4 Media	12.45	-	12.45	-	-	-	-	12.45	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mab	2.52	-	2.52	-	-	-	-	0.25	2.27	-	2.27	-	2.27	-	-	-	-	2.20	-	2.20	2.20	-	2.21	-	-	-	-
Sodium Bicarbonate	0.56	-	0.56	-	-	-	-	0.56	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Water	1227	-	1227	137.3	219.0	453.5	223.5	2169	90.70	-	90.70	256.5	90.70	27.61	37.56	111.7	27.61	16.42	-	16.67	16.67	-	16.67	76.88	127.5	250.1	124.9
Oxygen	-	1.30E-02	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.76E-02	-	-	-	-	-	-	-	-
Nitrogen	-	4.90E-02	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6.60E-02	-	-	-	-	-	-	-	-
Carbon Dioxide	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Acetic-Acid	-	-	-	-	-	0.82	-	0.66	0.16	-	0.16	-	0.16	-	-	0.16	-	3.99E-03	-	3.99E-03	-	-	3.99E-03	-	-	-	-
Hydrochloric acid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ammonium Sulfate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
TRIS Base	-	-	-	0.3163	0.52	-	1.13	1.21	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
TRIS HCl	-	-	-	0.94	1.55	-	0.34	3.63	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sodium Hydroxide	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
EDTA Disodium	-	-	-	1.25E-02	-	-	-	1.25E-02	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Disodium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.10E-02	1.82E-02	0.23	-
Monosodium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sodium Phosphate	-	-	-	6.26E-03	-	-	-	6.30E-02	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tributyl phosphate	-	-	-	-	-	-	-	-	-	-	-	4.33E-03	-	-	-	-	-	-	-	4.30E-03	4.34E-03	-	4.30E-03	-	-	-	-
Sodium Chloride	-	-	-	-	-	-	4.51	4.51	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.72	4.67	2.33
Guanidinium Chloride	-	-	-	-	8.26	-	-	8.26	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Potassium Chloride	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.00E-07	1.00E-06	-	-
Monopotassium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.00E-07	1.00E-06	-	-
Polysorbate 80	-	-	-	-	-	-	-	-	-	-	-	2.65E-03	-	-	-	-	-	-	-	2.70E-03	2.65E-03	-	2.70E-03	-	-	-	-
Total	1244	6.20E-02	1244	137.5	227.4	454.3	232.5	2203	93.27	0.00	93.27	256.5	93.27	27.61	37.56	112.0	27.61	18.72	8.36E-02	18.98	18.97	0.00	18.99	76.89	128.3	255.0	127.3

Table 5: Material and Energy Balance

Stream No.	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81
Temperature [C]	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.8	25.0	25.0	25.8	25.8	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.8	25.0	25.8	25.8	25.0
Pressure [bara]	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01
Enthalpy [kW-hr/batch]	40.63	335.8	28.40	1.01	8.00E-04	29.41	14.51	36.45	14.51	11.97	6.16	6.16	53.94	93.43	185.1	91.37	392.0	37.95	1.00E-02	37.95	14.51	15.12	46.85	14.51	7.79	7.79	-
Total Mass Flow Rate [kg/batch]	1406	11690	997.0	102.1	1.46	1099	497.4	1302	497.4	410.0	206.7	206.7	2002	3337	6453	3161	13838	1322	1.85	1322	497	518	1580	497	260	260	-
Molar Flow Rate [kmol/batch]																											
Biomass	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Impurities	-	9.16E-02	5.84E-03	-	-	5.84E-03	-	0.03	-	-	3.17E-02	1.03	-	-	-	-	0.03	-	-	-	-	-	-	-	-	-	-
BalanCD Media	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Feed 4 Media	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mab	-	0.22	1.98	-	-	1.98	-	-	-	-	1.92	2.92	-	-	-	-	0.19	1.73	-	1.73	-	-	-	-	1.64	1.64	-
Sodium Bicarbonate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Water	76.48	622.6	50.02	-	-	50.02	27.61	63.47	27.61	22.76	9.31	10.31	92.94	166.2	343.1	172.0	711.0	68.63	-	68.63	27.61	28.77	84.78	27.61	12.70	12.70	-
Oxygen	-	-	-	-	1.06E-02	-	-	-	-	-	-	-	-	-	-	-	-	-	1.34E-02	-	-	-	-	-	-	-	-
Nitrogen	-	-	-	-	4.00E-02	-	-	-	-	-	-	-	-	-	-	-	-	-	5.06E-02	-	-	-	-	-	-	-	-
Carbon Dioxide	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Acetic-Acid	-	3.99E-03	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hydrochloric acid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ammonium Sulfate	-	-	-	0.77	-	0.77	-	0.75	-	-	1.79E-02	1.02	-	-	-	-	1.79E-02	-	-	-	-	-	-	-	-	-	-
TRIS Base	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
TRIS HCl	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sodium Hydroxide	0.70	0.70	-	-	-	-	-	-	-	-	-	-	-	-	-	1.57	-	-	-	-	-	-	-	-	-	-	-
EDTA Disodium	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Disodium Phosphate	-	2.90E-02	-	-	-	-	-	-	-	-	-	-	4.57E-02	7.50E-02	0.13	-	0.22	2.61E-02	-	2.60E-02	-	-	2.54E-02	6.40E-04	6.40E-04	6.40E-04	-
Monosodium Phosphate	-	0.19	4.67E-02	-	-	4.67E-02	-	4.56E-02	-	-	1.10E-03	1.00	-	-	-	-	1.10E-03	-	-	-	-	-	-	-	-	-	-
Sodium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tributyl phosphate	-	0.70	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sodium Chloride	-	7.00	0.93	-	-	0.93	-	0.91	-	-	2.20E-02	1.02	6.71	5.69	4.33	-	15.88	0.87	-	0.86	-	-	0.84	2.12E-02	2.12E-02	2.12E-02	-
Guanidinium Chloride	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Potassium Chloride	-	1.00E-04	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Monopotassium Phosphate	-	5.00E-05	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Polysorbate 80	-	2.65E-03	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total	77.18	631.5	52.99	0.77	0.05	53.76	27.61	65.21	27.61	22.76	11.31	17.31	99.70	171.9	347.6	173.6	727.3	71.25	0.06	71.25	27.61	28.77	85.65	27.63	14.37	14.37	0.00

Stream No.	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108
Temperature [C]	25.00	-50.0	30.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0
Pressure [bara]	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01
Enthalpy [kW-hr/batch]	7.79	-15.61	2466	174.2	1.84	176.0	493.5	1.03	494.5	783.8	14.17	43.77	42.66	54.28	54.28	4.11	50.28	178.9	365.9	365.9	910.9	8447	0.17	8.06	7.73	9.58	25.70
Total Mass Flow Rate [kg/batch]	259.8	259.8	7.20E+04	5968	121.3	6089	1.69E+04	68.14	1.70E+04	2.69E+04	267.7	1.50E+03	1.46E+03	1.82E+03	1.82E+03	1.37E+02	1.68E+03	6108.98	1.25E+04	1.25E+04	3.12E+04	2.83E+05	7.22	274.3	264.1	330.1	887.0
Molar Flow Rate [kmol/batch]																											
Biomass	-	-	7.13	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Impurities	-	-	2.41	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BalanCD Media	-	-	1.89	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Feed 4 Media	-	-	10.94	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Mab	1.64	1.64	0.74	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sodium Bicarbonate	-	-	0.58	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Water	12.70	12.70	3802	331.3	-	331.3	938.7	-	938.7	1491	-	79.09	77.08	95.93	95.93	3.41	92.60	324.2	630.0	695.5	79.80	15589	0.34	15.22	14.62	18.31	48.59
Oxygen	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nitrogen	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Carbon Dioxide	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Acetic-Acid	-	-	0.82	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.49	-	-	-	-
Hydrochloric acid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	14.62	-	-	1680	-	-	-	-	-	-
Ammonium Sulfate	-	-	0.773	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
TRIS Base	-	-	1.21	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
TRIS HCl	-	-	3.63	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sodium Hydroxide	-	-	2.27	3.03	-	3.03	-	1.70	1.70	-	-	-	-	-	-	-	-	-	66.19	-	0.59	-	-	-	-	-	-
EDTA Disodium	-	-	1.30E-02	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Disodium Phosphate	6.40E-04	6.40E-04	0.28	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Monosodium Phosphate	-	-	0.23	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sodium Phosphate	-	-	6.25E-02	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tributyl phosphate	-	-	4.34E-03	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sodium Chloride	2.12E-02	2.12E-02	29.15	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Guanidinium Chloride	-	-	8.30	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Potassium Chloride	-	-	1.00E-04	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Monopotassium Phosphate	-	-	6.00E-05	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Polysorbate 80	-	-	2.65E-03	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total	14.37	14.37	3873	334.3	0.00	334.3	938.7	1.70	940.4	1491	0.00	79.09	77.08	95.93	95.93	3.41	92.60	338.9	696.2	695.5	1760	15589	0.82	15.22	14.62	18.31	48.59

Stream No.	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135
Temperature [C]	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	27.8	105.7	105.7	245.8	136.1	136.1	136.1	110.0	25.0	110.0	25.0	110.0	83.3	25.0	83.2
Pressure [bara]	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.66	1.45	1.24	1.24	3.45	3.24	3.24	3.24	3.03	1.01	3.03	1.50	3.03	1.50	1.10	1.50
Enthalpy [kW-hr/batch]	8447	6.55	6.55	6.38	7.90	27.72	8447	425.0	8277	395.0	8308	6042	6042	5335	4803	4698	4774	743.4	4039	4742	714.3	4742	3369	4742	3661	4.59	3619
Total Mass Flow Rate [kg/batch]	169.7	169.7	169.7	169.7	169.7	169.7	169.7	169.7	169.7	169.7	1523	2.30E+05	2.30E+05	2.30E+05	2.18E+05	2.18E+05	2.18E+05	3.36E+04	1.85E+05	1.85E+05	2.46E+04	1.11E+05	1.29E+05	7.39E+04	1.42E+04	252.00	1.43E+05
Molar Flow Rate [kmol/batch]																											
Biomass	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	7.13	-	7.13	-	7.13
Impurities	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2.41	-	2.41	-	2.41
BalanCD Media	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.89	-	1.89	-	1.89
Feed 4 Media	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	10.94	-	10.94	-	10.94
Mab	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.74	-	0.74	-	0.74
Sodium Bicarbonate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.58	-	0.58	-	0.58
Water	15589	11.80	12.58	12.11	15.12	50.62	15589	793	14780	689	83.96	75.96	75.96	75.96	72.16	72.16	72.16	11.10	61.06	61.06	1349	36.64	5188	24.42	5212	5.25E-02	5212
Oxygen	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Nitrogen	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Carbon Dioxide	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Acetic-Acid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.82	-	0.82	-	0.82
Hydrochloric acid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.00	-	0.00	1.52E-02	0.02
Ammonium Sulfate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.77	-	0.77	-	0.77
TRIS Base	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.21	-	1.21	-	1.21
TRIS HCl	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3.63	-	3.63	-	3.63
Sodium Hydroxide	-	0.74	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2.27	-	2.27	1.00E-06	2.27
EDTA Disodium	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.30E-02	-	1.30E-02	-	0.01
Disodium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.28	-	0.28	-	0.28
Monosodium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.23	-	0.23	-	0.23
Sodium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6.25E-02	-	6.25E-02	-	6.25E-02
Tributyl phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Sodium Chloride	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	29.15	-	29.15	-	29.15
Guanidinium Chloride	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	8.30	-	8.30	-	8.30
Potassium Chloride	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Monopotassium Phosphate	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Polysorbate 80	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Total	15589	12.54	12.58	12.11	15.12	50.62	15589	793.0	14780	688.8	83.96	75.96	75.96	75.96	72.16	72.16	72.16	11.10	61.06	61.06	1349	36.64	5258	24.42	5283	6.77E-02	5283

Stream No.	136	137	138	139	140	141	142	143	144	145	146
Temperature [C]	105.7	50.0	25	25	25	25	89.12	37	25	30	126.1
Pressure [bara]	1.65	1.45	1.01	1.01	1.01	1.01	1.703	1.358	3.771	3.426	3.24
Enthalpy [kW-hr/batch]	295.4	295.4	10.2	10.2	10.2	10.2	2307	419.0	.39E+06	1.39E+06	743.4
Total Mass Flow Rate [kg/batch]	1.15E+04	1.15E+04	1.31E+05	0.00E+00	1.31E+05	1.31E+05	1.31E+05	1.31E+05	3.16E+05	3.16E+05	33600
Molar Flow Rate [kmol/batch]											
Biomass	-	-	-	-	-	-	-	-	-	-	
Impurities	-	-	-	-	-	-	-	-	-	-	
BalanCD Media	-	-	-	-	-	-	-	-	-	-	
Feed 4 Media	-	-	-	-	-	-	-	-	-	-	
Mab	-	-	-	-	-	-	-	-	-	-	
Sodium Bicarbonate	-	-	-	-	-	-	-	-	-	-	
Water	6.38E+02	6.38E+02	-	-	-	-	-	-	315672.00	315672.00	36.64
Oxygen	-	-	1713.95	-	1713.95	1713.95	1713.95	1713.95	-	-	
Nitrogen	-	-	7368.80	-	7368.80	7368.80	7368.80	7368.80	-	-	
Carbon Dioxide	-	-	-	-	-	-	-	-	-	-	
Acetic-Acid	-	-	-	-	-	-	-	-	-	-	
Hydrochloric acid	-	-	-	-	-	-	-	-	-	-	
Ammonium Sulfate	-	-	-	-	-	-	-	-	-	-	
TRIS Base	-	-	-	-	-	-	-	-	-	-	
TRIS HCl	-	-	-	-	-	-	-	-	-	-	
Sodium Hydroxide	-	-	-	-	-	-	-	-	-	-	
EDTA Disodium	-	-	-	-	-	-	-	-	-	-	
Disodium Phosphate	-	-	-	-	-	-	-	-	-	-	
Monosodium Phosphate	-	-	-	-	-	-	-	-	-	-	
Sodium Phosphate	-	-	-	-	-	-	-	-	-	-	
Tributyl phosphate	-	-	-	-	-	-	-	-	-	-	
Sodium Chloride	-	-	-	-	-	-	-	-	-	-	
Guanidinium Chloride	-	-	-	-	-	-	-	-	-	-	
Potassium Chloride	-	-	-	-	-	-	-	-	-	-	
Monopotassium Phosphate	-	-	-	-	-	-	-	-	-	-	
Polysorbate 80	-	-	-	-	-	-	-	-	-	-	
Total	638.1	638.1	9082.75	0.00	9082.75	9082.75	9082.75	9082.75	315672.00	315672.00	36.64

PROCESS DESCRIPTION

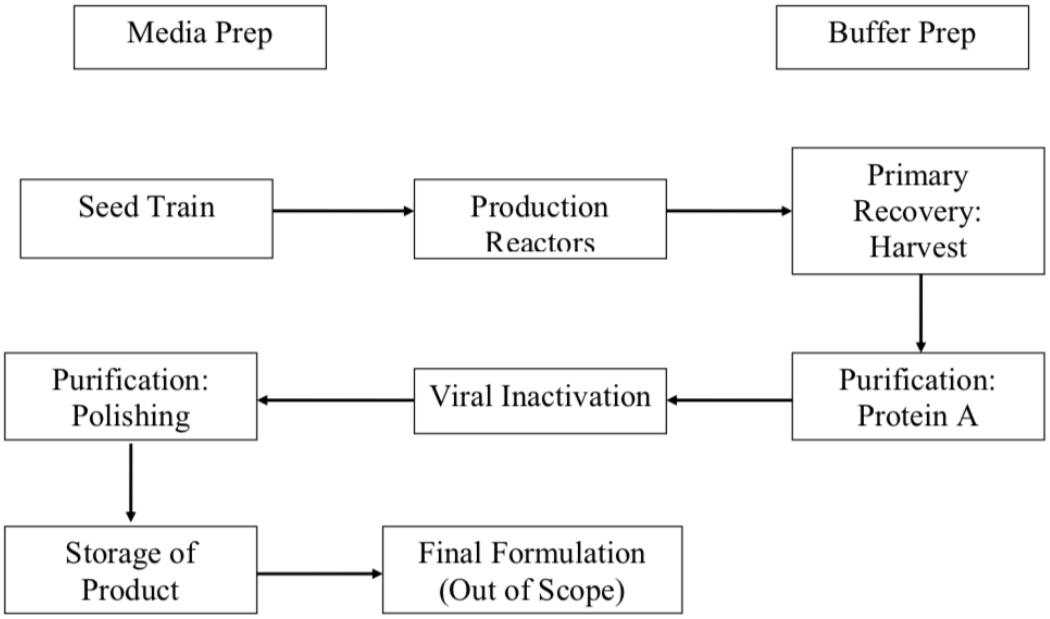


***Figure 5**: Process Block Flow Diagram*

Design Basis

The scope of this project was to design a facility that produced a minimum of 1000 kg of mAb per year. The block diagram (Figure 6) above, gives an overview of the entire process. The seed train must be inoculated from one 1 mL vial holding 1 x10^6 CHO cells, with only one vial used per batch. The doubling time for CHO cells was estimated to be 36 hours. Each step in the seed train was operated in a batch manner and was performed under sterile conditions. The cell culturing media was required to be a powdered, chemically-defined, serum-free media that was mixed into solution on site. The production bioreactor was designed to produce a minimum mAb titer (concentration per batch) of 1-2 g/L with the expectation that the titer could be increased to 5-10 g/L in the future. The production reactor could be operated in either a batch or a fed-batch manner. Throughout this final production step, the concentration of glucose in the reactor had to be maintained above 2 g/L. Per the project guidelines, it was assumed that each CHO cell produces 25 pg of mAb per day during both the seed train and bioreactor portions of the upstream process. These project specifications are summarized in Table 6 below.

Table 6: CHO Cell and mAb Specifications

CHO Cell/mAb Specifications	
CHO Cells per vial	1000000 cells
Cell Doubling Time	36 hours
mAb Production Minimum	1000 kg/yr
mAb Titer	1-2 g/L
CHO Cell - mAb Production Rate	25 pg/day
Prod. Bioreactor Glucose Minimum	2 g/L

The product leaving the seed train and bioreactors must be sanitized and purified to the standards set forth by the FDA for pharmaceutical processes [7]. The most significant of these regulations include having two purification steps that inactivate any biological contaminants including viruses. After the purification and viral inactivation steps, the final product was required to be packaged and stably stored for up to one year. Other considerations due to the sterile nature of the process include SIP (steam in place) and CIP (clean in place) of process vessels in between batches and the use of WFI (water for injection) as opposed to potable water in the process. The option was given in the project guidelines of purchasing WFI for $1/L or of purchasing potable water for $0.543/1000 L and purifying this water to meet the USP (United States Pharmacopeia) guidelines for WFI. Waste from the process was to be pretreated and disposed of using the existing city sewage system at the cost of $5/1000 gal. Existing electricity utility is also provided at the site, for a current rate of $0.05/kW-hr. The on-site utilities provided to the project team are summarized below in Table 7.

Table 7: Cost of On-Site Utilities

On-Site Utilities	
Electricity	$0.05/kW-hr
Sewer	$5/thousand gal
Water	$0.543/thousand L
WFI	$1/L

Not all parameters necessary to evaluate the project were provided by management, so some assumptions were made by the project evaluation and preliminary design team. These project assumptions are summarized in Table 8 below.

Table 8: Project Evaluation Parameters

Project Assumptions	
Service Factor	0.98
Project Life	25
Tax Rate	21%
Escalation Rate	2%
Inflation Rate	2%

Design Philosophy

The two main factors that influenced the design of this process were the minimum mAb production rate (1000 kg/yr) and the sterile nature of the process. The production rate determined the way that the upstream process was designed—both the amount of mAb produced in each batch and the number of batches per year were maximized to at least hit the minimum mAb production. The production rate was always the first and foremost priority in the design, and everything else was based upon meeting it. In regards to the mAb titer in the production reactor, this design is based solely on the current titer of 1-2 g/L. The optimization of the process production centered around increasing total mAb production in the process (minimum of 1000 kg/yr) rather than increasing the concentration of mAb in the product reactor (1-2 g/L). Potential ways that this design could be used to produce a larger titer of mAb will are addressed in the Process Scale Up subsection. The other main factor in the design was maintaining a sterile environment and dealing with the biological hazard both within and without the process properly. A large portion of the design is devoted to a water for injection/steam in place (SIP) system and a clean in place (CIP) system, both of which are necessary for keeping a biopharmaceutical manufacturing process sterile. Other important pieces of the design that were emphasized because of the sterile nature of the product are the viral inactivation steps and the waste treatment and disposal process. The following are examples of ways that the process was optimized in order to properly account for these two main factors.

Seed Train Densities

One of the keys to properly designing the seed train is managing the different phases of cell growth. For this design, much attention was given to selecting an optimum media for CHO growth and understanding how the media affected cell growth. The media that was selected for this process was BalanCD CHO Growth A media. This media was proven to be an optimal media for CHO production because of the length of time that cells remained viable in it [8]. In fact, cultures remained viable and growing in densities of up to 9 million cells/mL of media, a larger number than most other CHO media can support [8]. Knowing this about the media, the team designed the seed train to keep cells in each vessel as long as the log phase was continuing, and to remove the cells before they reached maximum density. It was established that the cells would be inoculated at $2x10^5$ cells/mL and harvested at $4x10^6$, a lower density than the maximum. Working within this range of densities allows the process to produce the required number of cells to produce the minimum amount of mAb per year.

Scheduling Optimization

Besides optimizing the cell culturing process, the second most important way to maximize production is by optimizing the scheduling of the process. Although each step in this process is batch, the steps can be scheduled in such a way as to maximize efficiency by minimizing the lag time between each step. One way that scheduling was used to optimize the process was by operating some of the downstream process steps in cycles. The centrifuge and first two chromatography columns processed only a portion of the product stream at a time, decreasing the size of the units or the number of required units to complete the process. Another way the

process was optimized was by debottlenecking it so that the cycle time, or time between batches could be decreased, increasing the number of batches per year. Once the original process was designed with the minimum, necessary pieces of equipment, the schedule was examined to see where the bottleneck in the process was. Figure 6 below is the equipment occupancy chart for the first 100 days of the original design. As is made clear by the chart, bioreactor R-301 is the bottleneck in the process. The minimum possible time between batches (cycle time) is 12 days, limiting the facility to just under 30 batches per year. With a production amount of 29.6 g/batch, this design won't meet the minimum mAb production requirement. To optimize this process, a second (and identical) R-301 bioreactor was added to the process. The operation of the two bioreactors is staggered, so that the reactors take turns being used in the process. The same equipment occupancy chart with a second R-301 bioreactor is displayed below in Figure 7. In the chart, R-301 a/b is the original reactor and STG01 is the second reactor. Adding a second R-301 reactor reduces the cycle time to 7 days, allowing the facility to process 51 batches and produce over 1500 kg of mAb each year. This optimized design is the one that was chosen for the rest of the process because it greatly increased the yearly production of mAb while only increasing the capital cost by a small amount.

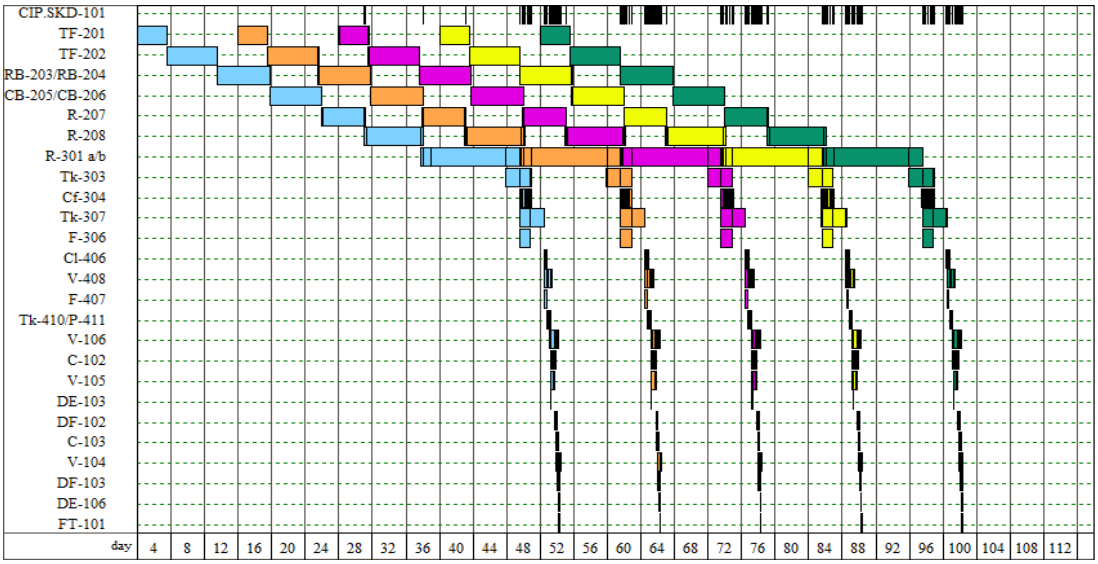


Figure 6: Equipment occupancy chart without cycle time optimization

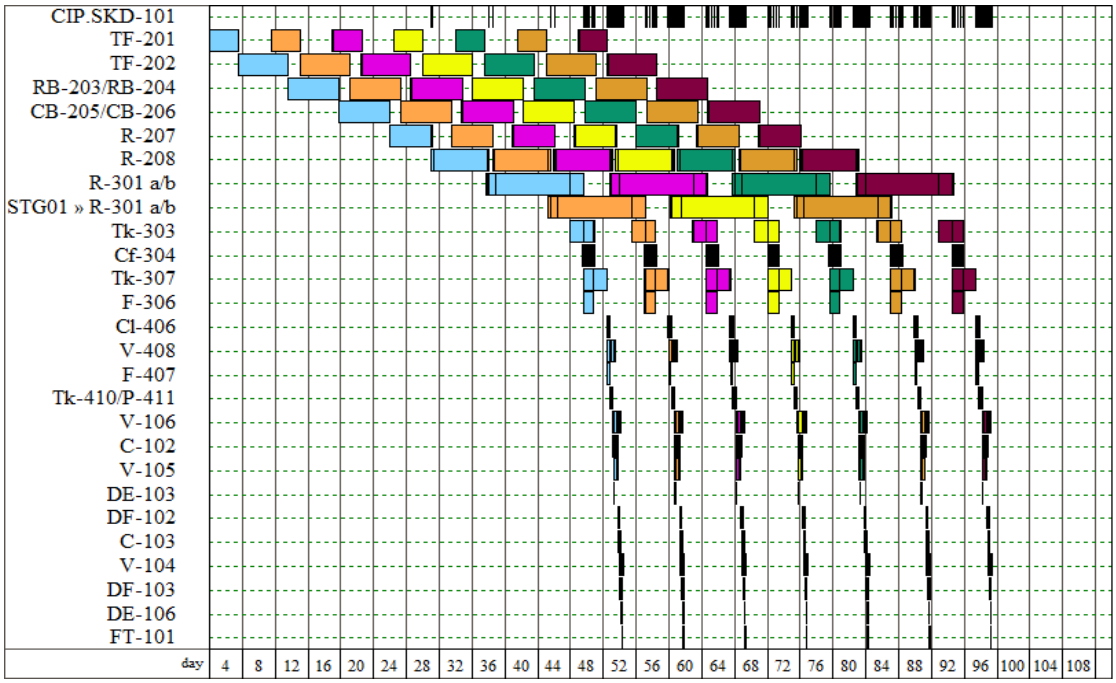


Figure 7: Equipment occupancy chart with cycle time optimization

Water for Injection

As specified in the project statement and made very clear in FDA and USP regulations, all water that is used in the process that in any way comes into contact with the product streams is required to be water for injection [9] Water for injection (WFI) is available for purchase for $1000/1000 L, however the cost of purchasing that much water adds up quickly when considering that one batch of mAb production requires nearly 130,000 L of water for injection, as well as another 25,000 kg of clean steam needed for steam in place (SIP) of process equipment. Purchasing that much water greatly increases the operating cost of the process. To make the process more cost-effective, a water for injection skid was designed that purifies potable water until it is up to the USP standard for WFI [10,11]The skid was designed so that it could handle potable water and even relatively "clean" waste streams from the process such as the diafiltration flush outlet stream. In order to realistically simulate the process, a water stream was designed using the maximum allowable contaminants in potable water per the EPA regulation [12]. The contaminants added to the water are listed in Table 9 below. Although there are more contaminants in potable water than those listed, these represent the variety of possible contaminants in water. Some of the contaminants listed, such as sodium, are not regulated by the EPA but were listed on the Boston, MA municipal water report [13]. Since much of the pharmaceutical industry is located in the Boson-Cambridge area, this water was compared to the EPA regulations to give a comprehensive water composition [14].

Table 9 – Potable Water Estimated Contaminants Concentration

Water Component	Concentration (mg/L)	Water Component	Concentration (mg/L)	Water Component	Concentration (mg/L)	Water Component	Concentration (mg/L)
Arsenic	0.010	Chlorine	4.0	Endotoxins	0.034	Mercury	0.002
Barium	2.0	Chlorine Dioxide	0.80	Fluoride	4.0	Nitrates/Nitrites	11
Benzene	0.005	Chlorite	1.0	Haloacetic Acids	0.060	Sodium	33
Chloramines	4.0	Coliform	50	Lead	0.015	Trihalomethanes	0.080

In the Economic Analysis – Optimization Analysis Section of the report, the designed WFI system is compared to buying the necessary WFI from an economics standpoint. It is estimated that the operating cost of producing WFI is $3-5/1000 L [15], which if true would make producing WFI a very attractive option. Some of the non-economic benefits of designing a WFI system is that it allows the manufacturing process to control the volume of WFI that is produced and stored at any one time. If WFI is purchased, the process is dependent upon the supply of another raw material instead of on a process that can be continuously run to produce more of the needed material.

Heat Integration

Another optimization step performed in the process is utilizing heat integration, both within the WFI system and the overall process. One example is using municipal water to cool down the bioreactors and then sending that same potable water to the WFI system to be processed into WFI. Combining these streams allows for the better utilization of resources and greatly reduces the amount of water bought only for cooling. In the WFI system, the purified water stream is pre-heated by exchanging heat with the hot water stream drained from the boiler and the WFI saturated steam. Next, the pre-heated purified water is boiled in the steam boiler by an electric coil and a steam coil fueled by the steam leaving the boiler and subsequent compressor. Integrating these heat streams allows WFI and Clean Steam to be produced and cooled to their respective correct states for a total of 306 kW. Finally, the compressed air that is supplied to the bioreactors is cooled to 37 C, the reactor temperature, by potable water that is then supplied to the WFI system. This integration of heat minimizes operating costs while also making good use of thermal energy conservation within the process.

Compressed Air

The final optimization step considered in the design of the process was compressing air for the bioreactors rather than buying compressed air. Over the course of one batch, 406.8 m^3 of air are fed into the three bioreactors in the process to maintain a constant oxygen concentration in the culture media. Compressed air is available in industrial sized cylinders with sizes up to 10,000 L per cylinder [16]. The issue with buying compressed air for this process is that one batch of would use 41 of these cylinders or almost 6 canisters per day. The required storage space and man power to use these canisters outweighs the ease of designing a compression skid that continuously filters, compresses, and cools the air for the reactor. The decision to design this skid, although not economically motivated, optimizes the functionality of the process and further minimizes the dependence of production upon supply of raw materials.

Media Prep

The process begins with cell culture media preparation. The serum-free media, BalanCD CHO Growth A Media, is mixed immediately prior to each new inoculation. For every L of media solution prepared, 23.1 g and 2.09 g of Growth A media and sodium bicarbonate are added respectively [17]. The first four steps of the seed train, t-flasks (TF-201) through cell bag bioreactor (CB-206), are inoculated with media that is prepared in sterile glassware in a sterile room. The glassware is sterilized in an autoclave after each use. Media for both seed train bioreactors, R-207 and R-208, is prepared in Media Prep Vessel 1, V-101, and is pumped into the seed train bioreactors using Media Prep Pump 1, P-102. Media Prep Vessel 1 is connected directly to the WFI system; media powder and sodium bicarbonate are manually added to the vessel. Using an impeller, the media ingredients are well-mixed to produce the inoculation solution. The amounts of media added to R-207 and R-208 for each batch is 165 L and 3325 L respectively. The inoculation media for the Production Bioreactor, R-301 A/B, is prepared in Media Prep Vessel 2, V-103, using the same method explained above. For each batch, 16,500 L of Growth A media solution will be pumped to R-301 using Media Prep Pump 2, P-104. The Production Bioreactor is operated as a fed-batch process, with BalanCD CHO Feed 4 media solution being added over the course of the reaction. The amounts of Feed 4 media powder and sodium bicarbonate added per L of solution are 107.45 g and 2.09 g respectively [17] The feed media is prepared in Feed Media Prep Vessel, V-105 A/B, using the same method explained above. The media fromV-105 A/B will be fed to R-301 A/B through Feed Media Pump, P-106. In order to minimize the time in between batches, two identical Production Bioreactors, R-301 A/B, were designed, each with its own Feed Media Prep Vessel, V-105 A/B, but sharing a Media Prep Vessel, V-103, and pumps P-104 and P-106.

Seed Train

The seed trains consists of a series of cell culture containers, each larger than the last, for the purpose of multiplying the number of cells from the cell source. A large number of cells is required to produce more mAbs, therefore the seed train is designed to maximize the number of cells entering the production bioreactor. The seed train begins by adding 5 mL of Growth A media solution to T-Flask 1, TF-201, thereby preparing it for inoculation. Next one 1 mL vial containing one million CHO cells is inoculated into TF-201. The CHO cells are incubated in T-Flask 1 for 3.5 days. After the allotted time has ended, the approximately $5x10^6$ cells are inoculated into TF-202 which contains 20 mL of inoculation solution. The cells are incubated in TF-202 for 6.5 days. Next the $1x10^8$ cells are inoculated in the Roller Bottle, RB-204, with an additional 475 mL of inoculation solution and incubated for 6.5 days. During incubation, the solution is constantly agitated as the Roller Bottle Roller, RB-203, keeps RB-204 in constant radial motion. This agitation keeps the cells in suspension and promotes good dispersion of nutrients throughout the media. Next the cells, now approximately $2x10^9$, are inoculated in Cell Bag Bioreactor, CB-206, with an addition of 9.5 L of Growth A media solution. The culture is agitated by Cell Bag Rocker, CB-205, through a continuous rocking motion during the 6.2 days of incubation time. During these steps of the seed train, the inoculation vessels and media preparation glassware were located in a sterile room and all transfers were performed under sterile conditions.

From CB-205, the $3.5x10^{10}$ cells in the culture are inoculated in a Seed Culture Bioreactor 1, R-207. The reactor is filled with 165 L of Growth A solution from V-101 by P-102 prior to inoculation. This cell culture is allowed to incubate for 6.5 days. During this time, R-207 is supplied with .25 m^3/min by Air Compressor, C-211, that helps to agitate the cells and maintains an adequate oxygen concentration in the solution for optimal cell growth. A vent is located on the reactor to allow excess carbon dioxide produced by the cells and inert nitrogen to leave the reactor. Using the vent, the pressure in the vessel is maintained at 1.013 bara. The cells in R-207 are additionally agitated by a low rpm impeller. After the 6.5 days are over, the $7x10^{11}$ cell culture is moved to the final seed train step, Seed Culture Bioreactor 2, R-208. R-208 is prepared with 3,325 L of Growth A media solution through the use of V-101 and P-102. The culture incubates for 6.5 days and is fed a constant supply of air throughout by C-211. Additionally, this reactor contains the same impeller and vent systems mentioned above for R-207. The air entering C-211 is first filtered through Air Cartridge Filter, F-210, before being compressed from 1.013 bara to 1.7 bara. This compression also raises the temperature of the ambient air from 25 to 89°C, so the air is cooled back to 37°C by Air Compressor After-Cooler, HE-212 using 3250 L/hr of cooling water. The reactors are maintained at 37°C through 11.4 and 243 kg/hr of cooling water flowing through their respective jackets (R-207 and R-208). After cooling off the reactors, this water is fed to the WFI system as potable feed water.

Production Bioreactors

From R-208, the $1.4x10^{13}$ culture is inoculated in the Production Bioreactor, R-301 A/B. Although each step in the seed train process has produced mAbs, the large number of cells in this reactor maximizes protein production. R-301 A/B is prepared for inoculation by pumping in 16,500 L of Growth A media from V-103 through P-104. The cells are then inoculated in the reactor and allowed to incubate for 9 days. During this time, 366 L of BalanCD CHO Feed 4 media are pumped from V-105 A/B to the reactor by P-106 each day. The total amount of Feed 4 media added to the production bioreactor is 20% of the volume of the Growth A media added to the same reactor [17] The purpose for adding Feed 4 media to the reactor is to maintain the glucose level within the reactor above 2 g/L, as well as to make sure that amount of nutrients is not a limiting factor to culture growth. R-301 has the same compressed air, cooling jack, impeller, and vent systems as described above for R-207 and R-208. 15 m^3/min of air and 1823 kg/hr of cooling water are provided to the reactor. In order to decrease the cycle time (time between batches) of the process, two identical Production Bioreactors and Feed Media Prep Vessels were designed. Each successive batch will switch between using R-301A and R-301B so that cells are always in one of the reactors.

Primary Recovery: Harvest

The solution leaving the production bioreactor, R-301 A/B, contains a variety of substances including cells, proteins (especially mAb), water, media, nutrients, and soluble gases. Once the mAb has been produced, the solution needs to be purified by removing any unnecessary components and concentrating the mAbs in solution. The production slurry, a total of 23,325 kilograms per batch, leaves the production bioreactor and is sent to Production Bioreactor Surge Tank, Tk-303 via Production Bioreactor Pump, P-302. After the complete transfer into the

surge tank, the reactor product drains out, in four equivalently-apportioned cycles, to centrifuge Cf-304. Here, the suspension is separated into layers based upon the density of the components via centrifugal force, and the cells are separated into their various components (lipids, proteins, water, etc.). Gravity serves to take 823 kg per batch of solid waste to Waste Holding Tank, Tk-701. The Centrifugal Pump, P-305, sends the other 22,463 kg per batch of liquid cell culture broth through Dead-End Filter 1, F-306, where any remaining cell solids or solid impurities are removed. The pores in the filter membrane are 0.2 µm in diameter, too small for cells to pass through, but large enough that smaller components, as well as those that are soluble, can pass through. From F-306, a cell-less solution is collected in Tk-307, where it awaits further purification. Any waste remaining in F-306 also collects in Tk-701.

Buffer Prep

In order to purify the mAb product, the solution must pass through multiple chromatography columns. These columns selectively bind to certain molecules in the solution while allowing others to pass through freely. Each column uses multiple types of buffers to process the solution: equilibration, wash, elution, and regeneration buffers. These buffers contain unique formulations of various chemicals, for which these specific formulations can be found in Table 17 in the Column Chromatography section of Equipment List and Unit Descriptions. For the first chromatography column, Protein A Chromatography, a total of four different buffers are prepared. The equilibration, wash, elution, and regeneration buffers are prepared in impeller-mixed vessels V-401, V-402, V-403, and V-404 respectively. A total of 2507, 4146, 8219, and 5097 kg/batch are prepared in the aforementioned vessels, respectively, before being pumped through Cl-406 via P-405. For the Cation-Exchange Chromatography Column, V-501, V-502, V-503, V-504, and V-505 are utilized for the preparation of buffers. These vessels are utilized for the equilibration, first wash, elution, regeneration, and final wash buffers, preparing 1405, 2345, 4806, 2387, and 1406 kg/batch, respectively, before sending them through the Cl-507 via P-506. Lastly, V-601, V-602, V-603, and V-604 are utilized in the preparation of the Hydrophobic Interaction Column buffers for equilibration, wash, elution, and regeneration, respectively. 2002, 3337, 6453, and 3161 kg/batch of these respective buffers are prepared in the vessels, followed by P-605 sending them through Cl-606.

Purification: Protein A

With the liquid cell culture broth in Tk-307, the equilibration buffer from V-401 is sent through the Protein A Chromatography Column, Cl-406, at 300 cm/hr in order to prepare the environment of the column to maximize mAb affinity. Then, the liquid cell culture broth, in two equivalent cycles, is loaded through Cl-406 at a linear velocity of 500 cm/hr in order to remove impurities. The Protein A column operates in a bind-elute mode, in which the mAb proteins bind to the protein A present on the column resin. Their affinity for the resin allows them to remain in the column after the liquid has been loaded through it, while other impurities flow through the column and into the waste stream. Five bed volumes of wash buffer from V-402 is then sent through the column at 300 cm/hr, cleaning any remaining impurities from the column. Now that impurities have been washed from the column, ten bed volumes of elution buffer from V-403 is loaded at 300 cm/hr. The mAbs are eluted from the Protein A resin,

flowing from Cl-406, through F-407 in order to filter out any potential aggregates or solids, and into the Viral Activation Vessel, V-408. Lastly, Cl-406 is regenerated by five bed volumes of buffer solution from V-404 at 300cm/hr.

Viral Inactivation

Two orthogonal viral inactivation steps are required for biopharmaceutical processes per FDA requirements [7]. These processes are designed to change the environment of any viruses that it denatures their protein structure such that they are rendered inviable. Any microbes, especially pathogenic, are a serious threat not only to cell cultures but to the public who consume pharmaceutical products. As such, these steps of the process are some of the most important.

After the process materials have gone through the protein A chromatography column, Cl-406, the 1687 kg of purified solution is collected in the Viral Inactivation Vessel, V-408. The elution buffer from the protein A column has a low pH and therefore can be used for viral inactivation. The purified solution is held in the surge tank with the elution buffer for 90 minutes to effectively inactivate any viruses [7]. Next, the stream is diluted with 500 L WFI and sent to Diafiltration Flush Tank 1, Tk-410. From this tank, the solution is pumped through Diafilter 1, F-412, and back to V-108 by Diafiltration Pump 1, P-411. While passing through the diafilter, soluble particles and liquids are separated from the product stream and sent to waste. After the solution has been washed in the diafiltration system and returned to the same viral inactivation vessel, V-508, 10.3 L of Polysorbate 80 solution is added to the 339 L of concentrated product solution and held for 90 minutes. This solution acts as a surfactant to break down lipids in the viruses, thus rendering them inactive. After the solution has been properly inactivated, it is filtered through Dead-End Filter 3, F-413, and sent to the Viral Inactivation Surge Tank, Tk-414, to await further purification. The 2025 kg of waste from F-412 are collected in Tk-701.

Purification: Polishing

While Protein A Chromatography is able to remove the vast majority of, and in some cases up to 99.5% of non-mAb components in the solution, we must still send the broth through polishing steps in order to ensure a pure mAb product before final storage and formulation. The first step in this polishing process is Cation-Exchange Chromatography, through Cl-507. From Tk-414, 347 kilograms of remaining cell broth is pumped via P-506 through Cl-507 at 500 cm/hr. As the equilibration buffer has already been sent from V-501, the pH of the column is below the isoelectric point of the mAb proteins. This environment makes the protein positively charged, causing it to bind to the negatively charged CEX resin, while other uncharged or positively charged impurities flow through the column and to the waste. After wash and elution from Cl-507, the solution flows into the Ammonium Sulfate Vessel, V-508. 102 kg of ammonium sulfate is added to V-508 and mixed for 30 minutes in order to precipitate mAb proteins out of the solution. The solution is then diluted with WFI and sent to Diafiltration Flush Tank 2, Tk-509, via P-605. It is passed through the diafilter, separating waste, after which the process stream is pumped to Cl-606. Cl-606 is the Hydrophobic Interaction Column, the last step in the polishing process. This column's resin binds to the hydrophobic regions of the antibodies. From V-601, V-

602, V-603, and V-604, the HIC equilibration, wash, elution, and regeneration buffers, respectively, are pumped via P-605 through each step of the HIC Chromatography. The bound and then eluted mAb in 1322 kg of solution are sent to HIC Surge Tank, Tk-607. The solution is once again diluted with WFI and sent through Diafilter 3, F-611, via P-610 before being sent through the last dead end filter F-612.

Storage of Product

After the final polishing steps, the product needs to be packaged and stored for sale. 260 kg of product is drawn out of the final filter and fed into twenty-two 12 L storage bags. Due to the biological nature of the components, the mAb product needs to be frozen in order to preserve the protein structure. To do so, eight storage bags at a time are placed in the Freeze-Thaw Cryovessel, V-613. V-613 provides controlled cooling from 25 to -50°C over the course of 4.5 hours [18]. This uniformly entraps solute molecules and prevents prolonged freeze-concentration stress. After each freeze cycle, the now-frozen solution in the storage bags are removed from V-613 and placed into the Storage Freezer, Fz-614, at -50 C. The mAbs are viable in their frozen state for at least one year.

Waste Treatment

Throughout the process, all 129000 kg of waste produced is collected in the Waste Holding Tank, Tk-701. The waste streams come from CIP and SIP streams, filter waste, centrifuge waste, and column waste. These materials must be treated so that they can be disposed of through the municipal sewage system. The waste from Tk-701 is continuously pumped by Waste Holding Pump, P-102, to the Neutralization Vessel, V-703 at a rate of 768 kg/hr. While the stream is traveling to the neutralization vessel, 80 kg/hr of saturated steam is continuously injected into the line, raising the temperature of the waste from 25 to 83°C. The heated waste collects in the neutralization tank. Here 36 kg of 37% (w/w) aqueous hydrochloric acid is added to the waste to bring the pH of the solution within the acceptable range. After the contents of the vessel have been mixed by an impeller for 30 minutes, the vessel is emptied into the municipal sewage system and more waste begins collecting in the neutralization tank.

Water for Injection

Producing pharmaceutical components requires high standards of purity and sterilization. As such, it was a necessity to use WFI throughout the process. For water to be classified as WFI, it must meet certain standards of purity and composition [11]. Although this water can be purchased in bulk, it is more cost-effective to design a system to make water for injection from potable water.

The WFI production system begins with the Potable Water Tank, Tk-801. This tank stores 1450 kg/hr of potable water from the city and 120 kg/hr of water from different points in the process. This water solution is pumped from Tk-801 through Dead-End Filter 5, F-803, to the Carbon Adsorption Column, Cl-804, by Potable Water Pump, P-802. F-803 removes any solid impurities, including bacteria, from the stream. In the carbon adsorption column, organic molecules are adsorbed onto the surface of the activated carbon, further purifying the water. In

order to maximize the productivity of the WFI process, two carbon columns operate on a cycle—while one is in operation, the other is being regenerated by washing with 75 L each of water, 0.5 M NaOH, and 0.5 M HCl. After leaving the carbon adsorption column, the water enters the Cation Exchange Column, Cl-805 and then the Anion Exchange Colulmn, Cl-806. In these columns, the stream is purified of cations and anions respectively as they bind to the adsorbents. These columns also undergo a wash once per batch of the process. After undergoing ion exchange, the stream is purified of any fine particulate matter through the Ultrafilter, F-807. The pore size on these filters are 100 D, leading to a high filtering ability [19]. After F-807, the stream finally enters F-808, the Reverse Osmosis unit. This final unit removes any leftover contaminants in the water. Lastly, 1531 kg/hr water enters a Purified Water Tank, Tk-809. Although this process is designed to run continuously, the process will need to be shut down once per batch to wash the activated carbon, cation exchange, and anion exchange columns with buffers that will remove any adsorbed materials and help maintain optimal purification of the water. The waste from the adsorption columns and dead-end filter are sent to process waste, while the waste streams from the ultrafiltration and RO units are recycled to the inlet of the potable water tank and recycled through the process.

After being processed through this filtering system, the once potable water can be classified as purified water. In order to complete the production of WFI, the water is pumped from the Purified Water Tank, Tk-809, through a series of heat exchangers to the Steam Boiler, HE-813, by Purified Water Pump, P-810. The first heat exchanger the water is pumped through is Purified Water Pre-Heater, HE-811. In this heat exchanger, the 1100 kg/hr of impure hot water leaving the bottom of the steam boiler heats the purified water from 25 to 29°C. In the second heat exchanger, the WFI Condenser, HE-812, the 1100 kg/hr of vaporized water for injection is condensed at a pressure of 3.24 bara as the purified water is further preheated to 105.7°C. Next the preheated, purified water enters the steam boiler where it is heated by an electric coil providing 166.5 kW of heating and a steam coil carrying the compressed steam from the boiler providing 77.89 kW of heating. As the water is boiled, it enters a compressor which superheats the steam by increasing the pressure from 1.24 to 3.45 bara and the temperature from 105.7 to 245.8°C. This superheated steam is then circulated through the steam coil where it is cooled from 245.8 to 136.1°C such that the steam is now saturated. From here 200 kg/hr of steam is drawn off for steam injection into the waste treatment line and for steam in place of the process. The rest of the steam (1100 kg/hr) is condensed in HE-812 and pumped to the WFI Storage

Tank, Tk-818, via WFI Storage Pump, P-817. Here the WFI collects until it is needed in the process. The WFI Process Supply Pumps 1 and 2, P-819 and P-820, pump water from Tk-818 throughout the entire process at a maximum of 30,000 L/hr. The 68.4 L/hr of water that exits the bottom of the boiler, HE-813, is pumped through the purified water preheater, HE-811, and recycled back to the potable water tank at the beginning of the WFI process.

Steam in Place and Clean in Place

The final part of the process is the SIP and CIP system. This system is one of the most important of the entire process because it is responsible for sterilizing all of the equipment and

maintaining the proper environment for mAb production. The SIP for the SIP system is produced during the WFI process and is simply stored in the SIP lines until it is needed. The CIP system is comprised of three vessels, V-901, V-902, and V-903, and a pump, P-904. Each vessel is used to prepare and store a different cleaning solution. Caustic Vessel 1, V-901, is used to prepare 0.5 M NaOH for cleaning the chromatography columns. In order to prepare this solution, 20g of solid NaOH is added to the vessel for every one liter of WFI. Caustic Vessel 2, V-902, is used to prepare 0.1 M NaOH for cleaning the rest of the vessels. For this solution, 4g of solid NaOH is added to the vessel for every L of WFI. Acid Vessel 1, V-903, is used to prepare 0.1 M HCl. This solution is prepared by mixing 2.47 L of 37% (w/w) HCl per L of WFI. The total amounts produced of each solution per batch are 6,063 L, 17,035 L, and 27,170 L for V-901, V-902, and V-903 respectively. CIP Pump, P-904, supplies the CIP solutions for the entire process and can supply up to 1200 L/hr. After each unit has completed its operations, different solutions are cycled through to remove any leftover waste or impurities. For all units except chromatography columns, respective cycles through the unit are WFI, 0.1 M NaOH, WFI, 0.1 M HCl, and WFI. Chromatography columns only have two CIP cycles- one 0.5 M NaOH cycle and a WFI cycle. The flow amounts for each unit are based upon equipment heuristics, summarized in Table 10 below.

Table 10: Heuristics

Unit Type	SIP Flow	WFI Flow	NaOH Flow	HCl Flow
Vessel	50 kg/m3	14 L/min.m	7 L/min.m	8 L/min.m
Centrifuge	600 kg/h	500 L	250 L	250 L
Diafilter	10 kg/m2	500 L	250 L	250 L
Column	-	3 Bed Vol	5 Bed Vol	-

Process Scale Up

One of the most important parts of designing this process is accounting for the potential to scale up the process in the future. There are a few ways this process could be scaled up to increase production. The first is mentioned in the design parameters for the project—increasing the mAb titer from 1-2 g/L to 5-10 g/L. This increase in the process titer could be accomplished by harvesting the cells from each step in the seed train at a larger cell density. By allowing the culture to grow longer in each step of the seed train, the amount of mAb produced in each step increases while the volume stays constant, effectively increasing the titer. Additionally, an increased amount of Feed 4 media can be fed to the production bioreactor through the process. This would give the culture more nutrients to use for growth, allowing the titer to continue to increase.

Another way to scale up the process is to build multiples of the entire process so that each process can be run individually. This will greatly increase the capital and operating costs, but it will also greatly increase the revenue. Although having multiples of the entire process running simultaneously works, the most effective way to scale up the process is by continuing to add staggered units to remove bottlenecks in the process. This method was used in this design by adding a second production bioreactor to decrease the cycle time from 12 to 7 days. As

bottlenecks in the process are removed, more batches can be processed per year, meaning more product is produced and more revenue is generated. This method is more effective than having multiples of the entire process because it prioritizes increasing the capital cost on adding units that will affect your cycle time rather than on those that won't.

UTILITY REQUIREMENTS

One of the most important manufacturing costs to account for when analyzing the economics of a project is the utility cost. Table 11, 12, and 13 summarize the electric, water, and sewer utility requirements and costs for the entirety of the project life.

Table 11: Electric Utility requirements

Electric Utilities						
Equipment	Equipment IID	Energy/batch (kW-hr)	Energy/2020 (kW-hr)	Energy/2021+	$/2020	$/2021+
Media Prep						
Media Prep Vessel 1	V-101	0.40	7.12	20.19	$ 0.36	$ 1.01
Media Prep Pump 1	P-102	2.15	38.63	109.46	$ 1.93	$ 5.47
Media Prep Vessel 2	V-103	0.33	5.97	16.92	$ 0.30	$ 0.85
Media Prep Pump 2	P-104	2.16	38.85	110.07	$ 1.94	$ 5.50
Feed Media Prep Vessel A/B	V-105 A/B	0.79	14.25	40.37	$ 0.71	$ 2.02
Feed Media Pump A/B	P-106 A/B	10.13	182.39	516.77	$ 9.12	$ 25.84
Seed Train						
Roller Bottle Roller	RB-203	1.49	26.78	75.89	$ 1.34	$ 3.79
Cell Bag Rocker Tray	CB-205	71.42	1285.63	3642.62	$ 64.28	$ 182.13
Seed Culture Bioreactor 1	R-207	1.36E-11	2.45E-10	6.95E-10	$ 0.00	$ 0.00
Seed Culture Bioreactor 2	R-208	2.72E-04	4.90E-03	1.39E-02	$ 0.00	$ 0.00
Air Compressor KO Drum	V-209	-	-	-	-	-
Air Cartridge Filter	F-210	-	-	-	-	-
Air Compressor	C-211	5.20E+03	9.35E+04	2.65E+05	$ 4,676.62	$ 13,250.41
Air Compressor After-Cooler	HE-212	-	-	-	-	-
Product Reactor/Centrifuge						
Production Bioreactor A/B	R-301 A/B	0.00295	0.05	0.15	$ 0.00	$ 0.01
Production Bioreactor Pump A/B	P-302	14.38	258.84	733.38	$ 12.94	$ 36.67
Production Bioreactor Surge Tank	Tk-303	-	-	-	-	-
Centrifuge	Cf-304	382	6884	19505	$ 344.21	$ 975.25
Centrifuge Pump A/B	P-305 A/B	11	203	576	$ 10.16	$ 28.78
Dead-End Filter 1	F-306	-	-	-	-	-
Centrifuge Surge Tank	Tk-307	-	-	-	-	-
Protein A Chromatography						
Protein A Buffer Prep Vessel 1	V-401	0.40	7.17	20.31	$ 0.36	$ 1.02
Protein A Buffer Prep Vessel 2	V-402	0.99	17.78	50.38	$ 0.89	$ 2.52
Protein A Buffer Prep Vessel 3	V-403	0.32	5.80	16.44	$ 0.29	$ 0.82
Protein A Buffer Prep Vessel 4	V-404	0.14	2.60	7.36	$ 0.13	$ 0.37
Protein A Column Feed Pump A/B	P-405 A/B	60.12	1082.14	3066.07	$ 54.11	$ 153.30
Protein A Chromatography Column	Cl-406	-	-	-	-	-
Dead-End Filter 2	F-407	-	-	-	-	-
Viral Inactivation Vessel	V-408	0.13	2.33	6.61	$ 0.12	$ 0.33
Viral Inactivation Pump A/B	P-409 A/B	1.48	26.64	75.48	$ 1.33	$ 3.77
Diafiltration Flush Tank 1	Tk-410	-	-	-	-	-
Diafiltration Pump 1 A/B	P-411 A/B	3.0525	54.945	155.6775	$ 2.75	$ 7.78
Diafilter 1	F-412	-	-	-	-	-
Dead-End Filter 3	F-413	-	-	-	-	-
Viral Inactivation Surge Tank	Tk-414	-	-	-	-	-
IEX Chromatography						
IEX Buffer Prep Vessel 1	V-501	0.13	2.34	6.64	$ 0.12	$ 0.33
IEX Buffer Prep Vessel 2	V-502	0.13	2.35	6.67	$ 0.12	$ 0.33
IEX Buffer Prep Vessel 3	V-503	0.41	7.34	20.79	$ 0.37	$ 1.04
IEX Buffer Prep Vessel 4	V-504	0.13	2.40	6.79	$ 0.12	$ 0.34
IEX Buffer Prep Vessel 5	V-505	0.03	0.56	1.58	$ 0.03	$ 0.08
IEX Feed Pump A/B	P-506 A/B	56.347	1014.25	2873.70	$ 50.71	$ 143.68
IEX Chromatography Column	Cl-507	-	-	-	-	-
Amm. Sulfate Vessel	V-508	0.03	0.59	1.68	$ 0.03	$ 0.08
Diafiltration Flush Tank 2	Tk-509	-	-	-	-	-
Diafiltration Pump 2 A/B	P-510 A/B	1.48	26.64	75.48	$ 1.33	$ 3.77
Diafilter 2	F-511	-	-	-	-	-

Electric Utilities						
Equipment	Equipment ID	Energy/batch (kW-hr)	Energy/2020 (kW-hr)	Energy/2021+	$/2020	$/2021+
HIC Chromatography						
HIC Buffer Prep Vessel 1	V-601	0.14	2.58	7.31	$ 0.13	$ 0.37
HIC Buffer Prep Vessel 2	V-602	0.42	7.49	21.22	$ 0.37	$ 1.06
HIC Buffer Prep Vessel 3	V-603	1.00	18.07	51.19	$ 0.90	$ 2.56
HIC Buffer Prep Vessel 4	V-604	0.40	7.18	20.35	$ 0.36	$ 1.02
Diafiltration/HIC Column Feed Pump A/B	P-605	44.13	794.35	2250.66	$ 39.72	$ 112.53
HIC Column	CI-606	-	-	-	-	-
HIC Surge Tank	Tk-607	-	-	-	-	-
HIC Surge Tank Pump A/B	P-608 A/B	1.85	33.30	94.35	$ 1.67	$ 4.72
Diafiltration Flush Tank 3	Tk-609	-	-	-	-	-
Diafilatration Pump 3 A/B	P-610 A/B	1.48	26.64	75.48	$ 1.33	$ 3.77
Diafilter 3	F-611	-	-	-	-	-
Dead-End Filter 4	F-612	-	-	-	-	-
Freeze-Thaw Cryovessel	V-613	198	3564	10098	$ 178.20	$ 504.90
Storage Freezer	Fz-614	7667.712	138019	391053	$ 6,900.94	$ 19,552.67
Waste Treatment						
Waste Holding Tank	Tk-701	-	-	-	-	-
Waste Holding Pump A/B	P-702	62.16	1118.88	3170.16	$55.94	$158.51
Neutralization Vessel	V-703	995.00	17910.00	50745.00	$895.50	$2,537.25
WFI System						
Potable Water Tank	Tk-801	-	-	-	-	-
Potable Water Pump A/B	P-802	504	9072.00	25704.00	$453.60	$1,285.20
Dead-End Filter 5	F-803	-	-	-	-	-
Carbon Adsorption Column A/B	CI-804 A/B	-	-	-	-	-
Cation Exchange Column	CI-805	-	-	-	-	-
Anion Exchange Column	CI-806	-	-	-	-	-
Ultrafilter	F-807	-	-	-	-	-
Reverse Osmosis System	F-808	-	-	-	-	-
Purified Water Tank	Tk-809	-	-	-	-	-
Purified Water Pump A/B	P-810 A/B	504	9072.00	25704.00	$453.60	$1,285.20
Purified Water Pre-Heater	HE-811	-	-	-	-	-
WFI Condenser	HE-812	-	-	-	-	-
Steam Boiler	HE-813	28744.8	517406.40	1465984.80	$25,870.32	$73,299.24
Steam Compressor KO Drum	Tk-814					
Steam Compressor	C-815	16205.28	291695.04	826469.28	$14,584.75	$41,323.46
Water Return Pump A/B	P-816 A/B	62.16	1118.88	3170.16	$55.94	$158.51
WFI Storage Pump A/B	P-817 A/B	504	9072.00	25704.00	$453.60	$1,285.20
WFI Storage Tank	Tk-818	-	-	-	-	-
WFI Process Supply Pump 1 A/B	P-819 A/B	-	-	-	-	-
WFI Process Supply Pump 2 A/B	P-820 A/B	672	12096.00	34272.00	$604.80	$1,713.60
Clean in Place						
Caustic Vessel 1	V-901	-	-	-	-	-
Caustic Vessel 2	V-902	-	-	-	-	-
Acid Vessel	V-903	-	-	-	-	-
CIP Pump A/B	P-904 A/B	62.16	1118.88	3170.16	$55.94	$158.51

Table 12: Water Utilities

Potable Water				
	WFI System	Seed Reactors	Production Reactor	Total
L of Water per batch	239,382	39,216	2,285,589	2,324,804
$/L	0.000543			
L/2020	4,308,868	705,879	41,140,600	41,846,479
L/2021+	12,208,459	1,999,992	116,565,033	118,565,024
$/2020	2,340	383	22,339	$22,722.64
$/2021+	6,629	1,086	63,295	$64,380.81

Table 13: Sewer Utilities

Sewer Costs	
L/batch	39221
$/gal	0.05
gal/2020	186501
gal/2021+	528419
$/2020	$ 9,325.05
$/2021+	$ 26,420.97

EQUIPMENT LIST AND UNIT DESCRIPTIONS

Seed and Production Bioreactors

The CHO cells for this design are provided in 1 mL vials containing 1 x 10^6 cells per vial. Each seed train may only use 1 vial for each batch of bioreactor product. Cell cultures go through four different phases: lag phase, log phase, stationary phase, and death phase. A generalization of the phases are shown in Figure 8.

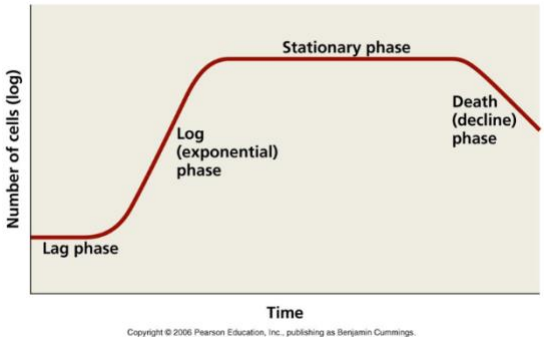


Figure 8 : Phases Over Time (time)

The goal in designing the seed train is to keep cells in the log phase for as long as possible, because in the log phase the culture grows exponentially. Exponential growth of cells is modeled by the following function:

$$A = A_o e^{rt} \qquad (1)$$

where A is the current number of cells, A_o is the initial number of cells, r is the growth rate constant (1 / hours), and t is time (hours). In the problem statement, the doubling time for CHO cells was stated to be 36 hours, meaning when $A=2*A_o$ when t=36h. With a doubling time, the above equation can be solved for r; for these CHO cells r=0.019254 (hr^{-1}). With this rate constant, the amount of time needed to obtain a certain number of cells from an initial amount of cells can be calculated. The main factor that determines whether a culture will remain in the log phase is the concentration of nutrients in the media. Powdered BalanCD® CHO Growth A Medium, a serum-free and chemically defined media, is used in the seed train. The media has a reported maximum cell viability of 9.0×10^6 cells/mL [8]. Cells are often inoculated into BalanCD media at a density of 2.0×10^5 cells/mL [8]. These two facts set the upper and lower limits for each seed train step.

The seed train was designed to inoculate each vessel at 2.0×10^5 cells/mL and harvest at 4.0×10^6 cells/mL. This lower harvest density than the reported maximum was selected in order to guarantee that the cells were still in the log phase throughout the entire culture. Using these densities and the initial amount of cells in the first step, as well as the exponential growth equation, Table 14 was created.

Table 14: Seed Train Steps

Seed Train Step	1	2	3	4	5	6	Prod Bio
Initial Cells	1.00E+06	5.00E+06	1.00E+08	2.00E+09	3.50E+10	7.00E+11	1.40E+13
Final Cells	5.00E+06	1.00E+08	2.00E+09	3.50E+10	7.00E+11	1.40E+13	2.10E+14
Time (hrs)	83.6	155.6	155.6	148.7	155.6	155.6	140.6
Time (days)	3.48	6.48	6.48	6.19	6.48	6.48	5.86
Volume (mL)	5.00	25.00	500	1.00E+04	1.75E+05	3.50E+06	1.40E+07
Volume Added (L)	0.005	0.02	0.475	9.5	165	3325	10500
Inoc Density (cell/mL)	2.00E+05	2.00E+05	2.00E+05	2.00E+05	2.00E+05	2.00E+05	1.00E+06
Harvest Density (cell/mL)	1.00E+06	4.00E+06	4.00E+06	3.50E+06	4.00E+06	4.00E+06	1.50E+07
mAb Produced (kg)	4.35E-07	1.62E-05	3.24E-04	5.42E-03	0.113	2.27	30.77
mAb Sum (kg)	4.35E-07	1.66E-05	3.41E-04	5.76E-03	0.119	2.39	33.15

In this table, the amount of media that was needed for a particular step was calculated by diluting the total number of cells at the beginning of that step to the desired inoculation density. Next, the final number of cells in each step was calculated by multiplying the desired harvest density by the total volume of the culture. Finally, the exponential growth equation was used to solve for the total amount of time the cells would need to grow exponentially in order to reach the final culture size. Table 14 was used to determine the size of the vessel in each seed train step, how long the cells needed to remain in that step, as well as how much media needed to be added to the previous broth to reach the desired volume. The last two rows in the table calculate the amount of mAb produced during each step and a running total of all the mAb produced so far. These values were calculated by multiplying the number of cells at any point in time by the mAb production rate of 25 pg(mAb)/cell.day.

The size of each seed train vessel was determined based on the maximum total volume that it would contain. For the smaller volumes, a culture vessel was chosen that was one nominal size greater than the volume required per batch. The vessels that were chosen are a 10 mL t-flask, a 35 mL t-flask, a 1 L roller bottle, and a 15 L cell bag. All of these vessels are sterile and disposable, which leads to lower operating costs and higher raw material costs. The bulk cost for each of these items as well as the roller bottle roller and cell bag rocker were found from online retailers [20,21].

The final two seed culture bioreactors and the production bioreactor were sized using the total volume each would contain during each batch. For the seed culture bioreactors, this volume is equal to the volume in the chart above. For the production bioreactor, this volume is equal to the volume in the chart plus 3,300 L for the Feed 4 fed-batch media. The maximum working capacity for each vessel is 90%, so the maximum volume was divided by 90% and then rounded up to the nearest whole number (in m^3). The sizes for the bioreactors are as follows: R-207 is .25 m^3, R-208 is 5 m^3, and R-301 is 30 m^3. 316L stainless steel was selected as the material of construction for the reactor due to its high resistance to corrosion and its sterile nature. For more details about the bioreactor sizing and costing, see the Vessels and Tanks section below.

Vessels and Tanks

All vessels and tanks in the process were sized based upon the maximum fluid volume that might be held in the vessel during a batch. This maximum volume is divided by a 90% working capacity factor and then rounded up to the next nominal size to determine the actual size of the vessel. The maximum fluid volumes and actual size of the tanks and vessels in the process are shown in Table 15 below. All vessels and tanks are made out of 316L stainless steel because of its anti-corrosive and sterile properties.

Table 15: Fluid Volume Compared to Tank and Vessel Volume

Equipment ID	Fluid Vol (m3)	Vessel Size (m3)
V-101	3.49	4.00
V-103	16.5	20.0
V-105 A/B	3.30	4.50
Tk-303	23.5	27.5
Tk-307	22.7	25.0
V-401	2.48	3.00
V-402	4.13	5.00
V-403	8.26	10.0
V-404	4.13	5.00
V-408	1.70	2.00
Tk-410	2.87	3.00
Tk-414	0.35	0.50
V-501	1.40	2.00
V-502	2.33	3.00
V-503	4.67	5.50
V-504	2.33	2.75

Equipment ID	Fluid Vol (m3)	Vessel Size (m3)
V-508	1.07	1.25
Tk-509	1.94	2.25
V-601	1.89	2.25
V-602	3.15	3.50
V-603	6.30	7.00
V-604	3.15	3.50
Tk-607	1.32	1.50
Tk-609	2.32	2.50
Tk-701	104	125
V-703	7.63	10.0
Tk-801	4.05	5.00
Tk-809	2.25	2.50
Tk-818	93.7	100.0
V-901	6.06	7.00
V-902	17.0	20.0
V-903	27.2	30.0

Compressors

In our process, we have both an air and a steam compressor. The air compressor allows us to provide sterile, compressed air to the bioreactors at 25 psia. The steam compressor drives the flow of the steam for both steam-in-place and waste steam injection at 50 psia. The power of each of the compressors was calculated based on the ideal work, gas horsepower, mechanical losses, brake horsepower, and adiabatic efficiency from the GPSA Handbook [22]. This method assumes:

- Mechanical losses are equal to $(GHP)^{0.4}$
- Compression follows a polytropic path

The team determined that both of the compressors would best operate as centrifugal single-stage compressors. This was determined using inlet flow, discharge pressure, and Figure 9, shown below. At the intended operating condition, 316L stainless steel is the required material of construction.

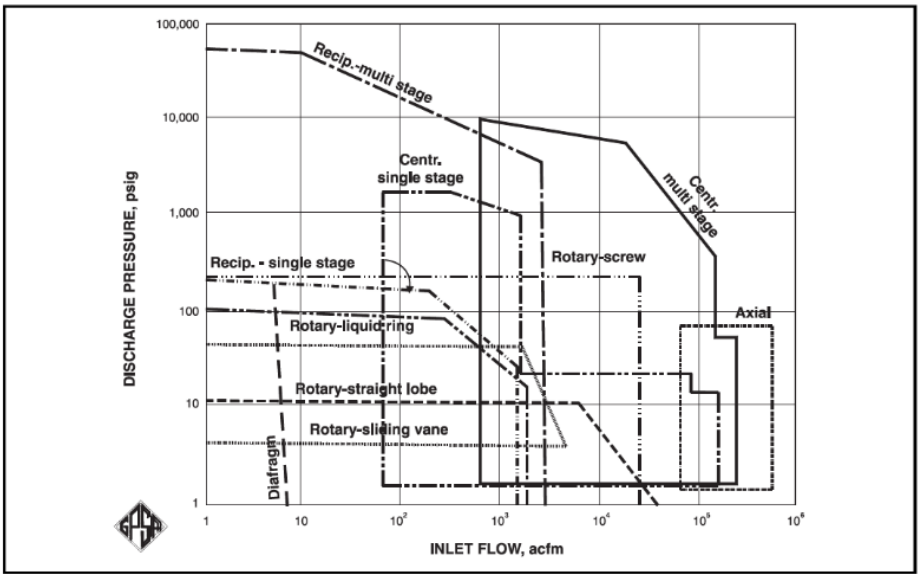


***Figure 9**:* Graphical display of suitable compressor operating ranges for compressor type selection [22]

To size the compressor drives, the overall BHP were rounded up to the next available standard drive size, as outlined by [23].

Centrifuge

After the cells and broth leave the production bioreactor, they are sent to the first harvesting step, centrifugation in Cf-304. The centrifuge is scheduled to perform four cycles per batch, processing 5831 kilograms per cycle in order to reduce the overall size and capital cost of the equipment. In order to design the centrifuge itself, the overall settling area ∑ was set at a maximum value of 130,000 m^2, based upon the suggested upper limit for an industrial-size centrifuge [7]. From this maximum ∑ value, the overall throughput was determined to be 1470 L/hr based off of calculations performed by SuperPro Designer.

Pumps

In bioprocessing industries, pumps are required to move fluids through tubing into processing equipment. These fluids can be buffer, media, WFI, or the biological broth itself. They must be selected and designed to minimize shearing and agitation of the biological fluids in order to protect against degradation that could diminish product quality. Diaphragm metering pumps have been selected for all applications in this design for their highly accurate volume control necessary in processes and for dosing [24]. A diaphragm pump operates by lifting and pressing a flexible seal on top of the chamber to suck in fluid during the lift and closing the outlet by creating a negative pressure gradient and entrapping that liquid in the pump fluid chamber. The movement is shown in Figure 10. Then, the diaphragm is pushed

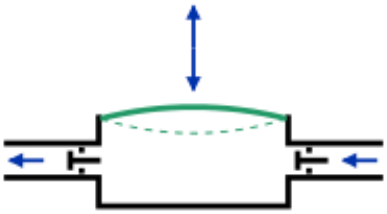


Figure 10: Pump Motion

down to create a positive pressure gradient, resulting in opening of the exit, closing of the inlet, and positive displacement of the fluid without creating a net pressure effect on the process stream. These motions are powered by an electric motor. Also, the diaphragm separates the pump drive from the product-wetted side. This separation means that mechanical seals are not needed, which ensures product sterilization, simplifies maintenance, and allows the pump to run dry [24]. Being able to run dry for a limited amount of time is a significant advantage that will allow the pumps to pull from different sources depending on valve configuration considered in the detail design, thus reducing the number of pumps required in the process. Applications for diaphragm positive displacement pumps include: chromatography, buffer inline dilution, homogenization, injection of fluids (e.g., liposomes) into extruders, coating operations, filling, caustic dilution, and aseptic transfer of proteins, cells, and other materials [24], which meet all demands of this design. It is also common practice to use pumps in diafiltration units. Costing information for the pumps and motors used in running these pumps is listed in Table 18 in the Fixed Capital Investment Summary.

Placement and quantity of pumps is considered for the main components of this preliminary design. Exact specifications and additional pumps of non-key process components can be completed in the detailed design stage if this project is pursued further. Areas without pumps in between process equipment can either be assumed to have pressure from previous pumps in combination with valve configurations sufficient enough to move the material to their desired locations, or to utilize gravity by placement of equipment below the previous process to move process flow, such as the Production Bioreactor Surge Tank (Tk-203) being designed to drain to the centrifuge. An example of a pump being used for multiple streams would be the Protein A Column Feed Tank (P-405 A/B). If valves and control systems are configured correctly during detailed design, this pump will be able to buffer the column by first emptying the contents of V-401, then run dry while the valves switch to allow the contents of V-402 to flow into the column, and continue that process until all buffers have been loaded. Next, the pump and valves could operate by transferring in the contents of the centrifuge Surge Tank (Tk-307). This capability coupled with the process design greatly reduces the number of pumps that would be placed in the facility. Pumps are not required in the preliminary stages of the seed train because the cell cultures will be transported by trained personnel due to the minimal size and delicate nature of the early seed train stages.

Table 16: Pump Sizes [25]

Pump	Flow Range (Lph)	Max Pressure (bar)	Motor Power (kW)
QF150	1-150	6	0.05
QF1200	6-1,200	6	0.37
QF4400	60-4,000	6	2.20
QF10K	500-10,000	6	3.00
QF20K	200-20,000	6	4.00

Sizing these pumps depends solely upon the flow required in a process stream. Due to the nature of the diaphragm pump, a net pressure difference is not put on the streams due to the

lift and press motion of the diaphragm that pulls in a volume of liquid to the pump and pushes it out. So, pressure of the stream must only be less than the maximum allowable working pressure of the pump (6 bar for each pump). Because there is no pressure greater than 6 bar in the process design, pressure is not a factor in pump selection. Table 16 is referred to in order to select the correct size for each pump in the design. All that needs to be known to select the size is the maximum and minimum flowrates. There are twenty four QF1200 pumps in the process: P-102 A/B, P-104 A/B, P-106 A/B, P-302 A/B, P-305 A/B, P-409 A/B, P-411 A/B, P-510 A/B, P-608 A/B, P-610 A/B, P-816 A/B, and P-904 A/B. There are fourteen QF10k pumps in the process: P-405 A/B, P-506 A/B, P-702 A/B, P-802 A/B, P-810 A/B, P-817 A/B, and P-820 A/B. There are four QF20k pumps in the process: P-605 A/B and P-819 A/B (Figure 11). A relatively low flowrate of 600 L/hr was selected for all streams containing CHO cells in order to protect the cells; therefore the majority of pumps were QF1200s. The flowrates for pumps serving chromatography columns were set by the column loading rate. The rest of the flowrates were determined by the desired production need i.e. the amount of water being pumped through the WFI system is determined by the total WFI production demand of 1300 kg/hr. The largest flowrate in the process is the WFI stream leaving the WFI Storage Tank (Tk-818) due to instantaneous WFI demand. This need can reach 29,000 liters per hour, and was outside of the range of the largest pump size. This issue was resolved by placing a 10,000 liter per hour (QF10k) pump in parallel with the 20,000 liter per hour (QF20K) pump to meet maximum instantaneous demand for WFI. Pump P-819 A/B, the 20,000 liter per hour pump, will always be running to provide WFI to the process and the other pump will only turn on if the demand reaches above 20,000 liters per hour.

Figure 11: Varying pump sizes [25]

Dead-End Filters

Dead-end filters are used throughout the process to remove unwanted solids, particularly biomass (CHO cells) and suspended impurities, from the product stream. The pore size for pharmaceutical dead-end filters is 0.2 µm, significantly smaller than the average mammalian cell size. Advantages of using dead-end filters include a very low capital cost and high recovery of product solution from bioreactor slurry. The required membrane surface area for each filter was calculated based upon the flow rate of the stream through the filter, which was usually set by the flow rate to or from some other point in the process. SuperPro Designer was used to model each dead-end filter, and the required surface area for each filter was determined using that model. The following surface areas were calculated for the various dead-end filters: 230 m^2 for F-306, 80 m^2 for F-407, 80 m^2 for F-413, 70 m^2 for F-612, and 120 m^2 for F-803. For all of the dead-end filtration units, 316L stainless steel is the material of construction for the filter housing, and pharmaceutical friendly membranes are selected.

Diafilters and Ultrafilters

Diafilters are used in this process to remove small particulates, soluble molecules, and non-water liquids from the product stream. These systems are capable of removing both small solid and liquid impurities through the use of multiple water flush cycles that dilute and concentrate the stream until only the desired components are left. For each diafiltration system, the inlet stream was diluted with 40% of the stream volume in WFI. Additionally, 500 L of water was flushed through the unit to aid in filtration. The product stream was concentrated 5 times through the filtration and the majority of chemicals and contaminants introduced into the stream at the previous chromatography column were removed. The required filter surface area for each diafiltration unit was calculated using the product stream and WFI diluant volumes inputted into a SuperPro Designer model. The required membrane areas are 26 m^2 for F-412, 16 m^2 for F-511, and 20 m^2 for F-611.

Ultrafilters are used in the WFI system to filter out very small suspended particulates from the water supply. Ultrafiltration membranes, along with the diafiltration membranes, have pore sizes that are 100 D, much smaller and finer than the pore sizes for dead-end filtration [19]. The required surface area for the ultrafiltration unit was determined using a SuperPro Designer model based upon the total water flow through the WFI system. The required membrane area for F-807 is 40 m^2. The same filters were selected for both the diafilters and ultrafilters [19]. For all of the filtration units, 316L stainless steel is the material of construction for the filter housing, and pharmaceutical friendly membranes are selected.

Chromatography Columns

This preliminary design utilizes three different chromatography columns to purify the mAb product stream. All three of the columns-Protein A, Ion Exchange, and Hydrophobic Interaction-are filled with an adsorptive resin and constructed of stainless steel to maximize sterilization and minimize impurities due to rust and corrosion. Figure 12 is an example of this type of column:

Figure 12: Process-Scale Chromatography Columns

In each of these columns, the goal is to bind the target protein, mAb, to the column resin and let impurities flow through. Affinity for Protein A, charge, and hydrophobicity are the characteristics, respectively, that each column is utilizing to target the mAbs.

Protein A

In order to design the Protein A Chromatography Column, some assumptions were required. Utilizing heuristics and common values from an article by Marichal-Gallardo and Alvarez, we assumed that the dynamic binding capacity of the resin is 55 g/L, the linear velocity of each buffer loading step is 300 cm/hr, and the bed height is 25 cm [7]. The final parameter needed to determine the overall bed volume of the chromatography column was the productivity of the column. As seen in the equations below, maximizing the productivity of the column increases the mass of product processed for a given column volume and time.

$$\text{Productivity (P)} = (\text{Mass of product/column volume})/\text{time} \tag{2}$$

$$P = \frac{1}{L((1/C_0u_L) + (N/Q_du_N))} \tag{3}$$

In the simplified second equation, L refers to the column bed height, C_O to the column loading concentration, u_L to the velocity of the load step, N to number of column volumes in non-load steps, u_N to velocity of non-loading steps, and Q_d to binding capacity. While most of the parameters were estimated, the velocity of the load step was increased up to the maximum load velocity of 500 cm/hr in order to maximize the productivity at the assumed column conditions. From this, we determined the optimal productivity to be 20.95 g/L*hr. From the estimated parameters and now-determined load velocity, a required bed volume of 413 liters was specified by SuperPro Designer. In order to determine what Protein A resin to buy for the process, several selection guides were considered. One resin in particular, mAbSelectSure, fits the capacity needs of our process, has a high binding capacity, and has a low affinity for host cell proteins, particles that tend to compete with mAb for resin binding positions [26].

IEX and HIC

Both the Ion Exchange and Hydrophobic Interaction Chromatography columns are integral components of the downstream polishing process. A similar approach to the previously stated PA Column design process was taken to determine the size and parameters of each of the two columns in the polishing process. The main change with regard to our assumptions about the IEX column was the dynamic binding capacity of the resin. The average dynamic binding capacity of an IEX resin is much higher than that of a Protein A resin, thus a DBC of 85 g/L was chosen [7]. The productivity of this column was determined to be 55.02 g/L*hr with the same maximum linear velocity of 500 cm/hr. The concentration of the IEX loading solution was much lower than the loading concentration of the Protein A column inlet, thus only a bed volume of 233 L was determined for its design. Using a selection guide similar to that which was used for Protein A resin, it was determined that Unosphere S Support Cation Exchange resin was the most optimal choice for the column, based upon its nature as a strong cation exchanger as well

as high DBC [27]. For Hydrophobic Interaction Chromatography, similar design guidelines to Protein A Columns were provided, thus a DBC of 55 g/L was assumed, as well as the same non-loading linear velocity of 300 cm/hr. Lastly, a productivity of 43.4 g/L*hr was calculated based on a 500 cm/hr loading flow rate. It was determined that the required bed volume for the HIC column is 629.5 L. The HIC resin, Methyl HIC Support was chosen as the resin due to its minimization of protein denaturing and affinity toward bimolecular hydrophobic regions [28].

Buffers

For each chromatography column there are various buffers with their own unique formulation. Equilibration buffers prepare a column for loading a sample by washing out any impurities and setting the proper pH. Wash buffers remove any molecules that haven't bonded to the column resin, leaving behind only the resin and the bonded molecules. Elution buffers change the environment inside the column in such a way that the molecules that were bonded to the resin are released. Regeneration buffers clean the column by removing any leftovers of the previous buffers and prepare the column to wait for the next load. The different buffer compositions for each column can be found below in Table 17.

Table 17: Buffer Solution Composition

Buffer Solution Compositions			
Buffer Solution	Component	Mass Fraction	kg/batch
Prot A Equil	EDTA Disodium	0.00168	4.2
	Sodium Phosphate	0.00409	10.3
	Tris Base	0.00197	4.9
	Tris HCl	0.00590	14.8
	Water for Injection (WFI)	0.986	2473
Prot A Wash	Guanidinium Chloride	0.0361	149.5
	Tris Base	0.00197	8.2
	Tris HCl	0.00592	24.5
	WFI	0.956	3964
Prot A Elution	Acetic Acid	0.006	49.3
	WFI	0.994	8170
Prot A Regen	Sodium Chloride	0.0194	97.0
	Tris base	0.00485	24.3
	Tris HCl	0.0146	72.8
	WFI	0.981	4903
IEX Equil	Potassium Chloride	0.000002	0.0028
	Potassium Di-hydrogen Phosphate	0.000002	0.0028
	Sodium Chloride	0.009	12.6
	Sodium HydroPhosphate	0.0011	1.5
	WFI	0.990	1391
IEX Wash 1	Potassium Chloride	0.000002	0.0047
	Potassium Di-hydrogen Phosphate	0.000002	0.0047
	Sodium Chloride	0.018	42.2
	Sodium HydroPhosphate	0.001	2.6
	WFI	0.981	2300
IEX Elute	Sodium Chloride	0.018	87.9
	Sodium Di-hydrogen Phosphate	0.000915	4.4
	WFI	0.981	4714
IEX Regen	Sodium Chloride	0.057	136
	WFI	0.943	2251
IEX Wash 2	Sodium Hydroxide	0.02	28.0
	WFI	0.98	1378
HIC Equil	Sodium Chloride	0.196	392
	Sodium HydroPhosphate	0.00310	6.2
	WFI	0.801	1603
HIC Wash	Sodium Chloride	0.100	332.5
	Sodium HydroPhosphate	0.00318	10.6
	WFI	0.897	2993
HIC Elute	Sodium Chloride	0.039	253
	Sodium HydroPhosphate	0.0029	18.5
	WFI	0.958	6182
HIC Regen	Sodium Hydroxide	0.02	62.9
	WFI	0.98	3098

For Protein A Chromatography, an equilibration, wash, elution, and regeneration buffer are prepared and sent through the column. The compositions of each of these buffer solutions were chosen based upon suggested compositions from both Bio-Rad and ThermoFisher [29]. One important consideration was that the elution buffer would provide a pH of 3 or lower, allowing for effective viral inactivation in V-408.

IEX Chromatography, or in this case Cation Exchange Chromatography requires five buffer solutions: equilibration, first wash, elution, regeneration, and second wash. The compositions of these buffers were determined both by the compatible buffer formulations from Marichal-Gallardo and Alvarez as well as considerations to guidelines from Bio-Rad and Pall, Inc. [30]. The most important aspect of this CEX buffer composition was to maintain a pH of around 6 pH, 1-1.5 pH below the isoelectric point of the antibody [31]. This ensures that the antibody is positively charged, and thus will bind to the CEX resin rather than flow through.

HIC Chromatography requires four different buffer solutions, also for an equilibration, wash, elution, and regeneration step. However, rather than each of the buffer solutions being different in component, the first three only differ in composition. The equilibration buffer has a strong concentration of sodium chloride in water, salting out the mAb proteins to allow for easier binding to the hydrophobic areas of the resin [32]. As the buffer steps continue to wash and elute, the concentration decreases, creating a concentration gradient and allowing the mAbs to release from the resin. The final step consists of sodium hydroxide and water, helping to release tightly-bound proteins [32].

Adsorption Columns

The WFI process utilizes three different adsorption columns to purify potable water. The activated carbon, cation exchange, and anion exchange columns were all sized in a similar manner, although they use different resins and serve to purify the water in different ways. The vessels for all three columns were sized as a regular tank, in a similar manner to the way described in the Vessels and Tanks section above. For the activated carbon column, the bed volume was calculated to be 276 L using a SuperPro Designer model with breakthrough time of 7 days (one complete process batch) and a water inlet flow of 2042 L/hr. Assuming a bed/column volume ratio of 0.5, the required vessel volume for Cl-804 A/B is 552 L and the actual vessel volume is set at 0.625 m^3. The same process was completed for Cl-805 and CL-806 leading to required volumes of 212 L and 175 L and vessel sizes of 0.25 m^3 and 0.20 m^3 respectively. All of the columns are to be made out of 316L stainless steel because of its anti-corrosive and sterile properties.

The volume of adsorbent for each column was calculated as half the total volume of the column. Granular activated carbon comes in a variety of sizes; 12 x 40 was chosen for the column because it is one of the most popular sized for aqueous phase adsorption [ ]. For the cation exchange column, the same resin was chosen as the resin in the mAb ion exchange column, UNOsphere S Media. AG 1-X2 was selected as the resin for the anion exchange column because of high resistance to oxidizing agents and ability to adsorb for long periods of time without washing [33]. Wash cycles were designed for all three columns using the same

solutions from the CIP system, making the cleaning process simpler and easier. Chemical reactivation of the activated carbon adsorbent with 0.1 M NaOH and 0.1 M HCl will occur after each batch to maintain optimal adsorption [34]. The anion and cation exchange columns are washed with 0.1 M NaOH and 0.1 M HCl respectively to clean the resin and prepare for the next batch. All of the modeling for these wash steps were performed in SuperPro Designer assuming 3 bed volumes of wash per solution per batch.

Reverse Osmosis

Reverse osmosis is one of the most prevalent methods for water purification, even being used to desalinate sea water. In this process, the reverse osmosis system serves as final purification "catch-all," removing any contaminants that were left over after the water was processed by the previous systems. Due to the complication of reverse osmosis membranes, a prepackaged RO skid sold by US Water Systems was selected to be used in the process [35]. The skid size was selected based upon the 11,000 gpd throughput required by the WFI process. Although they don't have a standard skid that can product that level of throughput, a US Water Systems employee confirmed that the price of a skid that size could be scaled up from the price of the largest skid using the six-tenths rule. The skid comes with standard filters, and replacements were also available through US Water Systems [36].

Air Cartridge Filter

In order to sterilize the air being brought into the bioreactor aeration system, an Air Cartridge Filter, F-210, is placed in the process stream before the Air Compressor, C-211. The total continuous air supply amount required to aerate the bioreactors was sent through a simulated dead-end filter to calculate the required membrane surface area of the filter. It was determined based upon this SuperPro Designer simulation that the size of the filter required is 10 m^2 of total filter surface area.

Shell-and-Tube Heat Exchanger

Throughout our process we have three separate shell-and-tube heat exchangers, all of 316L stainless steel material of construction. In the bioreactor aeration process, the filtered, compressed air is sent through the shell side of the Air Compressor After-Cooler, HE-212, where cooling water brings it from 89°C down to 37°C. The cooling water, in turn, is heated from 25°C to 30°C before being sent to Tk-801, the Potable Water Tank. In the WFI system, the Purified Water Pre-Heater, HE-811, allows for contact between the steam boiler bottoms liquid and incoming purified WFI, heating the WFI on the shell side from 22°C to 24.5°C and cooling the bottoms from 94.4°C to 50°C. In the WFI Condenser, HE-812, the WFI is preheated even more on the tube side from 24.5°C to 106.2°C while a portion of the steam produced in the boiler is condensed from 136.1°C to 110°C. Using these changes in temperature for ΔLMTD, heat duty provided by Aspen HYSYS, as well as known U values for a stainless steel air-water, water-water, and water-steam interface, the overall heat transfer area for each heat exchanger was calculated [37].

KO Drum

Two knockout drums are present in the process, one before the air compressor and one before the steam compressor. Both separators were sized using the guidelines provided by Svrcek and Monnery in their article, *Design Two-Phase Separators Within the Right Limits* [38]. The team compared the volume and cost of vertical and horizontal separators with and without demister pads. For both knockout drums, it was determined that horizontal orientation without demister pads provided the lowest cost while still providing the utility and equipment safety required before the compressors.

Steam Boiler

The steam boiler is the most important item in the WFI system, as it is what takes purified water and makes it into water for injection. The unit was modeled in aspen as a heat exchanger and a heater in series, since both an electric coil and a steam coil are located in the boiler. The combined heat transfer for both, 231 kW, as well as a net delta T of 0°C for the boiled water (the boiler is not superheating the steam) was used to size and cost the steam boiler. The steam boiler is made out of 316L stainless steel because of the material's anti-corrosive and sterile properties.

Freeze System

Before being sold to pharmaceutical companies for final formulation into a drug that can be sold to patients, it is required that the mAbs in solution be stored frozen for at least one year. This storage condition provides a challenge to the facility, as proteins must be handled carefully, with respect to ice crystallization fronts during freezing, as well as protein damage during freeze-thaw cycles [18]. It has been shown that another concern with freezing is production of soluble and insoluble aggregates of proteins in solution if the freezing process is uncontrolled or uneven. In order to address these concerns for product quality, it was decided that a temperature-controlled Freeze-Thaw Cryovessel, V-613, would be used to freeze the product after it has left the last filter. The cryovessel will be bought from Sartorius, specifically their Celsius FT100 model which is capable of freezing 100 L of product at a time. The freeze is temperature-controlled for 4.5 hours until the 3 cycles per batch of 100 L reach -50°C.

Storage Freezer

Once frozen, the 12 L bags of product will need to be maintained at a constant temperature for at least one year. In order to do this, the team identified laboratory deep-freeze cabinets which can hold 792 L of product, or sixty-six 12 L bags. In order to be able to hold an entire year's worth of product, 18 deep-freeze storage cabinets will be bought in order to store and maintain the mAb product at -50°C.

CIP

The CIP system is designed to contain enough of the various cleaning solution to clean the entire process one time. Using the CIP heuristics in Table 10, the total amount of each CIP solution was calculated. Accounting for a 90% working capacity of the vessels, the vessels sizes were determined to be 7, 20, and 30 m^3 for V-701, V-702, and V-703 respectively. All three of

these vessels are constructed of 316L stainless steel because of its anti-corrosive and sterile properties.

EQUIPMENT SPECIFICATION SHEETS

The equipment specification sheets were made for all capital costed equipment. Equipment type is ordered alphabetically in Figure 13 below.

Figure 13: Equipment Specification Sheets

Compressor		
Identification:	Item	Air Compressor
	Item No.	C-211
	No. Required	1
Function:	Air Compressor for clean air bubbles into bioreactors	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	105.7	245.8
Pressure [bara]:	1.24	3.45
Mass Flowrate	2.18E+05	2.18E+05
Molar Flowrate [kmol/batch]:		
Water	72.2	72.2
Total	72.2	72.2
Design Data:	**Power:**	5200 [kW]
	MOC:	316LSS
	Type:	Centrifigual Single Stage
Utilities:	**Electricity:**	[kW-hr]
	Comments and Drawings:	See PFD

Compressor		
Identification:	Item	Steam Compressor
	Item No.	C-815
	No. Required	1
Function:	Generate steam for SIP and for WFI once condensed	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	105.7	245.8
Pressure [bara]:	1.24	3.45
Mass Flowrate [kg/batch]:	2.18E+05	2.18E+05
Molar Flowrate [kmol/batch]:		
Water	72.2	72.2
Total	72.2	72.2
Design Data:	**Power:**	16205.3 [kW]
	MOC:	316LSS
	Type:	Centrifigual Single Stage
Utilities:	**Electricity:**	[kW-hr]
	Comments and Drawings:	See PFD

Centrifuge		
Identification:	Item	Centrifuge
	Item No.	Cf-304
	No. Required	1
Function:	Separates production reactor product broth into different components	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	37	44.1
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	2.3E+04	2.3E+04
Molar Flowrate [kmol/batch]:		
Biomass	7.1	7.1
Impurities	2.3	2.3
Feed 4 Media	12.8	12.8
Mab	2.6	2.6
Sodium Bicarbonate	0.6	0.6
Water	1.3E+03	1.3E+03
Total	1.3E+03	1.3E+03
Design Data:	**Diameter:**	1 [m]
	MOC:	316LSS
	Type:	Disc Stack
Utilities:	**Electricity:**	382.5 [kW-hr]
	Comments and Drawings:	See PFD

Column		
Identification:	Item	Protein A Chromatography
	Item No.	CI-406
	No. Required	1
Function:	Purify product	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	1.7E+04	4.2E+04
Molar Flowrate [kmol/batch]:		
Impurities	0.0	2.2
Feed 4 Media	0.0	12.5
Mab	0.0	2.5
Sodium Bicarbonate	0.0	0.6
Water	895.9	2259.9
Acetic-Acid	0.8	0.8
TRIS Base	1.7	1.2
TRIS HCl	1.9	3.6
EDTA Disodium	0.0	1.3E-02
Sodium Phosphate	0.0	6.3E-02
Sodium Chloride	4.5	4.5
Guanidinium Chloride	8.3	8.3
Total	914.2	2296.2
Design Data:	**Volume:**	0.42 [m^3]
	Diameter:	1.5 [m]
	MOC:	316LSS
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Column		
Identification:	Item	HIC Column
	Item No.	CI-507
	No. Required	1
Function:	Purify product	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	1.3E+04	1.3E+04
Molar Flowrate [kmol/batch]:		
Impurities	9.7E-02	9.7E-02
Mab	2.2	2.2
Water	672.58	672.59
Acetic-Acid	4.0E-03	4.0E-03
Sodium Hydroxide	0.7	0.7
Disodium Phosphate	2.6E-01	2.9E-02
Monosodium Phosphate	0	2.4E-01
Tributyl phosphate	0.0043	0.7
Sodium Chloride	7.7	7.9
Potassium Chloride	1.1E-06	1.0E-04
Monopotassium Phosphate	1.1E-06	5.0E-05
Polysorbate 80	2.7E-03	2.7E-03
Total	683.6	684.5
Design Data:	**Volume:**	0.25 [m^3]
	Diameter:	1.1 [m]
	MOC:	316LSS
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Column		
Identification:	Item	HIC Column
	Item No.	CI-606
	No. Required	1
Function:	Purify product	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	1.5E+04	1.5E+04
Molar Flowrate [kmol/batch]:		
Impurities	1E+00	3E-02
Mab	2.9	1.9
Water	785.0	779.6
Ammonium Sulfate	1E+00	2E-02
Disodium Phosphate	3E-01	2E-01
Monosodium Phosphate	1E+00	1E-03
Sodium Chloride	17.8	16.8
Total	810.0	798.6
Design Data:	**Volume:**	0.25 [m^3]
	Diameter:	1.1 [m]
	MOC:	316LSS
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Column		
Identification:	Item	Carbon Adsorption Column A/B
	Item No.	CI-804 A/B
	No. Required	2
Function:	remove organics	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	3.3E+04	3.1E+05
Molar Flowrate [kmol/batch]:		
Water	1740.0	1.6E+04
Hydrochloric acid	14.6	1.7E+03
Sodium Hydroxide	66.2	0.6
Total	1.8E+03	1.7E+04
Design Data:	**Volume:**	0.5 [m^3]
	Diameter:	0.5 [m]
	MOC:	316LSS
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Column		
Identification:	Item	Cation Exchange Column
	Item No.	CI-805
	No. Required	1
Function:	remove cations	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	2.8E+05	1.1E+03
Molar Flowrate [kmol/batch]:		
Water	1.6E+04	1.6E+04
Acetic-Acid	0.49	0
Total	1.6E+04	1.6E+04
Design Data:	**Volume:**	0.25 [m^3]
	Diameter:	0.75 [m]
	MOC:	316LSS
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Diafiltration System			
Identification:	Item	Diafiltration System 1	
	Item No.	Tk-410, P-411 A/B, F-412	
	No. Required	1	
Function:	concentrate product solution		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	25	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	2859.3	2859.3	
Molar Flowrate [kmol/batch]:			
Impurities	0.1	0.2	
Mab	2.3	2.2	
Water	155.9	155.8	
Acetic-Acid	0.2	0.2	
Total	158.4	158.3	
Tank Design Data:	**Volume:**	316LSS	[m^3]
	Diameter:	1	[m]
	MOC:	316LSS	
	Internals:	None	
Tank Utilities:	**Electricity:**	-	[kW-hr]
Pump Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Pump Utilities:	**Electricity:**	3.1	[kW-hr]
Filter Design Data:	**Area**	28	[m^2]
	MOC:	316LSS	
	Type:	Diafilter	
Filter Utilities:	**Electricity:**	-	
	Comments and Drawings:		See PFD

Diafiltration System			
Identification:	Item	Diafiltration System 2	
	Item No.	Tk-509, P-510 A/B, F-511	
	No. Required	1	
Function:	concentrate product solution		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	25	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	2006.5	2006.5	
Molar Flowrate [kmol/batch]:			
Impurities	5.84E-03	0.0617	
Mab	2.0	1.9	
Water	100.4	100.4	
Ammonium Sulfate	0.8	0.8	
Monosodium Phosphate	4.7E-02	4.7E-02	
Sodium Chloride	0.9	0.9	
Total	104.1	104.1	
Tank Design Data:	**Volume:**	2.25	[m^3]
	Diameter:	1	[m]
	MOC:	316LSS	
	Internals:	None	
Tank Utilities:	**Electricity:**	-	[kW-hr]
Pump Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Pump Utilities:	**Electricity:**	3.1	[kW-hr]
Filter Design Data:	**Area**	14	[m^2]
	MOC:	316LSS	
	Type:	Diafilter	
Filter Utilities:	**Electricity:**	-	
	Comments and Drawings:		See PFD

Diafiltration System			
Identification:	Item	Diafiltration System 3	
	Item No.	Tk-609, P-610 A/B, F-611	
	No. Required	1	
Function:	concentrate product solution		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	25	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	3142.4	2337.3	
Molar Flowrate [kmol/batch]:			
Impurities	3.0E-02	0.00	
Mab	1.7	1.6	
Water	160.9	125.1	
Ammonium Sulfate	7.5E-01	0.00	
Disodium Phosphate	2.6E-02	2.7E-02	
Monosodium Phosphate	4.6E-02	0.00	
Sodium Chloride	1.8	8.8E-01	
Total	165.2	127.7	
Tank Design Data:	**Volume:**	2.5	[m^3]
	Diameter:	1	[m]
	MOC:	316LSS	
	Internals:	None	
Tank Utilities:	**Electricity:**	-	[kW-hr]
Pump Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Pump Utilities:	**Electricity:**	3.1	[kW-hr]
Filter Design Data:	**Area**	14	[m^2]
	MOC:	316LSS	
	Type:	Diafilter	
Filter Utilities:	**Electricity:**	-	
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Media Prep Pump 1 A/B	
	Item No.	P-102 A/B	
	No. Required	2	
Function:	Feeds media to bioreactors 1 and 2		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	1.64E+04		
Molar Flowrate [kmol/batch]:			
BalanCD Media	21.13		
Sodium Bicarbonate	4.11		
Water	889.0		
Total	910.6		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Utilities:	**Electricity:**	2.15	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Media Prep Pump 2 A/B	
	Item No.	P-104 A/B	
	No. Required	2	
Function:	eeds inoc media to product bioreactor		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	16400		
Molar Flowrate [kmol/batch]:			
BalanCD Media	21.13		
Sodium Bicarbonate	4.11		
Water	889.02		
Total	910.6		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Utilities:	**Electricity:**	2.16	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Feed Media Pump A/B	
	Item No.	P-106 A/B	
	No. Required	2	
Function:	feeds inoc media to product bioreactor		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	3286.3		
Molar Flowrate [kmol/batch]:			
Feed 4 Media	4.23		
Sodium Bicarbonate	0.82		
Water	177.8		
Total	182.1		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Utilities:	**Electricity:**	10.13	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Feed Media Pump A/B	
	Item No.	P-106 A/B	
	No. Required	2	
Function:	feeds inoc media to product bioreactor		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	3286.33		
Molar Flowrate [kmol/batch]:			
Feed 4 Media	4.23		
Sodium Bicarbonate	0.82		
Water	177.8		
Total	182.12		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Utilities:	**Electricity:**	10.13	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Production Bioreactor	
	Item No.	P-302A/B	
	No. Required	2	
Function:	product to Tk-303		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	37		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	23300		
Molar Flowrate [kmol/batch]:			
Biomass	7.13		
Impurities	2.28		
Feed 4 Media	12.83		
Mab	2.6		
Sodium Bicarbonate	0.58		
Water	1264.62		
Total	1290.04		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Utilities:	**Electricity:**	14.38	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Centrifuge Pump A/B	
	Item No.	P-305 A/B	
	No. Required	2	
Function:	centrifuge to filter		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	44.1		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	22500		
Molar Flowrate [kmol/batch]:			
Biomass	0.14		
Impurities	2.21		
Feed 4 Media	12.45		
Mab	2.52		
Sodium Bicarbonate	0.56		
Water	1226.88		
Total	1244.76		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Utilities:	**Electricity:**	11	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Protein A Column Feed Pump A/B	
	Item No.	P-405 A/B	
	No. Required	2	
Function:	buffer to Prot A and Tk-307 to Prot A		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	42400		
Molar Flowrate [kmol/batch]:			
Impurities	2.21		
Feed 4 Media	12.45		
Mab	2.52		
Sodium Bicarbonate	0.56		
Water	2259.92		
Acetic-Acid	0.82		
TRIS Base	1.96625		
TRIS HCl	2.83		
Sodium Chloride	4.51		
Guanidinium Chloride	8.26		
Total	2296.17		
Design Data:	**Power:**	3	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF10k	
Utilities:	**Electricity:**	60.12	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Protein A Column Feed Pump A/B	
	Item No.	P-405 A/B	
	No. Required	2	
Function:	buffer to Prot A and Tk-307 to Prot A		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	42400		
Molar Flowrate [kmol/batch]:			
Impurities	2.21		
Feed 4 Media	12.45		
Mab	2.52		
Sodium Bicarbonate	0.56		
Water	2259.92		
Acetic-Acid	0.82		
TRIS Base	1.96625		
TRIS HCl	2.83		
Sodium Chloride	4.51		
Guanidinium Chloride	8.26		
Total	2296.17		
Design Data:	**Power:**	3	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF10k	
Utilities:	**Electricity:**	60.12	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Viral Inactivation Pump A/B	
	Item No.	P-409 A/B	
	No. Required	2	
Function:	Viral Inactivation Tank to D		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	26		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	2033.74		
Molar Flowrate [kmol/batch]:			
Impurities	0.2274		
Mab	4.47		
Water	107.37		
Acetic-Acid	0.16399		
Tributyl phosphate	0.0043		
Polysorbate 80	0.0027		
Total	112.25		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Utilities:	**Electricity:**	1.48	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	IEX Feed Pump A/B	
	Item No.	P-506 A/B	
	No. Required	2	
Function:	Viral Inactivation surge tan		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	12686.93		
Molar Flowrate [kmol/batch]:			
Impurities	0.0974		
Mab	2.21		
Water	672.58		
Acetic-Acid	0.00399		
Sodium Hydroxide	0.7		
Disodium Phosphate	0.2592		
Tributyl phosphate	0.0043		
Sodium Chloride	7.72		
Potassium Chloride	0.0000011		
Monopotassium Phosphate	0.0000011		
Polysorbate 80	0.0027		
Total	683.58		
Design Data:	**Power:**	3	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF10k	
Utilities:	**Electricity:**	56.347	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Diafiltration/HIC Column Feed Pump A/B	
	Item No.	P-605	
	No. Required	2	
Function:	HIC loading pump and amm. sulfate vessel to diafiltration		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	16258.4		
Molar Flowrate [kmol/batch]:			
Impurities	1.04		
Mab	4.9		
Water	834.56		
Ammonium Sulfate	1.79		
Sodium Hydroxide	1.57		
Disodium Phosphate	0.2507		
Monosodium Phosphate	1.05		
Sodium Chloride	18.68		
Total	863.86		
Design Data:	**Power:**	4	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF20K	
Utilities:	**Electricity:**	44.13	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	HIC Surge Tank Pump A/B	
	Item No.	P-608 A/B	
	No. Required	2	
Function:	HIC surge tank to diafiltrati		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	1581.49		
Molar Flowrate [kmol/batch]:			
Mab	3.37		
Water	81.33		
Disodium Phosphate	0.02664		
Sodium Chloride	0.8812		
Total	85.62		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Utilities:	**Electricity:**	1.85	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Waste Holding Pump A/B	
	Item No.	P-702	
	No. Required	2	
Function:	Pumps from waste holding		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.5		
Mass Flowrate [kg/batch]:	129000		
Molar Flowrate [kmol/batch]:			
Biomass	7.13		
Impurities	2.41		
BalanCD Media	1.89		
Feed 4 Media	10.94		
Mab	0.74		
Sodium Bicarbonate	0.58		
Water	5187.86		
Acetic-Acid	0.82		
Ammonium Sulfate	0.77		
TRIS Base	1.21		
TRIS HCl	3.63		
Sodium Hydroxide	2.27		
EDTA Disodium	0.013		
Disodium Phosphate	0.28		
Monosodium Phosphate	0.23		
Sodium Phosphate	0.0625		
Sodium Chloride	29.15		
Guanidinium Chloride	8.3		
Total	5258.3		
Design Data:	**Power:**	3	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF10k	
Utilities:	**Electricity:**	62.16	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Potable Water Pump A/B	
	Item No.	P-802	
	No. Required	2	
Function:	water into WFI		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	1820		
Molar Flowrate [kmol/batch]:			
Water	95.93		
Total	95.93		
Design Data:	**Power:**	3	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF10k	
Utilities:	**Electricity:**	504	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	Purified Water Pump A/B	
	Item No.	P-810 A/B	
	No. Required	2	
Function:	purified water to steam bo		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.66		
Mass Flowrate [kg/batch]:	230000		
Molar Flowrate [kmol/batch]:			
Water	75.96		
Total	75.96		
Design Data:	**Power:**	3	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF10k	
Utilities:	**Electricity:**	504	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	WFI Return Pump A/B	
	Item No.	P-816 A/B	
	No. Required	2	
Function:	Water return to WFI system		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	105.7		
Pressure [bara]:	1.6		
Mass Flowrate [kg/batch]:	11500		
Molar Flowrate [kmol/batch]:			
Water	638		
Total	638		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200	
Utilities:	**Electricity:**	62.2	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	WFI Storage Pump A/B	
	Item No.	P-817 A/B	
	No. Required	2	
Function:	Water return to storage tank		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	110		
Pressure [bara]:	3.03		
Mass Flowrate [kg/batch]:	185000		
Molar Flowrate [kmol/batch]:			
Water	61.06		
Total	61.06		
Design Data:	**Power:**	4	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF10k	
Utilities:	**Electricity:**	504	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	WFI process Supply Pump 1 A/B	
	Item No.	P-819 A/B	
	No. Required	2	
Function:	Main WFI process pump		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	110		
Pressure [bara]:	30.3		
Mass Flowrate [kg/batch]:	185000		
Molar Flowrate [kmol/batch]:			
Water	20.3		
Total	20.3		
Design Data:	**Power:**	4	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF20k	
Utilities:	**Electricity:**	504	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	WFI process Supply Pump 2 A/B	
	Item No.	P-820 A/B	
	No. Required	2	
Function:	Secondary WFI process pump		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	110		
Pressure [bara]:	3.03		
Mass Flowrate [kg/batch]:	185000		
Molar Flowrate [kmol/batch]:			
Water	40.7		
Total	40.7		
Design Data:	**Power:**	3	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF10k	
Utilities:	**Electricity:**	672	[kW-hr]
	Comments and Drawings:		See PFD

Diaphragm Pump			
Identification:	Item	CIP Pump A/B	
	Item No.	P-904 A/B	
	No. Required	2	
Function:	CIP pump		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	24600		
Molar Flowrate [kmol/batch]:			
Water	1350		
Total	1350		
Design Data:	**Power:**	0.37	[kW]
	MAWP:	6	[bar]
	MOC:	316LSS	
	Type:	QF1200k	
Utilities:	**Electricity:**	62.2	[kW-hr]
	Comments and Drawings:		See PFD

Bioreactor			
Identification:	Item	Seed Culture Bioreactor 1	
	Item No.	R-207	
	No. Required	1	
Function:	promote CHO cell growth		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	37	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	254.7	254.9	
Molar Flowrate [kmol/batch]:			
Biomass	1.4E-03	2.9E-02	
Impurities	5.0E-04	9.5E-02	
BalanCD Media	2.1E-01	8.8E-02	
Mab	2.7E-04	1.0E-02	
Sodium Bicarbonate	4.1E-02	4.4E-03	
Water	9.5	9.5	
Oxygen	0.6	0.5	
Nitrogen	2.2	2.2	
Carbon Dioxide	0.0	4.0E-02	
Total	12.5	12.5	
Design Data:	**Volume:**	0.25	[m^3]
	Diameter:	0.05	[m]
	MOC:	316LSS	
	Externals:	Jacketed	
	Internals:	Impeller	
Utilities:	**Electricity:**	0	[kW-hr]
	Comments and Drawings:		See PFD

Bioreactor			
Identification:	Item	Seed Culture Bioreactor 2	
	Item No.	R-208	
	No. Required	1	
Function:	promote CHO cell growth		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	37	37	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	5575.3	5579.5	
Molar Flowrate [kmol/batch]:			
Biomass	2.9E-02	5.7E-01	
Impurities	0.1	0.2	
BalanCD Media	4.4	1.9	
Mab	1.0E-02	2.1E-01	
Sodium Bicarbonate	8.3E-01	8.7E-02	
Water	189.0	190.8	
Oxygen	15.2	13.8	
Nitrogen	57.1	57.2	
Carbon Dioxide	0.0	0.8	
Total	265.8	265.6	
Design Data:	**Volume:**	5	[m^3]
	Diameter:	1.5	[m]
	MOC:	316LSS	
	Externals:	Jacketed	
	Internals:	Impeller	
Utilities:	**Electricity:**	2.72E-04	[kW-hr]
	Comments and Drawings:		See PFD

Bioreactor			
Identification:	Item	Production Bioreactor A/B	
	Item No.	R-301 A/B	
	No. Required	2	
Function:	promote mAb production		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	37	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	188186.12	1.88E+05	
Molar Flowrate [kmol/batch]:			
Biomass	0.6	7.1	
Impurities	0.2	2.3	
BalanCD Media	23.0	0.0	
Feed 4 Media	4.2	12.8	
Mab	0.2	2.6	
Sodium Bicarbonate	5.0	0.6	
Water	1257.6	1264.6	
Oxygen	1199.9	9.8	
Nitrogen	4514.9	4515.7	
Carbon Dioxide	0.0	1183.3	
Total	7001.3	6998.8	
Design Data:	**Volume:**	30	[m^3]
	Diameter:	2.46	[m]
	MOC:	316LSS	
	Externals:	Jacketed	
	Internals:	Impeller	
Utilities:	**Electricity:**	3.0E-03	[kW-hr]
	Comments and Drawings:		See PFD

Tank		
Identification:	Item	Production Bioreactor A/B
	Item No.	Tk-303 A/B
	No. Required	2
Function:		
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	37	37
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	2.33E+04	2.33E+04
Molar Flowrate [kmol/batch]:		
Biomass	7.1	7.1
Impurities	2.3	2.3
Feed 4 Media	12.8	12.8
Mab	2.6	2.6
Sodium Bicarbonate	0.6	0.6
Water	1264.6	1264.6
Oxygen	0.0	5.90E-03
Nitrogen	0.0	2.20E-02
Total	1290.0	1290.0
Design Data:	**Volume:**	27.5 [m^3]
	Diameter:	2.3 [m]
	MOC:	316LSS
	Internals:	None
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Tank		
Identification:	Item	Centrifuge Surge Tank
	Item No.	Tk-307
	No. Required	1
Function:	Centrifuge Surge	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	44.1	44.1
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	2.25E+04	22501.79
Molar Flowrate [kmol/batch]:		
Impurities	2.2	2.2
Feed 4 Media	12.5	12.5
Mab	2.5	2.5
Sodium Bicarbonate	0.6	0.6
Water	1226.7	1226.7
Oxygen	0.0	1.30E-02
Nitrogen	0.0	4.90E-02
Total	1244.4	1244.4
Design Data:	**Volume:**	25 [m^3]
	Diameter:	2.2 [m]
	MOC:	316LSS
	Internals:	None
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Tank		
Identification:	Item	Viral Inactivation Surge Tank
	Item No.	Tk-414
	No. Required	1
Function:	Viral Inactivation Surge	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	346.6	346.6
Molar Flowrate [kmol/batch]:		
Impurities	9.7E-02	9.7E-02
Mab	2.2	2.21
Water	16.67	16.67
Acetic-Acid	0.0	4.0E-03
Tributyl phosphate	4.3E-03	4.3E-03
Polysorbate 80	2.7E-03	2.7E-03
Total	19.0	19.0
Design Data:	**Volume:**	0.5 [m^3]
	Diameter:	0.5 [m]
	MOC:	316LSS
	Internals:	None
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Tank		
Identification:	Item	HIC Surge Tank
	Item No.	Tk-607
	No. Required	1
Function:	HIC Surge Tank	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	1581.5	1583.3
Molar Flowrate [kmol/batch]:		
Mab	3.4	3.4
Water	81.3	81.3
Oxygen	0.0	1.3E-02
Nitrogen	0.0	5.1E-02
Disodium Phosphate	2.7E-02	2.7E-02
Sodium Chloride	0.9	0.9
Total	85.6	85.7
Design Data:	**Volume:**	1.5 [m^3]
	Diameter:	1 [m]
	MOC:	316LSS
	Internals:	None
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Tank		
Identification:	Item	Waste Holding Tank
	Item No.	Tk-701
	No. Required	1
Function:	Hold Waste to neutralization	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	110	25
Pressure [bara]:	3.03	1.5
Mass Flowrate [kg/batch]:	2.08E+05	1.29E+05
Molar Flowrate [kmol/batch]:		
Biomass	7.1	7.1
Impurities	2.4	2.4
BalanCD Media	1.9	1.9
Feed 4 Media	10.9	10.9
Mab	0.7	0.7
Sodium Bicarbonate	0.6	0.6
Water	5190.0	5187.9
Acetic-Acid	0.8	0.8
Ammonium Sulfate	0.8	0.8
TRIS Base	1.2	1.2
TRIS HCl	3.6	3.6
Sodium Hydroxide	2.3	2.3
EDTA Disodium	1.3E-02	1.3E-02
Disodium Phosphate	0.3	0.3
Monosodium Phosphate	0.2	0.2
Sodium Phosphate	0.1	0.1
Sodium Chloride	29.2	29.2
Guanidinium Chloride	8.3	8.3
Total	5260.0	5258.3
Design Data:	**Volume:**	125 [m^3]
	Diameter:	3.75 [m]
	MOC:	316LSS
	Internals:	None
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Tank		
Identification:	Item	Potable Water Tank
	Item No.	Tk-801
	No. Required	1
Function:		
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.0	1.0
Mass Flowrate [kg/batch]:	3280.0	1820.0
Molar Flowrate [kmol/batch]:		
Water	173.0	95.9
Total	173.0	95.9
Design Data:	**Volume:**	[m^3]
	Diameter:	[m]
	MOC:	316LSS
	Internals:	None
Utilities:	**Electricity:**	[kW-hr]
	Comments and Drawings:	See PFD

Tank		
Identification:	Item	Purifed Water Tank
	Item No.	Tk-809
	No. Required	1
Function:		
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	1522.8	1522.8
Molar Flowrate [kmol/batch]:		
Water	84.0	84.0
Total	84.0	84.0
Design Data:	**Volume:**	[m^3]
	Diameter:	[m]
	MOC:	316LSS
	Internals:	None
Utilities:	**Electricity:**	[kW-hr]
	Comments and Drawings:	See PFD

Tank		
Identification:	Item	Steam Compressor KO Drum
	Item No.	Tk-814
	No. Required	1
Function:		
Operation:	Batch	
Materials Handled:	Inlet/Outlet	
Temperature [C]:	105.7	
Pressure [bara]:	1.24	
Mass Flowrate [kg/batch]:	2.18E+05	
Molar Flowrate [kmol/batch]:		
Water	72.2	
Total	72.2	
Design Data:	**Volume:**	[m^3]
	Diameter:	[m]
	MOC:	316LSS
	Internals:	None
Utilities:	**Electricity:**	[kW-hr]
	Comments and Drawings:	See PFD

Tank			
Identification:	Item	WFI Storage Tank	
	Item No.	Tk-818	
	No. Required	1	
Function:	WFI Storage		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:		110	
Pressure [bara]:		3.03	
Mass Flowrate [kg/batch]:		1.85E+05	
Molar Flowrate [kmol/batch]:			
Water		61.1	
Total		61.1	
Design Data:	**Volume:**	1	[m^3]
	Diameter:	1.75	[m]
	MOC:	316LSS	
	Internals:	None	
Utilities:	**Electricity:**		[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Media Prep Vessel 1	
	Item No.	V-101	
	No. Required	1	
Function:	Media preperation		
Operation:	Batch; outputs various streams		
Materials Handled:	Inlet/Outlet		
Temperature [C]:			
Pressure [bara]:			
Mass Flowrate [kg/batch]:	3480.5		
Molar Flowrate [kmol/batch]:			
BalanCD Media	4.5		
Sodium Bicarbonate	0.9		
Water	188.3		
Total	192.9		
Design Data:	**Volume:**	4	[m^3]
	Diameter:	1.25	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.4	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Media Prep Vessel 1	
	Item No.	V-101	
	No. Required	1	
Function:	Media preperation		
Operation:	Batch; outputs various streams		
Materials Handled:	Inlet/Outlet		
Temperature [C]:			
Pressure [bara]:			
Mass Flowrate [kg/batch]:	3480.5		
Molar Flowrate [kmol/batch]:			
BalanCD Media	4.5		
Sodium Bicarbonate	0.9		
Water	188.3		
Total	192.9		
Design Data:	**Volume:**	4	[m^3]
	Diameter:	1.25	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.4	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Media Prep Vessel 2	
	Item No.	V-103	
	No. Required	1	
Function:	Media preperation		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:		25	
Pressure [bara]:		1.01	
Mass Flowrate [kg/batch]:		1.64E+04	
Molar Flowrate [kmol/batch]:			
BalanCD Media		21.1	
Sodium Bicarbonate		4.1	
Water		889.0	
Total		910.6	
Design Data:	**Volume:**	20	[m^3]
	Diameter:	1.2	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.33	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Feed Media Prep Vessel A/B	
	Item No.	V-105 A/B	
	No. Required	1	
Function:	Final Media preperation		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:		25	
Pressure [bara]:		1.01	
Mass Flowrate [kg/batch]:		3286.33	
Molar Flowrate [kmol/batch]:			
Feed 4 Media		4.23	
Sodium Bicarbonate		0.82	
Water		177.8	
Total		182.12	
Design Data:	**Volume:**	4.5	[m^3]
	Diameter:	1.25	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.79	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Air Compressor KO Drum	
	Item No.	V-209	
	No. Required	1	
Function:	Air to KO drum		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:		140	
Pressure [bara]:		25	
Mass Flowrate [kg/batch]:		1E+05	
Molar Flowrate [kmol/batch]:			
Oxygen		1714.0	
Nitrogen		7368.8	
Total		9082.8	
Design Data:	**Volume:**	0.053	[m^3]
	Diameter:	0.23	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	-	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Protein A Buffer Prep Vessel 1	
	Item No.	V-401	
	No. Required	1	
Function:	Protein A Buffer preperation		
Operation:	Batch		
Materials Handled:	Outlet		
Temperature [C]:		31	
Pressure [bara]:		1.01	
Mass Flowrate [kg/batch]:		2507.7	
Molar Flowrate [kmol/batch]:			
Water		137.3	
TRIS Base		0.3	
TRIS HCl		0.9	
EDTA Disodium		1.3E-02	
Total		137.5	
Design Data:	**Volume:**	3	[m^3]
	Diameter:	1.25	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.4	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Protein A Buffer Prep Vessel 2	
	Item No.	V-402	
	No. Required	1	
Function:	Protein A Buffer preperation		
Operation:	Batch		
Materials Handled:	Outlet		
Temperature [C]:		25	
Pressure [bara]:		1.01	
Mass Flowrate [kg/batch]:		4126.1	
Molar Flowrate [kmol/batch]:			
Water		218.97	
TRIS Base		0.52	
TRIS HCl		1.55	
Guanidinium Chloride		8.26	
Total		227.43	
Design Data:	**Volume:**	5	[m^3]
	Diameter:	1.5	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.99	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Protein A Buffer Prep Vessel 3	
	Item No.	V-403	
	No. Required	1	
Function:	Protein A Buffer preperation		
Operation:	Batch		
Materials Handled:	Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	8219.5		
Molar Flowrate [kmol/batch]:			
Water	453.5		
Acetic-Acid	0.8		
Total	454.3		
Design Data:	**Volume:**	5	[m^3]
	Diameter:	1.5	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	1	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Protein A Buffer Prep Vessel 4	
	Item No.	V-404	
	No. Required	1	
Function:	Protein A Buffer preperation		
Operation:	Batch		
Materials Handled:	Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	5000.1		
Molar Flowrate [kmol/batch]:			
Water	223.5		
TRIS Base	1.1		
TRIS HCl	0.3		
Sodium Chloride	4.5		
Total	232.5		
Design Data:	**Volume:**	5	[m^3]
	Diameter:	1	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.14	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	Viral Inactivation Vessel	
	Item No.	V-408	
	No. Required	1	
Function:	Viral Inactivation		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	25	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	2033.8	2033.8	
Molar Flowrate [kmol/batch]:			
Impurities	0.2	0.2	
Mab	4.5	4.5	
Water	363.7	363.7	
Oxygen	0.0	1.8E-02	
Nitrogen	0.0	6.6E-02	
Acetic-Acid	1.6E-01	1.6E-01	
Tributyl phosphate	4.3E-03	4.3E-03	
Polysorbate 80	2.7E-03	2.7E-03	
Total	375.5	375.5	
Design Data:	**Volume:**	2	[m^3]
	Diameter:	1	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.13	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	IEX Buffer Vessel 1	
	Item No.	V-501	
	No. Required	1	
Function:	IEX Buffer preperation		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	1399.2		
Molar Flowrate [kmol/batch]:			
Water	76.9		
Disodium Phosphate	1.1E-02		
Potassium Chloride	1.0E-07		
Monopotassium Phosphate	1.0E-07		
Total	76.9		
Design Data:	**Volume:**	2	[m^3]
	Diameter:	1	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.13	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	IEX Buffer Prep Vessel 2	
	Item No.	V-502	
	No. Required	1	
Function:	IEX Buffer preperation		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	2342.3		
Molar Flowrate [kmol/batch]:			
Water	127.53		
Disodium Phosphate	1.82E-02		
Sodium Chloride	0.72		
Potassium Chloride	1.00E-06		
Monopotassium Phosphate	1.00E-06		
Total	128.27		
Design Data:	**Volume:**	316LSS	[m^3]
	Diameter:	1	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.13	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	IEX Buffer Prep Vessel 3	
	Item No.	V-503	
	No. Required	1	
Function:	IEX Buffer preperation		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	4806.1		
Molar Flowrate [kmol/batch]:			
Water	250.1		
Disodium Phosphate	0.2		
Sodium Chloride	4.7		
Total	255.0		
Design Data:	**Volume:**	5.5	[m^3]
	Diameter:	1.25	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.41	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	IEX Buffer Prep Vessel 4	
	Item No.	V-504	
	No. Required	1	
Function:	IEX Buffer preperation		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	2386.9		
Molar Flowrate [kmol/batch]:			
Water	124.9		
Sodium Chloride	2.3		
Total	127.3		
Design Data:	**Volume:**	1.75	[m^3]
	Diameter:	0.75	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.03	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel			
Identification:	Item	IEX Buffer Prep Vessel 5	
	Item No.	V-505	
	No. Required	1	
Function:	IEX Buffer preperation		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	1405.9		
Molar Flowrate [kmol/batch]:			
Water	76.5		
Sodium Hydroxide	0.7		
Total	77.2		
Design Data:	**Volume:**	1.75	[m^3]
	Diameter:	0.75	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.03	[kW-hr]
	Comments and Drawings:	See PFD	

Vessel		
Identification:	Item	Amm. Sulfate Vessel
	Item No.	V-508
	No. Required	1
Function:	Amm. Sulfate	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	1305.9	1307.3
Molar Flowrate [kmol/batch]:		
Impurities	3.75E-02	1.0
Water	59.3	60.3
Oxygen	0.0	1.06E-02
Nitrogen	0.0	4.00E-02
Ammonium Sulfate	0.8	1.8
Monosodium Phosphate	4.78E-02	1.0
Sodium Chloride	1.0	2.0
Total	65.1	71.1
Design Data:	**Volume:**	1.25 [m^3]
	Diameter:	0.75 [m]
	MOC:	316LSS
	Internals:	Impeller
Utilities:	**Electricity:**	0.03 [kW-hr]
	Comments and Drawings:	See PFD

Vessel		
Identification:	Item	HIC Buffer Prep Vessel 1
	Item No.	V-601
	No. Required	1
Function:	HIC Buffer preperation	
Operation:	Batch	
Materials Handled:	Inlet/Outlet	
Temperature [C]:	25	
Pressure [bara]:	1.01	
Mass Flowrate [kg/batch]:	2001.9	
Molar Flowrate [kmol/batch]:		
Water	92.9	
Disodium Phosphate	4.6E-02	
Sodium Chloride	6.7	
Total	99.7	
Design Data:	**Volume:**	2.25 [m^3]
	Diameter:	1 [m]
	MOC:	316LSS
	Internals:	Impeller
Utilities:	**Electricity:**	0.14 [kW-hr]
	Comments and Drawings:	See PFD

Vessel		
Identification:	Item	HIC Buffer Prep Vessel 2
	Item No.	V-602
	No. Required	1
Function:	HIC Buffer preperation	
Operation:	Batch	
Materials Handled:	Inlet/Outlet	
Temperature [C]:	25	
Pressure [bara]:	1.01	
Mass Flowrate [kg/batch]:	3336.6	
Molar Flowrate [kmol/batch]:		
Water	166.2	
Disodium Phosphate	7.5E-02	
Sodium Chloride	5.7	
Total	171.9	
Design Data:	**Volume:**	3.5 [m^3]
	Diameter:	1.25 [m]
	MOC:	316LSS
	Internals:	Impeller
Utilities:	**Electricity:**	0.42 [kW-hr]
	Comments and Drawings:	See PFD

Vessel		
Identification:	Item	HIC Buffer Prep Vessel 3
	Item No.	V-603
	No. Required	1
Function:	HIC Buffer preperation	
Operation:	Batch	
Materials Handled:	Inlet/Outlet	
Temperature [C]:	25	
Pressure [bara]:	1.01	
Mass Flowrate [kg/batch]:	6452.8	
Molar Flowrate [kmol/batch]:		
Water	343.1	
Disodium Phosphate	0.1	
Sodium Chloride	4.3	
Total	347.6	
Design Data:	**Volume:**	7 [m^3]
	Diameter:	1.5 [m]
	MOC:	316LSS
	Internals:	Impeller
Utilities:	**Electricity:**	1 [kW-hr]
	Comments and Drawings:	See PFD

Vessel		
Identification:	Item	HIC Buffer Prep Vessel 4
	Item No.	V-604
	No. Required	1
Function:	HIC Buffer preperation	
Operation:	Batch	
Materials Handled:	Inlet/Outlet	
Temperature [C]:	25	
Pressure [bara]:	1.01	
Mass Flowrate [kg/batch]:	3161.3	
Molar Flowrate [kmol/batch]:		
Water	172.0	
Sodium Hydroxide	1.6	
Total	173.6	
Design Data:	**Volume:**	3.5 [m^3]
	Diameter:	1.25 [m]
	MOC:	316LSS
	Internals:	Impeller
Utilities:	**Electricity:**	0.4 [kW-hr]
	Comments and Drawings:	See PFD

Vessel		
Identification:	Item	Freeze Thaw Cyrovessel
	Item No.	V-613
	No. Required	1
Function:	Freezing for storage and thawing	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	-50
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	259.8	259.8
Molar Flowrate [kmol/batch]:		
Mab	1.6	1.6
Water	12.7	12.7
Disodium Phosphate	6.4E-04	6.4E-04
Sodium Chloride	2.1E-02	2.1E-02
Total	14.4	14.4
Design Data:	**Volume:**	- [m^3]
	Diameter:	- [m]
	MOC:	316LSS
	Internals:	None
Utilities:	**Electricity:**	198 [kW-hr]
	Comments and Drawings:	See PFD

Vessel			
Identification:	Item	Neutralization Vessel	
	Item No.	V-703	
	No. Required	1	
Function:	Neutralization for disposal		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	83.3	83.3	
Pressure [bara]:	1.5	1.5	
Mass Flowrate [kg/batch]:	1.45E+04	1.43E+05	
Molar Flowrate [kmol/batch]:			
Biomass	7.1	7.1	
Impurities	2.4	2.4	
BalanCD Media	1.9	1.9	
Feed 4 Media	10.9	10.9	
Mab	0.7	0.7	
Sodium Bicarbonate	0.6	0.6	
Water	5210.0	5212.3	
Acetic-Acid	0.8	0.8	
Hydrochloric acid	1.5E-02	2.0E-02	
Ammonium Sulfate	0.8	0.8	
TRIS Base	1.2	1.2	
TRIS HCl	3.6	3.6	
Sodium Hydroxide	2.3	2.3	
EDTA Disodium	1.3E-02	1.0E-02	
Disodium Phosphate	0.3	0.3	
Monosodium Phosphate	0.2	0.2	
Sodium Phosphate	0.1	0.1	
Sodium Chloride	29.2	29.2	
Guanidinium Chloride	8.3	8.3	
Total	5280.0	5282.8	
Design Data:	**Volume:**	10	[m^3]
	Diameter:	1.5	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	0.98	[kW-hr]
	Comments and Drawings:		See PFD

Vessel			
Identification:	Item	Caustic Vessel 1	
	Item No.	V-901	
	No. Required	1	
Function:	CIP preperation		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	6089.5		
Molar Flowrate [kmol/batch]:			
Water	331.3		
Sodium Hydroxide	3.0		
Total	334.3		
Design Data:	**Volume:**	7	[m^3]
	Diameter:	1.5	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	-	[kW-hr]
	Comments and Drawings:		See PFD

Vessel			
Identification:	Item	Caustic Vessel 2	
	Item No.	V-902	
	No. Required	1	
Function:	CIP preperation		
Operation:	Batch		
Materials Handled:	Inlet/Outlet		
Temperature [C]:	25		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	1.70E+04		
Molar Flowrate [kmol/batch]:			
Water	938.7		
Sodium Hydroxide	1.7		
Total	940.4		
Design Data:	**Volume:**	20	[m^3]
	Diameter:	2	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	-	[kW-hr]
	Comments and Drawings:		See PFD

Vessel			
Identification:	Item	Acid Vessel	
	Item No.	V-903	
	No. Required	1	
Function:	CIP preperation		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	25	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	2.7E+04	1.5E+03	
Molar Flowrate [kmol/batch]:			
Water	0	79.1	
Total	0	79.1	
Design Data:	**Volume:**	30	[m^3]
	Diameter:	2.5	[m]
	MOC:	316LSS	
	Internals:	Impeller	
Utilities:	**Electricity:**	-	[kW-hr]
	Comments and Drawings:	See PFD	

Freezer			
Identification:	Item	Storage Freezer	
	Item No.	Fz-614	
	No. Required	18	
Function:	storage		
Operation:	Batch		
Materials Handled:	Inlet		
Temperature [C]:	-50		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	259.8		
Molar Flowrate [kmol/batch]:			
Mab	1.6		
Water	12.7		
Disodium Phosphate	6.4E-04		
Sodium Chloride	2.1E-02		
Total	14.4		
Design Data:	**Volume:**	0.79	[m^3]
	Diameter:	-	[m]
	MOC:	316LSS	
	Internals:	None	
Utilities:	**Electricity:**	7667.7	[kW-hr]
	Comments and Drawings:	See PFD	

Filter			
Identification:	Item	Air Cartridge Filter	
	Item No.	F-210	
	No. Required	1	
Function:	purifies the air		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	25	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	1.31E+05	1.31E+05	
Molar Flowrate [kmol/batch]:			
Oxygen	1714.0	1714.0	
Nitrogen	7368.8	7368.8	
Total	9082.8	9082.8	
Design Data:	**Area**	10	[m^2]
	MOC:	316LSS	
	Type:	Cartridge	
Utilities:	**Electricity:**	None	
	Comments and Drawings:	See PFD	

Filter			
Identification:	Item	Dead-End Filter 1	
	Item No.	F-306	
	No. Required	1	
Function:	Filter out solids		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	44.1	44.1	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	2.25E+04	22506.82	
Molar Flowrate [kmol/batch]:			
Biomass	0.1	0.1	
Impurities	2.2	2.2	
Feed 4 Media	12.5	12.5	
Mab	2.5	2.5	
Sodium Bicarbonate	0.6	0.6	
Water	1226.9	1226.9	
Total	1244.8	1244.8	
Design Data:	**Area**	230	[m^2]
	MOC:	316LSS	
	Type:	Dead-End	
Utilities:	**Electricity:**	None	
	Comments and Drawings:	See PFD	

Filter			
Identification:	Item	Dead-End Filter 1	
	Item No.	F-306	
	No. Required	1	
Function:	Filter out solids		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	44.1	44.1	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	2.25E+04	22506.82	
Molar Flowrate [kmol/batch]:			
Biomass	0.1	0.1	
Impurities	2.2	2.2	
Feed 4 Media	12.5	12.5	
Mab	2.5	2.5	
Sodium Bicarbonate	0.6	0.6	
Water	1226.9	1226.9	
Total	1244.8	1244.8	
Design Data:	**Area**	230	[m^2]
	MOC:	316LSS	
	Type:	Dead-End	
Utilities:	**Electricity:**	None	
	Comments and Drawings:	See PFD	

Filter			
Identification:	Item	Dead-Filter 2	
	Item No.	F-407	
	No. Required	1	
Function:	Filter out solids		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	25	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	1687.1	1687.1	
Molar Flowrate [kmol/batch]:			
Impurities	0.1	0.1	
Mab	2.3	2.3	
Water	90.7	90.7	
Acetic-Acid	0.2	0.2	
Total	93.3	93.3	
Design Data:	**Area**	80	[m^2]
	MOC:	316LSS	
	Type:	Dead-End	
Utilities:	**Electricity:**	None	
	Comments and Drawings:	See PFD	

Filter			
Identification:	Item	Dead-End Filter 3	
	Item No.	F-413	
	No. Required	1	
Function:	Filter out solids		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	26		
Pressure [bara]:	1.01		
Mass Flowrate [kg/batch]:	346.6	346.6	
Molar Flowrate [kmol/batch]:			
Impurities	0.1	0.1	
Mab	2.2	2.2	
Water	16.7	16.7	
Acetic-Acid	0.0	0.0	
Tributyl phosphate	0.0	0.0	
Polysorbate 80	0.0	0.0	
Total	19.0	19.0	
Design Data:	**Area**	80	[m^2]
	MOC:	316LSS	
	Type:	Dead-End	
Utilities:	**Electricity:**	None	
	Comments and Drawings:	See PFD	

Filter			
Identification:	Item	Dead-End Filter 4	
	Item No.	F-612	
	No. Required	1	
Function:	Filter out solids		
Operation:	Batch		
Materials Handled:	Inlet	Outlet	
Temperature [C]:	25	25	
Pressure [bara]:	1.01	1.01	
Mass Flowrate [kg/batch]:	259.77	0	
Molar Flowrate [kmol/batch]:			
Mab	1.64	0	
Water	12.7	0	
Disodium Phosphate	6.4E-04	0	
Sodium Chloride	2.1E-02	0	
Total	14.4	0	
Design Data:	**Area**	70	[m^2]
	MOC:	316LSS	
	Type:	Dead-End	
Utilities:	**Electricity:**	None	
	Comments and Drawings:	See PFD	

Filter		
Identification:	Item	Dead-End Filter 5
	Item No.	F-803
	No. Required	1
Function:	Filter out solids	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	1.82E+03	1.82E+03
Molar Flowrate [kmol/batch]:		
Water	95.9	96.0
Total	95.9	96.0
Design Data:	**Area**	120 [m^2]
	MOC:	316LSS
	Type:	Dead-End
Utilities:	**Electricity:**	None
	Comments and Drawings:	See PFD

Filter		
Identification:	Item	Ultrafilter
	Item No.	F-807
	No. Required	1
Function:	filter out suspended particulates	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	169.7	339.4
Molar Flowrate [kmol/batch]:		
Water	1.6E+04	1.6E+04
Total	1.6E+04	1.6E+04
Design Data:	**Area**	40 [m^2]
	MOC:	316LSS
	Type:	Ultrafilter
Utilities:	**Electricity:**	None
	Comments and Drawings:	See PFD

Filter		
Identification:	Item	Revere Osmosis System
	Item No.	F-808
	No. Required	1
Function:	Filter out remaining particles	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	25	25
Pressure [bara]:	1.01	1.01
Mass Flowrate [kg/batch]:	169.7	1692.5
Molar Flowrate [kmol/batch]:		
Water	1.5E+04	772.8
Total	1.5E+04	772.8
Design Data:	**Area**	84 [m^2]
	MOC:	316LSS
	Type:	-
Utilities:	**Electricity:**	None
	Comments and Drawings:	See PFD

Heat Exchanger		
Identification:	Item	Air Compressor After-Cooler
	Item No.	HE-212
	No. Required	1
Function:	Cool compressed air to acceptable temp for bioreactors	
Operation:	Batch	
Materials Handled:	Shell In	Shell Out Tube in Tube Out
Temperature [C]:	142	143 144 145
Pressure [bara]:	89.12	37 25 30
Mass Flowrate [kg/batch]:	1.31E+05	1.31E+05 3.16E+05 3.16E+05
Molar Flowrate [kmol/batch]:		
Water	0	0 3.2E+05 3.2E+05
Oxygen	1.7E+03	1.7E+03 0 0
Nitrogen	7.4E+03	7.4E+03 0 -
Total	9.1E+03	9.1E+03 3.2E+05 3.2E+05
Design Data:	**Area:**	77.2 [m^2]
	Duty:	23.3 [kW]
	MOC:	316LSS
	Type:	Shell and Tube
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Heat Exchanger		
Identification:	Item	Purified Water Pre-Heater
	Item No.	HE-811
	No. Required	1
Function:	Pre-heat purified water	
Operation:	Batch	
Materials Handled:	Shell In	Shell Out Tube in Tube Out
Temperature [C]:	25	25 105.7 50
Pressure [bara]:	1.66	1.45 1.6 1.45
Mass Flowrate [kg/batch]:	2.3E+05	2.3E+05 1.2E+04 1.2E+04
Molar Flowrate [kmol/batch]:		
Water	76.0	76.0 638.0 638.0
Total	76.0	76.0 638.1 638.1
Design Data:	**Area:**	0.2 [m^2]
	Duty:	2.82 [kW]
	MOC:	316LSS
	Type:	Shell and Tube
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Heat Exchanger		
Identification:	Item	WFI Condenser
	Item No.	HE-812
	No. Required	1
Function:	condense clean steam to WFI and raise temp of clean water going to boiler	
Operation:	Batch	
Materials Handled:	Shell In	Shell Out Tube in Tube Out
Temperature [C]:	136.1	110 25 105.7
Pressure [bara]:	3.24	3.03 1.45 1.24
Mass Flowrate [kg/batch]:	1.9E+05	1.9E+05 2.3E+05 2.3E+05
Molar Flowrate [kmol/batch]:		
Water	61.1	61.1 76.0 76.0
Total	61.1	61.1 76.0 76.0
Design Data:	**Area:**	17.3 [m^2]
	Duty:	501.2 [kW]
	MOC:	316LSS
	Type:	Shell and Tube
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

Heat Exchanger		
Identification:	Item	Steam Boiler
	Item No.	HE-813
	No. Required	1
Function:	Boiler to generate steam needed for SIP process	
Operation:	Batch	
Materials Handled:	Inlet	Outlet
Temperature [C]:	245.8	136.1
Pressure [bara]:	3.45	3.24
Mass Flowrate [kg/batch]:	4.5E+05	4.5E+05
Molar Flowrate [kmol/batch]:		
Water	148.0	782.3
Total	148.0	782.4
Design Data:	**Pressure:**	1.25 [barg]
	Duty:	231 [kW]
	MOC:	316LSS
	Type:	Boiler
Utilities:	**Electricity:**	- [kW-hr]
	Comments and Drawings:	See PFD

EQUIPMENT COST SUMMARY

Table 18: Fixed Capital Investment Summary

Equipment	Equipment ID	Total Module Cost
Media Prep		
Media Prep Vessel 1	V-101	$ 25,166.19
Media Prep Pump 1	P-102	$ 60,471.84
Media Prep Vessel 2	V-103	$ 39,727.54
Media Prep Pump 2	P-104	$ 60,471.84
Feed Media Prep Vessel A/B	V-105 A/B	$ 212,941.22
Feed Media Pump A/B	P-106 A/B	$ 60,471.84
Seed Train		
Roller Bottle Roller	RB-203	$ 1,460.00
Cell Bag Rocker Tray	CB-205	$ 8,405.00
Seed Culture Bioreactor 1	R-207	$ 47,608.53
Seed Culture Bioreactor 2	R-208	$ 234,298.58
Air Compressor KO Drum	V-209	$ 12,979.63
Air Cartridge Filter	F-210	$ 30,303.02
Air Compressor	C-211	$ 210,083.33
Air Compressor After-Cooler	HE-212	$ 322,058.62
Product Reactor/Centrifuge		
Production Bioreactor A/B	R-301 A/B	$ 606,595.88
Production Bioreactor Pump A/B	P-302	$ 60,471.84
Production Bioreactor Surge Tar	Tk-303	$ 242,437.24
Centrifuge	Cf-304	$ 30,000.00
Centrifuge Pump A/B	P-305 A/B	$ 60,471.84
Dead-End Filter 1	F-306	$ 1,125,523.46
Centrifuge Surge Tank	Tk-307	$ 224,253.13
Protein A Chromatography		
Protein A Buffer Prep Vessel 1	V-401	$ 87,927.46
Protein A Buffer Prep Vessel 2	V-402	$ 131,632.37
Protein A Buffer Prep Vessel 3	V-403	$ 238,579.89
Protein A Buffer Prep Vessel 4	V-404	$ 99,313.58
Protein A Column Feed Pump A/I	P-405 A/B	$ 85,505.68
Protein A Chromatography Colur	CI-406	$ 828,577.70
Dead-End Filter 2	F-407	$ 562,671.78
Viral Inactivation Vessel	V-408	$ 85,970.06
Viral Inactivation Pump A/B	P-409 A/B	$ 60,471.84
Diafiltration Flush Tank 1	Tk-410	$ 55,380.36
Diafiltration Pump 1 A/B	P-411 A/B	$ 60,471.84
Diafilter 1	F-412	$ 52,834.00
Dead-End Filter 3	F-413	$ 562,671.78
Viral Inactivation Surge Tank	Tk-414	$ 24,295.12
IEX Chromatography		
IEX Buffer Prep Vessel 1	V-501	$ 62,312.75
IEX Buffer Prep Vessel 2	V-502	$ 75,546.19
IEX Buffer Prep Vessel 3	V-503	$ 166,642.03
IEX Buffer Prep Vessel 4	V-504	$ 72,481.39
IEX Buffer Prep Vessel 5	V-505	$ 51,334.23
IEX Feed Pump A/B	P-506 A/B	$ 85,505.68
IEX Chromatography Column	CI-507	$ 611,319.69
Amm. Sulfate Vessel	V-508	$ 44,132.98
Diafiltration Flush Tank 2	Tk-509	$ 48,618.55
Diafiltration Pump 2 A/B	P-510 A/B	$ 60,471.84
Diafilter 2	F-511	$ 52,834.00

Equipment	Equipment ID	Total Module Cost
HIC Chromatography		
HIC Buffer Prep Vessel 1	V-601	$ 66,291.54
HIC Buffer Prep Vessel 2	V-602	$ 94,868.61
HIC Buffer Prep Vessel 3	V-603	$ 201,979.84
HIC Buffer Prep Vessel 4	V-604	$ 94,381.24
Diafiltration/HIC Column Feed Pump A/B	P-605	$ 94,859.12
HIC Column	CI-606	$ 1,084,557.03
HIC Surge Tank	Tk-607	$ 40,915.82
HIC Surge Tank Pump A/B	P-608 A/B	$ 60,471.84
Diafiltration Flush Tank 3	Tk-609	$ 50,954.94
Diafilatration Pump 3 A/B	P-610 A/B	$ 60,471.84
Diafilter 3	F-611	$ 52,834.00
Dead-End Filter 4	F-612	$ 517,990.90
Freeze-Thaw Cryovessel	V-613	$ 125,000.00
Storage Freezer	Fz-614	$ 316,588.32
Waste Treatment		
Waste Holding Tank	Tk-701	$ 959,200.24
Waste Holding Pump A/B	P-702	$ 85,505.68
Neutralization Vessel	V-703	$ 195,252.15
WFI System		
Potable Water Tank	Tk-801	$ 70,915.08
Potable Water Pump A/B	P-802	$ 85,505.68
Dead-End Filter 5	F-803	$ 728,296.16
Carbon Adsorption Column A/B	CI-804 A/B	$ 52,802.88
Cation Exchange Column	CI-805	$ 21,891.91
Anion Exchange Column	CI-806	$ 19,314.80
Ultrafilter	F-807	$ 158,502.00
Reverse Osmosis System	F-808	$ 28,157.73
Purified Water Tank	Tk-809	$ 70,936.20
Purified Water Pump A/B	P-810 A/B	$ 85,505.68
Purified Water Pre-Heater	HE-811	$ 358,646.63
WFI Condenser	HE-812	$ 186,056.99
Steam Boiler	HE-813	$ 928,021.27
Steam Compressor KO Drum	Tk-814	$ 36,831.55
Steam Compressor	C-815	$ 713,938.71
Water Return Pump A/B	P-816 A/B	$ 60,471.84
WFI Storage Pump A/B	P-817 A/B	$ 85,505.68
WFI Storage Tank	Tk-818	$ 533,651.11
WFI Process Supply Pump 1 A/B	P-819 A/B	$ 85,505.68
WFI Process Supply Pump 2 A/B	P-820 A/B	$ 94,859.12
Clean in Place		
Caustic Vessel 1	V-901	$ 154,884.36
Caustic Vessel 2	V-902	$ 360,946.09
Acid Vessel	V-903	$ 590,610.75
CIP Pump A/B	P-904 A/B	$ 60,471.84
Total Fixed Capital Investment		$ 17,618,056.19

FIXED CAPITAL INVESTMENT SUMMARY

In order to predict and calculate economic metrics for our project, we assumed that all fixed capital investments were incurred during the year 2019. The project, however, does not begin production until halfway through the year 2020.

Roller Bottle Roller and Cell Bag Rocker Tray

In order to approximate the cost of the Roller Bottle Roller, RB-203, and the Cell Bag Rocker Tray, CB-205, quotes from vendor catalogs were obtained [20,21]

Centrifuge

To estimate the capital investment of the disc-stack centrifuge Cf-304, an automatic disc-stack centrifuge with a capacity of 4000 liters per hour was found via a vendor. It was assumed that, while Cf-304 only requires 1470 liters per hour, the cost of the centrifuge from the vendor would provide a valid estimation and if anything an overestimation of the cost [39].

Chromatography Columns

In order to estimate the capital cost of the chromatography columns, the "six-tenths rule," as described in *Analysis, Synthesis, and Design of Chemical Processes*, was utilized to relate a cost estimate for a 90 liter chromatography column to the known required volume of our disparate columns [40]. The estimate of $200,000 for a 90 L column was given by Warner and Nochumson in *Rethinking the Economics of Chromatography* from BioPharm International journal [41]. This estimate was given in 2003, so the estimate was projected to 2019 dollars utilizing the CEPCI before the "six-tenths rule" was applied.

Freeze-Thaw Cryovessel

In order to approximate the capital investment of the Freeze-Thaw Cryovessel, V-613, a quote was obtained via phone call from a vendor for the Sartorius Celsius FT-100 Freeze-Thaw System, the system for which our cryovessel is based [42].

Storage Freezer

To estimate the cost of the Storage Freezer, Fz-614, a quote from a vendor catalog was obtained for one freezer. This was then multiplied by 18 to find the total capital investment in freezer storage [43].

Ultrafilter

In order to approximate the capital cost of the ultrafilter, a quote direct from vendor was obtained via email. The six ultrafilters in series were accounted for to obtain the total capital cost of the ultrafilter [19].

Reverse Osmosis System

To estimate the fixed capital investment of the Reverse Osmosis System, F-808, the "six-tenths rule" [40] was again utilized to relate the cost of a known piece and size of equipment from a vendor to the size of the equipment required for the process. The size of the RO System

provided by the vendor is 9200 gallons per day, while the WFI production process requires 11000 gallons per day of RO water [35].

General Equipment Costing

For all other major pieces of equipment, the Guthrie Method constants and correlations, given in *Analysis, Synthesis, and Design of Chemical Processes* [40], were utilized to calculate the "vanilla" purchased cost. A carbon steel material of construction and MAWP of 50 psig is what constitutes the vanilla cost for any piece of equipment. A summary of each piece of equipment costed from these correlations and the parameter used to do so is provided in Table 18 below.

Table 19*: Costing Parameter Values for Process Equipment*

Equipment	Equipment ID	Parameter Value	
Media Prep			
Media Prep Vessel 1	V-101	4.0	m^3
Media Prep Pump 1	P-102	0.4	kW
Media Prep Vessel 2	V-103	20.0	m^3
Media Prep Pump 2	P-104	0.4	kW
Feed Media Prep Vessel A/B	V-105 A/B	4.5	m^3
Feed Media Pump A/B	P-106 A/B	0.4	kW
Seed Train			
Roller Bottle Roller	RB-203	-	-
Cell Bag Rocker Tray	CB-205	-	-
Seed Culture Bioreactor 1	R-207	0.3	m^3
Seed Culture Bioreactor 2	R-208	5.0	m^3
Air Compressor KO Drum	V-209	0.1	m^3
Air Cartridge Filter	F-210	10.0	m^2
Air Compressor	C-211	0.7	barg
Air Compressor After-Cooler	HE-212	77.2	m^2
Product Reactor/Centrifuge			
Production Bioreactor A/B	R-301 A/B	30.0	m^3
Production Bioreactor Pump A/B	P-302	0.4	kW
Production Bioreactor Surge Tank	Tk-303	27.5	m^3
Centrifuge	Cf-304	-	-
Centrifuge Pump A/B	P-305 A/B	0.4	kW
Dead-End Filter 1	F-306	230.0	m^2
Centrifuge Surge Tank	Tk-307	25.0	m^3
Protein A Chromatography			
Protein A Buffer Prep Vessel 1	V-401	3.0	m^3
Protein A Buffer Prep Vessel 2	V-402	5.0	m^3
Protein A Buffer Prep Vessel 3	V-403	10.0	m^3
Protein A Buffer Prep Vessel 4	V-404	5.0	m^3
Protein A Column Feed Pump A/B	P-405 A/B	3.0	kW
Protein A Chromatography Column	Cl-406	-	-
Dead-End Filter 2	F-407	80.0	m^2
Viral Inactivation Vessel	V-408	2.0	m^3
Viral Inactivation Pump A/B	P-409 A/B	0.4	kW
Diafiltration Flush Tank 1	Tk-410	3.0	m^3
Diafiltration Pump 1 A/B	P-411 A/B	0.4	kW
Diafilter 1	F-412	-	-
Dead-End Filter 3	F-413	80.0	m^2
Viral Inactivation Surge Tank	Tk-414	0.5	m^3
IEX Chromatography			
IEX Buffer Prep Vessel 1	V-501	2.0	m^3
IEX Buffer Prep Vessel 2	V-502	3.0	m^3
IEX Buffer Prep Vessel 3	V-503	5.5	m^3
IEX Buffer Prep Vessel 4	V-504	2.8	m^3
IEX Buffer Prep Vessel 5	V-505	1.8	m^3
IEX Feed Pump A/B	P-506 A/B	3.0	kW
IEX Chromatography Column	Cl-507	-	-
Amm. Sulfate Vessel	V-508	1.3	m^3
Diafiltration Flush Tank 2	Tk-509	2.3	m^3
Diafiltration Pump 2 A/B	P-510 A/B	0.4	kW
Diafilter 2	F-511	-	-

Equipment	Equipment ID	Parameter Value	
HIC Chromatography			
HIC Buffer Prep Vessel 1	V-601	2.3	m^3
HIC Buffer Prep Vessel 2	V-602	3.5	m^3
HIC Buffer Prep Vessel 3	V-603	7.0	m^3
HIC Buffer Prep Vessel 4	V-604	3.5	m^3
Diafiltration/HIC Column Feed Pump A/B	P-605	4.0	kW
HIC Column	Cl-606	-	-
HIC Surge Tank	Tk-607	1.5	m^3
HIC Surge Tank Pump A/B	P-608 A/B	0.4	kW
Diafiltration Flush Tank 3	Tk-609	2.5	m^3
Diafilatration Pump 3 A/B	P-610 A/B	0.4	kW
Diafilter 3	F-611	-	-
Dead-End Filter 4	F-612	70.0	m^2
Freeze-Thaw Cryovessel	V-613	0.0	$ -
Storage Freezer	Fz-614	-	$ -
Waste Treatment			
Waste Holding Tank	Tk-701	125.0	m^3
Waste Holding Pump A/B	P-702	3.0	kW
Neutralization Vessel	V-703	10.0	m^3
WFI System			
Potable Water Tank	Tk-801	5.0	m^3
Potable Water Pump A/B	P-802	3.0	kW
Dead-End Filter 5	F-803	120.0	m^3
Carbon Adsorption Column A/B	Cl-804 A/B	0.5	m^2
Cation Exchange Column	Cl-805	0.3	m^2
Anion Exchange Column	Cl-806	0.2	m^2
Ultrafilter	F-807	-	-
Reverse Osmosis System	F-808	-	-
Purified Water Tank	Tk-809	2.5	m^3
Purified Water Pump A/B	P-810 A/B	3.0	kW
Purified Water Pre-Heater	HE-811	0.2	m^2
WFI Condenser	HE-812	17.3	m^2
Steam Boiler	HE-813	231.0	kW
Steam Compressor KO Drum	Tk-814	0.7	m^3
Steam Compressor	C-815	75.0	kW
Water Return Pump A/B	P-816 A/B	0.4	kW
WFI Storage Pump A/B	P-817 A/B	3.0	kW
WFI Storage Tank	Tk-818	100.0	m^3
WFI Process Supply Pump 1 A/B	P-819 A/B	3.0	kW
WFI Process Supply Pump 2 A/B	P-820 A/B	4.0	kW
Clean in Place			
Caustic Vessel 1	V-901	7.0	m^3
Caustic Vessel 2	V-902	20.0	m^3
Acid Vessel	V-903	30.0	m^3
CIP Pump A/B	P-904 A/B	0.4	kW

In order to convert the vanilla purchased costs to installed costs, the purchased costs were multiplied by the bare module factors in order to account for infrastructure and installation. Material factors also accounted for the use of stainless steel rather than carbon steel for each piece of equipment. From the bare module costs, the total module costs were calculated by factoring in 3% fees and 15% contingency, a factor of 1.18. All of the correlations and constants were created in the year 2001, so the CEPCI was utilized to project the CTM to the current year, 2019. The pertinent CEPCI figures for the Fixed Capital Investment Estimates are included in Table 20 below.

Table 20 : Chemical Engineering Plant Cost Index for Relevant Years

CEPCI	
2001	394.3
2003	401.3
2019	652.9

The total fixed capital investment for the project is $17.6 million. The 2019 total module costs for each piece of equipment are summarized in Table 18 in the Equipment Cost Summary section.

Working Capital

The chromatography column and adsorption column resin, granular activated carbon, and filter and membrane cartridges all pose working capital costs to our facility when they are purchased. This is because they are not completely used up during the year in which they are purchased, as raw materials are, nor are they pieces of equipment that can continue to hold value once they have been placed into service. For this reason they cannot be deducted as an operating cost or depreciated as a fixed capital cost. We will write off the price we paid for the material at the end of the year in which its equipment life has ended. Only then can we realize the full value of the equipment in our tax deductions. Table 21 below summarizes the working capital over the life of the project.

Table 21: Working Capital Summary

Working Capital Summary					
Equipment	Amount	Units	Equip. Life	$/L or $/Cartridge	$/Purchase
Protein A Resin	450	L	5 yrs	$ 16,802.00	$ 7,560,900.00
IEX Resin - Cation Exchange	700	L	5 yrs	$ 3,190.00	$ 2,233,000.00
HIC Resin	650	L	5 yrs	$ 4,440.00	$ 2,886,000.00
IEX Resin - Anion Exchange	350	L	5 yrs	$ 730.60	$ 255,710.00
RO Membrane	6	Cartridges	5 yrs	$ 422.00	$ 2,532.00
Granular Activated Carbon	4200	L	3 yrs	$ 7.94	$ 33,331.20
Dead-End Filter Cartridge	580	m^2	3 yrs	$ 17.00	$ 9,860.00
Diafilter	102	m^2	3 yrs	$ 5,375.33	$ 548,284.00

SAFETY, HEALTH, AND ENVIRONMENTAL CONSIDERATIONS

Overview

Environmental, health, and safety (EH&S) considerations are overseen and addressed by a process safety management (PSM) system. Good Manufacturing Practices (GMP) for the preparation of drug products in the United States are outlined by the FDA in their Code of Federal Regulations Title 21 Part 211. The PSM system must adequately cover GMP for the organization and personnel, building and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling control, holding and distribution, laboratory controls, records and reports, and returned and salvaged drug products [44].

Occupational Safety

Occupational safety is considered in this design for the purpose of protecting those who work in this facility. A large portion of this safety will come from training. The FDA requires that qualified personnel to undergo GMP training on a continuous basis to assure that they are familiar with CGMP requirements. Being familiar with training is one of the best ways to prevent incidents from occurring. Furthermore, consultants are required to be upheld to the same standard as facility employees. This ensures that everyone on the premises knows what is expected of them and knows how to handle themselves when working. Personnel must have good sanitation and health habits. This deters the spread and growth of potential pathogens that could infect the process. Any health conditions or concerns must be reported in order to not jeopardize the product quality.

Both a security measure and process safety measure, only authorized personnel may enter certain areas. Proper training is required in many areas of the facility, and anyone without that training poses an occupational safety risk to others, themselves, and the process.
Personal Protective Equipment (PPE) will be held to a high standard during operation. The proper protection of someone on site is crucial to their safety. Consequences of improper PPE may include skin and eye irritation, chemical burns, respiratory distress and choking, infection from foreign pathogens and contamination of the process. Gloves must be worn at all times in the lab. When removed, proper removal technique must be used and the gloves are to be disposed of in biohazard waste. Powered air purifying respirators (PAPRs) should be worn in media and buffer prep area as a secondary means of exposure control where potent compound exposure potential is possible, as indicated by air monitoring data.

Another form of occupational safety is ergonomics. Training on this subject will be included in the training program required of employees. For many board operators, ergonomics can play a significant role in occupational safety when spending many hours of a shift sitting at a control panel. Proper ergonomics will promote good posture and resting positions, this will minimize the chances of developing aches and pains that can result in injury if left unchecked.

When detailed design is considered, security measures should be taken to guard against external threats. Fences, security checkpoints, and random screenings will deter potential threats while also putting another layer of protection between the facility and the community.

Product Requirements

A quality department is responsible for the testing and approval or rejection of components, drug product containers, closures, packaging materials, in-process materials, and drug products [44]. An adequate number of personnel must be present for the quality department to perform its functions. Testing for hazardous biological contaminants will include tests for Retroviruses, in vitro assays, and in vivo assays [45]. This testing will occur between The Protein A Chromatography Column and viral inactivation tank in order to measure what level of contamination must be reduced. Testing will also occur before product freezing in the Freeze-Thaw Cryovessel to ensure product quality and safety. If there is a rejection by standards at the product step, more testing will be conducted after the HIC and IEX Chromatography columns in order to identify the step that is not effectively inactivating viral contaminants.

Equipment MOC must not alter the quality or purity of the product. No substances required for operation, such as lubricants or coolants, shall come into contact with any process components that could alter the quality or purity of the product. This risk is reduced by the use of the diaphragm pumps utilizing electric motors. The diaphragm separating the wetted and non-wetted side separates the process fluid from the rest of the pump housing.

Product must be quarantined until the quality department releases it. Procedures must outline that the oldest product must be distributed first and removal procedure if there is a recall of a batch of product. This is a procedural safeguard against release of low quality or contaminated product to further processing and potentially the larger community.

Industrial Health

All pieces of equipment in the process that come into contact with the process materials have a method of cleaning or sterilization. A Steam in Place system and a Clean In Place system are designed to sterilize and wash any piece of equipment that is not single use. All single use equipment is disposed of properly into biohazard waste containers that will be available on site.

Buildings must be maintained in a clean and sanitary condition with adequate lighting and in a good state of repair. Any in-process materials must be properly labeled, stored properly, disposed of in a timely and sanitary manner, and have written procedures.

Per FDA regulations, air must be supplied to the building under positive pressure to maintain airflow. Also, the quality of air must be high enough by passing the air through high-efficiency particulate filters [44].

The room in which media is prepared must have a method of disinfecting the room so that the conditions can remain sterile. This room in particular, due to the dust hazard present, must

utilize air filtration systems. These systems include but are not limited to: pre filters and particulate matter air filters. This prevents dust recirculation in the facility. Fume hoods will be placed over the buffer preparation areas to protect against volatile vapor hazards.

Medical gas containers will be available and on site. They must be portable and self-contained to ensure reliability and efficiency in case of emergency situations. This is a layer of protection in place to respond to health related incidents involving respiratory distress. On site HSE emergency response teams must be trained in storage, handling, and use of these pieces of equipment.

Environmental

Fugitive air emissions must be identified and mitigated if necessary. The vapors involved in the design of this process and their respective hazards to the environment have been summarized in Table 22 below. Nitrogen, carbon dioxide, and oxygen are all components of ambient air that have no fugitive emissions concerns other than the flammability of oxygen. However, oxygen will not be in high enough concentrations to be cause for concern. Ambient air is not flammable, so the flammability concern is not a pertinent risk as oxygen concentration will not be raised above ambient air concentration in this design. Steam is produced in this process, but there are no emission hazards associated with a release of steam to the atmosphere. Aqueous hydrochloric acid is utilized throughout the design. This is a volatile chemical and is known to have vapor emissions of the acid. HCl vapor is both toxic and a pollutant. A release of this vapor would most likely result in a pollutant concern because this vapor is highly soluble in water. This could result in large amounts being put into solution with rain water or large bodies of water. Acid rain is corrosive to metal structures and buildings, and aqueous HCl is toxic to aquatic organisms.

Table 22: In accordance to the Clean Air Act Amendments of 1990, Title I, Clean Air Act Amendments of 1990, Title III, Emergency Planning and Community Right-to-Know Act

Components	Flammable	Human Toxic	Volatile Organic	Hazardous Air Pollutant
Nitrogen				
Carbon Dioxide				
Oxygen	x			
Water (Steam)				
HCl		x		x

Fume hoods will be incorporated in the buffer preparation area to collect any HCl vapors that could evaporate off of the designed HCl solutions used in the process. This actively reduces the risk presented by HCl vapors to the environment.

Liquid and solid wastes in this design are treated in the waste process. Two steps are taken to ensure sewage feed requirements are met. The first step is the steam injection process mentioned in the process description. The purpose of this steam injection step is to kill, denature, and inactivate any biological components that could remain in the waste stream prior

to release into the sewage system. The steam does this by raising the process stream temperature above 80 degrees Celsius for over a minute to adequately ensure microbial death [46]. The second step is the aqueous HCl addition to the neutralization tank. This step acts to lower the caustic pH of the stream into an acceptable range for sewage (5 to 9 pH) and dilute the waste even further. Any inorganic components that do not contribute to pH in the waste will be diluted to a lower concentration due to this addition of the aqueous solution.

PROCESS SAFETY CONSIDERATIONS

Objective

In order to reduce the risk of the production process, a detailed safety evaluation was performed using various methods to challenge safety concerns from multiple perspectives. Our main focus is to identify and mitigate hazards such as: toxicity, flammability, reactivity, environmental hazards, and biological hazards.

The overlying goal is to create a process design that is inherently safe with low levels of risk due to the design and that safety is less reliant of safety precautions and protective systems. An inherently safer design evaluates alternatives and aims to consider all potential hazards. It is crucial for this to be done at the preliminary design stage to allow for minimal possible damage to the environmental, business, and personnel.

Taking into consideration the inherently safer design, additional safety evaluations are performed. A Hazard Identification Summary was created using Risk Rank Matrix. Material properties, inventory estimates, and process technology, equipment, & operating conditions are evaluated. The Potential consequences summary identifies the potential for equipment damage, environmental compliance, loss of life, disruption of other business units, legal/PR, and community impact.

This preliminary design is assumed to have appropriate traditional plant safeguards, written procedures, mitigation equipment, and the various safety systems including emergency shutdown systems.

Inherently Safer Design

When considering how to design an inherently safer process, strategies such as minimization or intensification, moderation or attenuation, substitution, and simplification should be evaluated. The strategies for this preliminary design are assessed in Table 23 below.

***Table 23**: Inherently Safer Design Summary*

Concept	Incorporation in Preliminary Design	Hazard Addressed
Attenuation	Vent lines incorporated into bioreactor and tank design	Relieves pressure buildup in reactors
Substitution	Using chemically defined media instead of serum media	Facility is animal free
Minimization	Centrifuge and chromatography processes utilize multiple cycles per batch to minimize process fluid under process conditions	Larger centrifuge size poses a larger mechanical hazard. Larger chromatography columns process larger amounts of hazardous materials at one time.
Minimization	Only preparing enough media or buffer for one process cycle to alleviate unnecessary storage	Large quantities of hazardous materials like acidic or caustic buffer preparation material being stored for long periods of time.
Intensification	Diafiltration steps after each chromatography step reduce biological and chemical contaminant risks	Possibility of contaminants making it to the end product.
Attenuation	Dilution of all acidic or caustic solutions	Reduces hazard of storage. Reduces storage pressure. Reduces initial atmospheric concentration if a release occurs.
Simplification	The use of disposable units in the seed train process.	It is less difficult to keep sterile conditions. It also reduces the number of cleaning steps in the process.
Substitution	Positive Displacement Diaphragm pumps were selected over cheaper centrifugal pumps.	Reduces the hazard of contamination of process flow with contaminants associated with centrifugal pumps in biological processes.
Substitution	Materials of construction are 316L (SS) instead of carbon steel	Reduces risk of corrosion and surface metal release into solution, thus reducing contamination risk.

Hazard Identification and Risk Analysis

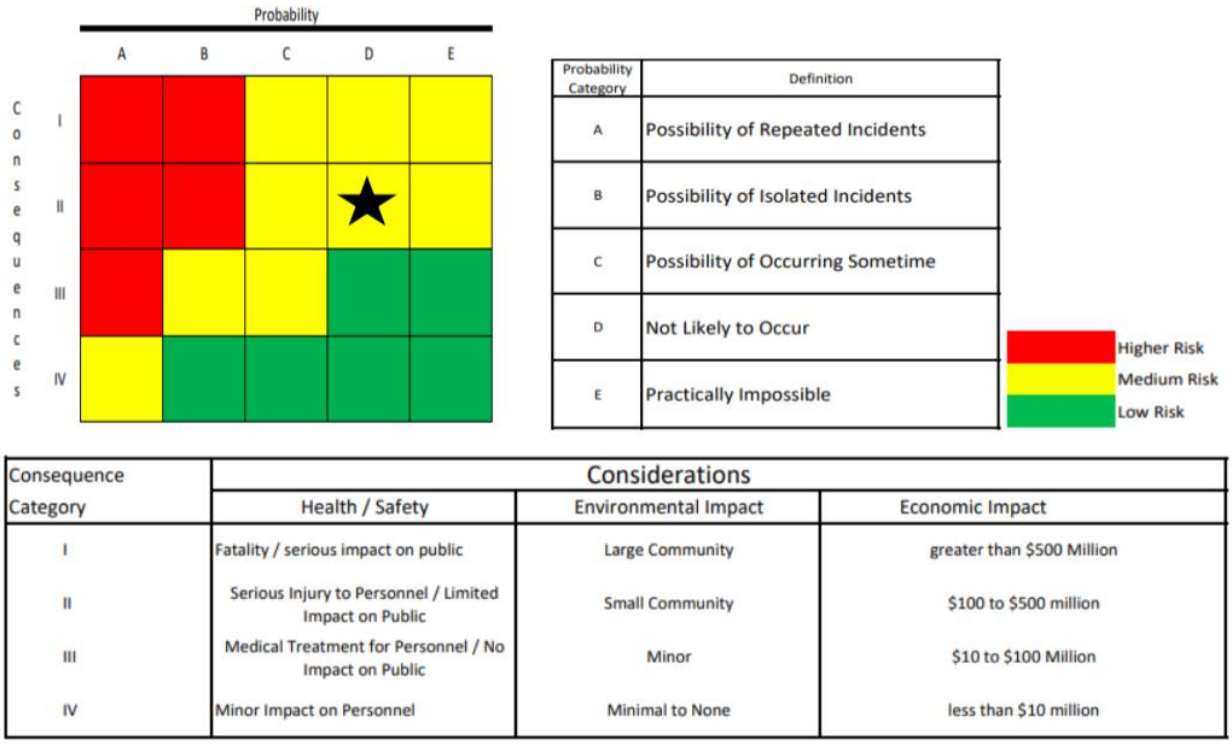
Near misses or injuries are typically traced back to the failure to identify hazards that could have been anticipated. Hazard identification is commonly sourced from the materials used and how they interact with other materials in the process, where the materials are stored, and the

equipment operating conditions. The source and the hazard are identified in the summary Table 23 and interaction matrix in Table 23.

The risk analysis is done using Figure 14. The potential risk is the product of consequences and probability. The consequences are based upon health/safety risk, environmental impact, and economic impact. Probability is the likelihood of an injury occurring. The hazards are rated by low, medium, and high risk in Table 24.

Table 24*: *HSE Hazard Identification Summary

Source	Hazard		Risk Rank
Material Properties	Acids (HCl and eluting)	Skin/eye irritant	Medium Risk
	Sodium Hydroxide (NaOH)	Skin/eye irritant	Medium Risk
	Steam	Burn risk	Low Risk
Inventory Estimates	Kill Tanks	pH out of range to sewer	Low Risk
		Large spill	Low Risk
	Media Prep Tanks	Media dust inhalation	Medium Risk
	Buffer Prep Tanks	Large spill	Medium Risk
	Final Formulation Storage	Refrigerant Spill	Medium Risk
Process Technology, Equipment, & Operating Conditions	Pumps	Leak of process material	Low Risk
	Filters	Flammability	Low Risk
	Seed Train	Broken Glassware	Low Risk
		Biological contamination	High Risk
	Bioreactors	Overpressure with closed vent	Medium Risk
	Centrifugation	Overturn	Low Risk
		Mechanical Strike to employee	Medium Risk
	Chromatography: Protein A	Blockage	Medium Risk
	Chromatography: Cation Exchange	Blockage	Medium Risk
	Chromatography: Hydrophobic Interaction	Blockage	Medium Risk
	Steam Boiler	Burn risk	Low Risk
		Blockage leading to overpressure	Medium Risk



Consequence Category	Considerations		
	Health / Safety	Environmental Impact	Economic Impact
I	Fatality / serious impact on public	Large Community	greater than $500 Million
II	Serious Injury to Personnel / Limited Impact on Public	Small Community	$100 to $500 million
III	Medical Treatment for Personnel / No Impact on Public	Minor	$10 to $100 Million
IV	Minor Impact on Personnel	Minimal to None	less than $10 million

***Figure 14**: Preliminary Design Risk Rank Matrix*

Interaction Matrix

In this process, a variety of chemicals are used for a variety of reasons. Chemical reactivity poses a threat to any process that contains chemicals that can mix and react with each other. This process contains inherently dangerous and reactive chemicals that can potentially react dangerously with each other. Table 25 is an interaction matrix for this design [47]. All of the chemical species in the process are included around the outside of the table. The cells inside the table describe the interaction between the species on the outside. This is useful to see the potential hazards that the process may contain if streams mix. For this process oxygen, ammonium sulfate, and hydrochloric acid are the most dangerous materials as they are incompatible with most of the other species present. The interaction matrix below contains all of the reaction information for each of the species present.

Table 25: *Chemical Interaction Matrix*

Potential Consequence Summary

Potential consequences are ranked based upon the immediate impact in Table 26.

***Table 26**: Potential Consequence Summary*

	Hazard	Equipment Damage	Environmental Compliance	Loss of Life	Disruption of Other Business Units	Legal/PR	Community Impact
1	Build up of inert gas in bioreactor	Low	None	Medium (OSHA breathing air requirements)	Medium (Too much inert gas stunts cell growth)	Low	None
2	Skin irritants	Low	None	None	None	Low	Low if allowed into sewage
3	Inhalation Hazard	Low	Low	Medium (OSHA breathing air requirements)	None	Low	None
4	Column Over-pressure	High	None	None	High	None	None
5	Pump loses contain-ment	High	None	None	High	None	None

Safety Assessment Summary

1. **Potential project termination**
    - After considering the aforementioned safety concerns in the hazard analyses, none of said concerns have high enough risk levels to warrant a project shutdown due to safety concerns.

2. **Major concerns requiring significant attention**
    - Dust inhalation hazard
    - If the waste line to sewage is out of the pH range requirements, a massive amount of materials will be put into the sewage line. Large environmental consequences could result in significant fines as well.

3. **Specific concerns - PSM related**

- Total employee participation in PSM practices and mindset is vital to maintaining a safer work environment. The facility will benefit if one hundred percent of employees participate in every required training, go about their work days while keeping PSM in mind and maintain good practicing integrity. Training will include the initial training as well as refresher training to keep employees up-to-date and in compliance with PSM.
- Process Hazard Analysis (PHA) is an integral part of PSM. They should be conducted regularly and identified hazards should be assessed and mitigated in a timely manner.
- Pre-Startup Safety Review (PSSR) for equipment will need to be handled very carefully and meticulously. With so many batch style pieces of equipment, PSSRs will be used daily. PSSRs will need to be reviewed and updated regularly to avoid miscommunication that could result in improper use of process equipment.
- Hot work will not be conducted on a regular basis in this facility. Typically, it should only be required in some instances of maintenance and repair. Regardless, hot work permits and procedures should be in place for the times it is needed.

4. **Specific concerns - RMP related**
    - If viral inactivation is not carried out to its fullest extent as designed, potential harm to the community end users and large regions could receive ineffective or harmful drugs.
    - HCl vapor release to the environment and surrounding communities is a significant environmental concern relating to the facilities relationship with the surrounding area.

Siting and Layout of Processes and Equipment

The FDA requires that the building have enough room for cleaning, maintenance, and proper operations. Enough space with defined areas must be designed in order to not mix up the different components. The layout must also flow in order to minimize contamination.

All chemical compounds used or stored on site must have appropriate labels and Safety Data Sheets (SDS) available. This provides a layer of protection against misidentification of materials and improper cleaning or response to exposure. Storage of chemicals relevant to this design must be categorized and separated based on properties. The following categories of chemicals must have their own storage areas:

- Inorganic salts (chlorides and phosphates)
- Inorganic corrosive bases that are dry (Dry Hydroxides and Carbon)
- Non-metal corrosive acid (Hydrochloric acid)

These separate storage containers will be dry, flame and tamper proof. Also, it is good practice to store all compounds at eye level with labels facing out for ease of identification and transportation. Benefits of storing these categories of compounds separately include ease of

identification, separation of potentially reactive mixtures, and simplification of spill cleaning procedures. Mixtures of compounds that are alike are easier to properly clean than differing compound mixtures [48].

The media preparation equipment will need to be in its own room due to dust hazards and the contamination threat it poses. The large vessels used in this area for media preparation will have pumps to deliver media to the bioreactors in a separate room.

OTHER IMPORTANT CONSIDERATIONS

HAZOP

The team performed a preliminary design HAZOP in order to account for and assess the potential consequences and probability of hazards to personnel and equipment. Safeguards and actions to be taken in the event of such a deviation were also considered. This HAZOP is detailed in Table 27 below.

***Table 27**: Preliminary Design HAZOP* [49]

Item	Deviation	Possible Causes	Consequences	Safeguards	Actions
1	Vent System Failure	Outlet blockage, motor failure	Build up of inert gas	Have additional venting systems and backup motors	Regular inspections of venting system
2	Unbalanced Centrifuge	Insufficient training / user error	Biological sample release, high-speed impact risk	Secondary containment of centrifuge during operation	Frequent training and procedural checklist
3	Caustic chemical exposure	Spill during buffer preparation or in kill tanks	Corrosive material, skin and eye irritant	PPE, available drainage	Frequent training and procedural checklist
4	Loss of biological containment in seed train	Loss of seal, spill during transportation	Spoiled Product, personnel exposure	Largest process steps do not require unloading out of process flow	Regular inspection of seals.

MANUFACTURING/OPERATION COSTS

Raw Materials

In order to estimate the annual manufacturing costs of the project facility, it was important to summarize the total raw materials costs incurred annually. Raw materials included chemicals used for buffer and media preparation, CHO cells, disposable inoculation equipment, freezer storage bags, and other miscellaneous chemicals introduced into the process. Table 28 below summarizes the total raw materials amounts and costs for the first half-year of the project and in every year after that.

Table 28: Raw Materials Summary

Raw Materials											
Buffer	kg/batch	Material	Fraction	Unit	ch	Unit/2020	Unit/2021+	$/Unit		$/2020	$/2021+
Prot A Equil	2507.54	EDTA Disodium	0.002	kg	4.2	75.7	214.5	$	197.00	$ 14,911.44	$ 42,249.09
		Sodium Phosphate	0.004	kg	10.3	184.6	522.9	$	44.40	$ 8,194.46	$ 23,217.64
		Tris Base	0.002	kg	4.9	88.7	251.3	$	158.00	$ 14,013.29	$ 39,704.31
		Tris HCl	0.006	kg	14.8	266.1	754.0	$	123.88	$ 32,966.97	$ 93,406.42
Prot A Wash	4146.36	Guanidinium Chloride	0.036	kg	149.5	2691.8	7626.9	$	73.60	$ 198,119.56	$ 561,338.74
		Tris Base	0.002	kg	8.2	147.2	417.0	$	158.00	$ 23,254.31	$ 65,887.22
		Tris HCl	0.006	kg	24.5	441.5	1251.0	$	123.88	$ 54,697.68	$ 154,976.75
Prot A Elution	8218.88	Acetic Acid	0.006	kg	49.3	887.6	2515.0	$	85.30	$ 75,715.61	$ 214,527.56
Prot A Regen	4999.82	Sodium Chloride	0.019	kg	97.0	1746.6	4948.6	$	22.24	$ 38,843.65	$ 110,057.02
		Tris base	0.005	kg	24.3	436.7	1237.2	$	158.00	$ 68,992.96	$ 195,480.04
		Tris HCl	0.015	kg	72.8	1309.6	3710.6	$	123.88	$ 162,237.32	$ 459,672.40
IEX Equil	1405.42	Potassium Chloride	0.000002	kg	0.00281	0.1	0.1	$	169.00	$ 8.55	$ 24.23
		Potassium Di-hydrogen phosphate	0.000002	kg	0.00281	0.1	0.1	$	82.54	$ 4.18	$ 11.83
		Sodium Chloride	0.009	kg	12.6	227.7	645.1	$	22.24	$ 5,063.56	$ 14,346.75
		Sodium HydroPhosphate	0.001	kg	1.5	27.8	78.8	$	76.84	$ 2,138.25	$ 6,058.38
IEX Wash	2344.71	Potassium Chloride	0.000002	kg	0.0	0.1	0.2	$	169.00	$ 14.27	$ 40.42
		Potassium Di-hydrogen phosphate	0.000002	kg	0.0	0.1	0.2	$	82.54	$ 6.97	$ 19.74
		Sodium Chloride	0.018	kg	42.2	759.7	2152.4	$	22.24	$ 16,895.42	$ 47,870.35
		Sodium HydroPhosphate	0.001	kg	2.6	46.4	131.5	$	76.84	$ 3,567.32	$ 10,107.40
IEX Elute	4806.07	Sodium Chloride	0.018	kg	87.9	1582.8	4484.5	$	22.24	$ 35,200.88	$ 99,735.83
		Sodium Di-hydrogen Phosphate	0.001	kg	4.4	79.2	224.3	$	82.54	$ 6,533.53	$ 18,511.68
HIC Equil	2001.94	Sodium Chloride	0.196	kg	392.4	7062.8	20011.4	$	22.24	$ 157,077.66	$ 445,053.36
		Sodium HydroPhosphate	0.003	kg	6.2	111.7	316.5	$	76.84	$ 8,583.66	$ 24,320.38
HIC Wash	3336.56	Sodium Chloride	0.100	kg	332.5	5985.6	16959.3	$	22.24	$ 133,120.38	$ 377,174.40
		Sodium HydroPhosphate	0.003	kg	10.6	191.0	541.3	$	76.84	$ 14,679.88	$ 41,592.99
HIC Elute	6452.78	Sodium Chloride	0.039	kg	252.7	4548.3	12886.9	$	22.24	$ 101,154.62	$ 286,604.77
		Sodium HydroPhosphate	0.003	kg	18.5	333.2	944.2	$	76.84	$ 25,605.74	$ 72,549.59
		Ammonium Sulfate	1	kg	102.13	1838.3	5208.6	$	53.28	$ 97,946.76	$ 277,515.81
		Polysorbate 80	1	kg	3.47	62.5	177.0	$	264.22	$ 16,503.18	$ 46,759.01
		Tri-n-butyl Phosphate	1	kg	1.16	20.9	59.2	$	354.37	$ 7,399.25	$ 20,964.53
		Sodium Hydroxide	1	kg	280	5046	14297	$	53.00	$ 267,441.50	$ 757,750.91
		Hydrochloric Acid	1	kg	615	11063	31345	$	21.64	$ 239,376.87	$ 678,234.45
		Sodium Chloride	1	kg	136	2454	6953	$	22.24	$ 54,579.63	$ 154,642.28
		BalanCD (Inoc Sltn)	1	kg	462	8319	23572	$	43.37	$ 360,821.91	$ 1,022,328.75
		Feed 4 Media (Rxn Feed)	1	kg	355	6383	18084	$	173.66	$ 1,108,408.21	$ 3,140,489.94
		Freezer bags (12L)	-	Bags	21.7	391.0	1108.0	$	455.26	$ 178,006.66	$ 504,428.08
		Air Cartridge Filter	-	Cartridge	-	1	2	$	4,196.07	$ 4,196.07	$ 8,392.14
		CHO Cells	-	Vials	1	18	51	$	729.00	$ 13,122.00	$ 37,179.00
		T-Flask 1	-	Flask	1	18	51	$	1.99	$ 35.90	$ 101.72
		T-Flask 2	-	Flask	1	18	51	$	3.56	$ 64.07	$ 181.52
		Roller Bottle	-	Bottle	1	18	51	$	19.50	$ 351.08	$ 994.73
		Cell Bag	-	Bags	1	18	51	$	430.36	$ 7,746.48	$ 21,948.36
Total Raw Material Cost										$3,557,601.66	$10,076,450.51

Utilities

Another major manufacturing cost are the utilities purchased on an annual basis: sewer, potable water, and electricity. Sewer costs are $0.05/gallon, potable water costs are $0.543/1000 liters, and electricity costs are $0.05/kW-hr. Utility consumption and costs are summarized in Tables 11, 12, and 13 in the Utility Requirements section of the report. The total utility costs incurred annually is $247,778.

Labor Costs

Along with utility and raw materials costs, generally the next most significant manufacturing cost is the cost of labor. In order to determine labor costs, we first needed to determine the total number of operator positions required for the facility at any one point in time. In order to estimate this, we utilized the Equipment Module Approach as outlined in *Analysis, Synthesis, and Design of Chemical Processes* and shown in Figure 15 below.

$$N_{OL} = (6.29 + 31.7P^2 + 0.23N_{np})^{0.5}$$

Figure 15: Equipment Module Approach Equation

In the equation, P represents the number of particulate solid handling steps and N_{np} represents the number of non-particulate processing steps. It was determined that P is equivalent to 40 while N_{np} is 13. However, according to the West Virginia University Department of Chemical Engineering, one should set P equal to zero if it is greater than two and now add P to the new N_{OL} value [50]. Utilizing this guideline, we determined N_{OL} to be 43.05. Assuming a 24-hour operating facility and that 4.5 operators are required for each position, this means there are 194 operators needed for the new facility. According to the Bureau of Labor Statistics, in the Pharmaceuticals and Medicine Manufacturing field, the annual mean wage for a Plant and System Operator is $51,280. With this known, we find our annual labor costs to be $9.95 million.

Other Manufacturing Costs

Outside of the three main categories of manufacturing costs already discussed, others include supervisory labor, lab costs, maintenance and repairs, local taxes and insurance, overhead costs, supplies, and administration costs. These other manufacturing costs are summarized with raw materials, utilities, and operating labor in Table 29 to give a summary of total manufacturing costs for the project. Taking all of these costs into account, the total annual operating cost for the project is $34.9 million.

Table 29: Manufacturing Costs

Cost Item	Multiplying Factor	Annual Cost
Direct Manufacturing Cost		
Raw Materials	C_{RM}	$ 10,076,450.51
Utilities	C_{UT}	$ 247,777.82
Operating Labor	C_{OL}	$ 9,948,320.00
Direct Supervisory and Labor	$0.18*C_{OL}$	$ 1,790,697.60
Maintenance and Repairs	0.06*Fixed Capital Investment (FCI)	$ 1,057,083.37
Operating Supplies	0.009*FCI	$ 158,562.51
Lab Charges	$0.15*C_{OL}$	$ 1,492,248.00
Fixed Manufacturing Costs		
Local Taxes and Insurance	0.032*FCI	$ 563,777.80
Plant Overhead Costs	$0.708*C_{OL}+0.036*FCI$	$ 7,677,660.58
General Manufacturing Expenses		
Administration Costs	$0.177*C_{OL}+0.009*FCI$	$ 1,919,415.15

ECONOMIC ANALYSIS

Revenue

There is not currently a standard market sales price for mAb products. Figure 16 compares the revenue per kilogram of production for different mAb derived pharmaceuticals and other similar pharmaceuticals. The estimated mAb sales price was determined by averaging these values, minus Humira which was an outlier. The estimated sales price for this project is $4.6 million/kg of mAb. This value is necessary to determine the annual revenue of the project. The effects of any error in this estimation are addresses in the following economic analyses. The annual revenue for this project is $6.96 billion.

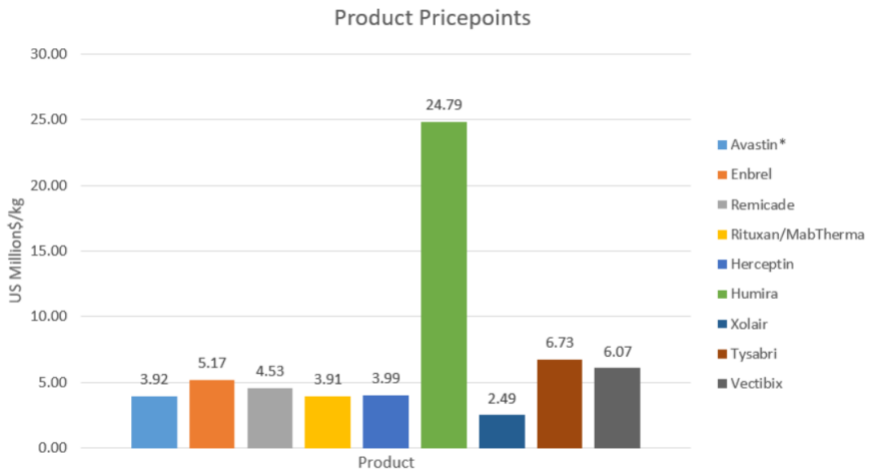


Figure 16: Sales Price of Various mAb Derived Pharmaceuticals

DCFROR and NPV Analysis

In order to evaluate the economic feasibility of the project, the discounted cash flow rate of return as well as the net present value were the primary metrics utilized. The following economic parameters were assumed in order to calculate the DCFROR and NPV for the project.

Project Life was assumed to be 25 years. All capital expenses are incurred during 2019. Production begins during mid-2020 and continues through 2045. NPV and DCFROR are based upon this assumed life of the project.

The Minimum Rate of Return was assumed to be 15% for the project. In order for the mAb production facility to be economically feasible, the project's DCFOR would need to be greater than 15%. When calculating net present value, this minimum rate of return was also utilized.

Tax Rate for the project is known to be 21%, as specified by the 2017 tax act (Pub. L. No. 115-97). The 2017 tax act taxes corporation at a flat rate of 21%, down from a previous maximum tax rate of 35% [51].

The MACRS Depreciation Basis for fixed capital investments was determined to be 10 years based on IRS Publication 946. The fixed capital investment can be recovered through tax deductions by the year 2030.

A cash flow table was constructed in order to analyze and evaluate the economic attractiveness of the mAb production facility project. An escalation rate of 2% was assumed and used to escalate all costs and revenues throughout the life of the project. The washout assumption was determined to be not valid, as the amount that costs and revenues increased was not equivalent.

We determined that the NPV of the project is $31.4 billion, and the current dollars DCFROR is 6350%. The NPV is greater than zero and the DCFROR is greater than the minimum DCFROR of 15%, thus the project is determined to be economically attractive.

Payback Period Analysis

Based off the cash flow table, the discounted payback period for the project was determined to 0.0185 years or 6.78 days. This means that as long as the facility operates for one week then it will make back all of its initial capital investment. However, it is known that it will actually take 51 days for the first batch of mAb to be produced. Only after this period will there be any product with which to create revenue. Thus, a more realistic payback period on the initial capital investment for the project is 51 days.

Optimization Analysis

A major consideration the preliminary design team made during the course of the design formulation was whether to buy Water for Injection for the process or to design a system to purify potable water and make our own WFI. Both designs were performed and an economic analysis on both options was performed for comparison. The comparison of buying and making the WFI is presented in Table 30 below.

Table 30: Economic Comparison between Buying and Making WFI

Parameter	Buying WFI	Making WFI	Incremental (Make-Buy)
Capital Investment	$13,212,739.50	$ 17,618,056.19	-
Annual Operating Costs	$46,497,275.90	$ 34,931,993.34	-
NPV @ ROR_{min}	$31,319,557,722.84	$ 31,367,659,455.95	$48,296,449.17
Today's Dollars DCFROR	74.4	63.5	0.9

One can see that the economic parameters when comparing the two options do not paint a simple black and white picture. If the facility buys its own WFI, this imposes a greater capital investment on the project as expected, due to the additional equipment required to purify the potable water. However, the annual operating costs are significantly increased if it buys its WFI, due to the additional raw material costs. The DCFROR of buying the WFI is over 1000 percentage points greater than when making your own WFI, but the NPV when making WFI is almost $50 million greater than buying it over the course of the 25-year project. In order to determine definitively the best option, the team performed an incremental analysis on the scenarios. Subtracting the buy option from the make option, one can see that the NPV of $48 million is still greater than zero and the DCFROR of 90% is greater than the minimum DCFROR if 15%. Thus, it is confirmed that making WFI is a more economically attractive option than buying it.

A cash flow table summarizing the revenues and expenses incurred during every year of the project life is included as Table 31 on the next page.

Cash Flow Table

Table 31

		0	1	2	3	4	5	6	7	8	9	10	11	12	13
End of Year	2019	2020 (mid year)	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
Production, (kg)		532.87	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81
x Sales Price, $/"unit"		4,692,000.00	4,784,000.00	4,876,000.00	4,968,000.00	5,060,000.00	5,152,000.00	5,244,000.00	5,336,000.00	5,428,000.00	5,520,000.00	5,612,000.00	5,704,000.00	5,796,000.00
Sales Revenue		2,500,245,869.60	7,222,926,734.40	7,361,829,171.60	7,500,751,608.80	7,639,654,046.00	7,778,556,483.20	7,917,458,920.40	8,056,361,357.60	8,195,263,794.80	8,334,166,232.00	8,473,068,669.20	8,611,951,106.40	8,750,853,543.60
+ Salvage Value	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
- Royalties (basis)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Net Revenue	0.00	2,500,245,869.60	7,222,926,734.40	7,361,829,171.60	7,500,751,608.80	7,639,654,046.00	7,778,556,483.20	7,917,458,920.40	8,056,361,357.60	8,195,263,794.80	8,334,166,232.00	8,473,068,669.20	8,611,951,106.40	8,750,853,543.60
- Raw Materials Costs	0.00	(3,628,753.69)	(10,479,508.53)	(10,681,037.54)	(10,882,566.55)	(11,084,095.56)	(11,285,624.57)	(11,487,153.58)	(11,688,682.59)	(11,890,211.60)	(12,091,740.61)	(12,293,269.62)	(12,494,798.63)	(12,696,327.64)
- Other Op Costs	0.00	(12,639,264.78)	(25,849,764.54)	(26,346,875.40)	(26,843,986.25)	(27,341,097.11)	(27,838,207.96)	(28,335,318.82)	(28,832,429.68)	(29,329,540.53)	(29,826,651.39)	(30,323,762.25)	(30,820,873.10)	(31,317,983.96)
- Depreciation	0.00	(1,761,805.62)	(3,171,250.12)	(2,537,000.09)	(2,029,600.07)	(1,624,384.78)	(1,298,450.74)	(1,153,982.68)	(1,153,982.68)	(1,155,744.49)	(1,153,982.68)	(577,872.24)		0.00
- Amortization	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
- Depletion	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
- Loss Forward	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
- Writeoff	0.00	0.00	0.00	0.00	0.00	(591,475.20)		(12,938,142.00)	(650,622.72)	0.00	0.00	(686,111.23)	(14,490,719.04)	0.00
Taxable Income	0.00	2,482,214,045.51	7,183,426,211.22	7,322,264,258.57	7,460,975,455.92	7,598,992,993.35	7,738,114,199.92	7,863,524,323.52	8,014,015,639.95	8,152,868,298.18	8,291,073,857.32	8,429,167,853.86	8,554,144,715.62	8,706,859,232.00
- Tax @ 21%	0.00	(521,264,949.58)	(1,508,519,504.36)	(1,537,675,494.30)	(1,566,804,845.74)	(1,595,788,528.60)	(1,625,003,981.98)	(1,651,340,107.90)	(1,682,943,284.39)	(1,712,102,342.62)	(1,741,125,510.04)	(1,770,125,207.31)	(1,796,370,390.28)	(3,047,393,731.20)
Net Income	0.00	1,960,949,095.93	5,674,906,706.86	5,784,588,764.27	5,894,170,610.18	6,003,204,464.75	6,113,110,217.94	6,212,184,215.62	6,331,072,355.55	6,440,765,955.56	6,549,948,347.28	6,659,042,646.55	6,757,774,325.34	5,659,465,500.80
+ Depreciation	0.00	1,761,805.62	3,171,250.12	2,537,000.09	2,029,600.07	1,624,384.78	1,298,450.74	1,153,982.68	1,153,982.68	1,155,744.49	1,153,982.68	577,872.24	0.00	0.00
+ Amortization	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
+ Depletion	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
+ Loss Forward	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
+ Writeoff	0.00	0.00	0.00	0.00	0.00	591,475.20	0.00	12,938,142.00	650,622.72	0.00	0.00	686,111.23	14,490,719.04	0.00
- Working Capital	(13,529,617.20)				0.00	(650,622.72)	0.00	(14,490,719.04)	(686,111.23)	0.00	0.00	(721,599.74)	(16,043,296.08)	0.00
- Fixed Capital	(17,818,056.19)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Escalation Factor	1.00	1.02	1.04	1.06	1.08	1.10	1.12	1.14	1.16	1.18	1.20	1.22	1.24	1.26
Cash Flow	(31,347,673.39)	1,962,710,901.57	5,678,077,956.98	5,787,125,764.36	5,896,200,210.25	6,004,769,702.01	6,114,408,668.68	6,211,785,621.06	6,332,190,849.71	6,441,921,700.05	6,551,102,329.96	6,659,504,830.28	6,756,221,348.30	5,659,465,500.80
Discounted factor (P/F i*,n)	1.00	0.85	0.73	0.62	0.53	0.46	0.39	0.33	0.28	0.24	0.21	0.18	0.15	0.13
Discounted Cash Flow	(31,347,673.39)	1,677,530,685.10	4,147,912,891.36	3,613,310,933.64	3,146,507,526.59	2,738,842,428.30	2,383,632,464.72	2,069,758,255.30	1,803,296,342.67	1,567,987,824.55	1,362,874,186.36	1,184,138,975.95	1,026,770,906.14	735,119,053.62

NPV @ i*	51,367,659,455.95	Minimum ROR
Escalated DCFROR	64.8	0.17
Today's Dollars DCFROR	63.5	0.15

	14	15	16	17	18	19	20	21	22	23	24	25	26
End of Year	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045
Production, (units)	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81	1,509.81
x Sales Price, $/"unit"	5,888,000.00	5,980,000.00	6,072,000.00	6,164,000.00	6,256,000.00	6,348,000.00	6,440,000.00	6,532,000.00	6,624,000.00	6,716,000.00	6,808,000.00	6,900,000.00	6,992,000.00
Sales Revenue	8,889,755,980.80	9,028,658,418.00	9,167,560,855.20	9,306,463,292.40	9,445,365,729.60	9,584,268,166.80	9,723,170,604.00	9,862,075,041.20	10,000,975,478.40	10,139,877,915.60	10,278,780,352.80	10,417,682,790.00	10,556,585,227.20
+ Salvage Value	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
- Royalties (basis)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Net Revenue	8,889,755,980.80	9,028,658,418.00	9,167,560,855.20	9,306,463,292.40	9,445,365,729.60	9,584,268,166.80	9,723,170,604.00	9,862,075,041.20	10,000,975,478.40	10,139,877,915.60	10,278,780,352.80	10,417,682,790.00	10,556,585,227.20
- Raw Materials Costs	(12,897,856.65)	(13,099,385.66)	(13,300,914.67)	(13,502,443.68)	(13,703,972.69)	(13,905,501.70)	(14,107,030.71)	(14,308,559.72)	(14,510,088.73)	(14,711,617.74)	(14,913,146.75)	(15,114,675.76)	(15,316,204.77)
- Other Op Costs	(31,815,094.82)	(32,312,205.67)	(32,809,316.53)	(33,306,427.39)	(33,803,538.24)	(34,300,649.10)	(34,797,759.96)	(35,294,870.81)	(35,791,981.67)	(36,289,092.53)	(36,786,203.38)	(37,283,314.24)	(37,780,425.09)
- Depreciation	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
- Amortization	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
- Depletion	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
- Loss Forward	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
- Writeoff	(721,599.74)	0.00	0.00	(16,800,384.34)	0.00	0.00	(792,576.77)	0.00	(17,337,110.28)	(828,065.28)	0.00	0.00	(20,393,520.58)
Taxable Income	8,844,321,429.59	8,983,246,826.66	9,121,450,624.00	9,242,854,036.99	9,397,858,218.66	9,536,062,016.00	9,673,475,236.56	9,812,469,610.66	9,933,336,297.72	10,088,049,140.05	10,227,081,002.66	10,365,284,800.00	10,483,095,078.75
- Tax @ 35%	(3,095,512,500.36)	(3,144,136,389.33)	(3,192,507,718.40)	(3,234,998,912.95)	(3,289,250,376.53)	(3,337,621,705.60)	(3,385,715,632.80)	(3,434,364,363.73)	(3,476,667,704.20)	(3,530,817,199.02)	(3,579,478,350.93)	(3,627,849,680.00)	(3,669,083,276.86)
Net Income	5,748,808,929.23	5,839,110,437.33	5,928,942,905.60	6,007,855,124.05	6,108,607,842.13	6,198,440,310.40	6,287,757,603.77	6,378,105,246.93	6,456,668,593.52	6,557,231,941.03	6,647,602,651.73	6,737,435,120.00	6,814,011,799.89
+ Depreciation	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
+ Amortization	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
+ Depletion	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
+ Loss Forward	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
+ Writeoff	721,599.74	0.00	0.00	16,800,384.34	0.00	0.00	792,576.77	0.00	17,337,110.28	828,065.28	0.00	0.00	20,393,520.58
- Working Capital	(757,088.26)	0.00	0.00	(18,129,687.05)	0.00	0.00	(828,065.28)	0.00	(18,630,924.48)	(863,553.79)	0.00	0.00	(899,042.30)
- Fixed Capital	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Escalation Factor	1.28	1.30	1.32	1.34	1.36	1.38	1.40	1.42	1.44	1.46	1.48	1.50	1.52
Cash Flow	5,748,775,440.72	5,839,110,437.33	5,928,942,905.60	6,006,525,821.33	6,108,607,842.13	6,198,440,310.40	6,287,722,115.25	6,378,105,246.93	6,455,374,779.32	6,557,196,452.52	6,647,602,651.73	6,737,435,120.00	6,833,506,278.16
Discounted factor (P/F i*,n)	0.11	0.09	0.08	0.07	0.06	0.05	0.04	0.04	0.03	0.03	0.02	0.02	0.02
Discounted Cash Flow	638,223,996.26	554,062,507.44	480,843,201.72	416,354,917.79	361,996,792.20	313,870,898.21	272,129,801.56	235,932,942.80	204,095,064.57	177,191,700.10	153,533,931.35	132,998,901.03	115,295,190.80

Table 31

Single Variable Sensitivity Analysis

Single variable sensitivity analysis is a qualitative economic evaluation of risk, performed by altering economic variables individually to see how the discounted cash flow rate of return (DCFROR) will be react. The analysis evaluates the parameter uncertainty and how it correlates to the project's viability. The analysis does not account for probability or variation so the analysis was done for years 2-25.

The uncertainty of the sales price ($/kg), annual profit, raw material or feed cost, and capital cost are analyzed. These parameters cause the most economic uncertainty, best predict the viability of the project, and account for the largest variability in the project's overall economics. The project life is assumed to be 25 years, and the capital cost estimates are preliminary estimations. The analysis will indicate where future focus or investments are best utilized.

The economic analysis provides a DCFROR of 6345.8%. The percent change in predictions is a form of statistical analysis that is used to find the variation in the parameters and degree of confidence. The sales price range of confidence is ± 20% and the fixed capital cost ranges from and -20% to 50%. Annual profit is ± 40% and raw materials ranges from -10% to 30%. A summary of the sensitivity analysis of the four parameters are shown throughout Tables 32-36.

In the sensitivity analysis, some assumptions are made. The key assumptions is that the isolated variable is the only value that changes and all other factors are constant. Another assumption is that production remains constant and therefore profit is constant (except when the sales price was varied).

Table 32: *Sales Price Calculations for Tornado Chart*

Sales Price (US Million$/kg)	% Change in prediction	DCFROR	% Change of DCFROR Prediction
3.68	-20%	51.01	-19.62%
4.6	0.00%	63.46	0.00%
5.52	20%	75.90	19.61%

Table 33: *Fixed Capital Investment Calculations for Tornado Chart*

Fixed Capital Investment	% Change in prediction	DCFROR	% Change of DCFROR Prediction
$(14,094,444.96)	-20%	71.34	12.42%
$(17,618,056.19)	0%	63.46	0.00%
$(21,141,667.43)	20%	57.18	-9.89%
$(31,712,501.15)	50%	49.84	-21.47%

Table 34: *Annual Profit Calculations for Tornado Chart*

Annual Profit	% Change in prediction	DCFROR	% Change of DCFROR Prediction
$ 3,400,714,074.58	-40%	62.38	-1.69%
$ 4,534,285,432.77	-20%	62.93	-0.84%
$ 5,667,856,790.97	0%	63.46	0.00%
$ 6,801,428,149.16	20%	63.98	0.83%
$ 7,934,999,507.36	40%	64.50	1.64%

Table 35: *Raw Material Investment Calculations for Tornado Chart*

Raw Material Cost	% Change in prediction	DCFROR	% Change of DCFROR Prediction
$ (6,287,705.12)	-10%	63.459	0.0006%
$(10,479,508.53)	0%	63.458	0.00%
$(13,623,361.09)	30%	63.457	0.0018%

Table 36: *Minimum and Maximum Percent Change of DCFROR Prediction*

	Min DCFROR [%]	MAX DCFROR [%]
Sales Price	-19.62%	19.61%
Annual Profit	-1.69%	1.64%
Fixed Capital Investment	-21.47%	12.42%
Raw Material Cost	0.0018%	0.0006%

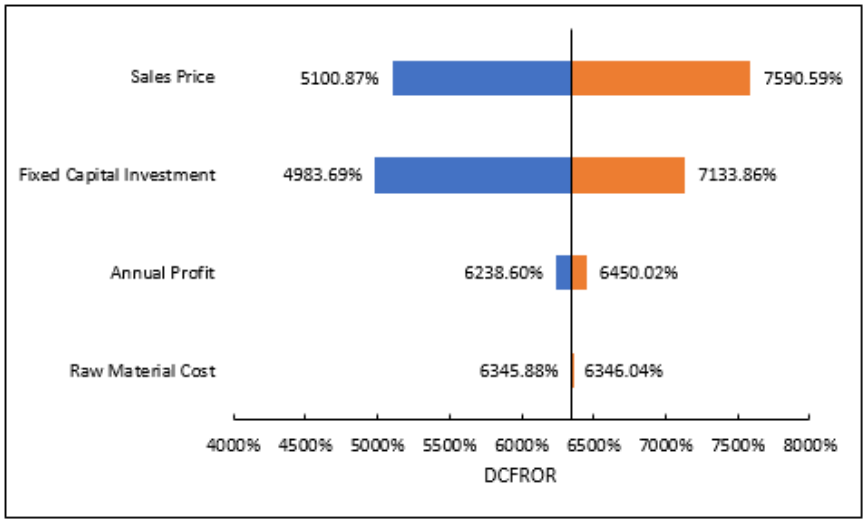


***Figure 17**: Tornado chart representing parameter sensitivities*

The tornado chart shown above in Figure 17 displays the DCFROR variation based off the calculated DCFROR of 6345.8%. The single most sensitive variable was the sales price as the profit is based on low titers sold for high dollars. Even a small change in sales price with drastically impact the profit margin for any given year. The next highest was the fixed capital investment. This impact is due to the cost being incurred at the beginning of the project life as this has a significant effect on the overall profit. This is a significant variable in the project's profitability and is the leading factor in the project's long-term success. The annual profit is not a very sensitive variable because the annual profit is such a large number that fluctuation has a small effect on the margins. The cost of the raw materials has a minimal effect on the viability of the project. The cost of the raw material is minuscule in comparison to the project's annual profit. Therefore, when the raw material price fluctuates, there is little to no effect on the DCFROR.

Break-Even Analysis

Break-even analysis was the final economic analysis that was performed for the project. This analysis is used to determine the value of some variable at which the project becomes profitable. For this project, the break-even sales price of mAb was determined by varying the sales price of mAb ($/kg) until the NPV of the project equals 0. The break-even price was

calculated to be $28,889.25/kg of mAb. As long as the sales price of mAb is above that value, the project will be economically attractive. This value is especially important if this production facility is ever contracted out to other companies. If that is the case, the other companies need to pay at least this price per kg of mAb for the process to be profitable.

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

The proposed design in this report meets the technical requirements for the manufacturing facility proposed by The Company management. Both the required annual production and production titer were fulfilled while also meeting the other specifications set forth in the project statement. The design is capable of producing 1514 kg/yr of mAb (29.6 kg/batch) at a titer of 2 g/L with a 7 day cycle time. Included in the design are a continuous water for injection production system, a full-scale SIP and CIP skid, waste treatment and disposal processes, and an air compression system—everything that is necessary for immediate full-scale production. Facility production can be scaled up by several methods including staggering more units to decrease the cycle time and harvesting the cells from each seed train step at a higher density (increasing the time of each seed train step) as the demand for mAb products grow.

The NPV of the project is $31.4 billion, and the current dollars DCFROR is 6350%. The total capital cost ($17.6 million) and annual operating cost ($34.9 million) are significantly smaller than the annual revenue ($6.96 billion). The payback period is one batch, approximately 51 days, and the break-even sales price is just under $29,000/kg mAb while the average sales price is $4.6 million/kg mAb. Taking all of these economic factors into consideration, this project is very economically attractive.

Analyzing the single variable sensitivity analysis, the mAb sales price and fixed capital investment have the greatest impact on the DCFROR. The analysis also reveals that even under less than optimal conditions, the project is still economically attractive. Incremental analysis comparing making WFI to purchasing WFI indicates that the project is economically attractive under with either method, but making WFI is the more attractive option.

Safety is of the utmost importance in this process because of the biological cultures that are worked with and because the product is being used in pharmaceuticals. The process is designed with a SIP and CIP system that maintains sterile conditions within each process unit. Only water for injection is used in the process and all the air that enters into the process is filtered prior to entering the process. The product stream is virally inactivated in two orthogonal steps and the waste stream is heated with steam and neutralized with acid to make it safe to enter the sewage system. The design was optimized to be inherently safer by preparing hazardous chemicals immediately prior to their use and by operating the centrifuge and chromatography columns in cycles. Both of these design decisions limit the hazard associated with moving and storing large amount of hazardous chemicals.

Overall, the project is both economically attractive and technically feasible. Thus, The Company management should move forward with the proposed project.

Recommendations

- Proceed with the detailed design of this process.
- Explore further reducing the cycle time by adding more staggered equipment. The additional capital costs will be outweighed by the increased revenue.
- Scale up the size of the WFI and SIP/CIP systems as the process is scaled up.
- Test BalanCD Growth A and Feed 4 media with CHO cells to determine the optimal inoculation and harvest densities and other optimal seed train conditions.
- Consider the use of single-use pumps instead of diaphragm pumps.

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Appendices

Appendix A: Economics

Table A.1 : Media Prep Vessel 1 Costing

Media Prep Vessel 1					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.625	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	996	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
4	1.52	1.25	0.792	0.395798588	
Fp	B1	B2			
0.794641763	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$6,402.56		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$4,565.46	$5,387.25	$ 8,920.45
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$6,025.02		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$8,314.53	$ 9,811.14	$ 16,245.74		

Table A.2 : Media Prep Vessel 2 Costing

Media Prep Vessel 2					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.6	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1024	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
20	1.52	1.2	0.664	0.331795907	
Fp	B1	B2			
0.782856092	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$18,310.73		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$12,984.95	$15,322.24	$ 25,371.26
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$5,324.28		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$7,347.51	$ 8,670.06	$ 14,356.28		

Table A.3 : Production Bioreactor Feed Media Prep Vessel Costing

Feed Media Prep Vessel (2X)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.625	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	996	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
4.5	1.52	1.25	0.792	0.395798588	
Fp	B1	B2			
0.794641763	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$6,857.91		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$46,176.86	$54,488.69	$ 90,224.87
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$6,025.02		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$8,314.53	$ 9,811.14	$ 16,245.74		

Table A.4 : Seed Train Equipment Costing

SEED TRAIN					
	batches per yr	OPERATING COSTS TOTAL	$ 8,197.53		
	51				
T-Flask 1					
$$	# in shipment	$$ each	Volume (100mL)	$$ per 2020	$/2021+
398.9	200	$ 1.99	15-38	$ 35.90	$ 101.72
https://www.sigmaaldrich.com/catalog/product/SIGMA/C6481?lang=en&region=US&cm_sp=Insite-_-prodRecCold_xviews-_-prodRecCold5-3					
T-Flask 2					
$$	# in shipment	$$ each	Volume (100mL)	$$ per yr	
427.1	120	$ 3.56	35-52.5	$ 64.07	$ 181.52
https://www.sigmaaldrich.com/catalog/product/SIGMA/C7106?lang=en&region=US&cm_sp=Insite-_-prodRecCold_xviews-_-prodRecCold5-2					
Roller Bottle					
$$	# in shipment	$$ each	Volume (100mL)	$$ per yr	
858.2	44	$ 19.50	1L	$ 351.08	$ 994.73
https://www.sigmaaldrich.com/labware/labware-products.html?TablePage=9577881					
Cell Bag					
$$	# in shipment	$$ each	Volume (100L)	$$ per yr	
430.36	1	$ 430.36	15L	$ 7,746.48	$ 21,948.36
https://ecatalog.corning.com/life-sciences/b2b/NO/en/Bioprocess-and-Scale-up/Single-Use-Technology/Rocker-Cell-Culture-Bags/Corning%C2%AE-Rocker-Cell-Culture-Bags/p/91-200-78					
		CTM in 2019			
Cell Bag Rocker Tray	CB-205	$ 8,405.00			
https://chemglass.com/chemcell-rocker-bioreactor-system-cell-culture-bags?AspxAutoDetectCookieSupport=1					
		CTM in 2019			
Roller Bottle Roller	RB-203	$ 1,460.00			
https://www.thomassci.com/Equipment/Roller-Bottle-Apparatus/_/Bottle/Tube-Roller?q=Roller%20Bottles					
https://www.socalbiomed.com/equipment/rockers-rollers-revolvers/tube-bottle-rollers/stackable-minirollertm-tube-bottle-mixer.html#specification.tab					
10W					

Table A.5 : Seed Culture Reactor Costing

Seed Culture Bioreactor 1 (R-207)					
CBM=Cp0*Fbm				Impeller Diamete	0.026
Volume [m^3]				Power Number	1.8
0.25	From Excel Calc	Diameter (m)		Liquid Density (k	1101
10<P<100 barg		0.052		RPS	0.083333
Jacketed Agitated Reactor 1			Min:0.1 Max:35[m^3]		Power [kW]
K1 (Table A.1)	K2	K3	Cp0		0.0
4.1052	0.532	-0.0005	$ 6,091.48		
Material	Fbm (Table A.7)	CBM	CTM	CTM 2019	
SS	4	$ 24,365.92	$ 28,751.79	$ 47,608.53	
Seed Culture Bioreactor 2 (R-208)					
CBM=Cp0*Fbm				Impeller Diamete	0.75
Volume [m^3]				Power Number	1.8
5	From Excel Calc	Diameter (m)		Liquid Density (k	1101
10<P<100 barg		1.5		RPS	0.0833333
Jacked Agitated Reactor 2			Min:0.1 Max:35[m^3]		Power [kW]
K1 (Table A.1)	K2	K3	Cp0		0.00027
4.1052	0.532	-0.0005	$ 29,978.35		
Material	Fbm (Table A.7)	CBM	CTM	CTM 2019	
SS	4	$ 119,913.41	$ 141,497.82	$ 234,298.58	

Table A.6 : Air Compressor Costing

Air Compressor (C-209)								
CBM=Cp0*FBM								
Design Pressure [barg]	Power Purchased [kW]							
0.703	27.35	30.93						
Compressor (Centrifugal, axial, reciprocating)		Min:450 Max:3000	C1,2,3=0	0.95				
K1 (Table A.1)	K2	K3	Cp0		Chosen CTM			
2.2897	1.3604	-0.1027	$10,776.48		$210,083.33			
Centrifugal								
Material	ID #	FBM (A.6/A.19)	CBM	CTM (2001)	CTM 2019			
SS	2	6.7	$72,202.43	$85,198.87	$141,076.19			
Axial								
Material	ID #	FBM (A.6/A.19)	CBM	CTM (2001)	CTM 2019			
SS	5	8	$86,211.86	$101,730.00	$168,449.19			
Reciprocating								
Material	ID #	FBM (A.6/A.19)	CBM	CTM (2001)	CTM 2019			
SS	11	7	$75,435.38	$89,013.75	$147,393.04			
Rotary	Min:18 Max:950							
K1 (Table A.1)	K2	K3	Cp0					
5.0355	-1.8002	0.8253	$14,216.97					
Material	ID #	FBM (A.6/A.19)	CBM	CTM (2001)	CTM 2019			
SS	8	5	$71,084.86	$83,880.14	$138,892.57			
CBM=Cp0*FBM								
Drive								
Material	ID # (Table A.6)	Fbm (Fig A.19)	K1 (Table A.1)	K2	K3			
Electric-totally enclosed	17	3.5	1.956	1.7142	-0.2282			
Cp0	CBM	limits [kW]	CTM	CTM 2019				
10090.76394	$ 35,317.67	75-2600	$ 41,674.86	$ 69,007.13				

Table A.7 : Air Compressor Knock Out Drum Costing

Air Compressor KO Drum					
CBM=Cp0(B1+B2*Fm*Fp	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
0.053	0.703	0.2286			
Fp	B1	B2			
0.536393497	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$1,259.01		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$6,642.94	$7,838.67	$ 12,979.63
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = 520 r	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$1,667.53		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$6,699.27	$ 7,905.13	$ 13,089.68

Table A.8 : Water Pre-Heater Costing

Purified Water Pre-Heater (HE-811)									
CBM=Cp0(B1+B2*Fm*Fp)		limits:5-140 barg							
Area (m^2)	Op Pressure [barg]	Design Pressure [ba	C1	C2	C3				
77.17363222	62.058	62.058	0.03881	-0.11272	0.08183				
			limits:10-1000						
Fp	B1	B2	K1	K2	K3	Cp0			
1	1.63	1.66	4.1884	-0.2503	0.1974	26,254.98			
Heat Exchanger (tube&shell) (U-tube)									
Material	ID # (Table A.3)	Fm (Fig A.18)	CBM	CTM	CTM 2019				
SS-shell/SS-Tube	5	2.8	164,828.78	$194,497.96	$322,058.62				
		35-70							
Q [Btu/hr]	U [Btu/ft^2*hrF]	T1 (Inlet tube)	T2 (outlet tube	t1 (inlet shell)	t2 (outlet shell	DelTlm [F]	A (ft^2)	A (m^2)	
7.61E+04	2	77	86	192.5	98.6	53.21	714.5706687	77.173632	

Table A.9 : Air filter Costing

Air Cartridge Filter (HE-811)								
Area (m^2)			C1	C2	C3			
10			0.03881	-0.11272	0.08183			
			limits:10-1000					
		Fbm	K1	K2	K3	Cp0	Cbm	CTM
		1.65	3.2107	0.7597	0.0027	9,399.40	15,509.01	18,300.63

Table A.10 : Production Bioreactor Costing

Production Bioreactor (R-301A/B)					
CBM=Cp0*Fbm				Impeller Diamete	1.2315
Volume [m^3]				Power Number	1.8
30		Diameter		Liquid Density (k	1000
10<P<100 barg		2.463		RPS	0.0833333
Fermenter Reactor			Min:0.1 Max:35[m^3]		Power [kW]
K1 (Table A.1)	K2	K3	Cp0		0.00295
4.1052	0.532	-0.0005	77613.55279		
Material	Fbm (Table A.7)	CBM	CTM	CTM 2019	
SS	4	$ 310,454.21	$ 366,335.97	$ 606,595.88	

Table A.11: Production Bioreactor Surge Tank Costing

Production Bioreactor Surge Tank (Tk-303)						
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5					
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute					
Without Demister						
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)				
27.5	1.52	2.3				
Fp	B1	B2				
1.042140843	2.25	1.82				
	min=.1, max = 628	vessel thickness> .25 in				
K1 (Table A.1)	K2	K3	Cp0			
3.4974	0.4485	0.1074	$23,197.38			
Vertical Process Vessel						
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019	
SS	20	3.1	$188,589.13	$222,535.17	$ 368,483.92	
Horizontal Process Vessel						
B1	B2					
1.49	1.52	min=.3, max = !	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0			
3.5565	0.3776	0.0905	$19,385.59			
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019	
SS	20	3.1	$124,078.76	$ 146,412.93	$ 242,437.24	

Table A.12 : Dead-End Filter Costing

Dead-End Filter 1 (F-306)					
CBM=Cp0*Fbm					
Area [m^2]		SuperPro			
230		$ 810,000.00			
10<P<100 barg					
Deadend Plate and Frame Filter			Min:0.5 Max:80[m^2]		
K1 (Table A.1)	K2	K3	Cp0		
4.28	0.352	0.0714	320022.23		
Material	Fbm (Table A.7)	CBM	CTM	CTM 2019	
SS	1.8	$ 576,040.01	$ 679,727.21	$ 1,125,523.46	

Table A.13 : Centrifuge Surge Tank Costing

Centrifuge Surge Tank (Tk-307)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
25	1.52	2.2			
Fp	B1	B2			
1.02	2.25	1.82			
	min=.1, max = 628	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$21,590.42		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$2,929,504.17	$3,456,814.92	$ 5,723,952.48
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = !	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$18,248.22		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$114,772.18	$ 135,431.17	$ 224,253.13

Table A.14 : Centrifuge Costing

Centrifuge (Cf-307)									
Automatic Disc Stack Solid Bowl Centrifuge									
$$ for Unit									
$ 30,000.00									
https://www.alibaba.com/product-detail/Automatic-Disc-Stack-Solid-Bowl-Centrifuge_60830647396.html?spm=a2700.7724857.normalList.32.17523744M489M2									

Table A.15 : Centrifuge Costing 2

CBM=Cp0*Fbm									
Diameter [m]									
1	Super pro doesn't have an area.....								
10<P<100 barg						Energy/cycle	95.6128		
Solid Bowl Centrifuge w/o motor			Min:0.3 Max:2 [m]			Energy/Batch	382.4512	kW-h	
K1 (Table A.1)	K2	K3	Cp0						
4.9697	1.1689	0.0038	93260.98542						
Material	Fbm (Table A.7)	CBM	CTM	CTM 2019					
SS	1.27	$ 118,441.45	$ 139,760.91						
CBM=Cp0*FBM									
Drive									
Material	ID # (Table A.6)	Fbm (Fig A.19)	K1 (Table A.1)	K2	K3	Cp0	CBM	limits [kW]	CTM
Gas Turbine	13	1.5	-21.7702	13.2175	-1.5279	1.69746E-22	$ 0.00	7500-23000	$ 0.00
Intern. Comb. Engine	14	1.5	2.7635	0.8574	-0.0098	580.0961725	$ 870.14	10-10,000	$ 1,026.77
Steam Engine	15	1.5	2.6259	1.4398	-0.1776	422.5713024	$ 633.86	70-7500	$ 747.95
Electric-explosion-proof	16	3.5	2.4604	1.4191	-0.1798	288.6689018	$ 1,010.34	75-2600	$ 1,192.20
Electric-totally enclosed	17	3.5	1.956	1.7142	-0.2282	90.36494737	$ 316.28	75-2600	$ 373.21
Electric-open/drip-proof	18	2	2.9508	1.0688	-0.1315	892.8941961	$ 1,785.79	75-2600	$ 2,107.23
https://www.alibaba.com/product-detail/Automatic-Disc-Stack-Solid-Bowl-Centrifuge_60830647396.html?spm=a2700.7724857.normalList.32.17523744M489M2									

Table A.16 : Protein A Buffer Prep Vessel 1 Costing

Protein A Buffer Prep Vessel 1 (V-401)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.625	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1002.3	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
3	1.52	1.25	0.797	0.39830213	
Fp	B1	B2			
0.794641763	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$5,442.99		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$36,649.69	$43,246.64	$ 71,609.76
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$6,051.71		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$8,351.36	$ 9,854.60	$ 16,317.70		

Table A.17 : Protein A Buffer Prep Vessel 2 Costing

Protein A Buffer Prep Vessel 2 (V-402)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.75	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	999	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
5	1.52	1.5	1.976	0.98784003	
Fp	B1	B2			
0.853570115	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$7,300.61		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$51,584.98	$60,870.27	$ 100,791.79
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$11,437.77		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$15,784.13	$ 18,625.27	$ 30,840.58		

Table A.18 : Protein A Buffer Prep Vessel 3 Costing

Protein A Buffer Prep Vessel 3 (V-403)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.6	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	995	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
10	1.52	1.2	0.645	0.32239934	
Fp	B1	B2			
0.782856092	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$11,305.77		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$75,374.12	$88,941.46	$ 147,273.34
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$5,218.13		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$7,201.01	$ 8,497.19	$ 14,070.04		

Table A.19 : Protein A Buffer Prep Vessel 4 Costing

Protein A Buffer Prep Vessel 4 (V-404)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.5	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1108	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
5	1.52	1	0.289	0.14427949	
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$7,300.61		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$46,730.45	$55,141.94	$ 91,306.54
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$2,969.55		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$4,097.98	$ 4,835.62	$ 8,007.04		

Table A.20 : Protein A Column Costing

Chromatography:Protein A			
Published Price			
Volume [L]	$$		
90	$ 200,000.00		
Estimated Price	6/10th Rule		
Volume [L]	CTM 2003	CTM 2019	
415	$ 500,395.45	$ 828,577.70	

Table A.21 : Dead End Filter 2 Costing

Dead-End Fliter 2 (F-407)				
CBM=Cp0*Fbm				
Area [m^2]				
80				
10<P<100 barg				
Deadend Plate and Frame Filter			Min:0.5 Max:80[m^2]	
K1 (Table A.1)	K2	K3	Cp0	
4.2756	0.352	0.0714	159985.5403	
Material	Fbm (Table A.7)	CBM	CTM	CTM 2019
SS	1.8	$ 287,973.97	$ 339,809.29	$ 562,671.78

Table A.22 : Viral Inactivation Vessel Costing

Viral Inactivation Vessel (V-408)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5			Impeller Diameter (m)	0.5
*vertical for compressors	*should be no less than 10 time the liquid volume pass			Power Number	1.8
Without Demister				Liquid Density (kg/m^3)	995
				RPS	1.6667
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]	Flat Paddle	
2	1.52	1	0.259	0.129565065	
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$4,386.77		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$28,079.23	$33,133.49	$ 54,863.95
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$11,536.25		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$15,920.03	$ 18,785.63	$ 31,106.11		

Table A.23 : Diafiltration Flush Tank 1 Costing

Diafiltration Flush Tank 1 (Tk-410)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
3	1.52	1			
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$5,442.99		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$34,840.04	$41,111.25	$ 68,073.88
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = !	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$5,718.25		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$28,343.52	$ 33,445.36	$ 55,380.36

Table A.24 : Dead End Filter 3 Costing

Dead-End Fliter 3 (F-413)				
CBM=Cp0*Fbm				
Area [m^2]		SuperPro		
80		$ 45,000.00		
10<P<100 barg				
Deadend Plate and Frame Filter			Min:0.5 Max:80[m^2]	
K1 (Table A.1)	K2	K3	Cp0	
4.2756	0.352	0.0714	159985.5403	
Material	Fbm (Table A.7)	CBM	CTM	CTM 2019
SS	1.8	$ 287,973.97	$ 339,809.29	$ 562,671.78

Table A.25 : Viral Inactivation Surge Tank Costing

Viral Inactivation Surge Tank (Tk-414)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
0.5	1.52	0.5			
Fp	B1	B2			
0.617856705	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$2,355.70		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$13,512.19	$15,944.38	$ 26,401.44
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max =	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$2,825.09		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$12,434.18	$ 14,672.33	$ 24,295.12

Table A.26 : Diafilter 1 Costing

Diafilter 1 (F-412)	
$$ Per Unit (14 m^2)	
$ 26,417.00	
# of Units	$$
2	$ 52,834.00

Table A.27 : IEX Buffer Prep Vessel 1 Costing

IEX Buffer Prep Vessel 1 (V-501)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.5	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	999.5	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
2	1.52	1	0.260	0.130151	
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$4,386.77		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$28,079.23	$33,133.49	$ 54,863.95
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$2,762.52		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$3,812.28	$ 4,498.49	$ 7,448.81		

Table A.28 : IEX Buffer Prep Vessel 2 Costing

IEX Buffer Prep Vessel 2 (V-502)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.5	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1004	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
3	1.52	1	0.261	0.130737	
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$5,442.99		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$34,840.04	$41,111.25	$ 68,073.88
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$2,771.24		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$3,824.31	$ 4,512.68	$ 7,472.31		

Table A.29 : IEX Buffer Prep Vessel 3 Costing

IEX Buffer Prep Vessel 3 (V-503)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.625	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1026	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
5.5	1.52	1.25	0.815	0.4077202	
Fp	B1	B2			
0.794641763	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$7,732.55		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$52,066.09	$61,437.99	$ 101,731.83
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$6,151.66		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$8,489.29	$ 10,017.37	$ 16,587.21		

Table A.30 : IEX Buffer Prep Vessel 4 Costing

IEX Buffer Prep Vessel 4 (V-504)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.5	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1023	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
2.75	1.52	1	0.266	0.1332111	
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$5,190.04		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$33,220.87	$39,200.63	$ 64,910.20
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$2,807.91		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$3,874.92	$ 4,572.40	$ 7,571.19		

Table A.31 : IEX Buffer Prep Vessel 5 Costing

IEX Buffer Prep Vessel 5 (V-505)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.375	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1004	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
1.75	1.52	0.75	0.062049011	0.0310245	
Fp	B1	B2			
0.676785058	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$4,099.65		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$24,878.38	$29,356.49	$ 48,609.82
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$1,010.39		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$1,394.34	$ 1,645.33	$ 2,724.40		

Table A.32 : IEX Chromatography Column Costing

IEX Chromatography Column (Cl-507)				
Published Price			SuperPro	
Volume [L]	$$		$$ 2019	
90	$ 200,000.00		$ 635,000.00	
Estimated Price	6/10th Rule			
Volume [L]	CTM 2003	CTM 2019		
250	$ 369,188.78	$ 611,319.69		

Table A.33 : Ammonium Sulfate Vessel Costing

Amm. Sulfate Vessel (V-508)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5			Impeller Diameter (m)	0.375
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute			Power Number	1.8
Without Demister				Liquid Density (kg/m^3)	1066.57
				RPS	1.6667
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]	Flat Paddle	
1.25	1.52	0.75	0.066	0.032957975	
Fp	B1	B2			
0.676785058	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$3,482.35		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$21,132.39	$24,936.21	$ 41,290.53
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$1,054.17		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$1,454.76	$ 1,716.62	$ 2,842.45		

Table A.34 : Diafiltration Flush Tank 2 Costing

Diafiltration Flush Tank 2 (Tk-509)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
2.25	1.52	1			
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$4,663.10		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$29,848.03	$35,220.67	$ 58,320.01
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = 520 m3	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$5,020.06		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$24,882.85	$ 29,361.76	$ 48,618.55

Table A.35 : Diafilter 2 Costing

Diafilter 2 (F-411)	
$$ Per Unit (14 m^2)	
$ 26,417.00	
# of Units	$$
2	$ 52,834.00

Table A.36 : HIC Buffer Prep Vessel 1 Costing

HIC Buffer Prep Vessel 1 (V-601)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.5	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1101	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
2.25	1.52	1	0.287	0.143368	
Fp	B1	B2			
0.736	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$4,663.10		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$29,848.03	$35,220.67	$ 58,320.01
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$2,956.38		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$4,079.81	$ 4,814.18	$ 7,971.53		

Table A.37 : HIC Buffer Prep Vessel 2 Costing

HIC Buffer Prep Vessel 2 (V-602)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.625	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1047	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
3.5	1.52	1.25	0.832	0.4160654	
Fp	B1	B2			
0.795	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$5,932.07		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$39,942.79	$47,132.49	$ 78,044.14
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$6,239.65		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$8,610.72	$ 10,160.65	$ 16,824.47		

Table A.38 : HIC Buffer Prep Vessel 3 Costing

HIC Buffer Prep Vessel 3 (V-603)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.75	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1015	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
7	1.52	1.5	2.007	1.0036613	
Fp	B1	B2			
0.853570115	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$8,976.99		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$63,429.97	$74,847.37	$ 123,935.70
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$11,565.83		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$15,960.85	$ 18,833.80	$ 31,185.87		

Table A.39 : HIC Buffer Prep Vessel 4 Costing

HIC Buffer Prep Vessel 4 (V-604)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.625	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1004	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
3.5	1.52	1.25	0.798	0.3989777	
Fp	B1	B2			
0.795	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$5,932.07		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$39,942.79	$47,132.49	$ 78,044.14
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$6,058.90		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$8,361.28	$ 9,866.32	$ 16,337.10		

Table A.40 : HIC Column Costing

HIC Column (Cl-606)			
Published Price			
Volume [L]	$$		
90	$ 200,000.00		
Estimated Price	6/10th Rule		
Volume [L]	CTM 2003	CTM 2019	
650	$ 654,986.73	$ 1,084,557.03	

Table A.41 : HIC Surge Tank Costing

HIC Surge Tank (Tk-607)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
1.5	1.52	1			
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$3,799.33		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$24,319.12	$28,696.57	$ 47,517.09
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = 520 m3	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$4,224.72		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$20,940.61	$ 24,709.92	$ 40,915.82

Table A.42 : Diafiltration Flush Tank 3 Costing

Diafiltration Flush Tank 3 (Tk-609)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
2.5	1.52	1			
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$4,930.42		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$31,559.07	$37,239.71	$ 61,663.21
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = 520 m3	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$5,261.30		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$26,078.61	$ 30,772.76	$ 50,954.94

Table A.43 : Dead-End Filter 4 Costing

Dead-End Fliter 4 (F-412)				
CBM=Cp0*Fbm				
Area [m^2]		SuperPro		
70		$ 45,000.00		
10<P<100 barg				
Deadend Plate and Frame Filter			Min:0.5 Max:80[m^2]	
K1 (Table A.1)	K2	K3	Cp0	
4.2756	0.352	0.0714	147281.3397	
Material	Fbm (Table A.7)	CBM	CTM	CTM 2019
SS	1.8	$ 265,106.41	$ 312,825.57	$ 517,990.90

Table A.44 : Diafilter 3 Costing

Diafilter 3 (F-412)	
$$ Per Unit (14 m^2)	
$ 26,417.00	
# of Units	$$
2	$ 52,834.00

Table A.45 : Freezer and cryovessel Costing

		# of Freezers		
Freezer	$17,588.24	18	$316,588.32	https://us.vwr.com/store/product/14459968/vwr-ultra-low-temperature-upright-freezers-and-freezer-packages-86-to-50c
Celsius FT100	$125,000.00			http://fedequip.com/inventory/Miscellaneous-Equipment/SARTORIUS-STEDIM-THAW-SYSTEM-MODEL-CELSIUS-FT100.html
				https://www.sartoriusglobal.com/_ui/images/h5f/hdc/8880818421790.pdf

Table A.46 : Waste Holding Tank Costing

Waste Holding Tank (Tk-701)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
125	2	3.75			
Fp	B1	B2			
1.552649308	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$81,302.77		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$895,147.34	$1,056,273.86	$ 1,749,026.63
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = 520 m3	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$55,747.40		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$490,916.22	$ 579,281.14	$ 959,200.24

Table A.47 : Neutralization Vessel Costing

Neutralization Vessel (V-703)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.75	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	995	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
10	2	1.5	1.968	0.983884714	
Fp	B1	B2			
0.921059723	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$11,305.77		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$84,189.73	$99,343.88	$ 164,498.15
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$11,405.66		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$15,739.82	$ 18,572.98	$ 30,754.00		

Table A.48 : Potable Water Holding Tank Costing

Potable Holding Tank (Tk-801)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
5	1.52	1			
Fp	B1	B2			
0.73571341	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$7,300.61		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$46,730.45	$55,141.94	$ 91,306.54
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = 520 m3	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$7,322.27		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$36,294.16	$ 42,827.10	$ 70,915.08

Table A.49 : Dead-End Filter 4 Costing

Dead-End Filter 4 (F-803)				
CBM=Cp0*Fbm				
Area [m^2]				
120				
10<P<100 barg				
Deadend Plate and Frame Filter			Min:0.5 Max:80[m^2]	
K1 (Table A.1)	K2	K3	Cp0	
4.2756	0.352	0.0714	207077.8355	
Material	Fbm (Table A.7)	CBM	CTM	CTM 2019
SS	1.8	$ 372,740.10	$ 439,833.32	$ 728,296.16

Table A.50 : Carbon Absorption Column A/B Costing

Carbon Adsorption Column A/B (Cl-804 A/B)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
0.5	1.52	0.5			
Fp	B1	B2			
0.617856705	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$2,355.70		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$13,512.19	$15,944.38	$ 52,802.88

Table A.51 : Cation Exchange Column Costing

Cation Exchange Column (Cl-805)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
0.25	1.52	0.75			
Fp	B1	B2			
0.676785058	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$1,846.32		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$11,204.22	$13,220.98	$ 21,891.91

Table A.52 : Anion Exchange Column Costing

Anion Exchange Column (Cl-806)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
0.2	1.52	0.5			
Fp	B1	B2			
0.617856705	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$1,723.39		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$9,885.27	$11,664.61	$ 19,314.80

Table A.53 : Ultrafilter Costing

Ultrafilter (F-807)	
$$ Per Unit (14 m^2)	
$ 26,417.00	
# of Units	$$
6	$ 158,502.00

Table A.54 : Reverse Osmosis System Costing

Reverse Osmosis System (F-808)	
Published Price	
Volume [L]	$$
9200	$ 25,295.00
Estimated Price	6/10th Rule
Volume [L]	CTM 2019
11000	$ 28,157.73

Table A.55 : Purified Water Tank Costing

Purified Water Tank (Tk-809)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
2.5	1.52	2.75			
Fp	B1	B2			
1.148211878	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$4,930.42		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$43,033.71	$50,779.78	$ 84,083.49
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = 520 m3	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$5,261.30		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$36,304.97	$ 42,839.86	$ 70,936.20

Table A.56 : Purified Water Pre-Heater Costing

Purified Water Pre-Heater (HE-811)									
CBM=Cp0(B1+B2*Fm*Fp)		limits:5-140 barg							
Area (m^2)	Op Pressure [barg]	Design Pressure [barg]	C1	C2	C3				
0.19471293	62.058	62.058	0.03881	-0.11272	0.08183				
			limits:10-1000						
Fp	B1	B2	K1	K2	K3	Cp0			
1	1.63	1.66	4.1884	-0.2503	0.1974	29,237.72			
Heat Exchanger (tube&shell) (U-tube)									
Material	ID # (Table A.3)	Fm (Fig A.18)	CBM	CTM	CTM 2019				
SS-shell/SS-Tube	5	2.8	183,554.42	$216,594.22	$ 358,646.63				
		35-70							
Q [Btu/hr]	U [Btu/ft^2*hrF]	T1 (Inlet tube)	T2 (outlet tube)	t1 (inlet shell)	t2 (outlet shell)	DelTlm [F]	A (ft^2)	A (m^2)	
9.63E+03	65	201.9	122	72	76.04	82.18	1.8028975	0.19471293	

Table A.57 : WFI Condenser Costing

WFI Condenser (HE-812)									
CBM=Cp0(B1+B2*Fm*Fp)		limits:5-140 barg							
Area (m^2)	Op Pressure [barg]	Design Pressure [barg]	C1	C2	C3				
17.27315736	62.058	62.058	0.03881	-0.11272	0.08183				
			limits:10-1000						
Fp	B1	B2	K1	K2	K3	Cp0			
1	1.63	1.66	4.1884	-0.2503	0.1974	15,167.81			
Heat Exchanger (tube&shell) (U-tube)									
Material	ID # (Table A.3)	Fm (Fig A.18)	CBM	CTM	CTM 2019				
SS-shell/SS-Tube	5	2.8	95,223.49	$112,363.72	$ 186,056.99				
		35-70							
Q [Btu/hr]	U [Btu/ft^2*hrF]	T1 (Inlet tube)	T2 (outlet tube)	t1 (inlet shell)	t2 (outlet shell)	DelTlm [F]	A (ft^2)	A (m^2)	
1.71E+06	120	76.04	223.3	277.1	230	88.89	159.936642	17.2731574	

Table A.58 : Steam Boiler Costing

Steam Boiler (HE-813)									
CBM=Cp0*Fbm*Fp*FT									
Design Pressure [barg]	Duty [kW]	Delta T							
1.25	231	0							
P<20 barg									
Steam Boiler			Min:1200 Max:9400 [kW]					FT: Superheat correction factor for steam boiler	
K1 (Table A.1)	K2	K3	Cp0	C1 (Table A.2)	C2	C3	Fp	FT	
6.9617	-1.48	0.3161	169628.1786	0	0	0	1.00	1	
Tube for nonreactive process heater									
Material	ID # (Table A.6)	Fbm (Fig A.19)	CBM	CTM	CTM 2019				
Stainless Steel	55	2.8	474,958.90	560451.5021	$ 928,021.27				

Table A.59 : Steam Compressor Costing

Steam Compressor (C-814)									
CBM=Cp0*FBM									
Design Pressure [barg]	Power Purchased [kW]								
3.5	75.00								
	9694.0983								
Compressor (Centrifugal, axial, reciprocating)		Min:450 Max:3000	C1,2,3=0	0.95					
K1 (Table A.1)	K2	K3	Cp0		Choosen CTM				
2.2897	1.3604	-0.1027	$30,161.65		$ 554,394.18				
Centrifugal									
Material	ID #	FBM (A.6/A.19)	CBM	CTM (2001)	CTM 2019				
SS	2	6.7	$202,083.04	$238,457.99	$ 394,849.65				
Axial									
Material	ID #	FBM (A.6/A.19)	CBM	CTM (2001)	CTM 2019				
SS	5	8	$241,293.18	$284,725.95	$ 471,462.27				
Reciprocating									
Material	ID #	FBM (A.6/A.19)	CBM	CTM (2001)	CTM 2019				
SS	11	7	$211,131.53	$249,135.21	$ 412,529.49				
Rotary	Min:18 Max:950								
K1 (Table A.1)	K2	K3	Cp0						
5.0355	-1.8002	0.8253	$36,445.98						
Material	ID #	FBM (A.6/A.19)	CBM	CTM (2001)	CTM 2019				
SS	8	5	$182,229.90	$215,031.28	$ 356,058.65				
CBM=Cp0*FBM									
Drive									
Material	ID # (Table A.6)	Fbm (Fig A.19)	K1 (Table A.1)	K2	K3				
Electric-totally enclosed	17	3.5	1.956	1.7142	-0.2282				
Cp0	CBM	limits [kW]	CTM	CTM 2019					
23329.85103	$ 81,654.48	75-2600	$ 96,352.28	$ 159,544.53					

Table A.60 : WFI Storage Tank Costing

WFI Storage Tank (Tk-817)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
100	1.52	1.75			
Fp	B1	B2			
0.912498468	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$66,680.68		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$493,324.74	$582,123.20	$ 963,906.25
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = 520 m3	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$47,173.71		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$273,121.27	$ 322,283.10	$ 533,651.11

Table A.61 : Steam Compressor KO Drum Costing

Steam Compressor KO (Tk-914)					
CBM=Cp0(B1+B2*Fm*Fp)	*L/D= 2.5 to 5				
*vertical for compressors	*should be no less than 10 time the liquid volume passing per minute				
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)			
0.65	3.67	1.1			
Fp	B1	B2			
0.981231557	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$2,613.67		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$20,350.32	$24,013.38	$ 39,762.45
Horizontal Process Vessel					
B1	B2				
1.49	1.52	min=.3, max = 520 m3	vessel thickness> .25 in		
K1 (Table A.1)	K2	K3	Cp0		
3.5565	0.3776	0.0905	$3,083.36		
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$18,850.29	$ 22,243.35	$ 36,831.55

Table A.62 : Caustic Vessel 1 Costing

Caustic Vessel 1 (V-701)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	0.75	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	1004	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
7	1.52	1.5	1.986		
Fp	B1	B2			
0.853570115	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$8,976.99		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$63,429.97	$74,847.37	$ 123,935.70
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$11,477.86		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$15,839.44	$ 18,690.54	$ 30,948.66		

Table A.63 : Caustic Vessel 2 Costing

Caustic Vessel 2 (V-702)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	1	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	997	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
20	1.52	2	8.309		
Fp	B1	B2			
0.97142682	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$18,310.73		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$141,556.42	$167,036.57	$ 276,586.81
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$31,286.13		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$43,174.86	$ 50,946.34	$ 84,359.28		

Table A.64 : Acid Vessel Costing

Acid Vessel (V-703)					
CBM=Cp0(B1+B2*Fm*Fp)			Impeller Diameter (m)	1.25	
*vertical for compressors		Flat Paddle	Power Number	1.8	
*L/D= 2.5 to 5			Liquid Density (kg/m^3)	995	
*should be no less than 10 time the liquid volume passing per minute			RPS	1.6667	
Without Demister					
Min Vessel Volume (m3)	Pressure (barg)	Diameter (m)	Power [kW]		
30	1.52	2.5	25.306		
Fp	B1	B2			
1.089283526	2.25	1.82			
	min=.1, max = 628 m3	vessel thickness> .25 in			
K1 (Table A.1)	K2	K3	Cp0		
3.4974	0.4485	0.1074	$24,786.98		
Vertical Process Vessel					
Material	ID # (Table A.3)	Fm (Fig A.18)	Cbm	CTM	CTM 2019
SS	20	3.1	$208,104.96	$245,563.85	$ 406,615.87
CBM=Cp0*Fm					
Mixers					
Impeller					
K1 (Table A.1)	K2	K3	Cp0		
3.8511	0.7009	-0.0003	$68,237.76		
Fbm (Table A.7)	Cbm	CTM	CTM 2019		
1.38	$94,168.11	$ 111,118.37	$ 183,994.88		

Table A.95 – WFI Incremental Analysis

End of Year	2019	2020 (mid year)	2021	2022	2023	2024	2025	2026	2027
Make WFI Cash Flow	(31,147,673.39)	1,962,710,901.57	5,678,077,956.98	5,787,125,764.36	5,896,200,210.25	6,004,769,702.01	6,114,408,668.68	6,211,785,621.06	6,332,190,849.71
Buy WFI Cash Flow	(26,450,783.50)	1,959,405,439.94	5,668,409,399.85	5,777,307,779.97	5,886,226,137.75	5,994,663,840.48	6,104,107,525.58	6,201,544,332.67	6,321,562,794.32
Incremental Cash Flow	(4,696,889.90)	3,305,461.63	9,668,557.13	9,817,984.40	9,974,072.51	10,105,861.52	10,301,143.10	10,241,288.39	10,628,055.39
Discounted factor (P/F i*,n)	1	0.854700855	0.730513551	0.624370556	0.533650048	0.456111152	0.389838592	0.333195378	0.284782374
Discounted Cash Flow	(4,696,889.90)	2,825,180.88	7,063,012.00	6,130,060.38	5,322,664.27	4,609,396.15	4,015,783.12	3,412,349.95	3,026,682.85

	9	10	11	12	13	14	15	16	17
End of Year	2028	2029	2030	2031	2032	2033	2034	2035	2036
Make WFI Cash Flow	6,441,921,700.05	6,551,102,329.96	6,659,584,830.28	6,756,221,748.30	5,659,445,500.80	5,748,773,440.72	5,839,110,437.33	5,928,942,905.60	6,006,525,821.33
Buy WFI Cash Flow	6,431,079,855.99	6,540,077,846.96	6,648,440,411.70	6,745,151,879.06	5,649,973,534.38	5,739,179,557.14	5,829,337,773.56	5,919,019,893.16	5,996,716,158.90
Incremental Cash Flow	10,841,844.05	11,024,483.01	11,144,418.58	11,069,869.24	9,471,966.42	9,593,883.58	9,772,663.77	9,923,012.44	9,809,662.43
Discounted factor (P/F i*,n)	0.243403738	0.208037383	0.177809729	0.151974128	0.129892417	0.11101916	0.094888171	0.081101001	0.069317094
Discounted Cash Flow	2,638,945.37	2,293,504.60	1,981,586.05	1,682,333.72	1,230,336.61	1,065,104.89	927,310.19	804,766.24	679,977.30

	18	19	20	21	22	23	24	25	26
End of Year	2037	2038	2039	2040	2041	2042	2043	2044	2045
Make WFI Cash Flow	6,108,607,842.13	6,198,440,310.40	6,287,722,115.25	6,378,105,246.93	6,455,374,779.32	6,557,196,452.52	6,647,602,651.73	6,737,435,120.00	6,833,506,278.16
Buy WFI Cash Flow	6,098,384,132.34	6,188,066,251.94	6,277,228,739.46	6,367,430,491.12	6,444,800,427.82	6,546,253,330.63	6,636,476,849.90	6,726,158,969.50	6,821,965,524.00
Incremental Cash Flow	10,223,709.79	10,374,058.46	10,493,375.79	10,674,755.81	10,574,351.50	10,943,121.89	11,125,801.83	11,276,150.50	11,540,754.16
Discounted factor (P/F i*,n)	0.05924538	0.050637077	0.043279553	0.036991071	0.0316163	0.027022478	0.023096135	0.019740287	0.01687204
Discounted Cash Flow	605,707.57	525,312.00	454,148.61	394,870.65	334,321.87	295,710.28	256,963.03	222,594.44	194,716.07

NPV @ i*	48,296,449.17	Minimum ROR
Escalated DCFROR	1.0	0.17
Today's Dollars DCFROR	**0.9**	0.15

Appendix B: Simulations

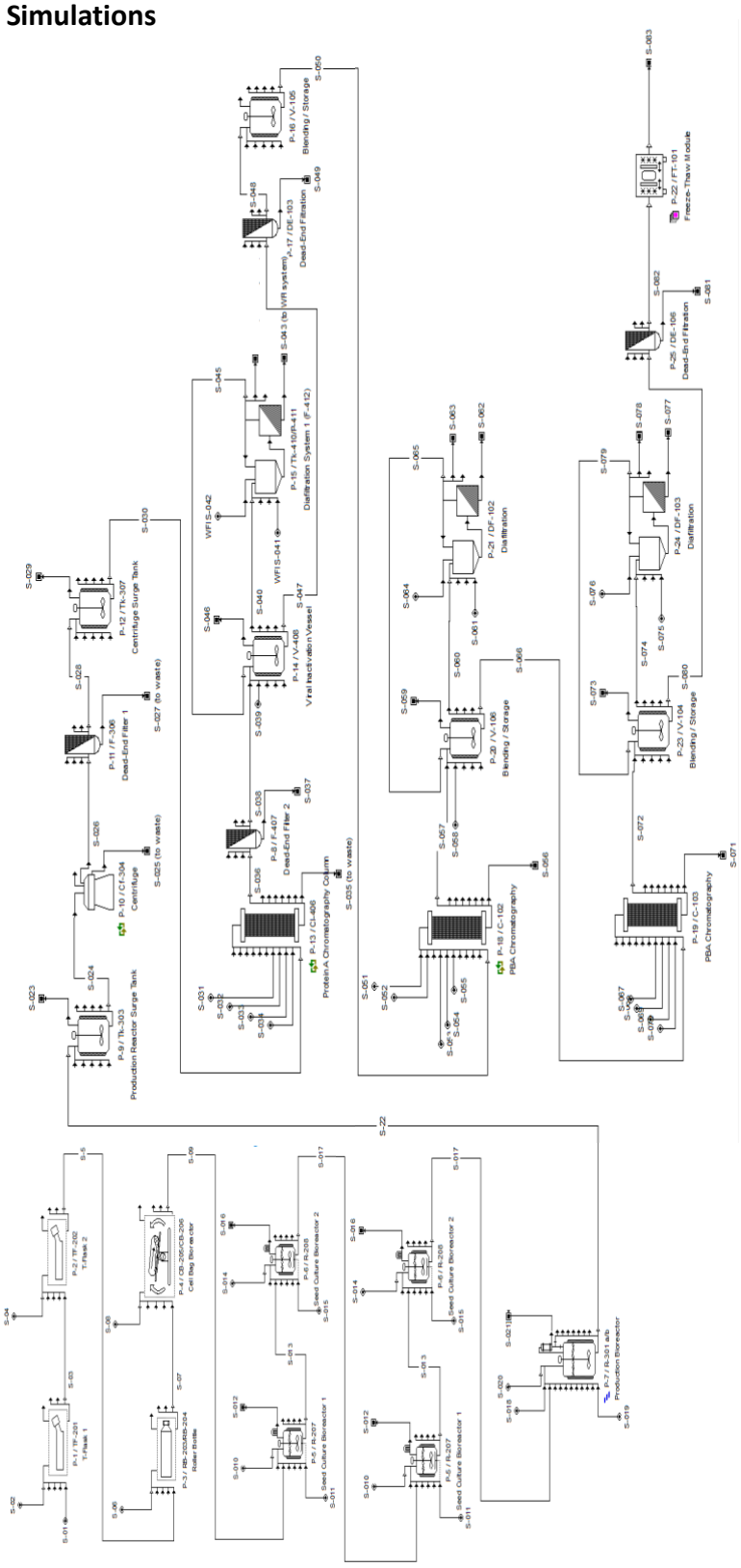

Figure B.1 : mAb production Process modeled in SuperPro

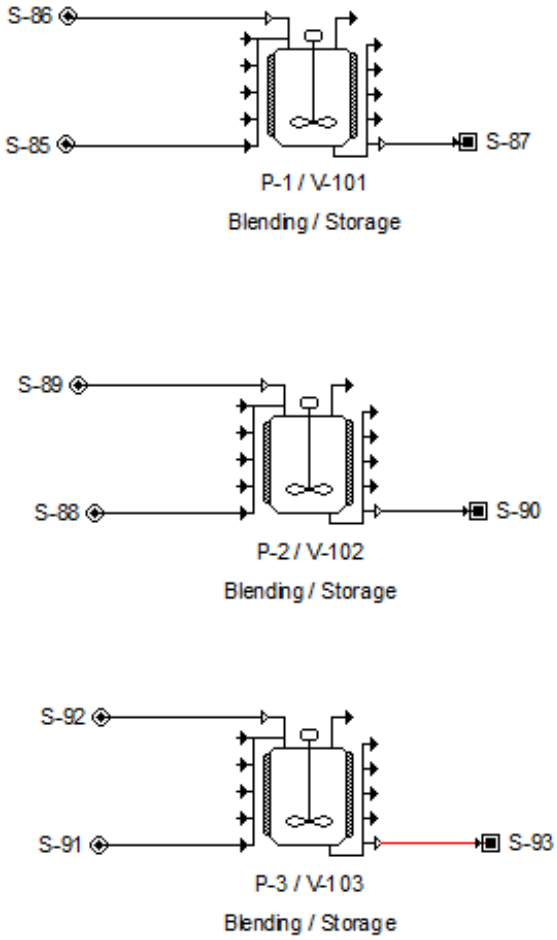

Figure B.2 : CIP Process modeled in SuperPro

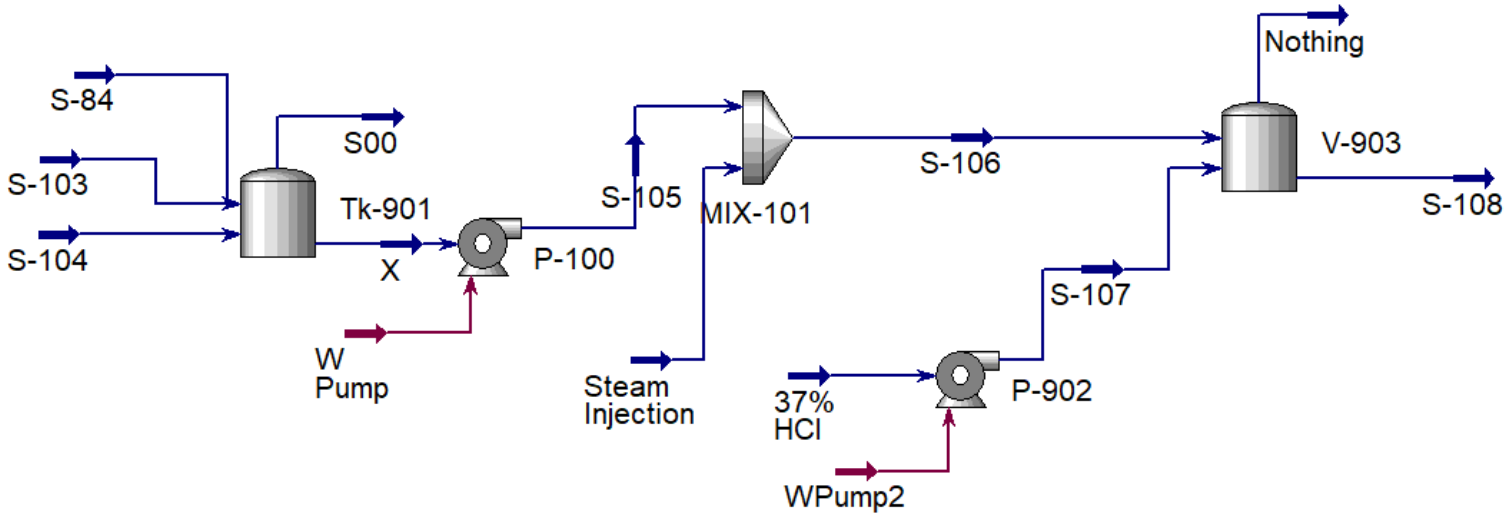

Figure B.3 : Waste Treatment Aspen HYSYS Simulation

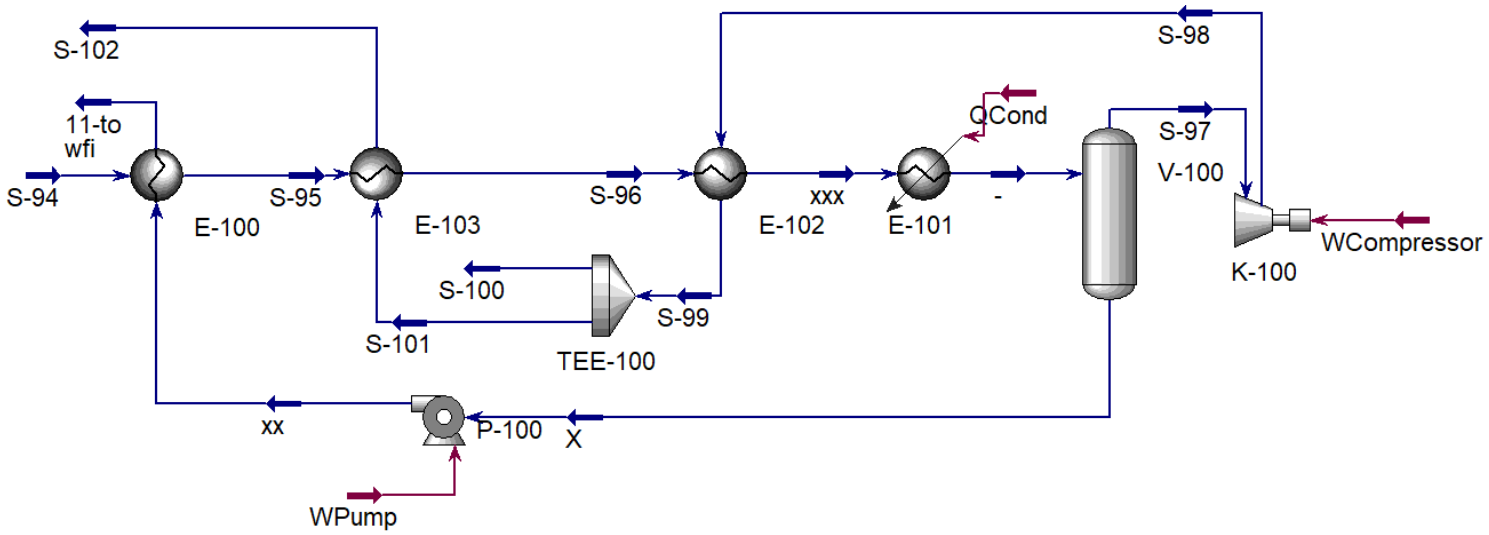

Figure B.4 : Steam Generation in WFI Unit Aspen HYSYS Simulation

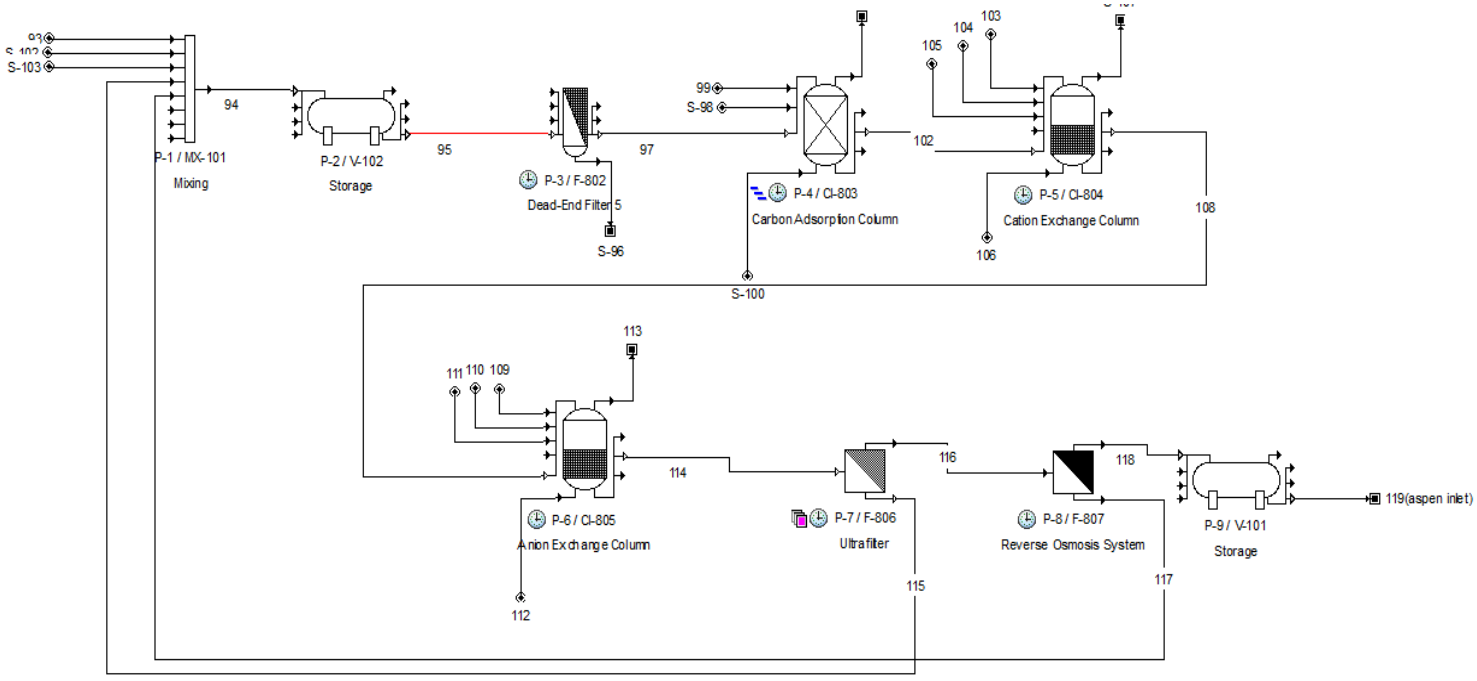

Figure B.5 : WFI generation from Potable water SuperPro Simulation

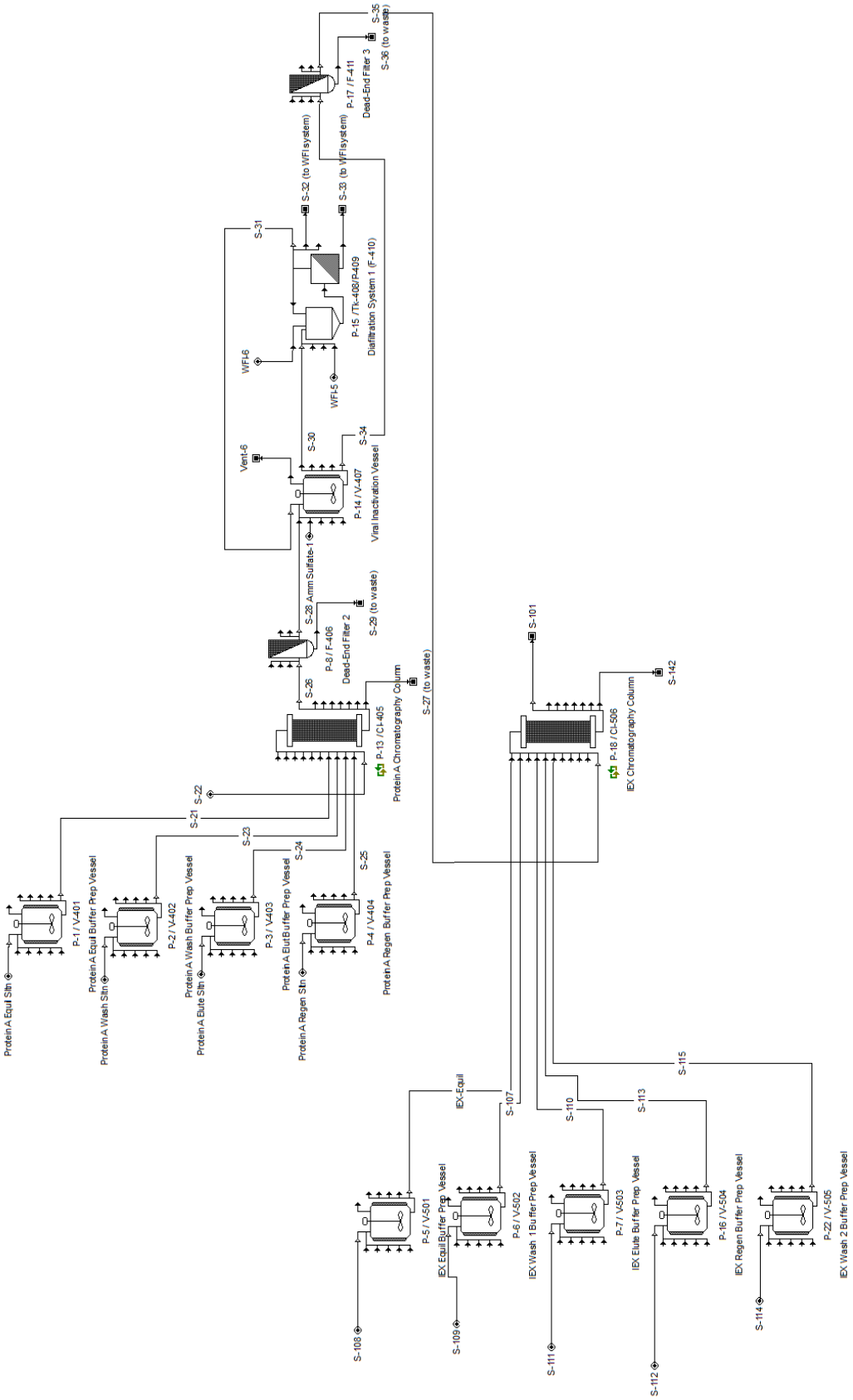

Figure B.6 : Protein A and IEX Buffer Solution Preparation SuperPro Simulation

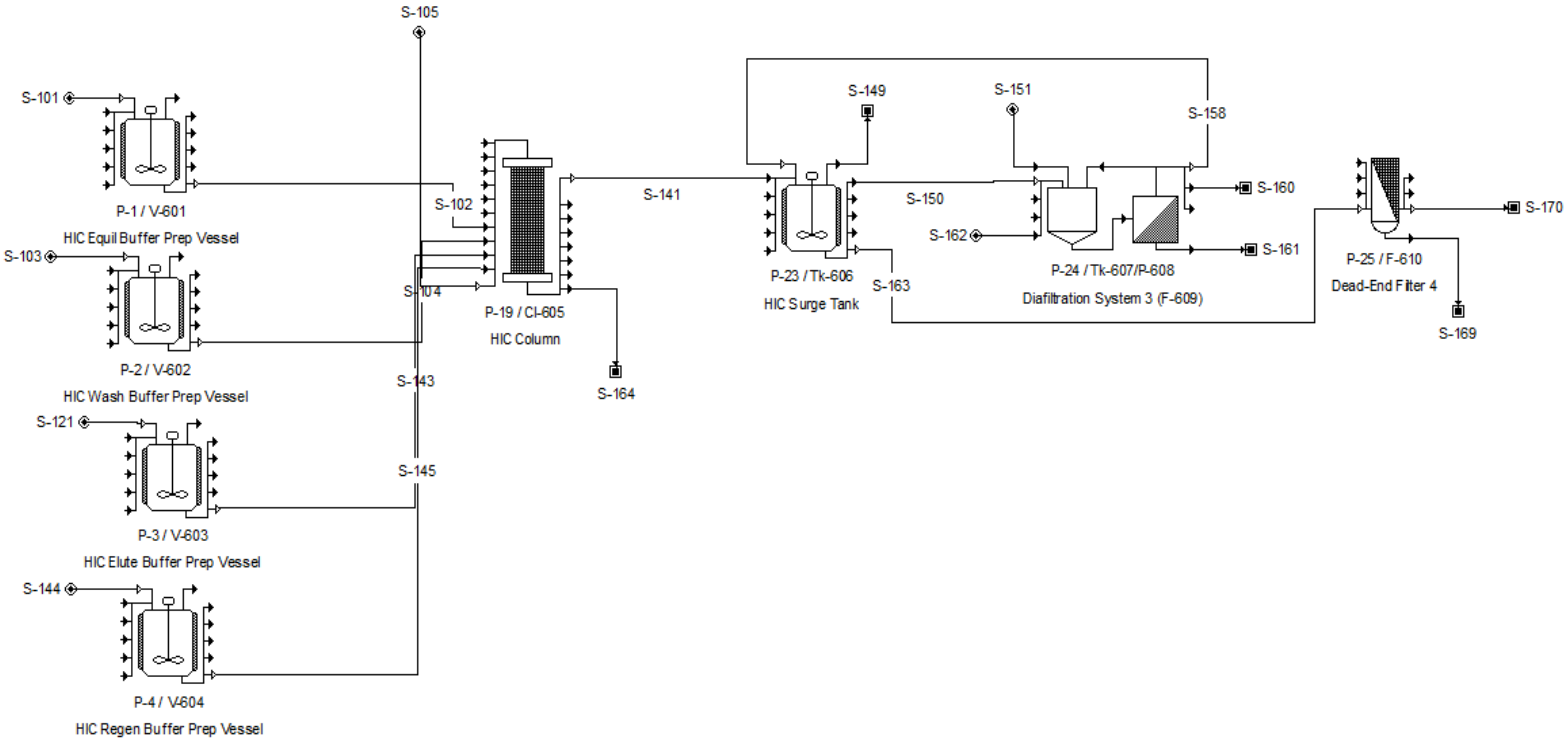

Figure B.7 : HIC Buffer Solution Preparation SuperPro Simulation

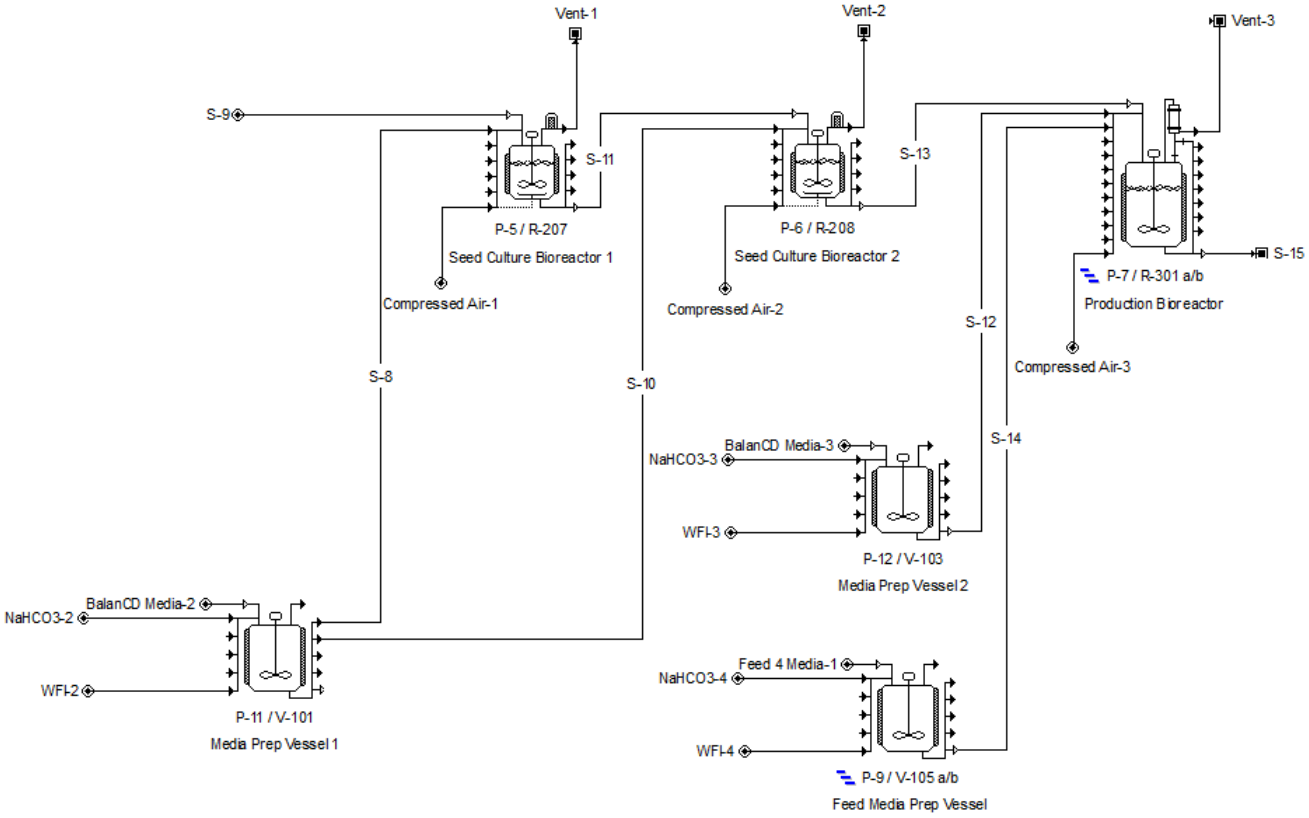

Figure B.8 : Media Preparation for Bioreactors SuperPro Simulation